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Abstract

Introduction

A new rehabilitative approach, called UPper Limb Children Action Observation Training (UP-CAT), based on the principles of Action Observation Training (AOT), has provided promising results for Upper Limb rehabilitation in children with UCP. This study will investigate if a new Information and Communication Technology (ICT) platform, named Tele-UPCAT, is able to deliver the AOT in a home setting and will measure its efficacy on children and young people with UCP.

Methods and Analysis.

A randomized, allocation concealed (waitlist-control) and evaluator-blinded clinical trial with two investigative arms will be carried out. The experimental group will perform AOT at home for 3 weeks using a dedicated and customized Tele-UPCAT system where they will watch video sequences of goal-directed actions and then carry out motor training of the same actions. The control group will continue standard care for 3 weeks after which they will also start Tele-UPCAT training. Based on a previous clinical study, a sample size of 12 patients per group is required and the primary outcome will be Assisting Hand Assessment. The Melbourne Assessment 2, ABILHAND, Participation and Environment Measure-Children and Youth (PEM-CY) and Cerebral Palsy Quality of Life Questionnaire (CP-QoL) will be included as secondary measures. Quantitative measures from sensorized objects and subject worn Actigraphs GXT3+ will be analysed. The assessment points will be the week before (T0) and after (T1) the period of AOT/Standard Care. Further assessments will be at T1 plus, the week after the AOT period for the waitlist group and at 8 (T2) and 24 weeks (T3) after AOT training.

Ethics and Dissemination

The trial has been approved by the Tuscany Paediatric Ethics Committee (169/2016). Publication of all outcomes will be in peer-reviewed journals and conference presentations.

Trial registration: ClinicalTrials.gov: NCT03094455 (16 March 2017). The trial was funded by Italian Ministry of Health grant: GR-2011-02350053

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Key words: action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Strenghts and limitation of this study

- A ICT platform, called Tele-UPCAT, will deliver the Action Observation Therapy (AOT) at home, thus allowing the rehabilitation for patients who live far from clinical centres.
- The validity of the study rehabilitation approach will be tested by a RCT.
- There will be the customization of the intervention involving children and young people with unilateral UCP at different functional levels and different ages.
- The sample size, even if calculated and powered on the previous clinical studies, is quite small.

- ICT platform does not permit to obtain quantitative measurements of visual attention during observation and manual activity periods of AOT session.

BACKGROUND

Cerebral palsy (CP) is the most common cause of childhood chronic physical disability in Europe and in other industrialised societies. [1] The incident rate is between 2 and 3 per 1000 live births and increases to 40–100 per 1000 live births among very premature and very low birth-weight babies which represent the population with highest rate of neurodevelopmental disorders. Unilateral Cerebral Palsy (UCP) (i.e. a motor impairment impacting one side of the body) constitutes the most frequent form of CP, about 30-40% of all affected children. [2]. Recent estimations of incidence and prevalence of CP have shown a significant increase in UCP in Europe over the last years. [2-4]. The Upper Limb (UL) of children with UCP is generally more involved than the lower limb and the consequent disability affects their participation, quality of life, independence at home, school and community. Many intervention models targeting deficits in UL function have been developed to promote better use of impaired arm and hand for routine bimanual activities and to achieve functional independence. [5-7]

In this field, one of the most recent models is the Action Observation Training (AOT), based on the discovery of the Mirror Neuron System, whose core regions are the ventral premotor and inferior parietal cortex. These areas are activated when individuals perform goal-directed motor acts (e.g. grasping an object) as well as if they simply observe the performance of the same or a similar action and trigger recruitment of the same network as the actual physical action. [8, 9] AOT is mainly based on observation of meaningful actions, and their successive imitation. AOT has been used as new intervention model in many adult studies for neurologic and non-neurologic diseases (such as Parkinson disease, stroke, orthopaedic surgery) and there is growing evidence of its effectiveness. [10-15]. Recent studies carried out in children with CP indicate positive effects on UL function also in young subjects. [16-18] We have recently carried out a clinical study called UP-CAT (UPper limb Children Action observation Training) on children with UCP based on AOT, providing evidence of its efficacy in improving UL activity performance in daily activities.

One of the limits of this approach was that only these children could be enrolled who were living near suitably equipped clinical centres and who had parents willing to commit to a 3-week intensive therapy program with consequencely high costs for both health services and families. Biotechnologies, tele-rehabilitation and eHealth could provide a promising approach to deliver tele-monitored home programs for a large number of subjects at a relatively low cost, as recently experienced by our group in the field of early intervention in preterm infants. [19-22] In this framework, Information and Communication Technologies (ICT) could represent a viable option in providing AOT programs at home, in a user-friendly, playful and rehabilitative setting.

METHODS/DESIGN

The overall aim of this clinical trial will be to investigate if a new ICT platform, named Tele-UPCAT, is able to provide the UP-CAT approach at home and to measure its efficacy in a clinical

population of children, adolescents and young adults with UCP. Participants will be evaluated through a Randomized Clinical Trial (RCT) comparing the effects of AOT for the UL provided by the Tele-UPCAT system (experimental group) to individuals receiving standard care (control group).
The primary aim will be to evaluate the immediate effects of this new approach (home AOT) on bimanual hand function (Assisting Hand Assessment, AHA) and to assess whether these effects will be retained at a medium-term follow-up.

The following hypotheses will be tested:
Children and young people with UCP receiving in home AOT, compared to the standard care (SC), will :

i) demonstrate more significant improvements in UL activity immediately following the intervention (AHA) at T1; [23-25]
ii) have sustained improvements on UL activity at medium-term follow-up (i.e. 8 weeks treatment, T2);
iii) benefit children and young people with UCP at different functional levels and different ages, due to the customization of the intervention (e.g. variety of AOT exercises fine-tuned by rehabilitation staff);
iv) report that ICT rehabilitation in a home setting is as comfortable, reliable, feasible and effective for UCP subjects and their families as rehabilitation in a clinical centre.

Secondary aims will be to investigate immediate (T1) and long-term clinical effects (T3, T4) on other activities and participation outcomes and to evaluate feasibility of ICT on assessing, monitoring and detecting changes in UL activity.
The following secondary hypotheses will be tested:
In a RCT of children and young people with UCP, compared to the standard care (SC), the in home AOT group (AOT) will have:

i) sustained improvements on bimanual activities might be retained at longer follow-ups (i.e. 24 weeks after treatment, T3, T4);
ii) improved participation (Participation and Environment Measure - Children and Youth, PEMCY) [26, 27] and perception of quality of life (Cerebral Palsy Quality of Life Questionnaire, CP-QOL); [28-30]
iii) ICT could
    a. monitor daily UL activity
    b. detect changes of UL activities during and after the AOT program;
    c. measure and detect changes in grasping time, force pressure during unimanual and bimanual activities.

Study design
The Tele-UPCAT trial is a randomized, allocation concealed (waitlist-controlled), and evaluator-blinded clinical trial with two investigative arms using an AOT intensive rehabilitation program of home based AOT compared to standard care in children and young people with UCP. The study will be designed as a waitlist controlled trial, in order to allow all enrolled subjects to perform AOT training either immediately or after a waitlist period. After obtaining informed

consent, participants will be block randomized into pairs according to the House functional classification system (HFCS) activity level (grades 2-3, 4-5 and 6-8) and age (5-14y, 15-20y), [31, 32] using a computer-generated set of random numbers. Randomization, sequence generation and preparation of group allocation materials will be carried out by an independent researcher who will be not involved in the trial. Pairs will be divided randomly into two groups with 1:1 experimental/standard care (waitlist) ratio. Participants allocated in the experimental group will immediately start AOT for a 3-weeks period, while those in the standard care group will continue with their usual care. In both cases, subjects and parents will be asked to take daily notes in a predefined diary of their daily activities. All subjects will be evaluated before (T0) and after (T1) the period of experimental training/standard care with standardized tests and questionnaires (see outcome measures). T1 will be the primary endpoint aimed at evaluating the short-term effects of AOT according to Consort Guidelines and the Spirit statement (see Figure 1). [33, 34]

After this phase, subjects previously allocated to the experimental group will continue standard care, while whose who started with standard care will then commence home based AOT. The subjects of this SC group will be re-assessed at the end of training (T1 plus). Further assessment of all participants will be performed after 8 weeks (T2) and 24 weeks (T3) from the end of AOT training (T1 or T1 plus, for the experimental and waitlist group, respectively), to evaluate the medium and long term effects of AOT.

In summary, assessments will be performed at:

- T0, baseline: the week before the period of AOT/Standard Care
- T1: at 1 week after period of AOT/Standard Care
- T1 plus: the week after period of AOT, for waitlist group
- T2: 8 weeks after end of AOT
- T3: 24 weeks after end of AOT.

The details of the study design are reported according to Consort guidelines in Figure 1. The programme of enrolment, interventions and assessments designed according to SPIRIT guidelines are shown in Figure 2. [34]

Blinding

All the clinical outcome measures (AHA, [23-25] Melbourne Assessment 2 MA-2 [35] and Box & Block Test [36]) will be videotaped and captured by a therapist blind to group assignment. Videotapes will be randomized and scored by assessors blind to group allocation and order of assessments.

Two independent researchers will comprise the data monitoring committee for this study. They will review all adverse events, subject participant retention in each study arm and compliance with study protocol at 12 weekly intervals. Subjects will have a study number in a dedicated data file. The file with study subject numbers and personal data will be stored in a password protected file, accessible only by the principal investigator. Enrolled subjects can withdraw from the study at any time but will still obtain their relative clinical assessments.

Study sample and recruitment

Enrolment and clinical trial will be carried out at the Department of Developmental Neuroscience of IRCCS Fondazione Stella Maris (FSM, Pisa, Italy), with the collaboration of the Unit of Children Rehabilitation of S.Maria Nuova Hospital (Reggio Emilia, Italy). ICT platforms have been designed

and built and will be provided by the BioRobotics Institute of Scuola Superiore Sant'Anna (Pontedera, Italy).
Potential participants will be identified according to inclusion criteria (see below), from UCP patients of the clinical departments. Suitable subjects and their parents will be invited to participate and will be enrolled in the RCT only after written consent has been obtained.

Inclusion criteria are participants with:
- confirmed diagnosis of spastic UCP; [2, 37]
- aged between 5 and 20 years at time of recruitment;
- predominant UL spasticity;
- mild to moderate impairment of UL function with minimal ability to grasp and hold objects with the affected hand (House functional classification system, HFCS score ≥ 2); [31, 32]
- sufficient cooperation, cognitive and communicative understanding to perform assessment and participate in intervention activities;
- subjects and parents willing to commit to the intensive therapy program for a 3-week period.

Subjects will be excluded in case of
- previous orthopaedic surgery or Botulinum Toxin A (BoNT-A) injection in the UL within 6 months prior to study entry.

Sample size
According to CONSORT guidelines, [33, 34] sample size estimates were based on projected treatment effect on the primary outcome measure, AHA. A minimum sample size of 10 per group will be required in order to detect a 1.40 effect size (value based on our preliminary data) at significant level of 0.05 and 80% power. [17, 18] Considering a 20% of possible drop-outs a minimum of 12 subjects per group will be recruited.

Study treatment

AOT library

On the basis of the previous clinical study, [17, 18] rehabilitation staff has created a library of rehabilitation packages composed of three different series of AOT exercises, which differ for complexity of action and range of UL capabilities conceived in relation to HFCS levels (≤ 4, 5-6, 7-8). [31, 32] Each serie is organized into customized sequences designed to cover unimanual and bimanual UL goal-directed actions with a variety of objects and toys commonly used in routine life. For each serie, experimental training is composed of 15 sets (8 unimanual followed by 7 bimanual) of routine UL activities, to be completed in 3 weeks (5 days per week). Each set has a general common goal (e.g. drinking a glass of water) composed of three sequential tasks of increasing complexity (e.g. from picking up a bottle of water, to opening the cap, to pouring the water into a glass). As previously indicated, in order to grade the activities according to the range of capabilities, three series of sets have been planned. The actions of each series have the same goal but the material and type of movement (i.e., range of movement, type of grasp) is customized in order to guarantee feasibility of the proposed activity while maintaining the same overall objective (see Table 1 and Figure 3a and Figure 3b). Each action of the three series performed by an actor is

videotaped so that the videos show only the hand and arm from the first perspective; each video is then edited to last 3 minutes. The actor uses one or two hands for unimanual and bimanual exercises respectively. When possible, videos are inverted, in order to have the same videos for right and left hand.

Table 1. List of goal-directed actions planned for the AOT training

Days	Action a	Action b	Action c
1	Uncover a little ball by lifting a box	Place a little ball in a glass	Fill a glass with water
2	Pick coloured card and match it to the same colour	Move a coloured card and place it on a base	Pick a card and place it on the similar one
3	Pick up a rubber stamp and move from/to different positions	Pick up a rubber stamp and press it against horizontal plane to print a figure	Pick up a rubber stamp and press it against sloping plane to print a figure
4	Pick up coin, put it in piggy bank through the slot on the top OR Pick up a magnet and place it on a horizontal magnetic board	Pick up coin, put it in piggy bank through the vertical slot on the side OR Pick up a magnet and place it on a sloping magnetic board	Pick up coin, put it in piggy bank through the horizontal slot on the side OR Pick up a magnet and place it on a vertical magnetic board
5	Pick up a wooden rubber stamp and move to different positions	Pick up a wooden rubber stamp and press it against horizontal plane to print a figure	Pick up a wooden rubber stamp and press it against sloping plane to print a figure
6	Move a spray can OR Move the bottle with a little ball inside	Place the spray can on a support OR Remove a little ball from the bottle	Put the spray can into a cup OR Press the catapult and launch a little ball
7	Move a container filled with shimmy powder	Open the container	Sprinkle shimmery powder on a paper
8	Place magnetic fish on a paper	Pick up fishing rod and catch magnetic fish	Pick up magnetic fish and place them in a container
9	Move a hole punch	Insert a sheet of paper and make holes	Match holes on sticks
10	Wet a cloth placing it in a container with water	Wring cloth and place it in a plate	Open a toy washing machine and insert the cloth inside
11	Pick up a card and place it	Pick up a card and insert it	Pick up a card and insert it

	on a support	in a clothespin	in a clothespin in a different orientation
12	Pick up and handle a piece of Play-Doh	Divide it in two pieces	Open a toy oven and insert a saucepan (with Play Doh in it)
13	Search for coin in the bag and place it on a support	Take the coin and insert it in a wallet	Open a box and place the wallet inside
14	Open a tube of tempera paint	Wet a brush with tempera paint	Make figure using a stencil with the brush dipped in tempera paint
15	Move a glitter glue tube	Open it	Decorate a frame by pasting pieces of mosaic

ICT platform

The AOT will be carried out through a dedicated platform (see Figure 4), designed to be user-friendly, by subjects at home in a playful setting with integrated smart features. The platform has been designed and developed by integrating two different modules:

- The Observation Module (OM) for the presentation of AOT videos and recording of subject's attention and exercise execution. This consists of a computer with 23" desktop, a dedicated software and a video camera. The Observation Module as been obtained by integrating a large all-in-one personal computer (All-in-One touch HP EliteOne 800 G2 - L3N93AV), a large switch and a video camera (GoPro HERO Session), which will record a whole field, including subject's face and hands and table with objects. The Observation Module is important to determine whether the subject is looking at the monitor during observation phase and has an overall view of the execution of actions. A dedicated software, aimed at guiding and motivating subjects to perform AOT (observation followed by execution) has been developed and customized based on the subject's. In particular, an interactive game with an engaging story which differs for every day of training has been developed for school aged children, while a slide-show with a voice-over is provided for adolescents and young people. The general architecture of the software is based on the following sequence: observation of a 3-minute video followed by execution of the same action for 3 minutes. Subsequently, the same video will be replayed and then executed a second time. As stated before, a 60-minute session, including rest intervals, of three different goal-directed actions of increasing complexity are observed and imitated twice every day. At the end of each day the software will terminate the session and automatically update it for the next day.
- The Motor Performance Module (MPM) for the execution of actions. This will be mainly composed of a kit of exactly the same common objects and toys shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists.

Experimental training

The ICT platform will be delivered to the subject's home for AOT training. Before delivering the platform, the most appropriate AOT exercises will be selected from the library and uploaded in the Observational Module (OM) so that each platform is customized. During the training sessions, each subject will sit on a chair with both arms placed on a table in front of a platform positioned at about 1 m. A parent will be seated on the subject's affected side to prompt attention during task execution and assist if necessary. The software will guide the subject in the sequence of observations and executions.

Standard care

Subjects previously allocated in the standard care group will continue their usual care for 3 weeks. All concurrent therapies will be recorded in a questionnaire in both groups.

Outcome measures

Description of sample

Children participating in the study will be classified according to HFCS, which assesses function of the impaired hand in children with CP.[31, 32] This classification consists of 9 grades ranging from a hand that is not used at all (grade 0) to one that is used spontaneously and independently from the other one (grade 8). Due to the general approach in classifying hand functional level, this scale can also be easily applied to young adults with UCP. HFCS will be used for all ages as a criterion for inclusion in this study (from grade 2 to grade 8). In addition, they will be classified according to the Manual Ability Classification System (MACS), a classification system of the child's ability to handle objects in daily activities on one of five levels. [38]

Primary outcome measure

On the basis of our scientific hypothesis and according to previous clinical experience, the primary outcome measure will be the AHA (version 5.0). [17, 18] This assessment measures UL function during bimanual activities by evaluating spontaneous use of assisting hand during a semi-structured age-appropriated 10-15-minute session with specific toys (Kids-AHA) or tasks (Ad-AHA) requiring bimanual handling. AHA is videotaped in a standardised manner and the subsequent scoring is carried out by a certified expert rater. For more details see http://www.ahanetwork.se. [23-25]

Other outcome measures

Other secondary measures will include measures of unimanual capacity (MA-2, and Box and Block Test, BBT) and bimanual daily activities at home and in the community (ABILHAND or ABILHAND-Kids). [35, 36, 39] Moreover, participation and quality of life will also be assessed. All assessment will be performed at T0, T1, T1 plus, T2 and T3 unless otherwise indicated.

i. The Melbourne Assessment 2 (MA2) measures unilateral UL function and it is a valid and reliable tool for evaluating quality of UL movement in children with neurological conditions for ages between 2.5 and 15 years. MA2 is a criterion-referenced test that extends and refines the scale properties of the original Melbourne Assessment (MUUL) and like MUUL

it can also be used for adolescents and young adults. MA2 measures four elements of UL movement quality: movement range, accuracy, dexterity and fluency. It comprises 14 test items of reaching, grasping, releasing and manipulating simple objects. The test is administered by video recording the child's performance for subsequent scoring (30 items score). It predominantly includes concepts within the body function domain as well as in the activity domain. [35]

ii. Box and Block Test (BBT) is a quick (2-5 minutes), simple and inexpensive test which measures unimanual dexterity in the activity domain. BBT is composed of a test box with 150 wooden blocks (25mm) with a partition in the middle. The patient must grasp one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute. The procedure must be repeated with the other hand. It can be used for a wide range of populations from childhood to adulthood. [36]

iii. ABILHAND is a semi-structured item-response questionnaire on a 3-point ordinal scale (impossible, difficult, easy) that measures daily manual activities referred to in the activity domain of ICF. It is scored by adolescents and young adults according to their perceived difficulties in performing daily bimanual tasks. A version for children called ABILHAND-Kids has been also validated and it is scored by parents. This test will be used at all assessment periods. [39]

iv. Participation and Environment Measure - Children and Youth (PEM-CY). It is a parent-reported instrument that evaluates participation and environment across home (ten items), school (five items) and community (ten items) settings. For each item, the parent is asked to identify how frequently (over the past four months) the child has participated (eight options: daily to never); how involved the child typically is while participating (five point scale: very involved to minimally involved); and whether the parent would like to see the child's participation in this type of activity change (no or yes, with five options for the type of change desired). For each setting, the parent is then asked to report on whether certain features of the environment make it easier or harder for the child to participate. [26, 27] This questionnaire will be used at T0 and T3.

v. Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years) evaluate quality of life in children and adolescents with CP. [28] These questionnaires will be used at T0 and T3.

vi. Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks, is a new assessment tool that consists of observation, followed by execution of three tasks of increasing difficulty (unimanual lifting, bimanual placing near and bimanual cooperation, holding and pulling) by means of a sensorized object. Two load-cells and a switch embedded in the sensorized object allow for the measurement of the following parameters: grasping time, maximum grasping force and delay time between unaffected and affected hand in reaching for the object. [40-42]

vii. Quantitative measurement of bimanual activities will be performed in all the subjects enrolled in the study by means of Actigraph GXT3+. Actigraphs wGT3X-BT and wActiSleep-BT, equipped with a Velcro strap bracelet, will be worn on both wrists. Moreover, participants will be asked to wear them for the whole 3-week period of AOT training or standard care, i.e. between T0 and T1 or T1 and T1 plus and between T0 and T1 or after T1 or T1 plus. All

the activities, concerning clinical assessments, training and daily life activities, or removal will be recorded in a dedicated diary. The actigraphs will also be worn during the clinical assessments.

viii. Cost effectiveness: A within trial cost-utility analysis will be conducted to synthesise the costs and benefits of the training program. Resource use (staff time, equipment and facility use) associated with the program will be collected alongside the RCT. Health care utilisation will be collected using a resource use questionnaire previously used in CP studies. Health utility will be derived from the adapted CHU-9D, a quality of life measure designed specifically for economic evaluation and which has been validated in an Australian population. [43-46]

Statistical analyses

Clinical data will be analysed by means of the Statistical Package for Social Sciences (SPSS). Means and standard deviation of clinical outcome scores for both groups will be calculated to identify potential baseline differences between groups. As a first step, normality of distributions will be verified by Shapiro-Wilk's test. Between-group differences for all selected outcome measures will be evaluated at T0, by means of t-test for unrelated samples or non-parametric Mann–Whitney U independent sample test, for normal or non-normal distributed data, respectively. To test our first hypothesis, between-group differences for primary and secondary outcome measures will be evaluated at the primary endpoint (T1), compared with T0, by means of parametric or non-parametric tests for unrelated samples. In addition, matched-pairs tests (t-tests or Wilcoxon) will be carried out in order to assess retention of effects at follow-up periods (T1 or T1 plus, T2 and T3) relative to assessment before AOT training (T0 or T1 for experimental or waitlist group respectively). Bonferroni corrections will not be carried out in relation to the exploratory nature of the current RCT study. To detect if significant changes will correlate to HFCS levels, a correlation analysis between score changes after AOT training (T1 or T1 plus) and assessment before AOT training (T0 or T1) will be carried out. Finally, an exploratory within-group analysis will be performed for the waitlist group comparing changes during AOT with respect to those of the first standard care period. [47]

ETHICS AND DISSEMINATION

This study protocol describes background, hypotheses, system, clinical and technologic outcome measures for a RCT designed to evaluate the Tele-UPCAT system as a new approach to deliver AOT to children and young people with UCP at home.

Full ethical approval has been obtained from the Tuscany Paediatric Ethics Committee (169/2016). The trial has been registered at http://www.clinicaltrials.gov (identifier NCT03094455). This study protocol is reported according to the SPIRIT (Standard Protocol Items: Recommendations for Intervention Trials) statement (SPIRIT 2013). [34] We anticipate that the results of this study will be disseminated through peer reviewed journals and national and international academic conferences. The results of this study will be of interest for rehabilitation trials based on AOT paradigm. Referring to a previous RCT study, [17, 18] we suggest that the home setting might increase accessibility of rehabilitation to a large number of children and young people with UCP

(e.g. subjects that live far from the clinical centres) with a large range of hand impairments (including also subjects with HFCS level lower than 6) and older age (5-20 years instead of 5-15). Moreover, if the Tele-UPCAT study, using a very simple ICT solution, demonstrates to be viable for delivering AOT at home with significant improvements in UL daily activities, it could lead to the application of new solution for cost efficient rehabilitation programs. Implementation of new smart technologies can i) provide user-friendly AOT programs at home; ii) remotely manage treatment by rehabilitation staff thus increasing the ratio 'number of patients per therapist'; iii) offer individualized and intensive training. It could become an economical and efficient rehabilitation program by achieving significant long-lasting effects in UL activity and participation through an easily implementable paradigm that could become an integral part of common clinical practice. Finally, this approach could become a rehabilitation tool and be applicable to broader populations of CP and other chronic disabilities.

PROJECT STATUS

This project began recruitment the 29 March 2017, and we expect to complete data collection for the last training the November 2017 and close the project in the April 2018.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This trial has been funded by the Italian Ministry of Health to GS and FC (RF 2011).

AUTHOR'S CONTRIBUTION

GS is the principal investigator of the project and mainly responsible of the clinical part of it while FC is the main responsible of the ICT platform. GS, EI, HF, KK, RB, AF and GC designed the research study. GS, EB, EI, SP and EB were responsible for the AOT library. GS, SP and ES were in charge for subject recruitment in Pisa and identification of type of exercise and software and AF for Reggio Emilia. GS and EB will collect the data and will monitor the training. FC, IM, MM and FFP with the supervision of PD have designed and built the new platform. GS and GC will take the lead roles on preparation of publications on the clinical outcomes of the study.
All authors have read and approved the final manuscript.

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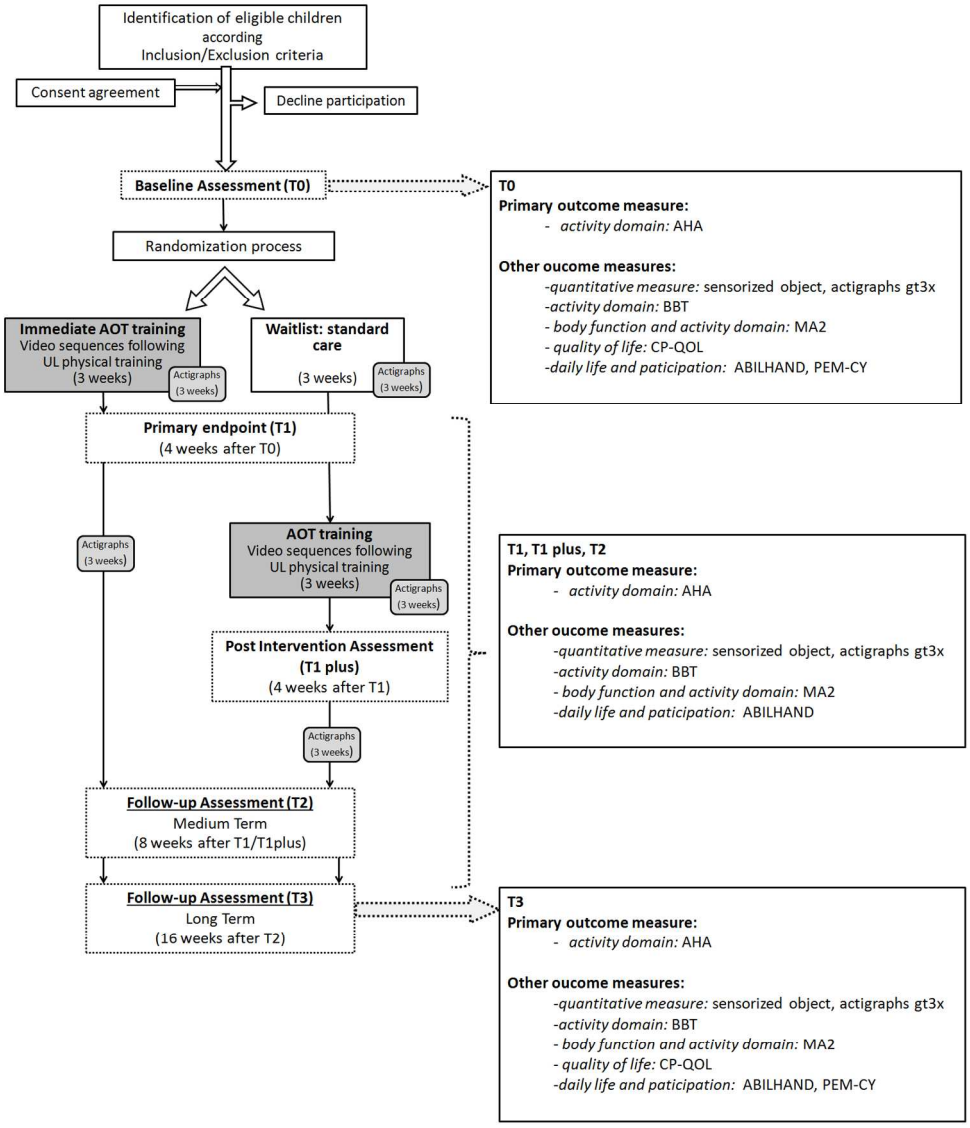
Figure 1. Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: -Participation and Environment Measure - Children and Youth

Figure 2. Schedule of enrolment, interventions, and assessments.

Figure 3a. Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

Figure 3b. Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

Figure 4. Tele-UPCAT platform.
Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected by the clinical staff in relation to HFCS level in the Clinical Interface (2). A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3). The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists. The integrated camera records subject's attention during the observation task and exercise execution.



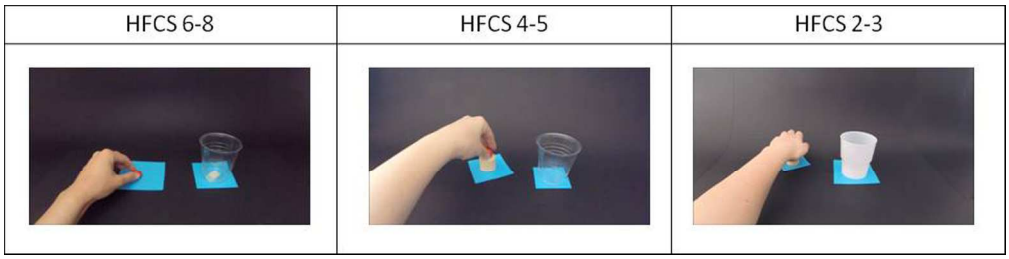
Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: - Participation and Environment Measure - Children and Youth

147x171mm (300 x 300 DPI)

	STUDY PERIOD				
	Enrolment	Post-allocation			
TIMEPOINT	*T0*	*T1*	*T1 plus**	*T2*	*T3*
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation	X				
INTERVENTIONS:					
AOT intervention	←	→			
Wait list control group	←	→	← →		
ASSESSMENTS:					
AHA	X	X	X	X	X
MA 2	X	X	X	X	X
BBT	X	X	X	X	X
ABILHAND (-Kids)	X	X	X	X	X
CP QoL	X				X
PEM-CY	X				X
Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks	X	X	X	X	X
Quantitative measurement of bimanual upper limb activities by means of Actigraph GXT3+	X	X	X	X	X

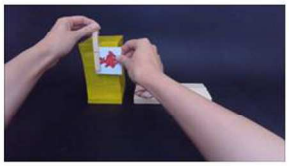
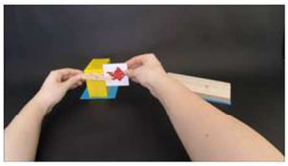
Schedule of enrolment, interventions, and assessments.

60x88mm (300 x 300 DPI)



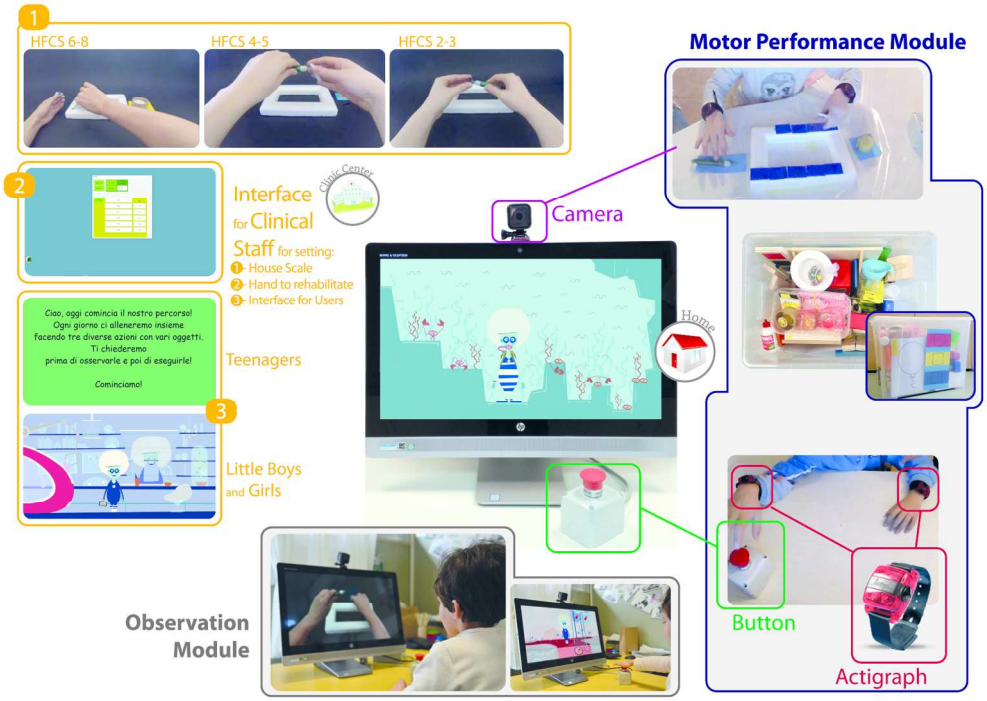
Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

170x42mm (300 x 300 DPI)

HFCS 6-8	HFCS 4-5	HFCS 2-3
		

Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

170x42mm (300 x 300 DPI)



Tele-UPCAT platform.

Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected by the clinical staff in relation to HFCS level in the Clinical Interface (2). A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3). The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists. The integrated camera records subject's attention during the observation task and exercise execution.

170x120mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1,2
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	5,6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	-
Sample size	7a	How sample size was determined	6
	7b	When applicable, explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	4
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	4
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	4,5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	5

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	-
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	11
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	-
	13b	For each group, losses and exclusions after randomisation, together with reasons	-
Recruitment	14a	Dates defining the periods of recruitment and follow-up	-
	14b	Why the trial ended or was stopped	-
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	-
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	-
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	-
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	-
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	-
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	-
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	-
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	-
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	-
Other information			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	2
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	2,12

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPper Limb Children Action Observation Training for Participants with Unilateral Cerebral Palsy

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Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Neurology, Paediatrics
Keywords:	action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPper Limb Children Action Observation Training for Participants with Unilateral Cerebral Palsy

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Word Count: 5680

Abstract

Introduction

A new rehabilitative approach, called UPper Limb Children Action Observation Training (UP-CAT), based on the principles of Action Observation Training (AOT), has provided promising results for Upper Limb rehabilitation in children with UCP. This study will investigate if a new Information and Communication Technology (ICT) platform, named Tele-UPCAT, is able to deliver the AOT in a home setting and will measure its efficacy on children and young people with UCP.

Methods and Analysis.

A randomized, allocation concealed (waitlist-control) and evaluator-blinded clinical trial with two investigative arms will be carried out. The experimental group will perform AOT at home for 3 weeks using a dedicated and customized Tele-UPCAT system where they will watch video sequences of goal-directed actions and then complete the motor training of the same actions. The control group will continue standard care for 3 weeks after which they will also start Tele-UPCAT training. Based on a previous clinical study, a sample size of 12 patients per group is required and the primary outcome will be Assisting Hand Assessment. The Melbourne Assessment 2, ABILHAND, Participation and Environment Measure-Children and Youth (PEM-CY) and Cerebral Palsy Quality of Life Questionnaire (CP-QoL) will be included as secondary measures. Quantitative measures from sensorized objects and subject worn Actigraphs GXT3+ will be analysed. The assessment points will be the week before (T0) and after (T1) the period of AOT/Standard Care. Further assessments will be at T1 plus, the week after the AOT period for the waitlist group and at 8 (T2) and 24 weeks (T3) after AOT training.

Ethics and Dissemination

The trial has been approved by the Tuscany Paediatric Ethics Committee (169/2016). Publication of all outcomes will be in peer-reviewed journals and conference presentations.

Trial registration: ClinicalTrials.gov: NCT03094455 (16 March 2017). The trial was funded by Italian Ministry of Health grant: GR-2011-02350053

Abstract words: 300

Key words: action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Strenghts and limitation of this study

- This is the first protocol study where an ICT platform is proposed, called Tele-UPCAT, to deliver the Action Observation Therapy (AOT) at home
- The study is a well designed RCT aimed to investigate the UP-CAT approach at home and to measure its efficacy in a clinical population of children, adolescents and young adults with UCP
- The Tele-UPCAT platform will allow to customize the intervention according to the different manual functional levels and the different ages of participants
- The sample size, even if calculated and powered on the previous clinical studies, is quite small.
- The Tele-UPCAT platform does not permit to obtain quantitative measurements of visual attention during observation and manual activity periods of AOT session.

BACKGROUND

Cerebral palsy (CP) is the most common cause of childhood chronic physical disability in Europe and in other industrialised societies. [1] The incident rate is between 2 and 3 per 1000 live births and increases to 40–100 per 1000 live births among very premature and very low birth-weight babies which represent the population with highest rate of neurodevelopmental disorders. Unilateral Cerebral Palsy (UCP) (i.e. a motor impairment impacting one side of the body) constitutes the most frequent form of CP, about 30-40% of all affected children. [2] Recent estimations of incidence and prevalence of CP have shown a significant increase in UCP in Europe over the last years. [3-4] The Upper Limb (UL) of children with UCP is generally more involved than the lower limb and the consequent disability affects their participation, quality of life, independence at home, school and community. Despite this large impact, the current clinical practice for UCP mainly include consultative intervention or time-limited therapy following pharmacological intervention. In the last decades, many intervention models targeting deficits in UL function have been developed to promote better use of impaired arm and hand for routine bimanual activities and to achieve functional independence. [5-8] In this field, one of the most recent models is the Action Observation Training (AOT), based on the discovery of the Mirror Neuron System, whose core regions are the ventral premotor and inferior parietal cortex. These areas are activated when individuals perform goal-directed motor acts (e.g. grasping an object) as well as if they simply observe the performance of the same or a similar action and trigger recruitment of the same network as the actual physical action. [9, 10] AOT is mainly based on observation of meaningful actions, and their successive imitation. AOT has been used as new intervention model in many adult studies for neurologic and non-neurologic diseases (such as Parkinson disease, stroke, orthopaedic surgery) and there is growing evidence of its effectiveness. [11-16] Recent studies carried out in children with CP indicate positive effects on UL function also in youngs. [17-19] We have recently completed a clinical study called UP-CAT (UPper limb Children Action observation Training) with children with UCP based on AOT, providing evidence of its efficacy in improving UL activity performance in daily activities. [19]

One of the limits of this approach was that only these children could be enrolled who were living near suitably equipped clinical centres and who had parents willing to commit to a 3-week intensive therapy program with consequencely high costs for both health services and families. In addition, the parents, even if able to participate, complained of the need to come every working day for three weeks and suggested to deliver the intervention at home. Biotechnologies, tele-rehabilitation and eHealth could provide a promising approach to deliver tele-monitored home programs for a large number of participants at a relatively low cost, as recently experienced by our group in the field of early intervention in preterm infants. [20-23] In this framework, Information and Communication Technologies (ICT) could represent a viable option in providing AOT programs at home, in a user-friendly, playful and rehabilitative setting.

METHODS/DESIGN

This study protocol, designed as an exploratory Randomized Clinical Trial (RCT), has the purpose to investigate the feasibility of a new ICT platform, named Tele-UPCAT, to provide the UP-CAT approach at home. Moreover, it aims to measure its efficacy in a group of children, adolescents and young adults with UCP comparing the effects of Tele-UPCAT approach (experimental group) with the standard care (control group).

The primary aim will be to evaluate the immediate effects (T1, in the week after the end of the treatment) of this new approach (home AOT) on bimanual hand function (Assisting Hand Assessment, AHA[24-26]) and to assess whether these effects will be retained at a medium and long

term follow-up (i.e. 8 and 24 weeks after the end of treatment, T2 and T3). In addition, the feasibility of the Tele-UPCAT system as a comfortable, reliable and customizable tool for delivering an home AOT to UCP participants and their families will be assessed by using semistructured interviews.

Secondary aims will be to investigate immediate (T1) and long-term clinical effects (T2, T3) on unimanual capacity (Melbourne Assessment 2, MA 2 [27] and Box and Block Test, BBT [28]) and on bimanual daily activities at home and in the community (ABILHAND-Kids [29]), participation (Participation and Environment Measure - Children and Youth, PEM-CY) [30, 31] and perception of quality of life (Cerebral Palsy Quality of Life Questionnaire, CP-QOL); [32-34]. Further aims will be the evaluation of feasibility of Tele-UPCAT platform on assessing, monitoring and detecting changes during and after the AOT program by comparing the data of the clinical outcome measures with those of quantitative measurement of manual activity. Finally, a cost-effective analysis will be carried out using both the perspective of the patient/caregivers and the healthcare system.

Study design

The Tele-UPCAT trial is an exploratory randomized, allocation concealed (waitlist-controlled), and evaluator-blinded clinical trial with two investigative arms using an AOT intensive rehabilitation program of home based AOT compared to standard care in children and young people with UCP. The study will be designed as a waitlist controlled trial, in order to allow all enrolled participants to perform AOT training either immediately or after a waitlist period. After obtaining informed consent, and completing baseline assessment (T0) participants will be block randomized into pairs according to the House functional classification system (HFCS) activity level (grades 2-3, 4-5 and 6-8) and age (5-14y, 15-20y), [35, 36] using a computer-generated set of random numbers. Randomization, sequence generation and preparation of group allocation materials will be carried out by an independent researcher who will be not involved in the trial. Pairs will be divided randomly into two groups with 1:1 experimental/standard care (waitlist) ratio. Participants allocated in the experimental group will immediately start AOT for a 3-weeks period, while those in the standard care group will continue with their usual care.

In both cases, AOT or standard care, participants and parents will be asked to take daily notes on a predefined diary of their daily activities, including therapies for their motor disability. In addition, to record the acceptability and feasibility of the training, participants and/or families allocated in the experimental group will fill in a multiple choice questionnaire (with box for notes) for grade their feelings about the proposed activities .

All participants will be re-evaluated after the period of experimental training/standard care (T1) with standardized tests and questionnaires (see outcome measures). T1 will be the primary endpoint aimed at evaluating the short-term effects of AOT according to Consort Guidelines (see Figure 1). [37]

After this phase, participants previously allocated to the experimental group will continue standard care, while whose who started with standard care will then commence home based AOT. The participants of this SC group will be re-assessed at the end of training (T1 plus). Further assessment of all participants will be performed after 8 weeks (T2) and 24 weeks (T3) from the end of AOT training (T1 or T1 plus, for the experimental and waitlist group, respectively), to evaluate the medium and long term effects of AOT. All the assessments will be carried out at home by trained therapists.

In summary, assessments will be performed at:

- T0, baseline: the week before the period of AOT/Standard Care
- T1: at 1 week after period of AOT/Standard Care
- T1 plus: the week after period of AOT, for waitlist group
- T2: 8 weeks after end of AOT
- T3: 24 weeks after end of AOT.

The details of the study design are reported according to Consort guidelines [37] (Figure 1), SPIRIT (Standard Protocol Items: Recommendations for Intervention Trials) statement [38] and TIDier (Template for Intervention Description and Replication) Checklist [39, 40] (Supplement Material 1 and 2). The programme of enrolment, interventions and assessments designed according to SPIRIT guidelines are shown in Figure 2.

Blinding

All the clinical outcome measures (AHA, [24-26] Melbourne Assessment 2 MA-2 [27] and Box & Block Test [28]) will be videotaped and captured by a therapist blind to group assignment. Videotapes will be randomized and scored by assessors blind to group allocation and order of assessments. During each assessment all the participants will wear two Actigraphs (wGT3X-BT, wActiSleep-BT), one for each wrist.
Two independent researchers (two child neurologists) without competing interests will comprise the data monitoring committee for this study. They will review all adverse events (deciding to stop the trial if necessary), subject participant retention in each study arm and compliance with study protocol at 12 weekly intervals. Participants will have a study number in a dedicated data file. The file with study partipants numbers and personal data will be stored in a password protected file, accessible only by the principal investigator. In order to promote participants's retention, all the assessment will be completed at home within flexible time windows. The clinical primary and secondary outcome measures that require the therapists will be the mandatory assessments, while the questionnaries could be completed within one week of when expected. Enrolled participants can withdraw from the study at any time; however, further assessments out of the research purpose, if clinically useful, will be done.

Study sample and recruitment
Enrolment and clinical trial management will be carried out by child neurologists and physiatrists at the Department of Developmental Neuroscience of IRCCS Fondazione Stella Maris (FSM, Pisa, Italy), with the collaboration of the Unit of Children Rehabilitation of S.Maria Nuova Hospital (Reggio Emilia, Italy).
Potential participants will be identified according to inclusion criteria (see below), from UCP patients of the clinical departments. Suitable participants and their parents will be invited to participate and will be enrolled in the RCT only after written consent has been obtained.

Inclusion criteria are participants with:
- confirmed diagnosis of spastic UCP; [2, 41]
- aged between 5 and 20 years at time of recruitment;
- predominant UL spasticity;
- minimal ability to grasp and hold objects, even passively, with the affected hand (House functional classification system, HFCS score ≥ 2); [35, 36]
- cognitive level within normal limits i.e. Intelligence Quotient ≥ 70, as assessed in the last year prior to recruitment by WPPSI-III, [42] WISC-IV [43] or WAIS [44]
- participants and parents willing to commit to the intensive th erapy program for a 3-week period.

Participants will be excluded in case of :
- previous orthopaedic surgery or Botulinum Toxin A (BoNT-A) injection in the UL within 6 months prior to study entry.

Sample size
Even if planned as an exploratory study, a sample size estimates, according to CONSORT guidelines, [37, 38] has been based on projected treatment effect on the primary outcome measure,

AHA. A minimum sample size of 10 per group will be required in order to detect a 1.40 effect size (value based on our preliminary data) at significant level of 0.05 and 80% power. [18, 19] Considering a 20% of possible drop-outs a minimum of 12 participants per group will be recruited.

Study treatment

The Tele-UPCAT system has been designed through the close collaboration between the rehabilitation staff (child neurologists and child therapists) of IRCCS Fondazione Stella Maris and biomedical engineers of BioRobotics Institute Scuola Superiore Sant'Anna. Taking into account the previous clinical experience on UPCAT, the main components of the Tele-UPCAT system, the AOT library of exercices and the experimental training have been defined. In general, the training will be structured in one session per day, to be executed 5 working days for 3 consecutive weeks (i.e. 15 sessions in total). The duration of daily sessions will be about 60 minutes per day for a total of 15 hours. The participants undergoing the AOT intervention through the Tele-UPCAT system will watch 3 minutes first-person video sequences of unimanual or bimanual goal-directed actions followed by their execution for 3 minutes. Each day 3 different actions will be proposed twice.

Tele-UPCAT system

Tele-UPCAT system (see Figure 3) has been designed and built and will be provided at home by the BioRobotics Institute of Scuola Superiore Sant'Anna (Pontedera, Italy).
It is a dedicated platform for delivering AOT designed to be user-friendly, by subjects at home in a playful setting with integrated smart features.

The platform has been designed and developed by integrating two different modules:

- The Observation Module (OM) for the presentation of AOT videos and recording of participant's attention and exercise execution. This consists of a computer with 23" desktop, a dedicated software and a video camera. The Observation Module has been obtained by integrating a large all-in-one personal computer (All-in-One touch HP EliteOne 800 G2 - L3N93AV), a large switch and a video camera (GoPro HERO Session), which will record a whole field, including subject's face and hands and table with objects. The Observation Module is important to determine whether the participant is looking at the monitor during observation phase and has an overall view of the execution of actions. A dedicated software, designed after a deep and specific literature analysis, was developed for guiding and motivating participants through the phases of AOT (observation followed by execution). In addition, the software was customized for the wide age range of participants providing an interactive game with an engaging story different for every day of training for school aged children, and a slide-show with a voice-over for adolescents and young people. The general architecture of the software is based on the following sequence: observation of a 3-minute video followed by execution of the same action for 3 minutes. Subsequently, the same video will be replayed and then executed a second time. As stated before, a 60-minute session, including rest intervals, of three different goal-directed actions of increasing complexity are observed and imitated twice every day. At the end of each day the software will terminate the session and automatically update it for the next day.
- The Motor Performance Module (MPM) for the execution of actions. This will be mainly composed of a kit of exactly the same common objects and toys shown in the videos and two Actigraphs (wGT3X-BT, wActiSleep-BT) worn one for each wrist.

The first prototype of Tele-UPCAT system has been widely tested before the beginning of the RCT in order to test the stability and reliability of the system.

AOT library

On the basis of the previous AOT exercises, [18, 19] rehabilitation staff (child neurologist and child therapists) has created a library of rehabilitation packages composed of three different series of AOT exercises suitable to be executed at home. They differ for complexity of action and range of UL capabilities conceived in relation to HFCS levels (≤ 4, 5-6, 7-8). [35, 36] Each serie is organized into customized sequences designed to cover unimanual and bimanual UL goal-directed actions with a variety of objects and toys commonly used in routine life. For each serie, experimental training is composed of 15 sets (8 unimanual followed by 7 bimanual) of routine UL activities, to be completed in 3 weeks (5 days per week). Each set has a general common goal (e.g. drinking a glass of water) composed of three sequential tasks of increasing complexity (e.g. from picking up a bottle of water, to opening the cap, to pouring the water into a glass). As previously indicated, in order to grade the activities according to the range of capabilities, three series of sets have been planned. The actions of each series have the same goal but the material and type of movement (i.e., range of movement, type of grasp) is customized in order to guarantee feasibility of the proposed activity while maintaining the same overall objective (see Table 1 and Figure 4). Each action of the three series performed by an actor is videotaped so that the videos show only the hand and arm from the first perspective; each video is then edited to last 3 minutes. A right-handed actor uses one or two hands for unimanual and bimanual exercises respectively for participants with right UCP. For the left UCP the previous videos where tipped over if they maintained the same characteristic of the setting and of the hand movement, while the remaining videos where specifically videotaped.

Table 1. List of goal-directed actions planned for the AOT training grouped in unimanual (white cells) and bimanual (grey cells) actions

Days	Action a	Action b	Action c
1	Uncover a little ball by lifting a box	Place a little ball in a glass	Fill a glass with water
2	Pick coloured card and match it to the same colour	Move a coloured card and place it on a base	Pick a card and place it on the similar one
3	Pick up a rubber stamp and move from/to different positions	Pick up a rubber stamp and press it against horizontal plane to print a figure	Pick up a rubber stamp and press it against sloping plane to print a figure
4	Pick up coin, put it in piggy bank through the slot on the top OR Pick up a magnet and place it on a horizontal magnetic board	Pick up coin, put it in piggy bank through the vertical slot on the side OR Pick up a magnet and place it on a sloping magnetic board	Pick up coin, put it in piggy bank through the horizontal slot on the side OR Pick up a magnet and place it on a vertical magnetic board
5	Pick up a wooden rubber stamp and move to different positions	Pick up a wooden rubber stamp and press it against horizontal plane to print a figure	Pick up a wooden rubber stamp and press it against sloping plane to print a figure
6	Move a spray can OR Move the bottle with a little ball inside	Place the spray can on a support OR Remove a little ball from the bottle	Put the spray can into a cup OR Press the catapult and launch a little ball

7	Move a container filled with shimmy powder	Open the container	Sprinkle shimmery powder on a paper
8	Place magnetic fish on a paper	Pick up fishing rod and catch magnetic fish	Pick up magnetic fish and place them in a container
9	Move a hole punch	Insert a sheet of paper and make holes	Match holes on sticks
10	Wet a cloth placing it in a container with water	Wring cloth and place it in a plate	Open a toy washing machine and insert the cloth inside
11	Pick up a card and place it on a support	Pick up a card and insert it in a clothespin	Pick up a card and insert it in a clothespin in a different orientation
12	Pick up and handle a piece of Play-Doh	Divide it in two pieces	Open a toy oven and insert a saucepan (with Play Doh in it)
13	Search for coin in the bag and place it on a support	Take the coin and insert it in a wallet	Open a box and place the wallet inside
14	Open a tube of tempera paint	Wet a brush with tempera paint	Make figure using a stencil with the brush dipped in tempera paint
15	Move a glitter glue tube	Open it	Decorate a frame by pasting pieces of mosaic

Experimental training

Before delivering the Tele-UPCAT platform, the training will be customized for each participant. The rehabilitation staff, on the basis of age and HFCS level, will select from the library the most appropriated AOT rehabilitation packages while the engineers will upload them in the Observational Module (OM). For the Motor Performance Module (MPM), the therapists will organize in a container all the objects identifying them with numbers relative to the training day (e.g. little ball number 1 which means day 1 of the training). In addition to that, a dedicated printed manual with instructions and guidelines related to the different steps of the training and for system management and setup will be provided. The manual contains also all the contacts of both technical and rehabilitation staff for remote assistance in case of doubts or problems during the training. Moreover, two Actigraphs (wGT3X-BT, wActiSleep-BT) will be initialized for the recording period (3 weeks).

The ICT platform will be delivered to the participant's home by the engineers that are in charge of the installation of the system. The families will identify a designated position with a table or a desk of about 80x100 cm near to a socket where the ICT platform will be placed. Engineers and rehabilitation staff will train both parents and participants about the correct use of the system, including safety aspects. Moreover, during the first two training days, a therapist will assist participants and their parents.

During the training sessions, each participant will sit on a chair with both arms placed on a table in front of a platform positioned at about 1 m. Especially when the participant will be a child, a parent will be seated on her/his affected side to prompt attention during task execution and assist if necessary. The software will guide the participant in the sequence of observations and executions.

Standard care

Participants previously allocated in the standard care group will continue their usual care for 3 weeks. Usual care for recruited participants could be consisted for physical or occupational therapy. The frequency and the type of all therapies will be recorded accurately by a diary in both groups.

Outcome measures

Description of sample

Children participating in the study will be classified according to HFCS, which assesses function of the impaired hand in children with CP.[35, 36] This classification consists of 9 grades ranging from a hand that is not used at all (grade 0) to one that is used spontaneously and independently from the other one (grade 8). Due to the general approach in classifying hand functional level, this scale can also be easily applied to young adults with UCP. HFCS will be used for all ages as a criterion for inclusion in this study (from grade 2 to grade 8). In addition, they will be classified according to the Manual Ability Classification System (MACS), a classification system of the child's ability to handle objects in daily activities on one of five levels. [45]

Primary outcome measure

On the basis of our scientific hypothesis and according to previous clinical experience, [18, 19] the primary outcome measure will be the AHA. The latest version 5.0 will be used. This assessment measures UL function during bimanual activities by evaluating spontaneous use of assisting hand during a semi-structured age-appropriated 10-15-minute session with specific toys or objects requiring bimanual handling. The school-kids form will be used for the assessment of UCP children 6-12 years old [24, 25] while the Adolescent version (Ad-AHA), using the board hame "Go with the Floe", [26] will be completed with participants older than 13 years. This last version, even if validated up to 18 years, will be used with potential participants 18-20 years old to guarantee the same assessment across all participants regardless of age. Moreover, AHA has been already used, even if not validated, in young people with UCP [46, 47]. The scale uses a Rasch measurement model which is a method to convert raw scores into a linear measure located on a unidimensional scale and more specifically to convert them into 0 to 100 logit-based AHA units, that will be used for the statistical analyses. All AHA assessments will be videotaped in a standardised manner and the subsequent scoring will be carried out by a certified expert rater who will be masked to group allocation and assessment order [24-26].

Other outcome measures

Other secondary measures will include measures of unimanual capacity (MA-2, [27] and BBT [28]) and bimanual daily activities at home and in the community (ABILHAND-Kids). [29] Moreover, participation and quality of life will also be assessed. All assessment will be performed at T0, T1, T1 plus, T2 and T3 unless otherwise indicated. Questionnaires will be completed by parents and/or participants at home and if doubts will occur, child neurologists or therapists will be available to discuss face to face items not clear to them.

i. The Melbourne Assessment 2 (MA2) [27] measures unilateral UL function and it is a valid and reliable tool for evaluating quality of UL movement in children with neurological conditions for ages between 2.5 and 15 years. MA2 is a criterion-referenced test that extends and refines the scale properties of the original Melbourne Assessment (MUUL) and like MUUL it can also be used for adolescents and young adults. MA2 measures four elements of UL movement quality: movement range, accuracy, dexterity and fluency. It comprises 14 test items of reaching, grasping, releasing and manipulating simple objects. The test is administered by video recording the child's performance for subsequent scoring (30 items

score). A raw score is provided for each of the four sections (Movement Range , Accuracy, Dexterity and Fluency) that will be analysed separately. It predominantly includes concepts within the body function domain as well as in the activity domain. Even if the MUUL and also the MA-2 have been validated up to 15 years, the first one has been used in studies involving patients with CP older than 15 year and in adults. [46-47] We have chosen to use the MA-2 also for participants older than 15 years to guarantee the same assessment across all participants regardless of age instead of using other scales (e.g. the Fugl-Meyer Assessment or the Action Research Arm test). [48]

ii. Box and Block Test (BBT) is a quick (2-5 minutes), simple and inexpensive test which measures unimanual dexterity in the activity domain. BBT is composed of a test box with a partition in the middle and 150 wooden blocks (25mm). The patient had to transport as many blocks as possible in 1 minute from one compartment to another. Firstly, the patient is asked to perform the test with the unaffected hand and then with the affected hand. The number of blocks transported by affected hand in 1 minute will be counted and considered for the main analyses. It can be used for a wide range of populations from childhood to adulthood. [28]

iii. ABILHAND-Kids [29] is a semi-structured item-response questionnaire on a 3-point ordinal scale (impossible, difficult, easy) that measures daily manual activities referred to in the activity domain of ICF. Parents will be instructed to rate their child's perceived difficulty in performing each activity taking account the performance of their child when performing the activity without technical or human assistance, regardless of the limb(s) and the strategies used. It has been validate for children aged 6-15 years but it has been used for larger ranges (6-19 years). [49] The questionnaire has been developed using the Rasch measurement model which provides a method to convert the ordinal raw scores into a linear logit measures located on a unidimensional scale, that will be used for the analyses.This questionnaire will be used at all assessment periods.

iv. Participation and Environment Measure - Children and Youth (PEM-CY). [30, 31] It is a parent-reported instrument that evaluates participation and environment across home (ten items), school (five items) and community (ten items) settings. For each item, the parent is asked to identify how frequently (over the past four months) the child has participated (eight options: daily to never); how involved the child typically is while participating (five point scale: very involved to minimally involved); and whether the parent would like to see the child's participation in this type of activity change (no or yes, with five options for the type of change desired). For each setting, the parent is then asked to report on whether certain features of the environment make it easier or harder for the child to participate. The following summary scores will be obtained: total score and score for each of the three setting-specific environmental supportiveness (home, school, community). Moreover the total number of supports and the total number of barriers will be computed.This questionnaire will be used at T0 and T3.

v. Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years) evaluate quality of life in children and adolescents with CP. [32-34] A score on a 0-100 scale will be obtained for each of computed sub-domains. In particular the Children form filled in by the parents assesses 7 subdomains (Social well-being and acceptance, Feelings about functioning, Participation and physical health, Emotional well-being and self-esteem, Access to services, Pain and impact of disability and Family health) and five subdomains (excluding Access to services and Family health to the previous) for the children version. The Teen form evaluates 7 subdomains (General well being and participation, Communication and physical health, School well being, Social well being, Access to services, Family health and Feeling about functioning) for the form filled in by the parents and 5 (excluding Access to services and Family health to the previous) for those filled in by the participants. These questionnaires will be used at T0 and T3.

vi. Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks, is a new assessment tool that consists of observation, followed by execution of three tasks of increasing difficulty (unimanual lifting, bimanual placing near and bimanual cooperation, holding and pulling) by means of a sensorized object. New technological tools such as sensorized objects can help in assessing the manipulation capabilities (reaching and grasping) in a quantitative but ecological way and the sensitivity to a training. Previous studies of the authors were focused on the development of sensozied toys for measuring infant's manipulation [50-52]. Starting from this experience, a new sensorized object has been designed and developed by the engineers tuning the sensors sensitivity and working range to the needs of participants with UCP.
Two load-cells and a switch embedded in the sensorized object allow for the measurement of the following parameters: grasping time, maximum grasping force and delay time between unaffected and affected hand in reaching for the object.

vii. Quantitative measurement of bimanual activities will be performed in all the participants enrolled in the study by means of Actigraph GXT3+. Actigraphs wGT3X-BT and wActiSleep-BT, equipped with a Velcro strap bracelet, will be worn, one for each wrists. As general rule, the experimental group have to wear the actigraphs between T0 and T1 and between T1 and T2 (total 6 weeks, 24 hours per day or as much as possible) while the control group are requested to wear them between T0 and T1, between T1 and T1 plus and, if possible also between T1 plus and T2 (total 9 weeks, 24 hours per day or as much as possible). All the daily activities, experimental training or usual care, or removal will be recorded in a dedicated diary. The actigraphs will also be worn, by all the participants, during each time point of clinical assessments with the outcome measures. Data will be mainly relative to the asymmetry index (AI), that is the difference between the mean activity of the dominant with those of the non dominant hand and it will be correlated with the clinical scores obtained in the clinical outcome measures (mainly AHA).

viii. Cost effectiveness: A within trial cost-utility analysis will be conducted to synthesise the costs and benefits of the training program. Resource use (staff time, equipment and facility use) associated with the program will be collected alongside the RCT. Health care utilisation will be collected using a resource use questionnaire previously used in CP studies. [53] Health utility will be derived from the adapted CHU-9D, [54] a quality of life measure designed specifically for economic evaluation and which has been validated in an Australian population. [55-57]

ix. A semi-guided face to face interview about the acceptability of the training will be completed immediately after the training period (T1 or T1 plus) trough a questionnaire. It will be done by the rehabilitation staff with the aim of investigating participant's and parents' opinions about the training in terms of customization of exercises, suitability to UCP children, feasibility at home, required effort by the participants, but also acceptability of actigraphs, suitability of the manual and of the software will be recorded.

Statistical analyses

Clinical data will be analysed by means of the Statistical Package for Social Sciences (SPSS). Means and standard deviation of clinical outcome scores for both groups will be calculated to identify potential baseline differences between groups. As a first step, normality of distributions will be verified by Shapiro-Wilk's test. Between-group differences for all selected outcome measures will be evaluated at T0, by means of t-test for unrelated samples or non-parametric Mann–Whitney U independent sample test, for normal or non-normal distributed data, respectively. To test our first hypothesis, an intention to treat analysis will be carried out, evaluating between-group differences for primary and secondary outcome measures at the primary endpoint (T1), compared with T0, by means of parametric or non-parametric tests for unrelated samples. The age, HFCS level,

characteristics of usual care (in both groups), supervision of caregiver will be analysed for further exploratory analyses. In addition, matched-pairs tests (t-tests or Wilcoxon) will be carried out in order to assess retention of effects at follow-up periods (T1 or T1 plus, T2 and T3) relative to assessment before AOT training (T0 or T1 for experimental or waitlist group respectively). Bonferroni corrections will not be carried out in relation to the exploratory nature of the current RCT study. To detect if significant changes will correlate to HFCS levels, a correlation analysis between score changes after AOT training (T1 or T1 plus) and assessment before AOT training (T0 or T1) will be carried out. Finally, an exploratory within-group analysis will be performed for the waitlist group comparing changes during AOT with respect to those of the first standard care period.

ETHICS AND DISSEMINATION

This study protocol describes background, hypotheses, system, clinical and technologic outcome measures for a RCT designed to evaluate the Tele-UPCAT system as a new approach to deliver AOT to children and young people with UCP at home.
Full ethical approval has been obtained from the Tuscany Paediatric Ethics Committee (169/2016, Protocol Version 5.0 of 10/11/2016) and any deviations from the protocol will be promptly notified to this Ethic Committee and applied only after its approval. The trial has been registered at http://www.clinicaltrials.gov (identifier NCT03094455). This study protocol is reported according to the SPIRIT statement (SPIRIT 2013) [38] and the TIDier guidelines [39, 40]. We anticipate that the results of this study will be disseminated through peer reviewed journals and national and international academic conferences only by the professionists directly involved in the clinical trial. The results of this study will be of interest for rehabilitation trials based on AOT paradigm. Referring to a previous RCT study, [18, 19] we suggest that the home setting might increase accessibility of rehabilitation to a large number of children and young people with UCP (e.g. participants that live far from the clinical centres) with a large range of hand impairments (including also participants with HFCS level lower than 6) and older age (5-20 years instead of 5-15). Moreover, if the Tele-UPCAT study, using a very simple ICT solution, demonstrates to be viable for delivering AOT at home with significant improvements in UL daily activities, it could lead to the application of new solution for cost efficient rehabilitation programs. Implementation of new smart technologies can i) provide user-friendly AOT programs at home; ii) remotely manage treatment by rehabilitation staff thus increasing the ratio ‘number of patients per therapist’; iii) offer individualized and intensive training. It could become an economical and efficient rehabilitation program by achieving significant long-lasting effects in UL activity and participation through an easily implementable paradigm that could become an integral part of common clinical practice. Finally, this approach could become a rehabilitation tool and be applicable to broader populations of CP and other chronic disabilities.

PROJECT STATUS

This project began recruitment the 29 March 2017, and we expect to complete data collection for the last training the November 2017 and close the project in the April 2018.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHOR’S CONTRIBUTION

GS is the principal investigator of the project and mainly responsible of the clinical part of it while FC is the main responsible of the ICT platform. GS, EI, HF, KK, RB, AF and GC designed the research study. GS, EB, EI, SP and EB were responsible for the AOT library. GS, SP and ES were in charge for participants' recruitment in Pisa and identification of type of exercise and software and AF for Reggio Emilia. GS and EB will collect the data and will monitor the training. FC, IM, MM and FFP with the supervision of PD have designed and built the new platform. GS and GC will take the lead roles on preparation of publications on the clinical outcomes of the study.
All authors have read and approved the final manuscript.

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Figure 1. Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: -Participation and Environment Measure - Children and Youth

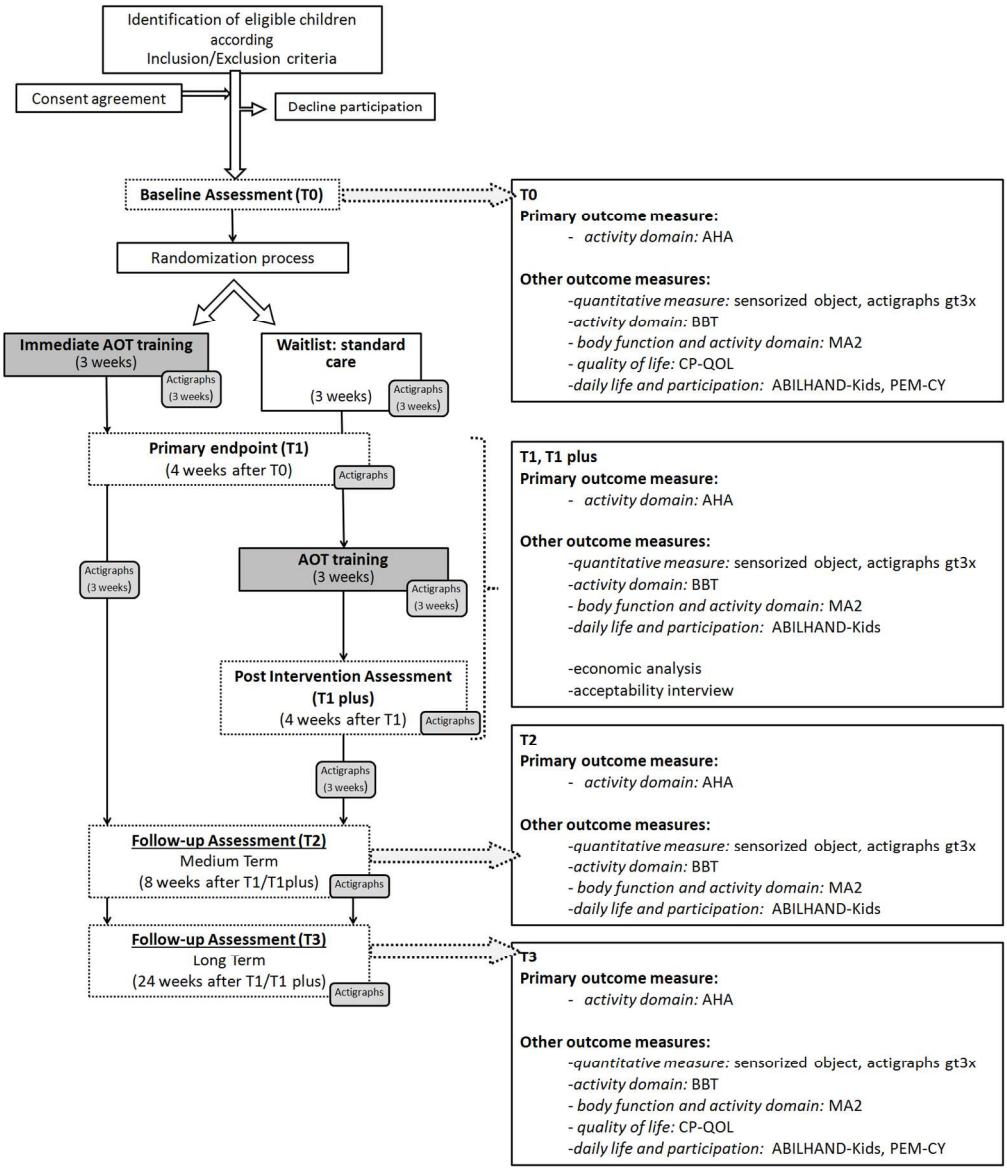
Figure 2. Schedule of enrolment, interventions, and assessments.

Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected by the clinical staff in relation to HFCS level in the Clinical Interface (2). A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3). The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists. The integrated camera records subject's attention during the observation task and exercise execution.

Figure 4. a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. **b)** Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

Supplement material 1. SPIRIT and TIDier checklists

Supplement material 2. Written informed consents (in Italian language)



Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: - Participation and Environment Measure - Children and Youth

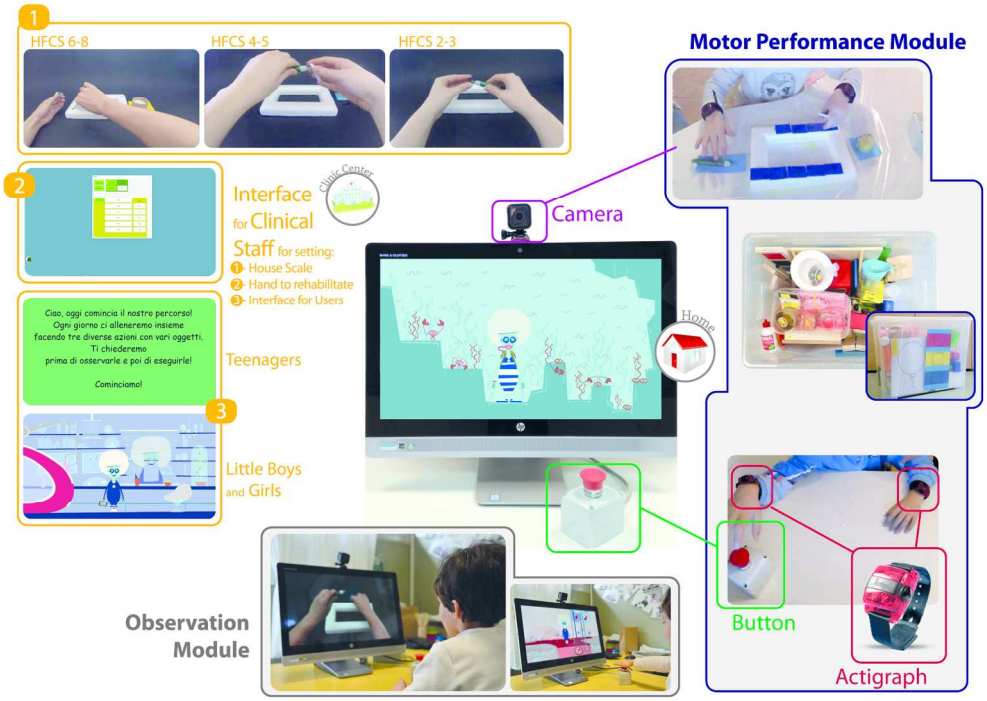
141x163mm (300 x 300 DPI)

	STUDY PERIOD				
	Enrollment	Post-allocation			
TIMEPOINT**	*T0*	*T_1*	*T_1 plus**	*T_2*	*T3*
ENROLLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation	X				
INTERVENTIONS:					
AOT intervention					
Wait list control group	←	→			
ASSESSMENTS:	←	→	←	→	
AHA	X	X	X	X	X
MA 2	X	X	X	X	X
BBT	X	X	X	X	X
ABILHAND-Kids	X	X	X	X	X
CP QoL	X				X
Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks	X	X	X	X	X
Quantitative measurement of bimanual upper limb activities by means of Actigraph GXT3+	X	X	X	X	X
Economic analysis		X	X		
Acceptability interview		X	X		

* only for wait-list group

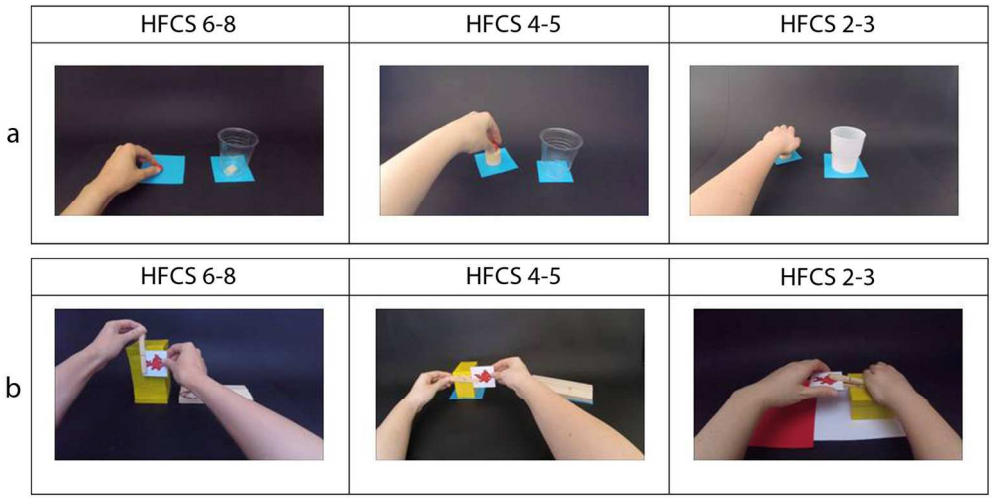
Schedule of enrolment, interventions, and assessments

60x88mm (300 x 300 DPI)



Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected by the clinical staff in relation to HFCS level in the Clinical Interface (2). A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3). The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists. The integrated camera records subject's attention during the observation task and exercise execution

170x120mm (300 x 300 DPI)



a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. b) Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal

170x83mm (300 x 300 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,12
	2b	All items from the World Health Organization Trial Registration Data Set	2,12
Protocol version	3	Date and version identifier	12
Funding	4	Sources and types of financial, material, and other support	2,12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,12
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	12

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	3
Objectives	7	Specific objectives or hypotheses	3,4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4,5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	4
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	4
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4,5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	5, 9-11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	5

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	5
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11, 12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11, 12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11, 12
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	5
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	5
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	5
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	12

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	5
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	5
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	12
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary material (in italian language)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	Page 2	_____
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	Pages 3-4	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	Pages 6-9	_____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	Pages 3-5	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	Pages 5-7	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	Pages 5, 8	_____
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	Page 8	_____

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	Page 6	_____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	Pages 6-8	_____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	_____N/A____	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____N/A____	_____
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	____N/A_____	_____

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
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MODULO INFORMATIVO
PER GENITORI/TUTORE LEGALE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentili Genitori/Tutore,
Le informazioni contenute nella scheda informativa seguente sono dettagliate e potrebbero risultare molto complesse.

Le chiediamo di accettare la partecipazione allo studio solo dopo avere letto con attenzione questo foglio informativo ed avere avuto un colloquio esauriente con il medico sperimentatore che le dovrà dedicare il tempo necessario per comprendere completamente ciò che le viene proposto.

Vostro/a figlio/a potrebbe essere idoneo a partecipare ad uno studio promosso dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni importanti riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non vi risultasse chiaro, potrete porre domande ai medici sperimentatori coinvolti dello studio. Prendetevi tutto il tempo necessario. La partecipazione di vostro/a figlio/a è volontaria e potrete ritirarla in qualsiasi momento.
Una volta che avrete letto questo modulo, avrete ricevuto risposta alle eventuali domande, e qualora decideste di far prendere parte vostro/a figlio/a allo studio, vi sarà chiesto di firmare un modulo di consenso, di cui riceverete una copia cartacea.

Cosa si propone lo studio

Vostro/a figlio/a è stato/a invitato/a a partecipare a questo studio per valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 bambini/adulti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei bambini che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 4 settimane; a termine delle quali i bambini di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i bambini saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T2). Per dettagli vedi Disegno dello studio Figura 1.

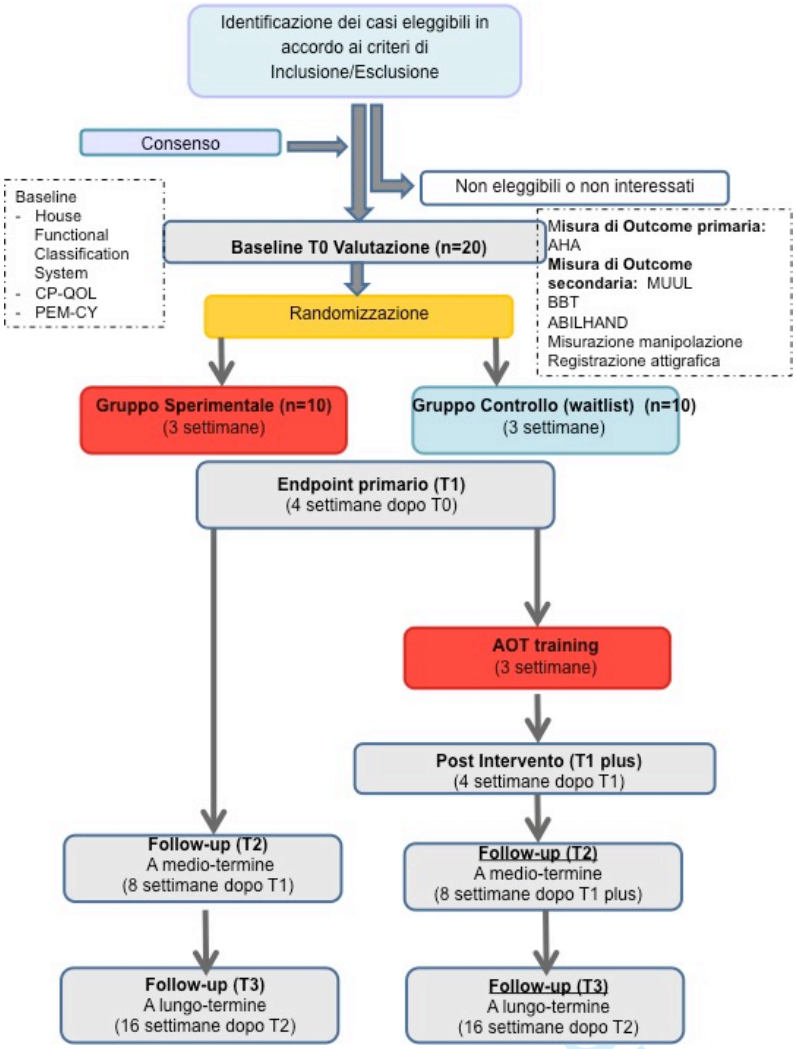


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i bambini arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolari di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I bambini che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i bambini allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la partecipazione allo studio

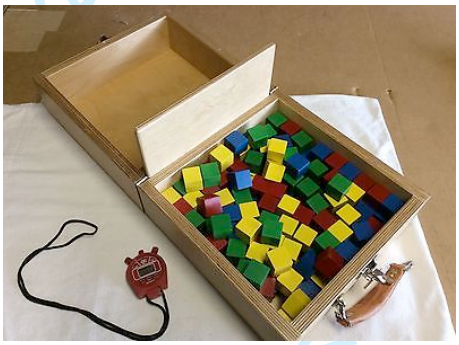
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



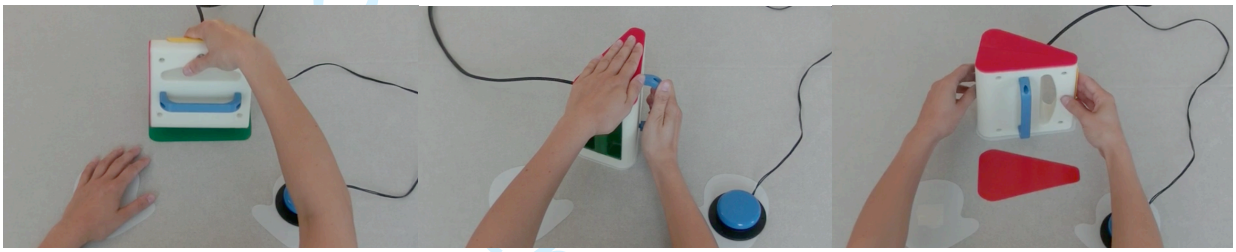
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND-Kids* è un breve questionario, validato in bambini con paralisi cerebrale infantile dai 6 ai 15 anni che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da un genitore in base alla difficoltà che ha il bambino a compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita nei bambini ed adolescenti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se doveste decidere di non prendere parte allo studio, o in caso doveste cambiare idea in seguito, vostro/a figlio/a non subirà alcuna penalità o perdita di benefici ai quali avrebbe altrimenti diritto. Le sue cure mediche attuali e future presso l'IRCCS

Fondazione Stella Maris non saranno compromesse dalla vostra decisione ed i medici continueranno a seguirlo/a con la dovuta attenzione.
Potrete ritirare l'adesione di vostro/a figlio/a allo studio in un qualsiasi momento dandone comunicazione al medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Procedure previste alla fine dello studio
Non è prevista alcuna procedura da attuarsi alla fine dello studio.

Informazione del medico di medicina generale /pediatra di libera scelta
Per la migliore tutela della salute di vostro/a figlio/a, vi verrà chiesto di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accettate di far partecipare vostro/a figlio/a.

Informazioni sui risultati dello studio
Qualora foste interessati, potrete chiedere al medico di comunicarvi i risultati generali dello studio ed in particolare quelli che riguardano vostro/a figlio/a.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i dati personali di Suo Figlio/a, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento

I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La partecipazione di Suo figlio/a allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione nella persona della Dr.ssa Giuseppina Sgandurra *, IRCCS Fondazione Stella Maris, Viale del Tirreno 331*. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la partecipazione di Suo figlio/a allo studio. In tal caso, i campioni biologici a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che riguardano Suo figlio/a, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi aggiuntivi a vostro carico derivanti dalla partecipazione allo studio. Non riceverete alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che vi è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data……..

Potrete segnalare qualsiasi fatto riteniate opportuno evidenziare, relativamente alla ricerca che riguarda vostro/a figlio/a, al Comitato Etico e/o alla Direzione sanitaria di questa struttura ospedaliera.

Per ulteriori informazioni e comunicazioni durante lo studio sarà a disposizione il seguente personale:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____
_____
Nome per esteso del medico Data Ora Firma
che ha consegnato l'informativa

CONSENSO INFORMATO PER GENITORI/TUTORE LEGALE

Versione 5.0 del 10/11/2016

Titolo Protocollo

Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Stella Maris, Prof. Giovanni Cioni IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 341/ ABC; 56128 Calambrone (Pisa), Italia Tel 050/886233.
e-mail: g.sgandurra@fsm.unipi.it

Io sottoscritta (madre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

Io sottoscritto (padre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

del minore _____ nato il ___/___/_____
residente a _____via/piazza _____

dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, della quale mi è stata consegnata una copia in data _____ alle ore _____ (indicare data e ora della consegna).

Dichiaro che mi sono stati chiaramente spiegati la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico.

DICHIARO inoltre che:

1. ho letto e compreso il foglio informativo fornito riguardo il progetto di ricerca e facente parte di questo consenso;
2. mi è stata data l'opportunità di porre qualsivoglia domanda allo sperimentatore dello studio e ho avuto risposte soddisfacenti;
3. mi è stato concesso il tempo sufficiente per riflettere sulle informazioni ricevute e per discuterne con terzi;
4. sono stato/a informato/a che il protocollo dello studio e tutti i moduli utilizzati hanno avuto il parere favorevole del Comitato Etico Pediatrico;
5. mi è stato chiaramente spiegato che posso decidere che il/la minore non prenda parte allo studio o ne esca in qualsiasi momento, senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
6. sono consapevole che la ricerca potrà essere interrotta in ogni momento, per decisione del responsabile della ricerca, senza pregiudizio per la salute del/della minore;
7. sono stato informato/a che sarò messo al corrente di qualsiasi nuovo dato che possa compromettere la sicurezza della ricerca e che, per ogni problema o per ulteriori domande, potrò rivolgermi ai medici presso i quali il/la minore è in cura;
8. per la migliore tutela della salute del/la minore, sono consapevole dell'importanza (e della mia responsabilità) di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accetto di far partecipare il/la minore; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici;

9. sono stato informato/a che i risultati dello studio saranno resi noti alla comunità scientifica, tutelando l'identità del minore secondo la normativa vigente sulla privacy.

10. sono consapevole che devo/dobbiamo ricevere una copia del presente modulo di consenso.

Sottoscrivendo questo modulo acconsento al trattamento dei dati personali di mio figlio/a e al loro trasferimento al di fuori dell'Unione europea (*da inserire se effettuato specificando gli estremi identificativi dei destinatari*) per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di:

□ **volere** □ **NON volere**
che il minore partecipi alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informati sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
informare il pediatra di libera scelta/medico di medicina generale della partecipazione allo studio (*è preferibile il suo coinvolgimento*)

_____ ___/___/_____ _____
_____
Nome per esteso del minore Data Ora Firma

_____ ___/___/_____ _____
_____
Nome per esteso Data Ora Firma
del genitore/tutore legale

_____ ___/___/_____ _____
_____
Nome per esteso Data Ora Firma
del genitore/tutore legal

Io sottoscritto Prof./Dr. …… (Cognome) …….. (Nome)

Dichiaro che i genitori/tutori legali del Paziente hanno firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle possibili alternative;
- aver verificato che i genitori/tutore legale abbiano sufficientemente compreso le informazioni fornitegli
- aver lasciato ai genitori/tutore legale il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato | Data | Ora | Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle "Modulo informativo per i genitori/tutore legale" dovrà essere consegnata ai genitori/tutori legali del Paziente

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

PRESIDENTE
Avv. Giuliano Maffei
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CENTRO DIURNO DI
RIABILITAZIONE PSICHIATRICA
La Scala di San Miniato (PI)
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MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

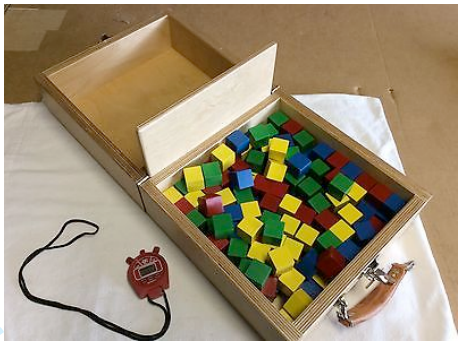
Perché facciamo questo studio?
La ricerca medica vuole migliorare la conoscenza sulle malattie.
Ti chiediamo di aiutarci a capire se l'uso di una terapia basata sull' osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato un' azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

Chi partecipa con me?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Che succede se partecipo?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo casuale ad uno dei due gruppi previsti nella prima fase dello studio: sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Inoltre ti saranno proposti, a dei tempi prestabiliti (quando ti arruoliamo, dopo che hai finito il trattamento o la fase di controllo, dopo che hai finito il trattamento se l'hai iniziato dopo, dopo 8 e dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!

Quanto durerà lo studio?
Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento). Ti verrà inoltre chiesto di effettuare i giochi e di compilare i questionari 3 o 4 volte.


Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?
Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?
Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio
Sei completamente libero di aderire o meno allo studio. Se deciderai di non partecipare, continuerai ad essere seguito periodicamente dalla tua equipe di riferimento del nostro centro clinico così come fatto fino ad ora.

Devo fornire il mio consenso per partecipare allo studio?
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare questo modulo di cui ti sarà data una copia.
Se decidi di non partecipare allo studio, o in caso dovessi cambiare idea in seguito, non succederà niente, continuerai a ricevere le cure a te necessarie presso questo ospedale.

E se dovessi avere delle domande?

Se hai delle domande puoi farle alla Dr.ssa Giuseppina Sgandurra durante il colloquio e potrai anche chiamarla al telefono al numero 050/886239: ti ascolterà e ti spiegherà tutto quello che desideri.

Data _____ ora _____ di consegna

_____Firma del medico che ha consegnato l'informativa

DICHIARAZIONE DI ASSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 6.0 del 29/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Il modulo informativo mi è stato consegnato il (data) _____ alle ore _____
Ho capito tutto quello che il medico mi ha spiegato.
Il Dottore ha ascoltato tutte le mie domande ed ha saputo rispondermi.
Se in futuro avrò bisogno di qualcos'altro i medici dello studio saranno a mia disposizione.

_____
Data e ora

_____
Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____
Firma del paziente. Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____ _____
Data/ora Firma del medico che ha informato il paziente

FONDAZIONE
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ISO 9001 BUREAU VERITAS Certification

MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 17 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Caro/a ……,
potresti essere idoneo a partecipare ad uno studio proposto dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non ti risultasse chiaro, puoi porre domande ai medici dello studio. Prenditi tutto il tempo necessario. Non sei obbligato a partecipare. Se accetti, potrai decidere di ritirare la tua partecipazione in qualsiasi momento.
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue eventuali domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare il modulo di cui ti sarà data una copia.

Quale è lo scopo di questo studio?
Sei stato/a invitato/a a partecipare a questo studio perché pensiamo che puoi aiutarci a capire se l'uso di una terapia basata sulla osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato una azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

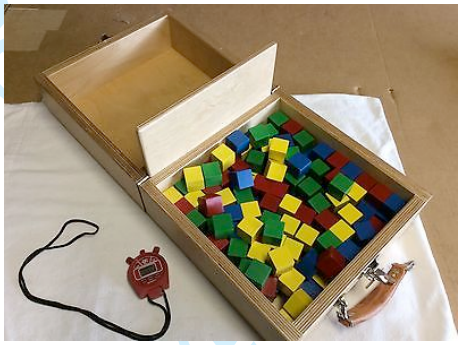
Quante persone parteciperanno?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Cosa comporta la partecipazione allo studio?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo random (casuale) ad uno dei due gruppi previsti nella prima fase dello studio:

sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre (durata 3 settimane) se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento).

Inoltre ti saranno proposti, a dei tempi prestabiliti (T0: quando ti arruoliamo, T1: dopo che hai finito il trattamento o la fase di controllo, T1 plus: dopo che hai finito il trattamento se l'hai iniziato dopo, T2: dopo 8 e T3: dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!



Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?

Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?

Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio o di ritirarmi dallo studio?

La tua partecipazione allo studio è volontaria.

Se decidi di non partecipare, o in caso dovessi cambiare idea in seguito, non subirai alcuna penalità o perdita di benefici ai quali avresti altrimenti diritto. Le tue cure mediche attuali e future presso l'IRCCS Fondazione Stella Maris non saranno compromesse dalla tua decisione ed i medici continueranno a seguirti con la dovuta attenzione.

Puoi ritirare la tua adesione allo studio in qualsiasi momento, comunicandolo al medico dello studio, la dottoressa *Giuseppina Sgandurra* senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che ti riguardano e potrai chiedere la cancellazione di quelli già raccolti. La tua partecipazione allo studio potrà essere interrotta se il medico valuterà che il nuovo trattamento non ha portato alcun giovamento o se si verificheranno effetti indesiderati. In questi

casi sarai tempestivamente informato dal medico e potrai discutere con lui circa ulteriori trattamenti validi per la tua patologia.

Cosa accadrà alle informazioni che sono state raccolte per lo studio?
Le informazioni mediche che ti riguardano come ad esempio l'età, il sesso, le caratteristiche della tua malattia, i risultati delle prove e il diario delle attività quotidiane saranno conservate presso un archivio della Fondazione Stella Maris.
I tuoi dati saranno archiviati in forma anonimizzata, il tuo nome sarà sostituito da un codice conosciuto solo da poche persone e quindi i tuoi dati saranno anonimi. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al tuo nominativo.
I dati dello studio potranno essere mostrati in occasione di convegni/congressi o pubblicati in riviste scientifiche per informare gli altri medici e i professionisti del settore sanitario.

Informazioni sui risultati dello studio
Alla fine dello studio sarai informato sui risultati della ricerca.

Ulteriori informazioni
Non sono previsti costi aggiuntivi a tuo carico derivanti dalla partecipazione allo studio.
Non riceverai alcun compenso economico per la partecipazione allo studio.
Il protocollo dello studio che ti è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data 22/11/2016.

Per ulteriori informazioni e comunicazioni potrai contattare il personale dello studio che sarà a tua disposizione:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha consegnato l'informativa — Data — Ora — Firma

MODULO DI CONSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 18 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Io sottoscritto (nome e cognome) _____
dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione allo studio in oggetto, secondo quanto riportato nel modulo informativo allegato, della quale mi è stata consegnata una copia in data _____ alle ore _____

Dichiaro che mi sono stati chiaramente spiegati la natura, lo scopo, i benefici attesi, i rischi e gli inconvenienti possibili dello studio clinico.

Dichiaro di aver potuto fare tutte le domande che ho ritenuto necessarie e di aver ricevuto risposte soddisfacenti, come pure di aver avuto la possibilità di informarmi in merito ai particolari dello studio con persona di mia fiducia.

Accetto dunque liberamente di partecipare alla ricerca, avendo compreso completamente il significato della richiesta e i rischi e benefici che possono derivare da questa partecipazione.

Acconsento al trattamento dei miei dati personali *e al loro trasferimento al di fuori dell'Unione europea (se applicabile)* per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

□ Desidero che mi siano comunicati i risultati dello studio.

__/__/____ _____ _____
Data Ora Firma del paziente

__/__/____ _____ _____
Data Ora Firma del medico che ha informato il paziente e registrato il suo consenso

FONDAZIONE
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Gentile Sig.ra/Sig.re, le informazioni contenute nel seguente foglio informativo sono dettagliate e potrebbero risultare
MOLTO COMPLESSE

Le chiediamo di accettare la partecipazione allo studio SOLO dopo avere letto con attenzione questo foglio informativo ed avere avuto un COLLOQUIO ESAURIENTE con il medico sperimentatore che le dovrà dedicare il TEMPO NECESSARIO
per comprendere completamente ciò che le viene proposto

INFORMAZIONI SCRITTE
PER IL PAZIENTE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentile Signora / Egregio Signore,
Le è stato chiesto di partecipare ad uno studio clinico sperimentale e questo documento ha lo scopo di informarLa sulla natura dello studio, sul fine che esso si propone, su ciò che comporterà per Lei una tale partecipazione, sui suoi diritti e le sue responsabilità.
La prego di leggere attentamente queste informazioni scritte prima di prendere una decisione in merito ad una eventuale Sua partecipazione allo studio. Lei avrà a disposizione tutto il tempo necessario per decidere se partecipare o meno.
Potrà, inoltre, porre liberamente qualsiasi domanda di chiarimento e riproporre ogni quesito che non abbia ricevuto una risposta chiara ed esauriente.
Nel caso in cui, dopo aver letto e compreso tutte le informazioni ivi fornite, decidesse di voler partecipare allo studio clinico, Le chiederò di voler firmare e personalmente datare il modulo di Consenso Informato allegato a questo documento.

Che cosa si propone lo studio

Valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 soggetti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei soggetti che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 3 settimane a termine delle quali i soggetti di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i soggetti saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T3). Per dettagli vedi Disegno dello studio Figura 1.

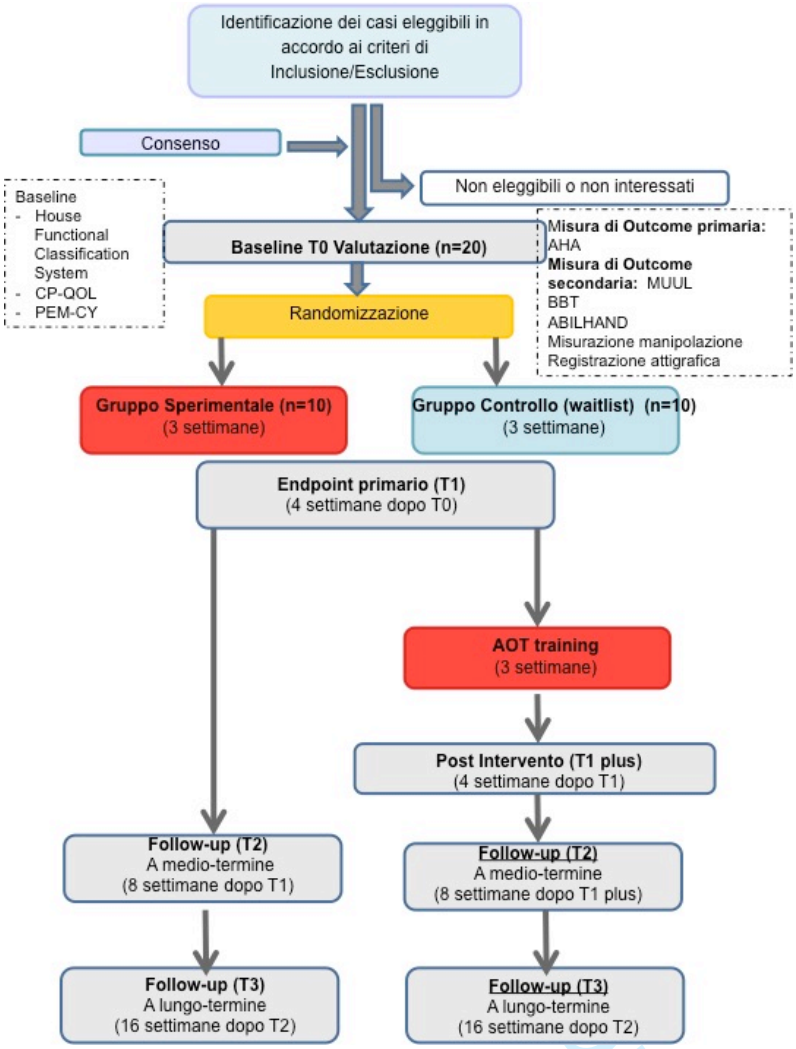


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i soggetti arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolati di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I soggetti che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i soggetti allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la Sua partecipazione allo studio

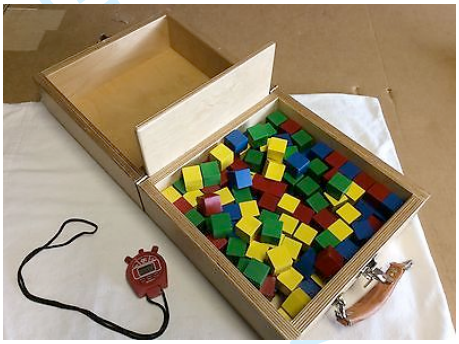
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



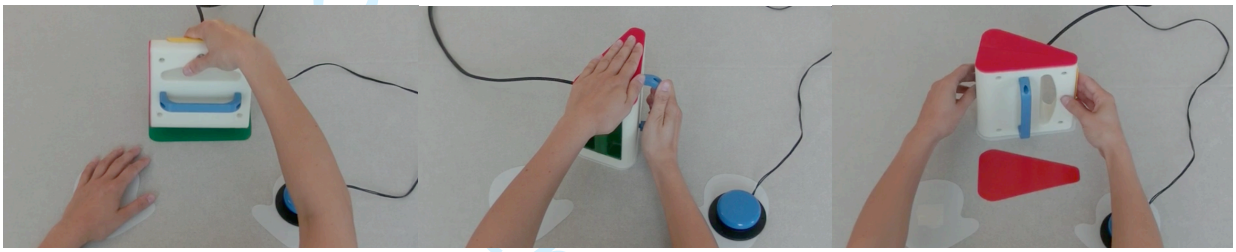
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni, ma utilizzati anche per l'età adulta. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND* è un breve questionario, validato in soggetti con paralisi cerebrale infantile che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da soggetto stesso in base alla difficoltà che esperimenta nel compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita in soggetti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se decide di partecipare, avrà il diritto di ritirarsi dallo studio in qualsiasi momento e senza l'obbligo di fornire spiegazioni, dandone tuttavia comunicazione al medico responsabile dello studio, la Dr.ssa Giuseppina Sgandurra.
Potrà ritirare la sua adesione allo studio in un qualsiasi momento dandone comunicazione al

medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Consenso ad informare il proprio medico di medicina generale
Per la migliore tutela della Sua salute, Le verrà chiesto di informare il Suo medico di medicina generale in merito alla sperimentazione alla quale accetta di partecipare.

Informazioni circa i risultati dello studio
Se Lei lo richiederà, alla fine dello studio potranno esserLe comunicati i risultati generali dello studio ed in particolare quelli che La riguardano.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:
Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all'età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento
I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti
Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi

direttamente al centro di sperimentazione nella persona della Dott.ssa Giuseppina Sgandurra. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. In tal caso, i dati acquisiti a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi a Suo carico derivanti dalla partecipazione allo studio. Non riceverà alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che Le è stato proposto è stato approvato dal Comitato Etico Pediatrico Toscano in data…… Il Comitato Etico ha tra le altre cose verificato la conformità dello studio alle Norme di Buona Pratica Clinica della Unione Europea ed ai principi etici espressi nelle Dichiarazione di Helsinki.

Lei potrà segnalare qualsiasi fatto ritenga opportuno evidenziare, relativamente alla ricerca che La riguarda, al Comitato Etico e/o alla Direzione Sanitaria di questa struttura ospedaliera.

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	g.sgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha consegnato l'informativa | Data | Ora | Firma

MODULO DI CONSENSO INFORMATO

V 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Io sottoscritto/a _____ nato/a il ___/___/_____ residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza) _____

DICHIARO

- di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, facente parte di questo consenso, della quale mi è stata consegnata una copia in data _____ alle ore _____ (*indicare data e ora della consegna*);
- che mi sono stati chiaramente spiegati e di aver compreso la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico;
- di aver avuto l'opportunità di porre domande chiarificatrici e di aver avuto risposte soddisfacenti;
- di aver avuto tutto il tempo necessario prima di decidere se partecipare o meno;
- di non aver avuto alcuna coercizione indebita nella richiesta del Consenso;
- che mi è stato chiaramente spiegato di poter decidere liberamente di non prendere parte allo studio o di uscirne in qualsiasi momento senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
- di essere consapevole dell'importanza (e della mia responsabilità) di informare il mio medico di medicina generale della sperimentazione alla quale accetto di partecipare; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici.

Sottoscrivendo questo modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di

□ **volere** □ **NON volere**
partecipare alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informato sui risultati di questa ricerca dal medico dello studio

□ **volere** □ **NON volere**
essere informato sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
Informare il medico di medicina generale della partecipazione allo studio

_____ ___/___/_____ _____ _____
Nome per esteso del paziente (adulto, minore maturo) Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso rappresentante legale Data Ora Firma

Io sottoscritto Prof./Dr. …… ……
Cognome Nome

Dichiaro che il Paziente ha firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito al Paziente esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle sue possibili alternative;
- aver verificato che il Paziente abbia sufficientemente compreso le informazioni fornitegli
- aver lasciato al Paziente il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato
Data Ora Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle “Informazioni Scritte per il Paziente” dovrà essere consegnata al Paziente stesso

FONDAZIONE
STELLA MARIS - *IRCCS*
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OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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CENTRO DIURNO DI
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INFORMATIVA E MANIFESTAZIONE DEL CONSENSO
AL TRATTAMENTO DEI DATI PERSONALI

Titolo Protocollo
Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
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e-mail: g.sgandurra@fsm.unipi.it

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris in accordo alle responsabilità previste dalle norme della buona pratica clinica (decreto-legge n. 211/2003), tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine esclusivamente in funzione della realizzazione dello studio.
Il trattamento dei dati personali relativi tra cui età, sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano, raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati unitamente a tale codice, alla Sua data di nascita, al sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento
I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che, il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione. Sperimentatore principale Dr.ssa Giuseppina Sgandurra , IRCCS Fondazione Stella Maris. Viale del Tirreno 331, 56128 Calambrone (Pisa), *g.sgandurra@fsm.unipi.it.*

Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca.

Consenso

Sottoscrivendo tale modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

Nome e Cognome dell'interessato (in stampatello) _____

Firma dell'interessato _____

Data _____

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Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPper Limb Children Action Observation Training for Participants with Unilateral Cerebral Palsy

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Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPper Limb Children Action Observation Training for Participants with Unilateral Cerebral Palsy

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Abstract

Introduction:

A new rehabilitative approach, called UPper Limb Children Action Observation Training (UP-CAT), based on the principles of Action Observation Training (AOT), has provided promising results for Upper Limb rehabilitation in children with UCP. This study will investigate if a new Information and Communication Technology (ICT) platform, named Tele-UPCAT, is able to deliver AOT in a home setting and will test its efficacy on children and young people with UCP.

Methods and Analysis:

A randomized, allocation concealed (waitlist-control) and evaluator-blinded clinical trial with two investigative arms will be carried out. The experimental group will perform AOT at home for 3 weeks using a dedicated and customized Tele-UPCAT system where they will watch video sequences of goal-directed actions and then complete the motor training of the same actions. The control group will continue standard care for 3 weeks after which they will also start Tele-UPCAT training. Based on a previous clinical study, a sample size of 12 patients per group is required and the primary outcome will be Assisting Hand Assessment. The Melbourne Assessment 2, ABILHAND, Participation and Environment Measure-Children and Youth (PEM-CY) and Cerebral Palsy Quality of Life Questionnaire (CP-QoL) will be included as secondary measures. Quantitative measures from sensorized objects and subject worn Actigraphs GXT3+ will be analysed. The assessment points will be the week before (T0) and after (T1) the period of AOT/Standard Care. Further assessments will be at T1 plus, the week after the AOT period for the waitlist group and at 8 (T2) and 24 weeks (T3) after AOT training.

Ethics and Dissemination:

The trial has been approved by the Tuscany Paediatric Ethics Committee (169/2016). Publication of all outcomes will be in peer-reviewed journals and conference presentations.

Trial registration: ClinicalTrials.gov: NCT03094455 (16 March 2017). The trial was funded by Italian Ministry of Health grant: GR-2011-02350053

Abstract words: 299

Key words: action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Strengths and limitation of this study

- This is the first protocol study where an ICT platform is proposed, called Tele-UPCAT, to deliver the Action Observation Therapy (AOT) at home
- The study is a well-designed RCT aimed to investigate the UP-CAT approach at home and to measure its efficacy in a clinical population of children, adolescents and young adults with UCP.
- The Tele-UPCAT platform allows individualised customization of the intervention according to the different manual functional levels and the different ages of participants.
- The sample size, even if calculated and powered on the previous clinical studies, is modest.
- The Tele-UPCAT platform does not obtain quantitative measurements of force and pressure hand measurements during AOT session.

BACKGROUND

Cerebral palsy (CP) is the most common cause of childhood chronic physical disability in Europe and in other industrialised societies. [1] The incident rate is between 2 and 3 per 1000 live births and increases to 40–100 per 1000 live births among very premature and very low birth-weight babies which represent the population with highest rate of neurodevelopmental disorders. Unilateral Cerebral Palsy (UCP) (i.e. a motor impairment impacting one side of the body) constitutes the most frequent form of CP, about 30-40% of all affected children. [2] Recent estimations of incidence and prevalence of CP have shown a significant increase in UCP in Europe over the last years. [3-4] The Upper Limb (UL) of children with UCP is generally more involved than the lower limb and the consequent disability affects their participation, quality of life, independence at home, school and community. Despite this large impact, the current clinical practice for UCP mainly include consultative intervention or time-limited therapy following pharmacological intervention. In the last decades, many intervention models targeting deficits in UL function have been developed to promote better use of impaired arm and hand for routine bimanual activities and to achieve functional independence. [5-8] In this field, one of the most recent models is the Action Observation Training (AOT), based on the discovery of the Mirror Neuron System, whose core regions are the ventral premotor and inferior parietal cortex. These areas are activated when individuals perform goal-directed motor acts (e.g. grasping an object) as well as if they simply observe the performance of the same or a similar action and trigger recruitment of the same network as the actual physical action. [9, 10] AOT is mainly based on observation of meaningful actions, and their successive imitation. AOT has been used as new intervention model in many adult studies for neurologic and non-neurologic diseases (such as Parkinson disease, stroke, orthopaedic surgery) and there is growing evidence of its effectiveness. [11-16] Recent studies carried out in children with CP indicate positive effects on UL function in younger population. [17-19] We have recently completed a clinical study called UP-CAT (UPper limb Children Action observation Training) with children with UCP based on 3 weeks of AOT, providing evidence of its efficacy in improving UL activity performance in daily activities. [19] To date, the UP-CAT study has only been carried out in a clinical rehabilitation setting with children who were living near the two clinical centres and whose parents are willing to commit to a 3-week intensive therapy program with consequently high costs for both health services and families. In addition, the parents, even if able to participate, found the need to attend every working day for three weeks too burdensome and suggested the delivery of the intervention at home. Biotechnologies, tele-rehabilitation and eHealth provide a promising approach to deliver tele-monitored home programs for a large number of participants at a relatively low cost. In this field our group has recently experienced the design, the build and the clinical validation of new technological Information and Communication Technologies (ICT) for providing in the first year of life tele-rehabilitation programs at home for infants at risk for developing neurodevelopmental disorders [20-23] In this context, similar approaches could represent a viable option in providing AOT programs at home, in a user-friendly, playful and rehabilitative setting in children. The present study protocol, designed as an exploratory Randomized Clinical Trial (RCT), has the purpose to investigate the feasibility of a new ICT platform, named Tele-UPCAT, to provide the UP-CAT approach at home. This pilot RCT aims to measure its efficacy in a group of children, adolescents and young adults with UCP comparing the effects of Tele-UPCAT approach (experimental group) with the standard care (control group).

The primary aim will be to evaluate the immediate effects (T1, in the week after the end of the treatment) of this new approach (home AOT) on bimanual hand function (Assisting Hand Assessment, AHA[24-26]) and to assess whether these effects will be retained at a medium and long term follow-up (i.e. 8 and 24 weeks after the end of treatment, T2 and T3). In addition, the feasibility of the Tele-UPCAT system as a comfortable, reliable and customizable tool for delivering an home AOT to UCP participants and their families will be assessed using semi-structured interviews.

Secondary aims will be to investigate the immediate (T1) and long-term clinical effects (T2, T3) on unimanual capacity (Melbourne Assessment 2, MA 2 [27] and Box and Block Test, BBT [28]) and on bimanual daily activities at home and in the community (ABILHAND-Kids [29]), participation (Participation and Environment Measure - Children and Youth, PEM-CY) [30, 31] and perception of quality of life (Cerebral Palsy Quality of Life Questionnaire, CP-QOL); [32-34]. Further aims will be the evaluation of feasibility of Tele-UPCAT platform on assessing, monitoring and detecting changes during and after the AOT program by comparing the data of the clinical outcome measures with those of quantitative measurement of manual activity, obtained using sensorized objects and Tele-UPCAT platform. Finally, a cost-effective analysis will be carried out using both the perspective of the patient/caregivers and the healthcare system.

METHODS/DESIGN

Study design

The Tele-UPCAT trial is an exploratory randomized, allocation concealed (waitlist-controlled), and evaluator-blinded clinical trial with two investigative arms using an AOT intensive rehabilitation program of home based AOT compared to standard care in children and young people with UCP. The study is a waitlist controlled trial, in order to allow all enrolled participants to perform AOT training either immediately or after a waitlist period. After obtaining informed consent, and completing baseline assessment (T0) participants will be block randomized into pairs according to the House functional classification system (HFCS) activity level (grades 2-3, 4-5 and 6-8) and age (5-14y, 15-20y), [35, 36] using a computer-generated set of random numbers. Randomization, sequence generation and preparation of group allocation materials will be carried out by an independent researcher who will be not involved in the trial. Pairs will be divided randomly into two groups with 1:1 experimental/standard care (waitlist) ratio. Participants allocated in the experimental group will immediately start AOT for a 3-weeks period, while those in the standard care group will continue with their usual care.

In both cases, AOT or standard care, participants and parents will be asked to take daily notes on a predefined diary of their daily activities, including therapies for their motor disability. In addition, to record the acceptability and feasibility of the training, participants and/or families allocated in the experimental group will fill in a multiple choice questionnaire (with box for notes) for ascertaining the perception about their experiences of using the Tele-UPCAT system.

All participants will be re-evaluated after the period of experimental training/standard care (T1) with standardized tests and questionnaires (see outcome measures). T1 will be the primary endpoint aimed at evaluating the short-term effects of AOT according to CONSORT Guidelines (see Figure 1). [37]

After this phase, participants previously allocated to the experimental group will continue standard care, while who's who started with standard care will then commence home based AOT. The participants of this SC group will be re-assessed at the end of training (T1 plus). Further assessment of all participants will be performed after 8 weeks (T2) and 24 weeks (T3) from the end of AOT training (T1 or T1 plus, for the experimental and waitlist group, respectively), to evaluate the medium and long term effects of AOT. All the assessments will be carried out at home by trained therapists.

In summary, assessments will be performed at:

- T0, baseline: the week before the period of AOT/Standard Care
- T1: at 1 week after period of AOT/Standard Care
- T1 plus: the week after period of AOT, for waitlist group
- T2: 8 weeks after end of AOT
- T3: 24 weeks after end of AOT.

The details of the study design are reported according to CONSORT guidelines [37] (Figure 1), SPIRIT (Standard Protocol Items: Recommendations for Intervention Trials) statement [38] and TIDier (Template for Intervention Description and Replication) Checklist [39, 40] (Supplement Material 1 and 2). The programme of enrolment, interventions and assessments designed according to SPIRIT guidelines are shown in Figure 2.

Blinding

All the clinical outcome measures (AHA, [24-26] Melbourne Assessment 2 MA-2 [27] and Box & Block Test [28]) will be videotaped by a therapist blind to group assignment. Videotapes will be randomized and scored by assessors blind to group allocation and order of assessments. During each assessment all the participants will wear two Actigraphs (wGT3X-BT, wActiSleep-BT), one for each wrist.

Two independent researchers (two child neurologists) without competing interests will comprise the data monitoring committee for this study. They will review all adverse events (deciding to stop the trial if necessary), subject participant retention in each study arm and compliance with study protocol at 12 weekly intervals. Participants will have a study number in a dedicated data file. The file with study participants numbers and personal data will be stored in a password protected file, accessible only by the principal investigator. In order to promote participant's retention, all the assessment will be completed at home. The clinical primary and secondary outcome measures will be completed within one week of when expected. Enrolled participants are ethically able to withdraw from the study at any time, and have been notified there usual follow-up and clinical care would not be impacted.

Study sample and recruitment

Enrolment and clinical trial management will be carried out by child neurologists and physiatrists at the Department of Developmental Neuroscience of IRCCS Fondazione Stella Maris (FSM, Pisa, Italy), with the collaboration of the Unit of Children Rehabilitation of S.Maria Nuova Hospital (Reggio Emilia, Italy).

Potential participants will be identified according to inclusion criteria (see below), from UCP patients of the clinical departments. Suitable participants and their parents will be invited to participate and will be enrolled in the RCT only after written consent has been obtained.

Inclusion criteria are participants with:

- confirmed diagnosis of spastic motor type UCP; [2, 41]
- aged between 5 and 20 years at time of recruitment;
- predominant UL spasticity;
- House functional classification system, (HFCS) score $\geq$ 2 that is, able to passively hold an object in the hand or better [35, 36]
- cognitive level within normal limits i.e. Intelligence Quotient $\geq$ 70, as assessed in the last year prior to recruitment on the WPPSI-III, [42] WISC-IV [43] or WAIS [44]
- participants and parents willing to commit to the intensive therapy program for a 3-week period.

Participants will be excluded in case of:

- previous orthopaedic surgery or Botulinum Toxin A (BoNT-A) injection in the UL within 6 months prior to study entry.

Sample size

Even if planned as an exploratory study, a sample size estimates, according to CONSORT guidelines, [37, 38] have been based on projected treatment effect on the primary outcome measure, AHA. Taking account of the study design and the stratification, a minimum sample size of 10 per group will be required in order to detect a 1.40 effect size (value based on our preliminary data) at

significant level of 0.05 and 80% power. [18, 19] Considering a 20% of possible drop-outs a minimum of 12 participants per group will be recruited, total sample of 24 participants.

Study treatment

The Tele-UPCAT system has been designed through the close collaboration between the rehabilitation staff (child neurologists and child therapists) of IRCCS Fondazione Stella Maris and biomedical engineers of BioRobotics Institute Scuola Superiore Sant'Anna. Taking into account the previous clinical experience on UPCAT, the main components of the Tele-UPCAT system (e.g. the size of the screen, the need of a guide for alternating the time of observation and of execution, the key words for catching the attention, etc), the AOT library of exercises (e.g. the adapation of the objects for enlarging the exercises to more impaired hands) and the experimental training (e.g. time and duration) have been defined. In general, the training will be structured in one session per day, to be executed 5 working days for 3 consecutive weeks (i.e. 15 sessions in total). The duration of daily sessions will be about 60 minutes per day for a total of 15 hours. The participants undergoing the AOT intervention through the Tele-UPCAT system will watch 3 minutes first-person video sequences of unimanual or bimanual goal-directed actions followed by their execution for 3 minutes. Each day 3 different actions will be proposed twice.

Tele-UPCAT system

Tele-UPCAT system (see Figure 3) has been designed and built and will be provided at home by the BioRobotics Institute of Scuola Superiore Sant'Anna (Pontedera, Italy).
It is a dedicated platform for delivering AOT designed to be user-friendly, by subjects at home in a playful setting with integrated smart features.

The platform has been designed and developed by integrating two different modules:

- The Observation Module (OM) for the presentation of AOT videos and recording of participant's attention and exercise execution. This consists of a computer with 23" desktop, a dedicated software and a video camera. The Observation Module has been obtained by integrating a large all-in-one personal computer (All-in-One touch HP EliteOne 800 G2 - L3N93AV), a large switch and a video camera (GoPro HERO Session), which will record a whole field, including subject's face and hands and table with objects. The Observation Module is important to determine whether the participant is looking at the monitor during observation phase and has an overall view of the execution of actions. A dedicated software, designed after a deep and specific literature analysis, was developed for guiding and motivating participants through the phases of AOT (observation followed by execution). In addition, the software was customized for the wide age range of participants providing an interactive game with an engaging story different for every day of training for school aged children, and a slide-show with a voice-over for adolescents and young people. The general architecture of the software is based on the following sequence: observation of a 3-minute video followed by execution of the same action for 3 minutes. Subsequently, the same video will be replayed and then executed a second time. As stated before, a 60-minute session, including rest intervals, of three different goal-directed actions of increasing complexity are observed and imitated twice every day. At the end of each day the software will terminate the session and automatically update it for the next day.
- The Motor Performance Module (MPM) for the execution of actions. This will be mainly composed of a kit of exactly the same common objects and toys shown in the videos and two Actigraphs (wGT3X-BT, wActiSleep-BT, for more details see http://actigraphcorp.com/support/activity-monitors/gt3x/) worn one for each wrist. With this

design it will be possible to measure the upper limb activity during the AOT training while the lack of sensorized toys embedded in the MPM will not allow to measure quantitative measures of hand activity (e.g. force or pressure) during the AOT training.

The first prototype of Tele-UPCAT system has been widely tested before the beginning of the RCT in order to test the stability and reliability of the system.

AOT library

On the basis of the previous AOT exercises, [18, 19] rehabilitation staff (child neurologist and child therapists) has created a library of rehabilitation packages composed of three different series of AOT exercises suitable to be executed at home. They differ for complexity of action and range of UL capabilities conceived in relation to HFCS levels (≤ 4, 5-6, 7-8). [35, 36] Each series is organized into customized sequences designed to cover unimanual and bimanual UL goal-directed actions with a variety of objects and toys commonly used in routine life. For each series, experimental training is composed of 15 sets (8 unimanual followed by 7 bimanual) of routine UL activities, to be completed in 3 weeks (5 days per week). Each set has a general common goal (e.g. drinking a glass of water) composed of three sequential tasks of increasing complexity (e.g. from picking up a bottle of water, to opening the cap, to pouring the water into a glass). As previously indicated, in order to grade the activities according to the range of capabilities, three series of sets have been planned. The actions of each series have the same goal but the material and type of movement (i.e., range of movement, type of grasp) is customized in order to guarantee feasibility of the proposed activity while maintaining the same overall objective (see Table 1 and Figure 4). Each action of the three series performed by an actor is videotaped so that the videos show only the hand and arm from the first perspective; each video is then edited to last 3 minutes. A right-handed actor uses one or two hands for unimanual and bimanual exercises respectively for participants with right UCP. For the left UCP the previous videos where reversed if they maintained the same characteristic of the setting and of the hand movement, while the remaining videos where specifically videotaped.

Table 1. List of goal-directed actions planned for the AOT training grouped in unimanual (white cells) and bimanual (grey cells) actions

Days	Action a	Action b	Action c
1	Uncover a little ball by lifting a box	Place a little ball in a glass	Fill a glass with water
2	Pick coloured card and match it to the same colour	Move a coloured card and place it on a base	Pick a card and place it on the similar one
3	Pick up a rubber stamp and move from/to different positions	Pick up a rubber stamp and press it against horizontal plane to print a figure	Pick up a rubber stamp and press it against sloping plane to print a figure
4	Pick up coin, put it in piggy bank through the slot on the top OR Pick up a magnet and place it on a horizontal magnetic board	Pick up coin, put it in piggy bank through the vertical slot on the side OR Pick up a magnet and place it on a sloping magnetic board	Pick up coin, put it in piggy bank through the horizontal slot on the side OR Pick up a magnet and place it on a vertical magnetic board
5	Pick up a wooden rubber stamp and move to	Pick up a wooden rubber stamp and press it against	Pick up a wooden rubber stamp and press it against

	different positions	horizontal plane to print a figure	sloping plane to print a figure
6	Move a spray can OR Move the bottle with a little ball inside	Place the spray can on a support OR Remove a little ball from the bottle	Put the spray can into a cup OR Press the catapult and launch a little ball
7	Move a container filled with shimmy powder	Open the container	Sprinkle shimmery powder on a paper
8	Place magnetic fish on a paper	Pick up fishing rod and catch magnetic fish	Pick up magnetic fish and place them in a container
9	Move a hole punch	Insert a sheet of paper and make holes	Match holes on sticks
10	Wet a cloth placing it in a container with water	Wring cloth and place it in a plate	Open a toy washing machine and insert the cloth inside
11	Pick up a card and place it on a support	Pick up a card and insert it in a clothespin	Pick up a card and insert it in a clothespin in a different orientation
12	Pick up and handle a piece of Play-Doh	Divide it in two pieces	Open a toy oven and insert a saucepan (with Play Doh in it)
13	Search for coin in the bag and place it on a support	Take the coin and insert it in a wallet	Open a box and place the wallet inside
14	Open a tube of tempera paint	Wet a brush with tempera paint	Make figure using a stencil with the brush dipped in tempera paint
15	Move a glitter glue tube	Open it	Decorate a frame by pasting pieces of mosaic

Experimental training

Before delivering the Tele-UPCAT platform, the training will be customized individually for each participant. The rehabilitation staff will select, on the basis of age and HFCS level, from the library the most appropriated AOT rehabilitation packages for each participant, then the engineers will upload them in the Observational Module (OM). For the Motor Performance Module (MPM), the therapists will organize a container of all the objects identifying them with numbers relative to the training day (e.g. little ball number 1 which means day 1 of the training). In addition, a dedicated printed manual with instructions and guidelines related to the different steps of the training and for system management and the setup will be provided. The manual contains also all the contacts of both technical and rehabilitation staff for remote assistance in case of any problems during the training. Two Actigraphs (wGT3X-BT, wActiSleep-BT) will be initialized for the recording period (3 weeks) to be worn on each wrist.

The ICT platform will be delivered to the participant's home by the engineers that are in charge of the installation of the system. The families will identify a designated position with a table or a desk of about 80x100 cm near to a socket where the ICT platform will be placed. Engineers and rehabilitation staff will train both parents and participants about the correct use of the system, including safety aspects. During the first two training days, a therapist will visit each participant and their parents to confirm the set-up.

During the training sessions, each participant will sit on a chair with both arms placed on a table in front of a platform positioned at about 1 m. Especially when the participant will be a child, a parent will be seated on her/his more impaired side to prompt attention during task execution and assist if necessary. The software will guide the participant in the sequence of observations and executions.

Standard care
Participants previously allocated in the standard care group will continue their usual care for 3 weeks. Usual care for recruited participants could be consisted for physical or occupational therapy. The frequency and the type of all therapies will be recorded accurately by a diary in both groups.

Outcome measures

Description of sample

Children participating in the study will be classified according to HFCS, which assesses function of the impaired hand in children with CP.[35, 36] This classification consists of 9 grades ranging from a hand that is not used at all (grade 0) to one that is used spontaneously and independently from the other one (grade 8). Due to the general approach in classifying hand functional level, this scale can also be easily applied to young adults with UCP. HFCS will be used for all ages as a criterion for inclusion in this study (from grade 2 to grade 8). In addition, they will be classified according to the Manual Ability Classification System (MACS), a classification system of the child's ability to handle objects in daily activities on one of five levels. [45]

Primary outcome measure

On the basis of our scientific hypothesis and according to previous clinical experience, [18, 19] the primary outcome measure will be the AHA. The latest version 5.0 will be used. This assessment measures UL function during bimanual activities by evaluating spontaneous use of assisting hand during a semi-structured age-appropriated 10-15-minute session with specific toys or objects requiring bimanual handling. The school-kids form will be used for the assessment of UCP children 6-12 years old [24, 25] while the Adolescent version (Ad-AHA), using the board game "Go with the Floe", [26] will be completed with participants older than 13 years. This last version, even if validated up to 18 years, will be used with potential participants 18-20 years old to guarantee the same assessment across all participants regardless of age. Moreover, AHA has been already used, even if not validated, in young people with UCP [46, 47]. The scale uses a Rasch measurement model which is a method to convert raw scores into a linear measure located on a unidimensional scale and more specifically to convert them into 0 to 100 logit-based AHA units, that will be used for the statistical analyses. All AHA assessments will be videotaped in a standardised manner and the subsequent scoring will be carried out by a certified expert rater who will be masked to group allocation and assessment order [24-26].

Other outcome measures
Other secondary measures will include measures of unimanual capacity (MA-2, [27] and BBT [28]) and bimanual daily activities at home and in the community (ABILHAND-Kids). [29] Moreover, participation and quality of life will also be assessed. All assessment will be performed at T0, T1, T1 plus, T2 and T3 unless otherwise indicated. Questionnaires will be completed by parents and/or participants at home and if doubts will occur, child neurologists or therapists will be available to discuss face to face items not clear to them.

i. The Melbourne Assessment 2 (MA2) [27] measures unilateral UL function and it is a valid and reliable tool for evaluating quality of UL movement in children with neurological

conditions for ages between 2.5 and 15 years. MA2 is a criterion-referenced test that extends and refines the scale properties of the original Melbourne Assessment (MUUL) and like MUUL it can also be used for adolescents and young adults. MA2 measures four elements of UL movement quality: movement range, accuracy, dexterity and fluency. It comprises 14 test items of reaching, grasping, releasing and manipulating simple objects. The test is administered by video recording the child's performance for subsequent scoring (30 items score). A raw score is provided for each of the four sections (Movement Range, Accuracy, Dexterity and Fluency) that will be analysed separately. It predominantly includes concepts within the body function domain as well as in the activity domain. Even if the MUUL and also the MA-2 have been validated up to 15 years, the first one has been used in studies involving patients with CP older than 15 year and in adults. [46-47] We have chosen to use the MA-2 also for participants older than 15 years to guarantee the same assessment across all participants regardless of age instead of using other scales (e.g. the Fugl-Meyer Assessment or the Action Research Arm test). [48]

ii. Box and Block Test (BBT) is a quick (2-5 minutes), simple and inexpensive test which measures unimanual dexterity in the activity domain. BBT is composed of a test box with a partition in the middle and 150 wooden blocks (25mm). The patient had to transport as many blocks as possible in 1 minute from one compartment to another. Firstly, the patient is asked to perform the test with the unaffected hand and then with the affected hand. The number of blocks transported by affected hand in 1 minute will be counted and considered for the main analyses. It can be used for a wide range of populations from childhood to adulthood. [28]

iii. ABILHAND-Kids [29] is a semi-structured item-response questionnaire on a 3-point ordinal scale (impossible, difficult, easy) that measures daily manual activities referred to in the activity domain of ICF. Parents will be instructed to rate their child's perceived difficulty in performing each activity taking account the performance of their child when performing the activity without technical or human assistance, regardless of the limb(s) and the strategies used. It has been validate for children aged 6-15 years but it has been used for larger ranges (6-19 years). [49] The questionnaire has been developed using the Rasch measurement model which provides a method to convert the ordinal raw scores into a linear logit measures located on a unidimensional scale, that will be used for the analyses. This questionnaire will be used at all assessment periods.

iv. Participation and Environment Measure - Children and Youth (PEM-CY). [30, 31] It is a parent-reported instrument that evaluates participation and environment across home (ten items), school (five items) and community (ten items) settings. For each item, the parent is asked to identify how frequently (over the past four months) the child has participated (eight options: daily to never); how involved the child typically is while participating (five point scale: very involved to minimally involved); and whether the parent would like to see the child's participation in this type of activity change (no or yes, with five options for the type of change desired). For each setting, the parent is then asked to report on whether certain features of the environment make it easier or harder for the child to participate. The following summary scores will be obtained: total score and score for each of the three setting-specific environmental supportiveness (home, school, community). Moreover the total number of supports and the total number of barriers will be computed. This questionnaire will be used at T0 and T3.

v. Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years) evaluate quality of life in children and adolescents with CP. [32-34] A score on a 0-100 scale will be obtained for each of computed sub-domains. In particular the Children form filled in by the parents assesses 7 subdomains (Social well-being and acceptance, Feelings about functioning, Participation and physical health, Emotional well-being and self-esteem, Access to services, Pain and impact of disability and Family health) and five subdomains

(excluding Access to services and Family health to the previous) for the children version. The Teen form evaluates 7 subdomains (General well-being and participation, Communication and physical health, School well-being, Social well-being, Access to services, Family health and Feeling about functioning) for the form filled in by the parents and 5 (excluding Access to services and Family health to the previous) for those filled in by the caregivers. These questionnaires will be used at T0 and T3.

vi. Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks, is a new assessment tool that consists of observation, followed by execution of three tasks of increasing difficulty (unimanual lifting, bimanual placing near and bimanual cooperation, holding and pulling) by means of a sensorized object. New technological tools such as sensorized objects can help in assessing the manipulation capabilities (reaching and grasping) in a quantitative but ecological way and the sensitivity to a training. Previous studies of the authors were focused on the development of sensozied toys for measuring infant's manipulation [50-52]. Starting from this experience, a new sensorized object has been designed and developed by the engineers tuning the sensors sensitivity and working range to the needs of participants with UCP.
Two load-cells and a switch embedded in the sensorized object allow for the measurement of the following parameters: grasping time, maximum grasping force and delay time between unaffected and affected hand in reaching for the object. This set-up is out of Tele-UPCAT system even if it was designed and developed in parallel.

vii. Quantitative measurement of bimanual activities will be performed in all the participants enrolled in the study by means of Actigraph GXT3+, as components of Motor Performance Module of Tele-UPCAT system. Actigraphs wGT3X-BT and wActiSleep-BT, equipped with a Velcro strap bracelet, will be worn, one for each wrists. As general rule, the experimental group have to wear the actigraphs not only during the training sessions but also between T0 and T1 and between T1 and T2 (total 6 weeks, 24 hours per day or as much as possible) while the control group are requested to wear them between T0 and T1, between T1 and T1 plus and, if possible also between T1 plus and T2 (total 9 weeks, 24 hours per day or as much as possible). All the daily activities, experimental training or usual care, or removal will be recorded in a dedicated diary. The Actigraphs will also be worn, by all the participants, during each time point of clinical assessments with the outcome measures. Data will be mainly relative to the asymmetry index (AI), that is the difference between the mean activity of the dominant with those of the non dominant hand and it will be correlated with the clinical scores obtained in the clinical outcome measures (mainly AHA).

viii. Cost effectiveness: A within trial cost-utility analysis will be conducted to synthesise the costs and benefits of the training program. Resource use (staff time, equipment and facility use) associated with the program will be collected alongside the RCT. Health care utilisation will be collected using a resource use questionnaire previously used in CP studies. [53] Health utility will be derived from the adapted CHU-9D, [54] a quality of life measure designed specifically for economic evaluation and which has been validated in an Australian population. [55-57]

ix. A semi-guided face to face interview about the acceptability of the training will be completed immediately after the training period (T1 or T1 plus). It will be performed by the rehabilitation staff with the aim of investigating participant's and parents' opinions about the training in terms of customization of exercises, suitability to UCP children, feasibility at home, required effort by the participants and acceptability of Actigraphs, suitability of the manual and of the software will be recorded.

Statistical analyses

Clinical data will be analysed by means of the Statistical Package for Social Sciences (SPSS). Means and standard deviation of clinical outcome scores for both groups will be calculated to identify potential baseline differences between groups. As a first step, normality of distributions will be verified by Shapiro-Wilk's test. Between-group differences for all selected outcome measures will be evaluated at T0, by means of t-test for unrelated samples or non-parametric Mann–Whitney U independent sample test, for normal or non-normal distributed data, respectively. To test our first hypothesis, an intention to treat analysis will be carried out, evaluating between-group differences (delta scores) for primary and secondary outcome measures at the primary endpoint (T1), compared with T0 (T1-T0), by means of parametric or non-parametric tests for unrelated samples. The age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver, acceptability of therapy (measured by semi structured interview) will be analysed for further secondary exploratory analyses in order to determine if some of these variables are predictive of better responses to the Tele-UPCAT training. In addition, a matched-pairs test (t-tests or Wilcoxon) will be carried out in order to assess retention of effects at follow-up periods (T1 or T1 plus, T2 and T3) relative to assessment before AOT training (T0 or T1 for experimental or waitlist group respectively). Bonferroni corrections will not be carried out in relation to the exploratory nature of the current RCT study and the relative small number of the study sample. To detect if significant changes will correlate to HFCS levels, a correlation analysis between score changes after AOT training (T1 or T1 plus) and assessment before AOT training (T0 or T1) will be carried out. Finally, an exploratory within-group analysis will be performed for the waitlist group comparing changes during AOT with respect to those of the first standard care period.

ETHICS AND DISSEMINATION

This study protocol describes background, hypotheses, system, clinical and technological outcome measures for a RCT designed to evaluate the Tele-UPCAT system as a new approach to deliver AOT to children and young people with UCP at home.
Full ethical approval has been obtained from the Tuscany Paediatric Ethics Committee (169/2016, Protocol Version 5.0 of 10/11/2016) and any deviations from the protocol will be promptly notified to this Ethic Committee and applied only after its approval. The trial has been registered at http://www.clinicaltrials.gov (identifier NCT03094455). This study protocol is reported according to the SPIRIT statement (SPIRIT 2013) [38] and the TIDier guidelines [39, 40]. We anticipate that the results of this study will be disseminated through peer reviewed journals and national and international academic conferences only by the professionals directly involved in the clinical trial. The results of this study will be of interest for rehabilitation trials based on AOT paradigm. Referring to a previous RCT study, [18, 19] we suggest that the home setting might increase accessibility of rehabilitation to a large number of children and young people with UCP (e.g. participants that live far from the clinical centres) with a large range of hand impairments (including also participants with HFCS level lower than 6) and older age (5-20 years instead of 5-15). Moreover, if the Tele-UPCAT study, using a very simple ICT solution, demonstrates to be viable for delivering AOT at home with significant improvements in UL daily activities, it could lead to the application of new solution for cost efficient rehabilitation programs. Implementation of new smart technologies can i) provide user-friendly AOT programs at home; ii) remotely manage treatment by rehabilitation staff thus increasing the ratio 'number of patients per therapist'; iii) offer individualized and intensive training. It could become an economical and efficient rehabilitation program by achieving significant long-lasting effects in UL activity and participation through an easily implementable paradigm that could become an integral part of common clinical practice. Finally, this approach could become a rehabilitation tool and be applicable to broader populations of CP and other chronic disabilities.

PROJECT STATUS

This project began recruitment the 29 March 2017, and we expect to complete data collection for the last training the November 2017 and close the project in the April 2018.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

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AUTHOR'S CONTRIBUTION

GS is the principal investigator of the project and mainly responsible of the clinical part of it while FC is the main responsible of the ICT platform. GS, EI, HF, KK, RB, AF and GC designed the research study. GS, EB, EI, SP and EB were responsible for the AOT library. GS, SP and ES were in charge for participants' recruitment in Pisa and identification of type of exercise and software and AF for Reggio Emilia. GS and EB will collect the data and will monitor the training. FC, IM, MM and FFP with the supervision of PD have designed and built the new platform. GS and GC will take the lead roles on preparation of publications on the clinical outcomes of the study.
All authors have read and approved the final manuscript.

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Figure 1. Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: -Participation and Environment Measure - Children and Youth

Figure 2. Schedule of enrolment, interventions, and assessments.

Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected in the Clinical Interface (2) by the clinical staff in relation to HFCS level (6-8, 4-5 or 2-3), Side of impaired hand and Type of interface. A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3) for Teenagers or little Boys and Girls. The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists and a Button. The integrated camera records subject's attention during the observation task and exercise execution.

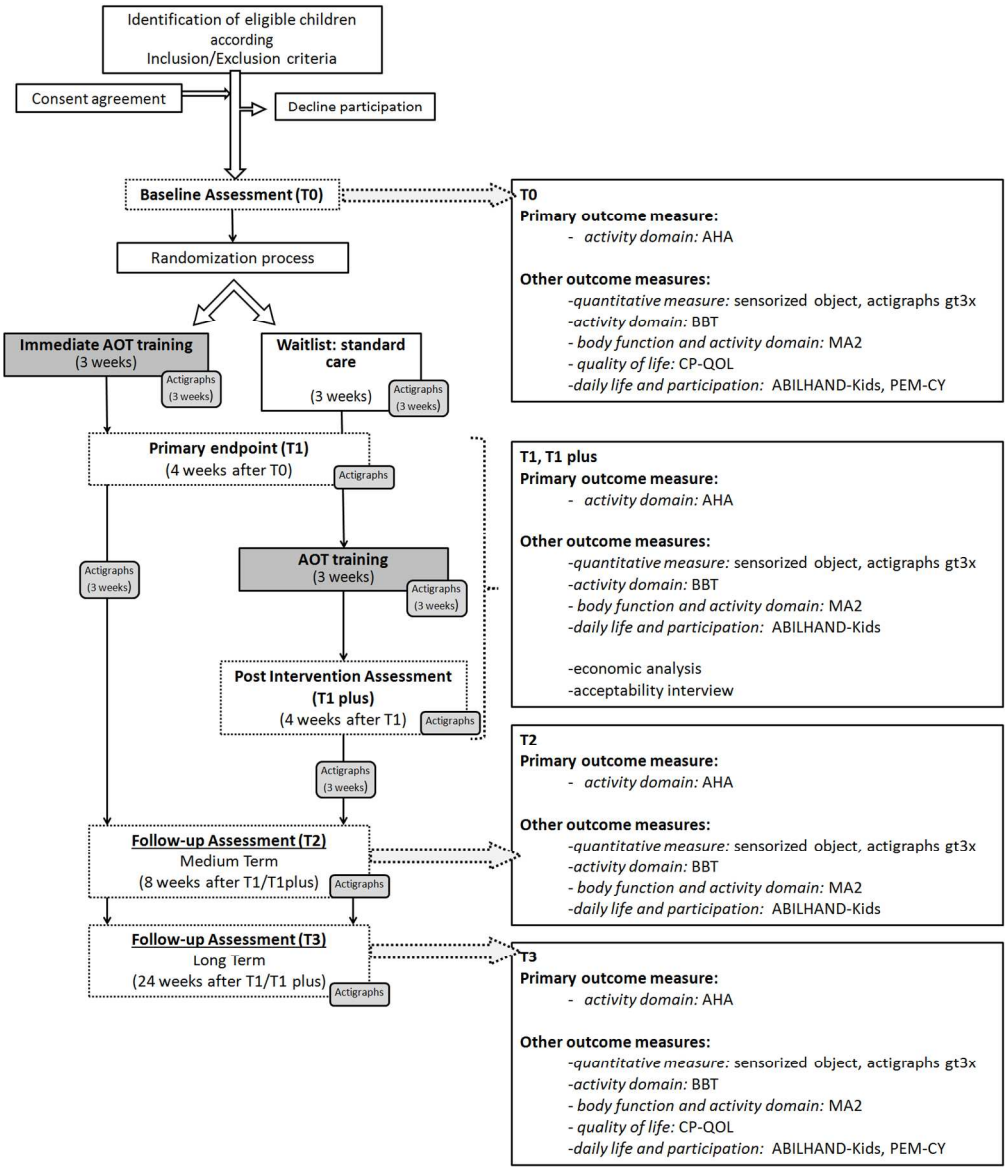
Figure 4. a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. **b)** Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

Supplement material 1. SPIRIT and TIDier checklists

Supplement material 2. Written informed consents (in Italian language)

Supplement material 3. Written informed consents (in English language)

Supplement material 4. Tele-UPCAT acceptability interview



Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: - Participation and Environment Measure - Children and Youth

141x163mm (300 x 300 DPI)

	STUDY PERIOD				
	Enrollment	Post-allocation			
TIMEPOINT**	*T0*	*T_1*	*T_1 plus**	*T_2*	*T3*
ENROLLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation	X				
INTERVENTIONS:					
AOT intervention					
Wait list control group	←	→			
ASSESSMENTS:	←	→	←	→	
AHA	X	X	X	X	X
MA 2	X	X	X	X	X
BBT	X	X	X	X	X
ABILHAND-Kids	X	X	X	X	X
CP QoL	X				X
Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks	X	X	X	X	X
Quantitative measurement of bimanual upper limb activities by means of Actigraph GXT3+	X	X	X	X	X
Economic analysis		X	X		
Acceptability interview		X	X		

* only for wait-list group

Schedule of enrolment, interventions, and assessments

60x88mm (300 x 300 DPI)

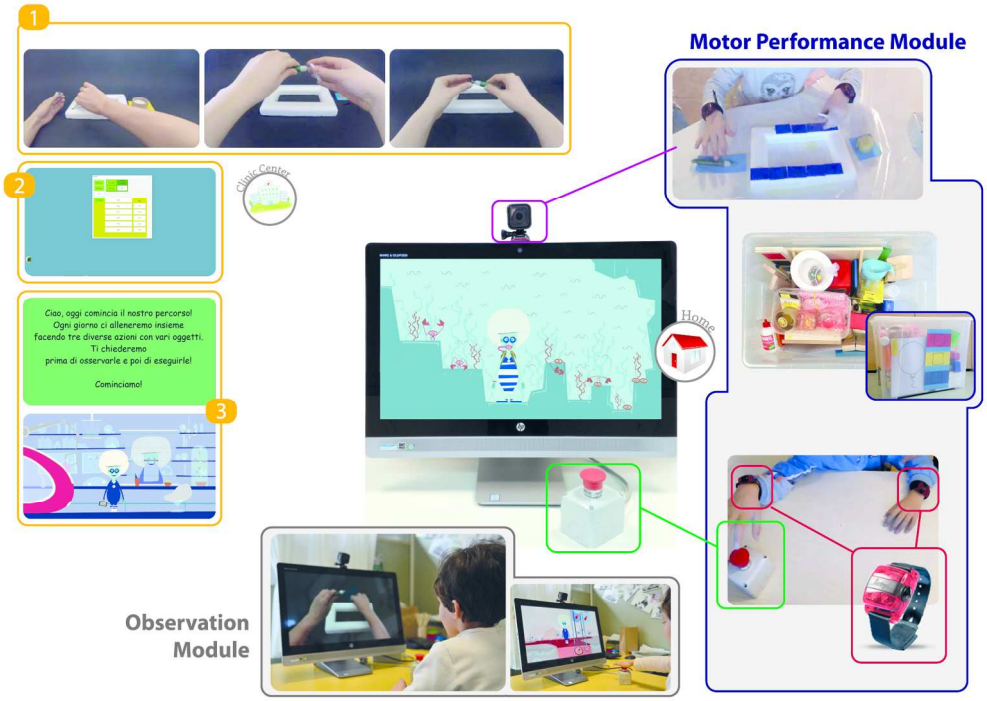
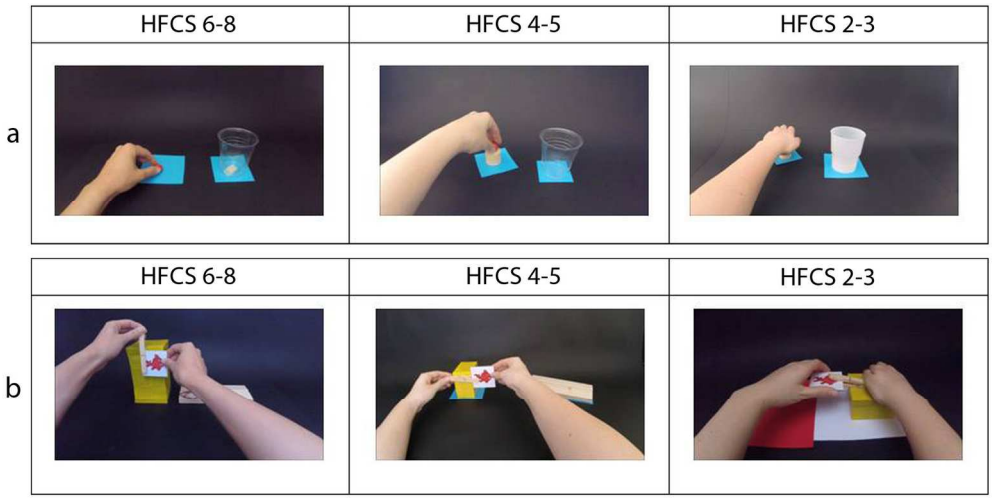


Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected in the Clinical Interface (2) by the clinical staff in relation to HFCS level (6-8, 4-5 or 2-3), Side of impaired hand and Type of interface. A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3) for Teenagers or little Boys and Girls. The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists and a Button. The integrated camera records subject's attention during the observation task and exercise execution.

170x120mm (300 x 300 DPI)



a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. b) Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal

170x83mm (300 x 300 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,13
	2b	All items from the World Health Organization Trial Registration Data Set	2,13
Protocol version	3	Date and version identifier	13
Funding	4	Sources and types of financial, material, and other support	2,13
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,13
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3,4
	6b	Explanation for choice of comparators	3,4
Objectives	7	Specific objectives or hypotheses	3,4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4,5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8,9
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	4
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5,6
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5,6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	4
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4,5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	5, 9-11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	5

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	5
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11, 12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11, 12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11, 12
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	5
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	5
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	5
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	12

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	5
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	5
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	12
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary material (2 and 3)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

TIDieR
Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	Page 2	_____
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	Pages 3-4	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	Pages 6-9	_____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	Pages 3-5	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	Pages 5-8	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	Pages 5, 8	_____
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	Page 8	_____

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	Page 6	_____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	Pages 6-8	_____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	_____N/A____	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____N/A____	_____
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	____N/A_____	_____

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

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MODULO INFORMATIVO
PER GENITORI/TUTORE LEGALE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentili Genitori/Tutore,
Le informazioni contenute nella scheda informativa seguente sono dettagliate e potrebbero risultare molto complesse.

Le chiediamo di accettare la partecipazione allo studio solo dopo avere letto con attenzione questo foglio informativo ed avere avuto un colloquio esauriente con il medico sperimentatore che le dovrà dedicare il tempo necessario per comprendere completamente ciò che le viene proposto.

Vostro/a figlio/a potrebbe essere idoneo a partecipare ad uno studio promosso dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni importanti riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non vi risultasse chiaro, potrete porre domande ai medici sperimentatori coinvolti dello studio. Prendetevi tutto il tempo necessario. La partecipazione di vostro/a figlio/a è volontaria e potrete ritirarla in qualsiasi momento.
Una volta che avrete letto questo modulo, avrete ricevuto risposta alle eventuali domande, e qualora decideste di far prendere parte vostro/a figlio/a allo studio, vi sarà chiesto di firmare un modulo di consenso, di cui riceverete una copia cartacea.

Cosa si propone lo studio

Vostro/a figlio/a è stato/a invitato/a a partecipare a questo studio per valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 bambini/adulti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei bambini che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 4 settimane; a termine delle quali i bambini di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i bambini saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T2). Per dettagli vedi Disegno dello studio Figura 1.

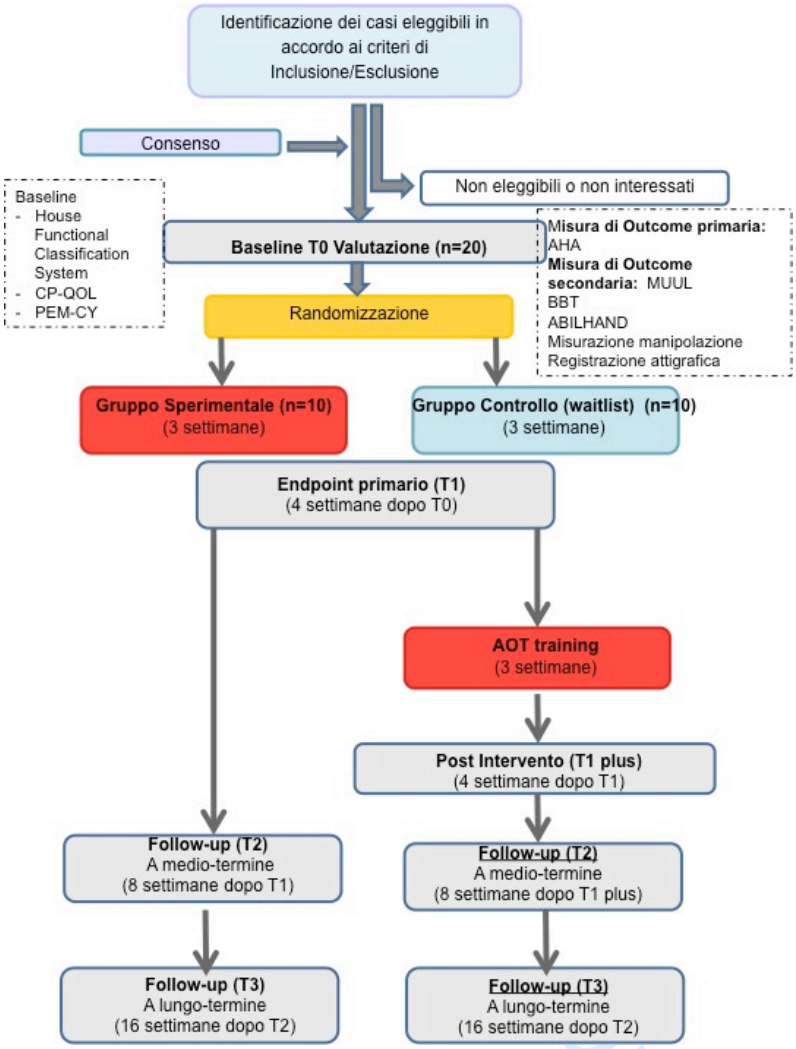


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i bambini arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolari di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I bambini che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i bambini allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la partecipazione allo studio

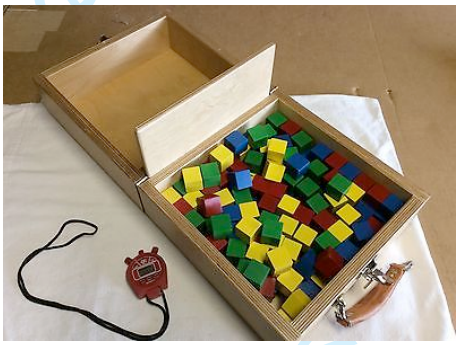
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



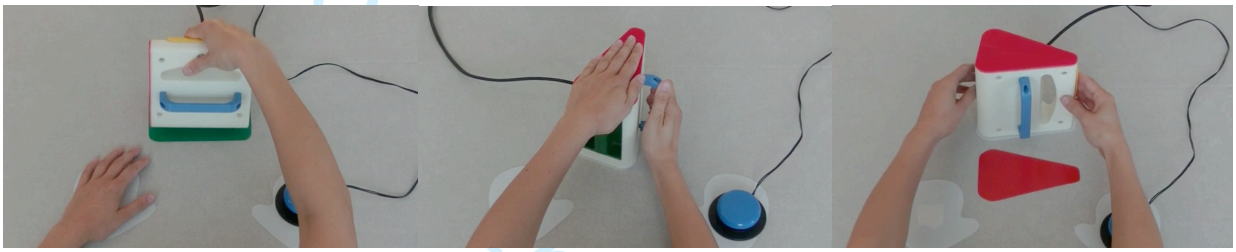
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND-Kids* è un breve questionario, validato in bambini con paralisi cerebrale infantile dai 6 ai 15 anni che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da un genitore in base alla difficoltà che ha il bambino a compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita nei bambini ed adolescenti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se doveste decidere di non prendere parte allo studio, o in caso doveste cambiare idea in seguito, vostro/a figlio/a non subirà alcuna penalità o perdita di benefici ai quali avrebbe altrimenti diritto. Le sue cure mediche attuali e future presso l'IRCCS

Fondazione Stella Maris non saranno compromesse dalla vostra decisione ed i medici continueranno a seguirlo/a con la dovuta attenzione.
Potrete ritirare l'adesione di vostro/a figlio/a allo studio in un qualsiasi momento dandone comunicazione al medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Procedure previste alla fine dello studio
Non è prevista alcuna procedura da attuarsi alla fine dello studio.

Informazione del medico di medicina generale /pediatra di libera scelta
Per la migliore tutela della salute di vostro/a figlio/a, vi verrà chiesto di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accettate di far partecipare vostro/a figlio/a.

Informazioni sui risultati dello studio
Qualora foste interessati, potrete chiedere al medico di comunicarvi i risultati generali dello studio ed in particolare quelli che riguardano vostro/a figlio/a.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i dati personali di Suo Figlio/a, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento

I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La partecipazione di Suo figlio/a allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione nella persona della Dr.ssa Giuseppina Sgandurra *, IRCCS Fondazione Stella Maris, Viale del Tirreno 331*. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la partecipazione di Suo figlio/a allo studio. In tal caso, i campioni biologici a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che riguardano Suo figlio/a, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi aggiuntivi a vostro carico derivanti dalla partecipazione allo studio. Non riceverete alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che vi è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data……..

Potrete segnalare qualsiasi fatto riteniate opportuno evidenziare, relativamente alla ricerca che riguarda vostro/a figlio/a, al Comitato Etico e/o alla Direzione sanitaria di questa struttura ospedaliera.

Per ulteriori informazioni e comunicazioni durante lo studio sarà a disposizione il seguente personale:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____

_____

Nome per esteso del medico che ha consegnato l'informativa | Data | Ora | Firma

CONSENSO INFORMATO PER GENITORI/TUTORE LEGALE

Versione 5.0 del 10/11/2016

Titolo Protocollo

Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Stella Maris, Prof. Giovanni Cioni IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 341/ ABC; 56128 Calambrone (Pisa), Italia Tel 050/886233.

e-mail: g.sgandurra@fsm.unipi.it

Io sottoscritta (madre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

Io sottoscritto (padre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

del minore _____ nato il ___/___/_____
residente a _____via/piazza _____

dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, della quale mi è stata consegnata una copia in data _____ alle ore _____ (indicare data e ora della consegna).

Dichiaro che mi sono stati chiaramente spiegati la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico.

DICHIARO inoltre che:

1. ho letto e compreso il foglio informativo fornito riguardo il progetto di ricerca e facente parte di questo consenso;
2. mi è stata data l'opportunità di porre qualsivoglia domanda allo sperimentatore dello studio e ho avuto risposte soddisfacenti;
3. mi è stato concesso il tempo sufficiente per riflettere sulle informazioni ricevute e per discuterne con terzi;
4. sono stato/a informato/a che il protocollo dello studio e tutti i moduli utilizzati hanno avuto il parere favorevole del Comitato Etico Pediatrico;
5. mi è stato chiaramente spiegato che posso decidere che il/la minore non prenda parte allo studio o ne esca in qualsiasi momento, senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
6. sono consapevole che la ricerca potrà essere interrotta in ogni momento, per decisione del responsabile della ricerca, senza pregiudizio per la salute del/della minore;
7. sono stato informato/a che sarò messo al corrente di qualsiasi nuovo dato che possa compromettere la sicurezza della ricerca e che, per ogni problema o per ulteriori domande, potrò rivolgermi ai medici presso i quali il/la minore è in cura;
8. per la migliore tutela della salute del/la minore, sono consapevole dell'importanza (e della mia responsabilità) di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accetto di far partecipare il/la minore; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici;

9. sono stato informato/a che i risultati dello studio saranno resi noti alla comunità scientifica, tutelando l'identità del minore secondo la normativa vigente sulla privacy.

10. sono consapevole che devo/dobbiamo ricevere una copia del presente modulo di consenso.

Sottoscrivendo questo modulo acconsento al trattamento dei dati personali di mio figlio/a e al loro trasferimento al di fuori dell'Unione europea (*da inserire se effettuato specificando gli estremi identificativi dei destinatari*) per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di:

□ **volere** □ **NON volere**
che il minore partecipi alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informati sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
informare il pediatra di libera scelta/medico di medicina generale della partecipazione allo studio (*è preferibile il suo coinvolgimento*)

_____ ___/___/_____ _____ _____
Nome per esteso del minore Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso Data Ora Firma
del genitore/tutore legale

_____ ___/___/_____ _____ _____
Nome per esteso Data Ora Firma
del genitore/tutore legal

Io sottoscritto Prof./Dr. …… (Cognome) …….. (Nome)

Dichiaro che i genitori/tutori legali del Paziente hanno firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle possibili alternative;
- aver verificato che i genitori/tutore legale abbiano sufficientemente compreso le informazioni fornitegli
- aver lasciato ai genitori/tutore legale il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato | Data | Ora | Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle "Modulo informativo per i genitori/tutore legale" dovrà essere consegnata ai genitori/tutori legali del Paziente

FONDAZIONE
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ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

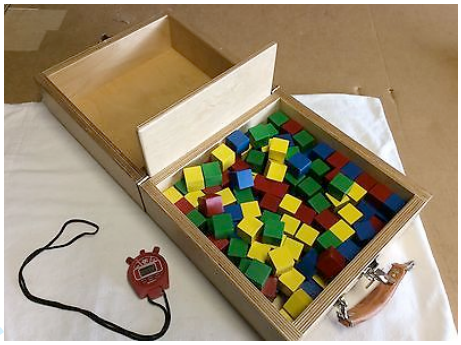
Perché facciamo questo studio?
La ricerca medica vuole migliorare la conoscenza sulle malattie.
Ti chiediamo di aiutarci a capire se l'uso di una terapia basata sull' osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato un' azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

Chi partecipa con me?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Che succede se partecipo?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo casuale ad uno dei due gruppi previsti nella prima fase dello studio: sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Inoltre ti saranno proposti, a dei tempi prestabiliti (quando ti arruoliamo, dopo che hai finito il trattamento o la fase di controllo, dopo che hai finito il trattamento se l'hai iniziato dopo, dopo 8 e dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!

Quanto durerà lo studio?
Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento). Ti verrà inoltre chiesto di effettuare i giochi e di compilare i questionari 3 o 4 volte.


Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?
Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?
Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio
Sei completamente libero di aderire o meno allo studio. Se deciderai di non partecipare, continuerai ad essere seguito periodicamente dalla tua equipe di riferimento del nostro centro clinico così come fatto fino ad ora.

Devo fornire il mio consenso per partecipare allo studio?
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare questo modulo di cui ti sarà data una copia.
Se decidi di non partecipare allo studio, o in caso dovessi cambiare idea in seguito, non succederà niente, continuerai a ricevere le cure a te necessarie presso questo ospedale.

E se dovessi avere delle domande?

Se hai delle domande puoi farle alla Dr.ssa Giuseppina Sgandurra durante il colloquio e potrai anche chiamarla al telefono al numero 050/886239: ti ascolterà e ti spiegherà tutto quello che desideri.

Data _____ ora _____ di consegna

_____Firma del medico che ha consegnato l'informativa

DICHIARAZIONE DI ASSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 6.0 del 29/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Il modulo informativo mi è stato consegnato il (data) _____ alle ore _____
Ho capito tutto quello che il medico mi ha spiegato.
Il Dottore ha ascoltato tutte le mie domande ed ha saputo rispondermi.
Se in futuro avrò bisogno di qualcos'altro i medici dello studio saranno a mia disposizione.

_____
Data e ora

_____
Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____
Firma del paziente. Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____ _____
Data/ora Firma del medico che ha informato il paziente

FONDAZIONE
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ISO 9001 BUREAU VERITAS Certification

MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 17 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Caro/a ……,
potresti essere idoneo a partecipare ad uno studio proposto dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non ti risultasse chiaro, puoi porre domande ai medici dello studio. Prenditi tutto il tempo necessario. Non sei obbligato a partecipare. Se accetti, potrai decidere di ritirare la tua partecipazione in qualsiasi momento.
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue eventuali domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare il modulo di cui ti sarà data una copia.

Quale è lo scopo di questo studio?
Sei stato/a invitato/a a partecipare a questo studio perché pensiamo che puoi aiutarci a capire se l'uso di una terapia basata sulla osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato una azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

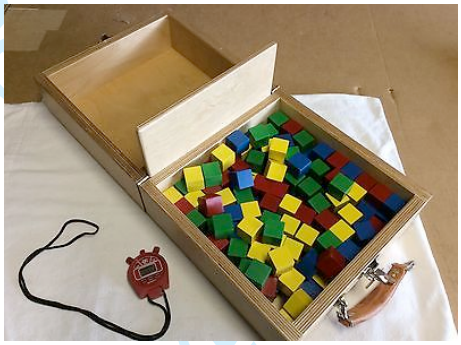
Quante persone parteciperanno?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Cosa comporta la partecipazione allo studio?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo random (casuale) ad uno dei due gruppi previsti nella prima fase dello studio:

sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre (durata 3 settimane) se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento).

Inoltre ti saranno proposti, a dei tempi prestabiliti (T0: quando ti arruoliamo, T1: dopo che hai finito il trattamento o la fase di controllo, T1 plus: dopo che hai finito il trattamento se l'hai iniziato dopo, T2: dopo 8 e T3: dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!



Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?

Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?

Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio o di ritirarmi dallo studio?

La tua partecipazione allo studio è volontaria.

Se decidi di non partecipare, o in caso dovessi cambiare idea in seguito, non subirai alcuna penalità o perdita di benefici ai quali avresti altrimenti diritto. Le tue cure mediche attuali e future presso l'IRCCS Fondazione Stella Maris non saranno compromesse dalla tua decisione ed i medici continueranno a seguirti con la dovuta attenzione.

Puoi ritirare la tua adesione allo studio in qualsiasi momento, comunicandolo al medico dello studio, la dottoressa *Giuseppina Sgandurra* senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che ti riguardano e potrai chiedere la cancellazione di quelli già raccolti. La tua partecipazione allo studio potrà essere interrotta se il medico valuterà che il nuovo trattamento non ha portato alcun giovamento o se si verificheranno effetti indesiderati. In questi

casi sarai tempestivamente informato dal medico e potrai discutere con lui circa ulteriori trattamenti validi per la tua patologia.

Cosa accadrà alle informazioni che sono state raccolte per lo studio?
Le informazioni mediche che ti riguardano come ad esempio l'età, il sesso, le caratteristiche della tua malattia, i risultati delle prove e il diario delle attività quotidiane saranno conservate presso un archivio della Fondazione Stella Maris.
I tuoi dati saranno archiviati in forma anonimizzata, il tuo nome sarà sostituito da un codice conosciuto solo da poche persone e quindi i tuoi dati saranno anonimi. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al tuo nominativo.
I dati dello studio potranno essere mostrati in occasione di convegni/congressi o pubblicati in riviste scientifiche per informare gli altri medici e i professionisti del settore sanitario.

Informazioni sui risultati dello studio
Alla fine dello studio sarai informato sui risultati della ricerca.

Ulteriori informazioni
Non sono previsti costi aggiuntivi a tuo carico derivanti dalla partecipazione allo studio.
Non riceverai alcun compenso economico per la partecipazione allo studio.
Il protocollo dello studio che ti è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data 22/11/2016.

Per ulteriori informazioni e comunicazioni potrai contattare il personale dello studio che sarà a tua disposizione:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha consegnato l'informativa — Data — Ora — Firma

MODULO DI CONSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 18 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Io sottoscritto (nome e cognome) _____
dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione allo studio in oggetto, secondo quanto riportato nel modulo informativo allegato, della quale mi è stata consegnata una copia in data _____ alle ore _____

Dichiaro che mi sono stati chiaramente spiegati la natura, lo scopo, i benefici attesi, i rischi e gli inconvenienti possibili dello studio clinico.

Dichiaro di aver potuto fare tutte le domande che ho ritenuto necessarie e di aver ricevuto risposte soddisfacenti, come pure di aver avuto la possibilità di informarmi in merito ai particolari dello studio con persona di mia fiducia.

Accetto dunque liberamente di partecipare alla ricerca, avendo compreso completamente il significato della richiesta e i rischi e benefici che possono derivare da questa partecipazione.

Acconsento al trattamento dei miei dati personali *e al loro trasferimento al di fuori dell'Unione europea (se applicabile)* per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

□ Desidero che mi siano comunicati i risultati dello studio.

__/__/____ _____ _____
Data Ora Firma del paziente

__/__/____ _____ _____
Data Ora Firma del medico che ha informato il paziente e registrato il suo consenso

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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Tel. 050 886661-0571 43289

CENTRO DIURNO DI
RIABILITAZIONE PSICHIATRICA
La Scala di San Miniato (PI)
Tel. 0571 419868

Gentile Sig.ra/Sig.re, le informazioni contenute nel seguente foglio informativo sono dettagliate e potrebbero risultare
MOLTO COMPLESSE

Le chiediamo di accettare la partecipazione allo studio SOLO dopo avere letto con attenzione questo foglio informativo ed avere avuto un COLLOQUIO ESAURIENTE con il medico sperimentatore che le dovrà dedicare il TEMPO NECESSARIO
per comprendere completamente ciò che le viene proposto

INFORMAZIONI SCRITTE
PER IL PAZIENTE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentile Signora / Egregio Signore,
Le è stato chiesto di partecipare ad uno studio clinico sperimentale e questo documento ha lo scopo di informarLa sulla natura dello studio, sul fine che esso si propone, su ciò che comporterà per Lei una tale partecipazione, sui suoi diritti e le sue responsabilità.
La prego di leggere attentamente queste informazioni scritte prima di prendere una decisione in merito ad una eventuale Sua partecipazione allo studio. Lei avrà a disposizione tutto il tempo necessario per decidere se partecipare o meno.
Potrà, inoltre, porre liberamente qualsiasi domanda di chiarimento e riproporre ogni quesito che non abbia ricevuto una risposta chiara ed esauriente.
Nel caso in cui, dopo aver letto e compreso tutte le informazioni ivi fornite, decidesse di voler partecipare allo studio clinico, Le chiederò di voler firmare e personalmente datare il modulo di Consenso Informato allegato a questo documento.

Che cosa si propone lo studio

Valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 soggetti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei soggetti che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 3 settimane a termine delle quali i soggetti di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i soggetti saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T3). Per dettagli vedi Disegno dello studio Figura 1.

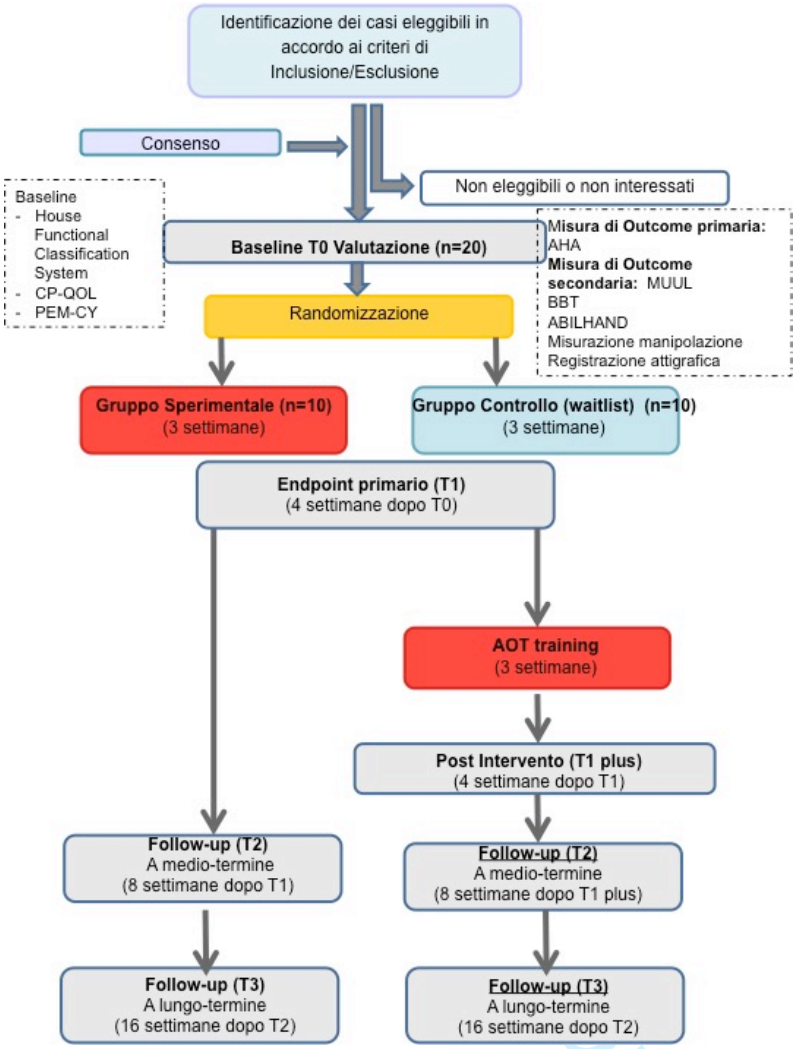


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i soggetti arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolati di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I soggetti che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i soggetti allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la Sua partecipazione allo studio

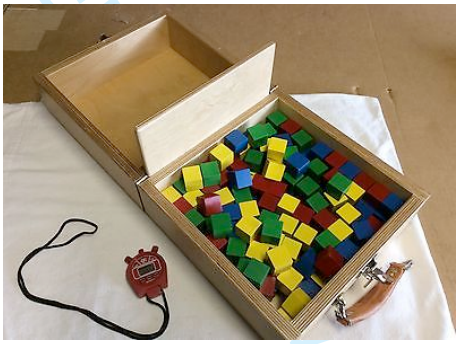
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



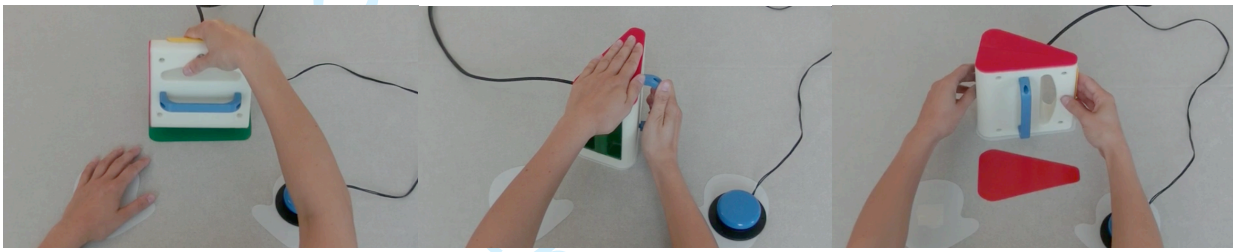
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni, ma utilizzati anche per l'età adulta. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND* è un breve questionario, validato in soggetti con paralisi cerebrale infantile che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da soggetto stesso in base alla difficoltà che esperimenta nel compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita in soggetti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se decide di partecipare, avrà il diritto di ritirarsi dallo studio in qualsiasi momento e senza l'obbligo di fornire spiegazioni, dandone tuttavia comunicazione al medico responsabile dello studio, la Dr.ssa Giuseppina Sgandurra.
Potrà ritirare la sua adesione allo studio in un qualsiasi momento dandone comunicazione al

medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Consenso ad informare il proprio medico di medicina generale

Per la migliore tutela della Sua salute, Le verrà chiesto di informare il Suo medico di medicina generale in merito alla sperimentazione alla quale accetta di partecipare.

Informazioni circa i risultati dello studio

Se Lei lo richiederà, alla fine dello studio potranno esserLe comunicati i risultati generali dello studio ed in particolare quelli che La riguardano.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:

Titolari del trattamento e relative finalità

Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all'età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati

Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento

I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi

direttamente al centro di sperimentazione nella persona della Dott.ssa Giuseppina Sgandurra. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. In tal caso, i dati acquisiti a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi a Suo carico derivanti dalla partecipazione allo studio. Non riceverà alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che Le è stato proposto è stato approvato dal Comitato Etico Pediatrico Toscano in data…… Il Comitato Etico ha tra le altre cose verificato la conformità dello studio alle Norme di Buona Pratica Clinica della Unione Europea ed ai principi etici espressi nelle Dichiarazione di Helsinki.

Lei potrà segnalare qualsiasi fatto ritenga opportuno evidenziare, relativamente alla ricerca che La riguarda, al Comitato Etico e/o alla Direzione Sanitaria di questa struttura ospedaliera.

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	g.sgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha consegnato l'informativa | Data | Ora | Firma

MODULO DI CONSENSO INFORMATO

V 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Io sottoscritto/a _____ nato/a il ___/___/_____ residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza) _____

DICHIARO

- di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, facente parte di questo consenso, della quale mi è stata consegnata una copia in data _____ alle ore _____ (*indicare data e ora della consegna*);
- che mi sono stati chiaramente spiegati e di aver compreso la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico;
- di aver avuto l'opportunità di porre domande chiarificatrici e di aver avuto risposte soddisfacenti;
- di aver avuto tutto il tempo necessario prima di decidere se partecipare o meno;
- di non aver avuto alcuna coercizione indebita nella richiesta del Consenso;
- che mi è stato chiaramente spiegato di poter decidere liberamente di non prendere parte allo studio o di uscirne in qualsiasi momento senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
- di essere consapevole dell'importanza (e della mia responsabilità) di informare il mio medico di medicina generale della sperimentazione alla quale accetto di partecipare; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici.

Sottoscrivendo questo modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di

□ **volere** □ **NON volere**
partecipare alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informato sui risultati di questa ricerca dal medico dello studio

□ **volere** □ **NON volere**
essere informato sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
Informare il medico di medicina generale della partecipazione allo studio

_____ ___/___/_____ _____ _____
Nome per esteso del paziente (adulto, minore maturo) Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso rappresentante legale Data Ora Firma

Io sottoscritto Prof./Dr. …… ……
Cognome Nome

Dichiaro che il Paziente ha firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito al Paziente esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle sue possibili alternative;
- aver verificato che il Paziente abbia sufficientemente compreso le informazioni fornitegli
- aver lasciato al Paziente il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato
Data Ora Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle “Informazioni Scritte per il Paziente” dovrà essere consegnata al Paziente stesso

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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RIABILITAZIONE PSICHIATRICA
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Tel. 0571 419868

INFORMATIVA E MANIFESTAZIONE DEL CONSENSO
AL TRATTAMENTO DEI DATI PERSONALI

Titolo Protocollo
Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233.
e-mail: g.sgandurra@fsm.unipi.it

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris in accordo alle responsabilità previste dalle norme della buona pratica clinica (decreto-legge n. 211/2003), tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine esclusivamente in funzione della realizzazione dello studio.
Il trattamento dei dati personali relativi tra cui età, sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

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Modalità del trattamento
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Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione. Sperimentatore principale Dr.ssa Giuseppina Sgandurra , IRCCS Fondazione Stella Maris. Viale del Tirreno 331, 56128 Calambrone (Pisa), *g.sgandurra@fsm.unipi.it.*

Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca.

Consenso

Sottoscrivendo tale modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

Nome e Cognome dell'interessato (in stampatello) _____

Firma dell'interessato _____

Data _____

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
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ISO 9001
BUREAU VERITAS
Certification

INFORMATIVE MODULE FOR PARENTS/LEGAL TUTORS

Version 5.0 of 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 5.0 V **and date** of 10/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear parents/legal tutor,
the information contained in this informative document are detailed and can be very complex. We ask you to accept the participation in the trial only after you have carefully read this document and have had an exhaustive conversation with the investigator that must devote the necessary time to fully understand what it is proposed.

Your son/daughter may be eligible to participate in a study of the IRCCS Fondazione Stella Maris. This module provides important information on the purposes, risks and possible benefits of this study. If some aspect of this module are not clear, you can ask questions to doctors researchers involved in the study. Take all the time necessary. Your son/daughter's participation is voluntary and you may withdraw it at any time. Once you have read this form, you will receive answers to any questions, and if you decide to take your son/daughter to study, you will be asked to sign a consent form, which you will receive a printed copy.

Which are the aims of the study

The study aims to evaluate the feasibility and effectiveness of the Action Observation Training (AOT) with regard to the standard care in home-based rehabilitation in children and adults with hemiplegia.

A second goal will be to measure and monitor the movements of the upper limbs through the use of actigraphs, simple commercial instruments such as watches (see below), whose data will be compared with the clinical results.

What is AOT?

The recent discovery of the Mirror Neuron System (SNS) has promoted the development of the Action-Observation Training (AOT), a therapy based on the observation of goal-directed actions followed by their motor replication as a model for motor learning.
AOT has been used with promising results in some studies in adult with stroke and recently also in children with Cerebral Palsy showing positive effects on the upper limb function. In particular, the IRCCS Fondazione Stella Maris (FSM) has carried out in a group of 24 children with hemiplegia Preliminary data support the hypothesis that AOT can improve the upper limbs function in children with hemiplegia. Based on these promising results, this study has been proposed.

The recruitment will be made by the FSM . We propose to select 20 participants aged between 5-20 years with unilateral cerebral palsy with a predominant spasticity pattern that interferes with the upper limb function; sufficient cooperation in the activities to be proposed; parents or legal tutor or adult with hemiplegia available to collaborate in 3- consecutive weeks of intensive home training program.

Recruitment will take place after the signing of informed consent by the subjects and/or by the parents or the legal tutor. The enrolled subjects will be divided randomly into two groups: experimental and standard care (control) groups. Subjects assigned to the experimental group will begin with the AOT for a period of 3 weeks, while those in the control or standard care will continue as they normally do by making a diary of any rehabilitation activities they conduct.
All subjects will be evaluated before (T0) and after (T1) the experimental / standard care period with standardized scales and tests. At the end of this period to those individuals who have not carried out the experimental training have the opportunity to carry out the training. The training will be offered with the same details and it will last three weeks at the end of which the subjects of this group will be re-evaluated with standardized scales and test (T1 plus). All subjects will be re-evaluated after 8 weeks from T1/T1 plus (T2) and after 16 weeks of T1 (T3).
These evaluations will be performed in order to evaluate the effects of training at short term (T1 and T1 plus) and at medium (T2) and long term (T3). For details see Study Design Figure 1.

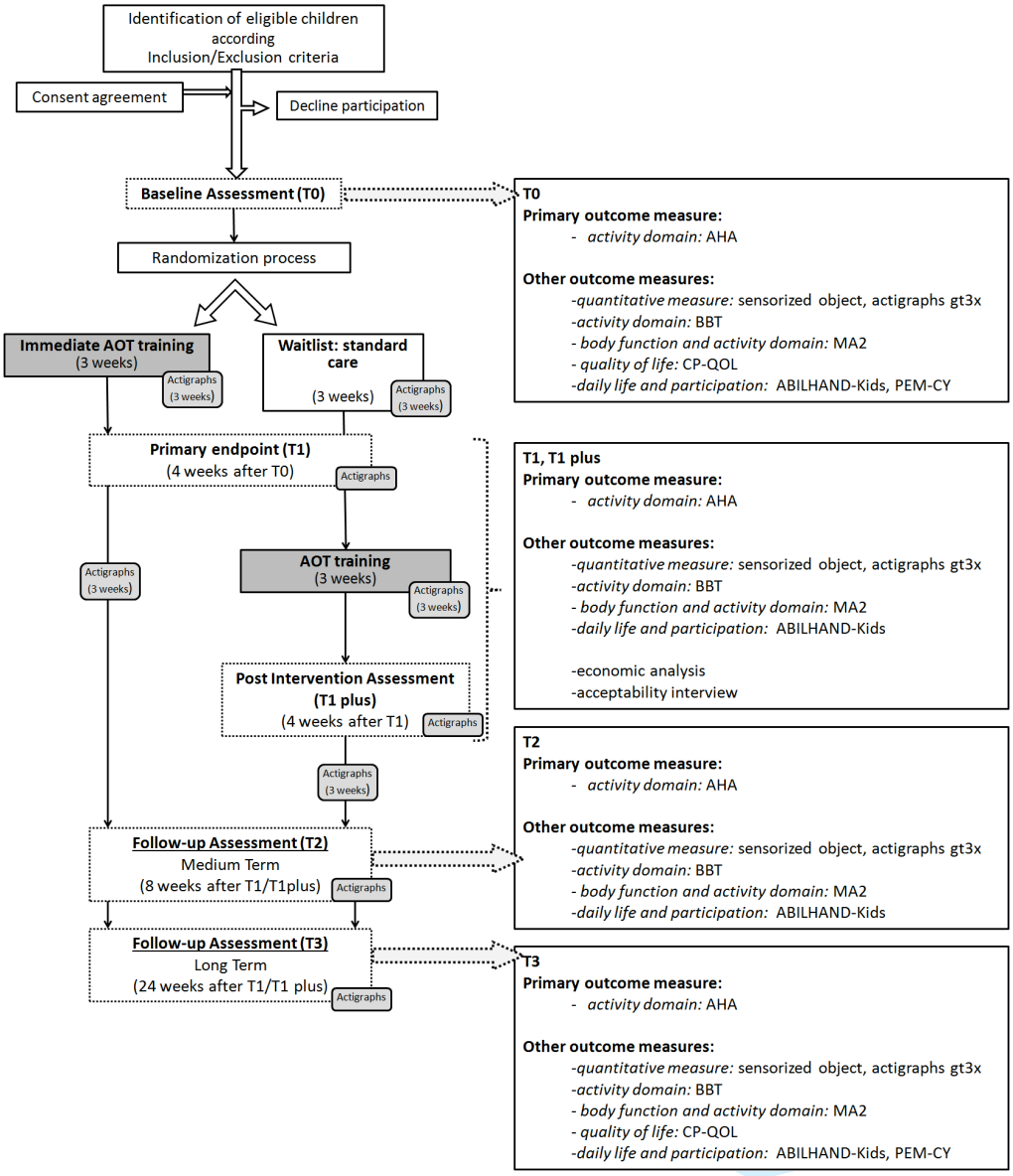


Figure 1: Flow-chart of Clinical Study

Summarizing all subjects will be assessed using standardized scales and tests at different times: T0, T1, T2, T3.

- T0: in the week before the beginning of the AOT training / standard care period
- T1: in the week after the AOT training / standard care
- T1 plus: in the week after the AOT training. This evaluation will be carried out only in the group of subjects who will undergo training in the second phase.
- T2: 8 weeks after the end of experimental training
- T3: 16 weeks after T2.

AOT training will be performed through a dedicated and personalized platform that will be delivered at home along with the useful material for training. The treatment will be performed by the participants, with the supervision of the parents, it will last about one hour per day, for 5 days a week for 3 weeks (total of 15 days). During the first two / three days of training, a therapist will support parents or adult hemiplegic subjects in the management of the training.

During the 3-week training sessions, the subjects will wear two actigraphs on the wrists (Figure 1) every day as long as possible. Subjects who will initially be allocated to the control group will be asked to keep a diary of any rehabilitation activities that they normally conduct and will be asked to wear actigraphs every day as long as possible, such as subjects assigned to the experimental group. It will be required to keep the actigraphs also in the 3 weeks following the end of the training.

The actigraph is a non-invasive motion accelerometer sensor that is worn on the wrist like a watch, is comfortable and water resistant. Today the actigraph is a trendy tool in use by youth and adults for fitness tracking and daily calorie consumption. The model used in this study is shown in the picture below.

Figure 2: wGT3X-BT

Recruitment will take place only after the informed consent has been given.
During the recruitment some clinical data (including age, gender, brain injury characteristics, affected side, manual functional level at the Home Functional Classification System) will be recorded and a dedicated database will be created.
To protect privacy and anonymity, to each subject will be assigned a numeric code that will be kept in separate form, so the database will not contain any identifying data. Access to such data will be restricted to the only staff directly involved in the study and all data will be processed in anonymous form.

What does your participation in the study involve?

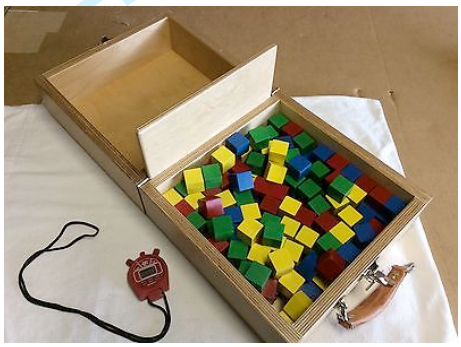
The study lasts 12 months, during this period a group of at least 20 children and young adults (5-20 years) with congenital hemiplegia will be enrolled at the IRCCS Fondazione Stella Maris . Participation will be voluntary on the basis of informed consent. The study will include a specific rehabilitation training, home-based AOT, through an ad hoc platform that will allow to conduct a personalized AOT training.

The clinical assessment (tests and questionnaires) is normally used for the functional evaluation in subjects with congenital hemiplegia:

The protocol will consist of the following tests:

1- Assisting Hand Assessment (AHA) is a scale that allows to evaluate manual and bimanual functionality.

2- Box and Block Test (BBT) is used to evaluate manual dexterity in which it is required to grasp, one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute.



3- *Melbourne Assessment of Upper Limb Function (MA2)*. It is a standardized instrument for measuring the capacity and quality of movement of the 'upper limb in children with Cerebral Palsy aged between 2 and 15 years, but it is also used for adults. It will be used at all evaluation times.

4- *ABILHAND* is a short questionnaire, validated in patients with cerebral palsy that measures 21 daily bimanual activities. The rating is assigned by the subject or the parent based on the experiences in daily accomplish, each task has a score of 3 points (impossible, difficult, easy). It will be used at all evaluation times.

5- *Participation and Environment Measure - Children and Youth (PEM-CY)*. This is a measure of participation and environmental factors at home, at school and in the community. It will be used at T0 and T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL -child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL -Teen, 13-18 years)*. These questionnaires are used to assess the quality of life in people with cerebral palsy. It will be used at T0 and T3.

7- *instrumental measurement of the manipulation during uni and bimanual tasks executed after observation.* It is an object containing two load cells to measure the force exerted (compression or traction) when grasped by the plegic hand and an on-off switch to evaluate the contact of the unaffected hand. An additional switch is placed at the starting point on the table under the more affected hand to record the moment when it starts moving toward the object. The instrument is used immediately after viewing three manipulation tasks carried out with three different types of grip: a one-hand task performed with the more affected hand, a two-hand bimanual task for the two hands, and a two-hand co-operation task for the two hands.

TASK 1. TASK 2. TASK 3.

The entire evaluation will last approximately one hour.

8- The use of the a*ctigraph in daily life.* The recruited subjects wear two actigraphs (Figure 2) outside of the clinical evaluation on his wrists (one for each wrist) for three-week periods (AOT experimental phase, phase control, phase follow-up). At the end of the registration period, the actigraph will turn off themselves and will be returned directly or by mail service to the examiner.

Benefits from participation in the study

Based on the literature and the preliminary results obtained in our previous studies, we expected that AOT training could improve the use of the upper limb in everyday life activities.

Possible risks

There are no direct risks or side effect related to the participation.

Possible alternatives

The alternative is not participate in the study.

What happen if you decide to do not take part in the study or retire from the study

The participation is voluntary. If you decide to attend, you will be able to withdraw from the study at any time and without the obligation to provide explanations, however, by notifying the doctor responsible for the study, Dr. Giuseppina Sgandurra.
If this is the case, no additional data will be collected and you can ask for the deletion of those already collected.

Information of General practitioner /pediatrician
For the best protection of the health of your child, you will be asked to inform the family doctor/paediatrician of the participation on the trial.

Information about the results of the study
If you require it, at the end of the study, results of the study and, in particular, those concerning you may be provided.

INFORMATION RELATING TO PERSONAL DATA PROCESSING:
Treatment holders and their purpose
The IRCCS Fondazione Stella Maris in accordance with the responsibilities provided by the rules of good practice, will process your personal data, particularly on health essential to the objective of the study, other data related to your origin and to the characteristics of your medical condition only solely on the basis of your study. For this purpose, the data provided will be collected by the Testing Center and processed in anonymity and in the privacy of the data. The processing of personal data related to 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphic records are essential for conducting the study: the refusal to provide will keep you from participating.

Nature of data
The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored for at least 7 (seven) years from the end of the study in this code, to your date of birth, the 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphs records are necessary for carrying out the study. Only the physician and authorized clinicians will be able to link this code to your name.

Treatment Mode
Data, whether processed by electronic means, will only be published in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, in such a way as to guarantee the confidentiality of your identity.

Exercise of rights
You may exercise your rights under art. 7 of the Code (eg. Access to your personal data, integrate, update, correct and object to their treatment for legitimate reasons, etc.) Applying directly to the testing center in the person of Dr. Giuseppina Sg andurra. You may terminate your participation at any time without giving any justification. In this case, the acquired data related to you will be destroyed. Further data will not be collected for you, without prejudice to the use of those already collected to determine, without altering the results of the search: even for the data already collected, you may ask for the cancellation.

Further information

There are no charge costs due to participation in the study. You will not receive any financial compensation for participating in the study.

The protocol of the study proposed to you has been approved by the Tuscan Ethics Pediatric Committee on 22/11/2016. The Ethics Committee has, among other things, verified the compliance of the study with the European Good Clinical Practice and the ethical principles expressed in the Helsinki Declaration.

You may report any matter you may find relevant to the Ethics Committee and / or the Health Care Department of this hospital structure regarding the research you are concerned with.

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	g. Sgandurra @ fsm.unipi.it	

_____ ___ / ___ / _____ _____ _____

Name of Doctor's who delivered the information | Date | Time | Signature

INFORMED CONSENT FOR PARENTS/LEGAL TUTOR
Version 5.0 of 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*

Version 5.0 V **and date** of 10/11 / 2016

Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella M aris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

I signed (mother/guardian) _ born on ___/___/___ ___ living in _ Street _ phone _ address (if different from the residence) _ I, the undersigned (parent/guardian) _ born on ___/___/___ ___ living in _ Street _ phone _ address (if different from residence) _ of the child _ born on ___/___/___ ___ living in _ Street _

I acknowledge that I have received from Dr. _ the explanations regarding the request to participate in the research, according to the informative document, which I had a copy dated _ _ _ _ _ _ _ _ _ _ _ _ _ _ at _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ (indicate date and time of delivery). I declare that it have been clearly explained the nature, purpose, procedures, expected benefits, risks and possible drawbacks and alternatives of the trial.

DECLARE in addition that:

1. I have read and understood the information provided about the research project and the informative part of this document;
2. it was given the opportunity to ask any questions to the investigator of the study and I had satisfactory answers;;
3. it was allowed enough time to reflect on the information received and to discuss with third parties;
4. I have been informed that the study protocol and all the modules that are used have had a favourable opinion of the Ethics Committee;
5. It was clearly explained that I can decide that the child cannot s not participate in the study or can withdraw at any time, without providing justification, and that these

decisions will not change in any way the relationships with physicians and with the structure that are treating him;

6. I am aware that the research can be interrupted at any time by decision of the head of research, without prejudice to the health of the child;
7. I have been informed that I will be informed of any new information which might affect the safety of the research and that, for every problem or if I have additional questions, I can ask to doctors;
8. for the best protection of the health of the minor, are aware of the importance (and responsibility) to inform the family doctor/paediatrician of the trial to which I agree to involve the child
9. I was informed that the study results will be made available to the scientific community, while protecting the identitication of the child in accordance with current legislation on privacy
10. I am aware that I/we must receive a copy of this consent form

By submitting this form I consent to the processing of personal data of my child and to their transfer outside the European Union (to be entered if performed by specifying the identity of recipients) for the purposes of research in limits and in the manner specified in the information provided hereby.

DECLARE therefore that I:

□ **want** □ **DON'T WANT**
that my child participate
□ in one under clinical evaluation
□ both under clinical evaluation and at home

□ **want** □ **DON'T WANT**
I will be informed about the results of research by the doctor of the study, also in relation to the unexpected news that might be accidentally encountered with the investigations required by the study

□ **want** □ **DON'T WANT**
inform your paediatrician/general practitioner of your involvement in the study

_____ ___/___/_____ _____ _____

Complete name of the child Date Time Signature

_____ ___/___/_____ _____ _____

Complete name of the parent/caregiver Date Time Signature

_____ ___/___/_____ _____ _____

Complete name of the parent/caregiver Date Time Signature

I signed Prof./Dr. …… (Surname) ……..… (Name)

I declare that the parents/guardians of Patient signed spontaneously his participation in the study

I also declare to:

- providing comprehensive explanations of the purpose of the study, the procedures, the potential risks and benefits and possible alternatives;
- I have verified that the parents/legal guardian have sufficiently understood the information provided
- Having left to the parents/legal tutor the necessary time and opportunity to ask questions about the study
- I am not exercising any coercion or unjustified influence in the Consent's request

_____ ___/___/_____ _____

_____

Name of doctor whom deliver consensus Date Time Signature

NOTA BENE

a copy of this form, signed and dated, attached to "information form for parents/legal guardian" should be delivered to parents/legal guardians of Patient

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
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Tel. 0571 419868

ISO 9001 BUREAU VERITAS Certification

INFORMATIVE MODULE
FOR PATIENTS AGED 7-13 YEARS
Version 6 .0 of 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

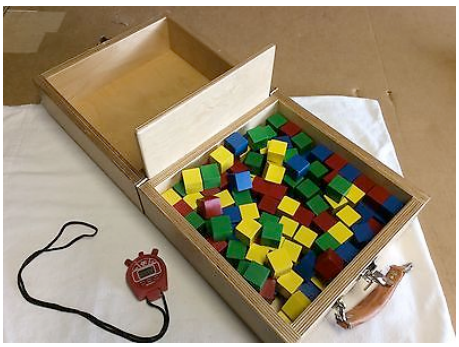
Why do we do this study?
Medical research wants to improve knowledge about diseases. We ask you to help us to understand whether the use of an "action observation-based therapy" may be helpful to improve the functionality of your affected arm. The observational therapy involves the viewing of short videos, to be observed carefully, which showed an 'action done with the hands and soon after you will be asked to perform the same movement trying to imitate as much as possible.
In addition we will ask you to wear bracelets, similar to a watch, to better measure and monitor the movements of your arms.

Who participates with me?
They will attend 20 children / teenagers and young adults aged 5-20 years. Everyone will be with similar motor difficulties like yours.

What happens if I participate?
If you decide to take part in the study at the beginning you will randomly assigned to one of two groups: experimental or control. If you will be assigned to the experimental group immediately you will begin a training based on action observation at home while if you will assigned to the control group you will be offered to wait about 4 weeks before starting the same type of therapy and in the meantime you will continue to do what you are doing now. So in each case you will do an action observation training immediately or after 4 weeks. In both cases you will be asked to wear bracelets, similar to a watch, on your wrists.
The therapy that you will do before or after is basically based on a computer program where "Ubi", an extra-terrestrial, will help you step by step in doing the exercises.

Additionally at a pre-set time (T0: when we enrol you, T1: T1: after the treatment or the control phase, T1 plus: after the treatment if you have started after, T2: after 8 weeks and T3: after 16 weeks from the end of the treatment) specific scales and questionnaires will be proposed to you and your parents that help us to understand how you use your hands!

How long will the study last?
The study will last one year. If you agree to join the study your participation lasts 3 weeks (treatment duration). You will also be asked to do the tests and fill out the questionnaires 3 or 4 times.



Some examples of games

There are benefits expected from my participation in the study?
We expect that this therapy could help you in improving the use of your hands

What are the risks of the study?
There are no risks because it is a very simple treatment which can be done safely at home and the assessments are those that normally you carry our during the clinical evaluation in the clinical centre.

What happen if I decide to do not take part in the study
You are completely free to join or not to the study. If you decide to do not participate, you will continue to be periodically monitored by your clinical team as well as done so far.

Do I have to give my consent to participate in the study?
Once you have read this information form and have asked your questions, you will decide if take part in the study. If you want to participate, you will need to sign this form for which you will be given a copy for you.
If you decide to do not take part in the study, or if you change your mind afterwards, nothing will happen, you will continue to receive the necessary care at this hospital.

And should I have any questions?
If you have any questions you can ask them to Dr. Giuseppina Sgandurra at the interview and can also call on the telephone number 050/886239: listens to you and explain to you everything you want.

Date _____ time _____ delivery

Signature of the Doctor who delivered the information

DECLARATION OF CONSENT
FOR PATIENTS AGED 7-13 YEARS
Version 6 .0 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
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The information form was delivered to me on (date) _____ at _____
I understood everything the doctor explained to me.
The Doctor has listened to all my questions and has answered me.
If in the future I'll need something else, the doctors of the study will be at my disposal.

_____
Date and time

_____
Write your name here if you would like to take part in the study

_____
Signing the patient. Enter your name in the block here if you would like to take part in the study

_____ _____
Date hour Doctor's signature that informed the patient

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INFORMATIVE MODULE
FOR PATIENTS AGED 14 - 17 YEARS
Version 6 .0 of 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear ……..,
may be eligible to participate in this clinical study proposed by IRCCS Fondazione Stella Maris.
This module provides information on the purposes, risks and potential benefits of this study. If some aspect of this form does not make you clear, you can ask questions to doctors of the study. Take all the time you need. You are not obligated to participate. If you accept, you may choose to withdraw your participation at any time.
Once you have read this form and answered your questions, you will be asked to decide if you would like to participate in the study. If you want to participate, you will need to sign the form for which you will be given a copy to you.

What is the purpose of this study?
We are inviting you to participate in this study because we think that you can help us to understand if the use of action observation therapy can be helpful in improving the functionality of your arm. The action observation therapy involves the viewing of short videos, to be observed carefully, which shows an 'action done with the hands" and soon after you will be asked to perform the same movement trying to imitate them as much as possible. In addition we will ask you to wear bracelets, similar to a watch, to better measure and monitor the movements of your arms.

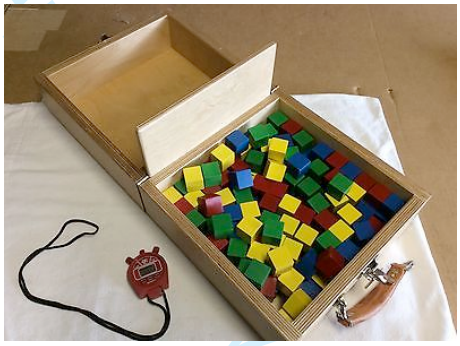
How many people will participate?
They will attend 20 children / teenagers and young adults aged 5-20 years. Everyone will be with similar motor difficulties like yours.

What does participating in the study mean?
If you decide to take part in the study at the beginning you will randomly assigned to one of two groups: experimental or control. If you will be assigned

to the experimental group immediately you will begin a training based on action observation at home (3 weeks) while if you will be assigned to the control group you will be offered to wait about 4 weeks before starting the same type of therapy and in the meantime you will continue to do what you are doing now. So in each case you will do an action observation training immediately or after 4 weeks. In both cases you will be asked to wear bracelets, similar to a watch, on your wrists. The therapy that you will do before or after is based on a computer program where "Ubi", an extra-terrestrial, will help you step by step in the exercises you do.

The study will last one year. If you accept to take part in the study your participation is 3 weeks (duration of treatment).

Additionally at a pre-set time (T0: when we enrol you, T1: T1: after the treatment or the control phases, T1 plus: after the treatment if you have started after, T2: after 8 weeks and T3: after 16 weeks from the end of the treatment) will be proposed specific scales and questionnaires that help us to understand how you use your hands!



Some examples of games

There are benefits expected from my participation in the study?
We expect that this therapy could help you in improving the use of your hands

What are the risks of the study?
There are no risks involved because it is a very simple treatment that you can done safely at home and assessments are those that normally our during the clinical evaluation in the clinical center.

What if I decide not to take part in the study or withdraw from the study?
Your participation in the study is voluntary.
If you decide to do not participate, or if you change your mind afterwards, you will not have any penalty or loss of benefits that you would otherwise have been entitled to. Your current and future medical care in the Fondazione IRCCS Stella Maris will not be affected by your decision, and doctors continue to follow you with due attention.
You can withdraw your participation in the study at any time communicating with Dr. *Giuseppina Sgandurra* providing any justification. In this case no additional data will be collected about you and you will be able to request the deletion of those already collected. Your participation in the study may be interrupted if your doctor evaluates that the new treatment has not benefited or if you

experience any side effects. In these cases, you will be promptly informed by your doctor and you will be able to discuss with him about further treatments that are valid for your condition.

What will happen to the information that was collected for the study?
The medical information about you such as age, sex, characteristics of your diseases, the results of the tests and the diary of daily activities will be kept in an archive of Fondazione Stella Maris.
Your data will be archived in anonym form, your name will be replaced by a code known only to a few people and your data will be anonymous. Only the physician and authorized persons will be able to link this code to your name.
Study data can be displayed at conferences/congresses or published in scientific journals to inform other doctors and health professionals.

Information on the results of the study
At the end of the study you will be informed on the results of the research.

Further information
There are no additional costs incurred from your participation in the study. You will not receive any financial compensation for participating in the study.
The study protocol have been written in accordance with the requirements of Good Clinical Practice and the Declaration of Helsinki, and was approved by the Ethics Committee of the Pediatric Tuscany Region on 22/11/2016.

For more information and communications, you can contact the study staff who will be at your disposal:

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	gsgandurra@fsm.unipi.it	

_____ ___ / ___ / _____ _____ _____
Name of Doctor's Date Time Signature
who delivered the information

INFORMED CONSENT
FOR PATIENTS AGED 14 -17 YEARS
Version 6 .0 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

I am signed (name and surname) _____ I declare that I have received information from Dr. _____ full explanations regarding the request for participation in the study in question, as indicated in the attached information form, of which I was given a copy on _____ at _____

I state that I have clearly understood the nature, purpose, expected benefits, risks and disadvantages of the clinical trial.

I declare that I have been able to do all the questions I have found necessary and have received satisfactory answers, as well as having been able to tell me about the details of the study with a person of my confidence.

I therefore agree to participate in the research, having fully understood the meaning of the request and the risks and benefits that may result from this participation.

I agree that my personal data *and their transfer outside the European Union (if applicable)* for research purposes to the extent and in the manner indicated in this document.
□ I wish the results of the study were communicated to me.

__ / __ / ____ _____
_____ Signature of the patient
Date hour
__ / __ / ____ _____ _____
_____ Doctor's signature that informed the patient and registered his consent
Date hour

FONDAZIONE
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Tel. 050 886111

Dear Mrs / Mrs, the information contained in the following informative module is detailed and could be very complex

we ask you to accept the participation in the study ONLY after reading this carefully document and interviewing the investigator who will dedicate to you all the time necessary to fully understand what we are proposing to you

INFORMATIVE MODULE FOR THE PATIENT

Version 5.0 of the 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 5.0 V **and date** of 10/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear ____ ,
we ask you to take part in this clinical study, this document is intended to provide you all the information about the study: the purpose, what you will be asked, which are your rights and responsibilities. Read the information carefully before making a decision about your participation in the study. You will have all the time you need to decide whether you want participate or not.
You will be free to ask any questions until you have received a clear and comprehensive answer for yourself.
If, after reading and understanding all the information you decide to participate in the clinical trial, you will need to sign the Consensus Information Form attached to this document.

Which are the aims of the study

The study aims to evaluate the feasibility and effectiveness of the Action Observation Training (AOT) with regard to the standard care in home-based rehabilitation in children and adults with hemiplegia.

A second goal will be to measure and monitor the movements of the upper limbs through the use of actigraphs, simple commercial instruments such as watches (see below), whose data will be compared with the clinical results.

What is AOT?

The recent discovery of the Mirror Neuron System (SNS) has promoted the development of the Action-Observation Training (AOT), a therapy based on the observation of goal-directed actions followed by their motor replication as a model for motor learning.

AOT has been used with promising results in some studies in adult with stroke and recently also in children with Cerebral Palsy showing positive effects on the upper limb function. In particular, the IRCCS Fondazione Stella Maris (FSM) has carried out in a group of 24 children with hemiplegia Preliminary data support the hypothesis that AOT can improve the upper limbs function in children with hemiplegia. Based on these promising results, this study has been proposed.

The recruitment will be made by the FSM . We propose to select 20 participants aged between 5-20 years with unilateral cerebral palsy with a predominant spasticity pattern that interferes with the upper limb function; sufficient cooperation in the activities to be proposed; parents or legal tutor or adult with hemiplegia available to collaborate in 3- consecutive weeks of intensive home training program.

Recruitment will take place after the signing of informed consent by the subjects and/or by the parents or the legal tutor. The enrolled subjects will be divided randomly into two groups: experimental and standard care (control) groups. Subjects assigned to the experimental group will begin with the AOT for a period of 3 weeks, while those in the control or standard care will continue as they normally do by making a diary of any rehabilitation activities they conduct.

All subjects will be evaluated before (T0) and after (T1) the experimental / standard care period with standardized scales and tests. At the end of this period to those individuals who have not carried out the experimental training have the opportunity to carry out the training. The training will be offered with the same details and it will last three weeks at the end of which the subjects of this group will be re-evaluated with standardized scales and test (T1 plus). All subjects will be re-evaluated after 8 weeks from T1/T1 plus (T2) and after 16 weeks of T1 (T3).

These evaluations will be performed in order to evaluate the effects of training at short term (T1 and T1 plus) and at medium (T2) and long term (T3). For details see Study Design Figure 1.

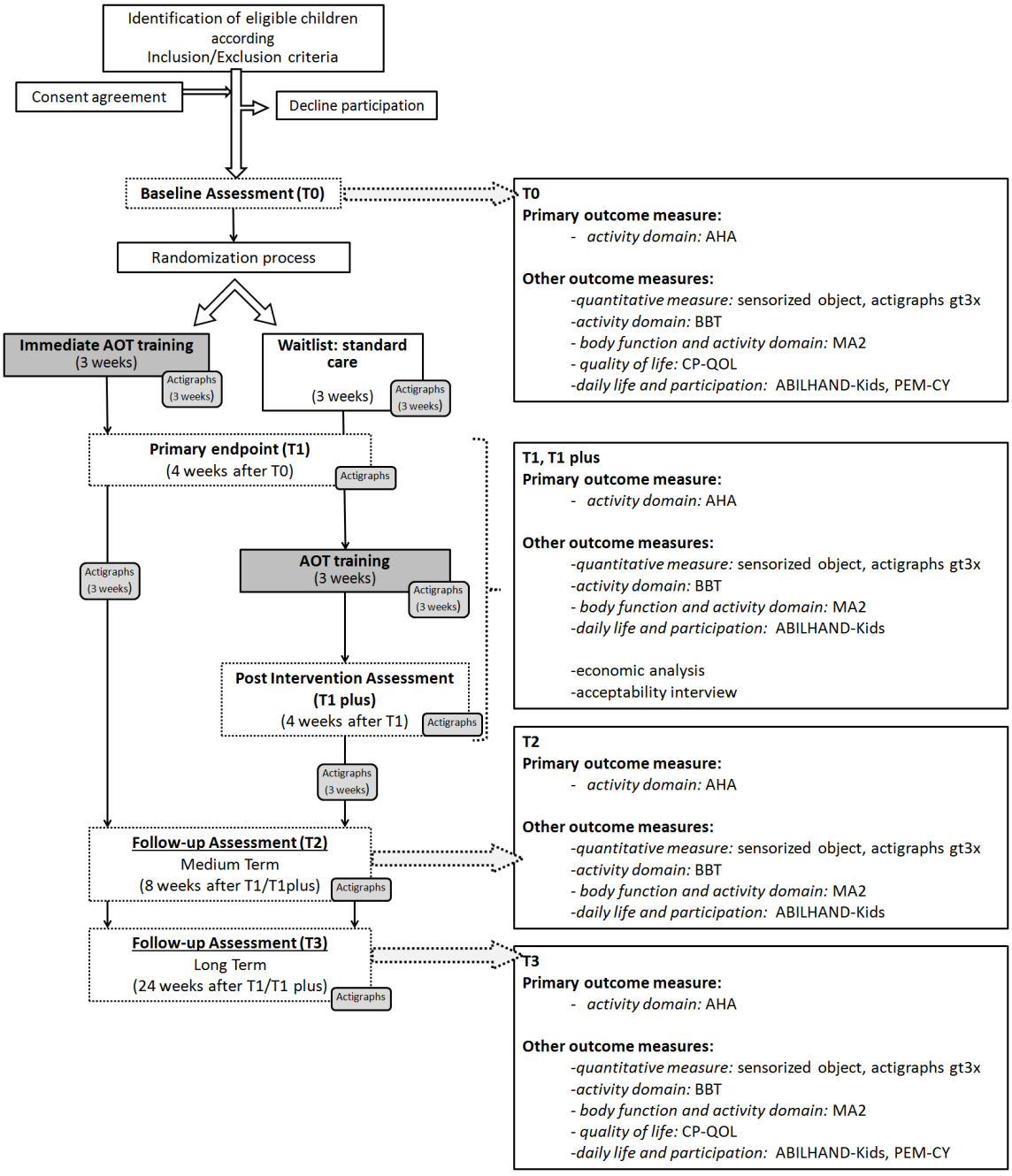


Figure 1: Flow-chart of Clinical Study

Summarizing all subjects will be assessed using standardized scales and tests at different times:
T0, T1, T2, T3.

- T0: in the week before the beginning of the AOT training / standard care period
- T1: in the week after the AOT training / standard care
- T1 plus: in the week after the AOT training. This evaluation will be carried out only in the group of subjects who will undergo training in the second phase.
- T2: 8 weeks after the end of experimental training
- T3: 16 weeks after T2.

AOT training will be performed through a dedicated and personalized platform that will be delivered at home along with the useful material for training. The treatment will be performed by the participants, with the supervision of their parents, it will last about one hour per day, for 5 days a week for 3 weeks (total of 15 days). During the first two / three days of training, a therapist will support parents or adult hemiplegic subjects in the management of the training.

During the 3-week training sessions, the subjects will wear two actigraphs on the wrists (Figure 1) every day as long as possible. Subjects who will initially be allocated to the control group will be asked to keep a diary of any rehabilitation activities that they normally conduct and will be asked to wear actigraphs every day as long as possible, such as subjects assigned to the experimental group. It will be required to keep the actigraphs also in the 3 weeks following the end of the training.

The actigraph is a non-invasive motion accelerometer sensor that is worn on the wrist like a watch, is comfortable and water resistant. Today the actigraph is a trendy tool in use by youth and adults for fitness tracking and daily calorie consumption. The model used in this study is shown in the picture below.

Figure 2: wGT3X-BT

Recruitment will take place only after the informed consent has been given.
During the recruitment some clinical data (including age, gender, brain injury characteristics, affected side, manual functional level at the Home Functional Classification System) will be recorded and a dedicated database will be created.
To protect privacy and anonymity, to each subject will be assigned a numeric code that will be kept in separate form, so the database will not contain any identifying data. Access to such data will be restricted to the only staff directly involved in the study and all data will be processed in anonymous form.

What does your participation in the study involve?
The study lasts 12 months, during this period a group of at least 20 children and young adults (5-20 years) with congenital hemiplegia will be enrolled at the IRCCS Fondazione Stella Maris. Participation will be voluntary on the basis of informed

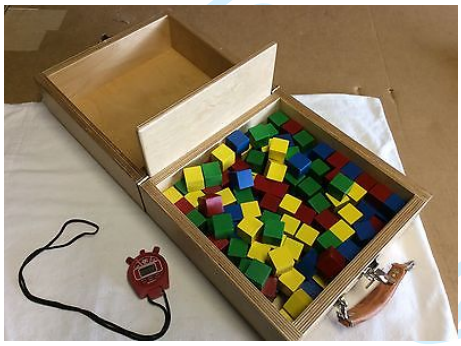
consent. The study will include a specific rehabilitation training, home-based AOT, through an ad hoc platform that will allow to conduct a personalized AOT training.

The clinical assessment (tests and questionnaires) is normally used for the functional evaluation in subjects with congenital hemiplegia:

The protocol will consist of the following tests:

1- Assisting Hand Assessment (AHA) is a scale that allows to evaluate manual and bimanual functionality.

2- Box and Block Test (BBT) is used to evaluate manual dexterity in which it is required to grasp, one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute.



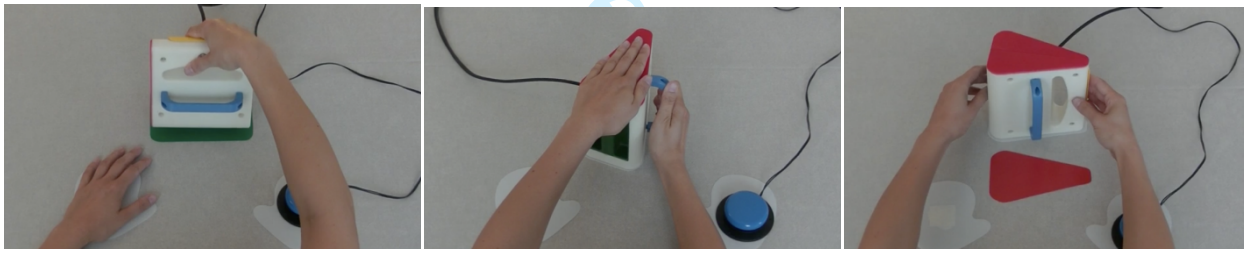
3- *Melbourne Assessment of Upper Limb Function (MA2)*. It is a standardized instrument for measuring the capacity and quality of movement of the 'upper limb in children with Cerebral Palsy aged between 2 and 15 years, but it is also used for adults. It will be used at all evaluation times.

4- *ABILHAND* is a short questionnaire, validated in patients with cerebral palsy that measures 21 daily bimanual activities. The rating is assigned by the subject or the parent based on the experiences in daily accomplish, each task has a score of 3 points (impossible, difficult, easy). It will be used at all evaluation times.

5- *Participation and Environment Measure - Children and Youth (PEM-CY).* This is a measure of participation and environmental factors at home, at school and in the community. It will be used at T0 and T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL - child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL -Teen, 13-18 years).* These questionnaires are used to assess the quality of life in people with cerebral palsy. It will be used at T0 and T3.

7- *instrumental measurement of the manipulation during uni and bimanual tasks executed after observation.* It is an object containing two load cells to measure the force exerted (compression or traction) when grasped by the plegic hand and an on-off switch to evaluate the contact of the unaffected hand. An additional switch is placed at the starting point on the table under the more affected hand to record the moment when it starts moving toward the object. The instrument is used immediately after viewing three manipulation tasks carried out with three different types of grip: a one-hand task performed with the more affected hand, a two-hand bimanual task for the two hands, and a two-hand co-operation task for the two hands.



TASK 1. TASK 2. TASK 3.

The entire evaluation will last approximately one hour.

8- The use of the a*ctigraph in daily life.* The recruited subjects wear two actigraphs (Figure 2) outside of the clinical evaluation on his wrists (one for each wrist) for three-week periods (AOT experimental phase, phase control, phase follow-up). At the end of the registration period, the actigraph will turn off themselves and will be returned directly or by mail service to the examiner.

Benefits from participation in the study

Based on the literature and the preliminary results obtained in our previous studies, we expected that AOT training could improve the use of the upper limb in everyday life activities.

Possible risks
There are no direct risks or side effect related to the participation.

Possible alternatives
The alternative is to do not participate in the study.

What happen if you decide to do not take part in the study or retire from the study
The participation is voluntary. If you decide to attend, you will be able to withdraw from the study at any time and without the obligation to provide explanations, however, by notifying the doctor responsible for the study, Dr. Giuseppina Sgandurra.
If this is the case, no additional data will be collected and you can ask for the deletion of those already collected.

I consent to informing your general practitioner
For the best protection of your health, you will be asked to inform your doctor of the experiment you are willing to attend.

Information about the results of the study
If you require it, at the end of the study, results of the study and, in particular, those concerning you may be provided.

INFORMATION RELATING TO PERSONAL DATA PROCESSING:
Treatment holders and their purpose
The IRCCS Fondazione Stella Maris in accordance with the responsibilities provided by the rules of good practice, will process your personal data, particularly on health essential to the objective of the study, other data related to your origin and to the characteristics of your medical condition only solely on the basis of your study. For this purpose, the data provided will be collected by the Testing Center and processed in anonymity and in the privacy of the data. The processing of personal data related to 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphic records are essential for conducting the study: the refusal to provide will keep you from participating.

Nature of data
The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored for at least 7 (seven) years from the end of the study in this code, to your date of birth, the 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphs records are necessary for carrying out

the study. Only the physician and authorized clinicians will be able to link this code to your name.

Treatment Mode

Data, whether processed by electronic means, will only be published in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, in such a way as to guarantee the confidentiality of your identity.

Exercise of rights

You may exercise your rights under art. 7 of the Code (eg. Access to your personal data, integrate, update, correct and object to their treatment for legitimate reasons, etc.) Applying directly to the testing centre in the person of Dr. Giuseppina Sgandurra. You may terminate your participation at any time without giving any justification. In this case, the acquired data related to you will be destroyed. Further data will not be collected for you, without prejudice to the use of those already collected to determine, without altering the results of the search: even for the data already collected, you may ask for the cancellation.

Further information

There are no charge costs due to participation in the study. You will not receive any financial compensation for participating in the study.

The protocol of the study proposed to you has been approved by the Tuscan Ethics Paediatric Committee on 22/11/2016. The Ethics Committee has, among other things, verified the compliance of the study with the European Good Clinical Practice and the ethical principles expressed in the Helsinki Declaration.

You may report any matter you may find relevant to the Ethics Committee and / or the Health Care Department of this hospital structure regarding the research you are concerned with.

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	g. Sgandurra @ fsm.unipi.it	

_____ ___ / ___ / _____ _____

_____

Name of Doctor's Date
Time Signature
who delivered the information

INFORMED FORM OF CONSENT

V 5.0 of the 10/11 / 2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*

Version 5.0 V **and date** of 10/11 / 2016

Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella M aris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

I signed _____ born ___ / ___ / _____ resident to _____ via / square _____ Tel ._____ domicile (if different from residence) _____

DECLARE

- had received from Dr. _____ exhaustive explanations about the request to participate in the present research, as reported in the information document, part of this agreement, which I was given a copy on _____ at _____ *(insert date time of delivery);*
- that I have been clearly explained and I have understood the nature, purpose, procedures, the expected benefits, risks and possible inconveniences and alternatives of the clinical study;
- that I have had the opportunity to ask questions and to have had satisfactory answers;
- that you have had all the time you need before deciding whether to participate or not;

- that I have not had any unjustified coercion in the request for Consent;
- that I was clearly asked that I could freely decide to do not take part in the study or to leave at any time without giving any justification, and that those decisions will not in any way modify the relationship with the physicians and the structure that are treating me ;
- I am aware of the importance (and of my responsibility) to inform my general practitioner of the experiment I am willing to attend
-

By subscribing to this form, I consent to the processing of my personal data for the purposes of the search within the limits and with the methods indicated in the information provided to me with this document.

I therefore declare of

□ **want** □ **NOT want**
□ participate in one under clinical evaluation
□ both under clinical evaluation and at home

□ **want** □ **NOT want**
be informed of the results of this research by the medical practitioner

□ **want** □ **NOT want**
be informed on the results of the research by the medical practitioner, also in relation to unexpected news that should be accidentally encountered with the investigations provided by the study

□ **want** □ **NOT want**
Inform your doctor of general practitioner in study participation

_____ ___ / ___ / _____ _____
_____
Full patient name (adult, lower mature) Date
Time Signature

_____ ___ / ___ / _____ _____
_____
Name for Extended Legal Representative Date
Time Signature

I signed Prof./Dr. ....
Surname Name

I declare that the Patient has spontaneously signed his participation in the study

I also declare:

- providing the patient with comprehensive explanations regarding the purposes of the study, the procedures, possible risks and benefits and possible alternatives there are to;
- have verified that the patient has sufficiently understood the information provided to him / her
- having left to the Patient the time needed and the opportunity to ask questions about the study
- not exercising any coercion or unjustified influence in the Consent's request

_____ ___/___/_____ _____
_____
Name of Doctor's Date Date Time Signature
who provided the information and
gathered informed consent

Please note

a copy of this form, signed and dated, enclosed with the "Written Information for the Patient" must be delivered to the Patient

Semi-structured qualitative interview about acceptability of AOT training

Answer to these questions with your parents, feel free to add your comments

Customization of exercises				
1	Did the exercises seem suitable for you (materials, type of actions...)?	yes, at all	yes, in part	no
2	Were exercises difficult for you (required perfomance)?	yes, all of them	yes, many of them	no
3	Did you notice an increasing difficulty (from the easiest the first day to the most difficult)?	yes		no
4	Did exercises seems like other typical activities/daily life actions?	yes, all of them	yes, many of them	no
5	Do you think that AOT activities had a role in promoting your ability?	yes, at all	yes, in part	no
Suitability of children with UCP for the Tele-UPCAT system in their own home				
6	Did you like to do the training at home?	yes		no
7	Did you like to perform exercises without a therapist?	yes, at all	yes, in part	no
8	Who helped you for the training?			
Feasibility at home				
9	Did you have a suitable table where the system was placed?	yes		no
10	If no, did you need to re-organize your home space?	yes, at all	yes, in part	
11	Do you judge the whole system bulky?	yes		no
12	Was the management of the system difficult?	yes, at all	yes, in part	no
Required effort by the participants				
13	Was the effort (about 1 hour per day) feasible for you?	yes, at all	yes, in part	no
14	Did you change your daily routine to do the training?	yes, at all	yes, in part	no
15	Did you have to renounce to something (sport, freetime, holidays..)?	yes, at all	yes, in part	no
16	Did you like to have a fixed time for the training each day?	yes, at all	yes, in part	no
17	Do you think that you could proceed the training for more days?	yes, at all	yes, in part	no
18	Were the exercises too hard (difficult, long..) for you?	yes, at all	yes, in part	no

Semi-structured qualitative interview about acceptability of AOT training

Answer to these questions with your parents, feel free to add your comments

Acceptability of Actigraphs				
19	Did you like to wear Acrigraphs?	yes		no
20	Did Actigraphs annoy you?	yes	yes, sometimes	no
21	Did you wear them for the whole day?	yes, at all	yes, in part	no
22	Did you remember how to wear them (orientation)?	yes		no
23	Did you remember to fill in your diary?	yes	yes, sometimes	no
Suitability of the manual				
24	Was the manual enough clear?	yes, at all	yes, in part	no
25	Did you have any difficulties in finding/preparing the material?	yes	yes, sometimes	no
26	Were the instructions for the managining of the system complete and clear?	yes	yes, sometimes	no
Software				
27	Did you like Ubi (for children)/slides (for adolescents)?	yes, at all	yes, in part	no
28	Do you think that something need to be changed?	yes		no
29	Was the managing of the software difficult?	yes, at all	yes, in part	no
30	Did you have technical issues/troubles?	yes	yes, sometimes	no
31	Did you need technical assistance?	yes	yes, sometimes	no

BMJ Open

Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPper Limb Children Action Observation Training for Participants with Unilateral Cerebral Palsy

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Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Neurology, Paediatrics
Keywords:	action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPper Limb Children Action Observation Training for Participants with Unilateral Cerebral Palsy

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Word Count: 5904

Abstract

Introduction:

A new rehabilitative approach, called UPper Limb Children Action Observation Training (UP-CAT), based on the principles of Action Observation Training (AOT), has provided promising results for Upper Limb rehabilitation in children with UCP. This study will investigate if a new Information and Communication Technology (ICT) platform, named Tele-UPCAT, is able to deliver AOT in a home setting and will test its efficacy on children and young people with UCP.

Methods and Analysis:

A randomized, allocation concealed (waitlist-control) and evaluator-blinded clinical trial with two investigative arms will be carried out. The experimental group will perform AOT at home for 3 weeks using a dedicated and customized Tele-UPCAT system where they will watch video sequences of goal-directed actions and then complete the motor training of the same actions. The control group will continue standard care for 3 weeks after which they will also start Tele-UPCAT training. Based on a previous clinical study, a sample size of 12 patients per group is required and the primary outcome will be Assisting Hand Assessment. The Melbourne Assessment 2, ABILHAND, Participation and Environment Measure-Children and Youth (PEM-CY) and Cerebral Palsy Quality of Life Questionnaire (CP-QoL) will be included as secondary measures. Quantitative measures from sensorized objects and subject worn Actigraphs GXT3+ will be analysed. The assessment points will be the week before (T0) and after (T1) the period of AOT/Standard Care. Further assessments will be at T1 plus, the week after the AOT period for the waitlist group and at 8 (T2) and 24 weeks (T3) after AOT training.

Ethics and Dissemination:

The trial has been approved by the Tuscany Paediatric Ethics Committee (169/2016). Publication of all outcomes will be in peer-reviewed journals and conference presentations.

Trial registration: ClinicalTrials.gov: NCT03094455 (16 March 2017). The trial was funded by Italian Ministry of Health grant: GR-2011-02350053

Abstract words: 299

Key words: action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Strengths and limitation of this study

- This is the first protocol study where an ICT platform is proposed, called Tele-UPCAT, to deliver the Action Observation Therapy (AOT) at home
- The study is a well-designed RCT aimed to investigate the UP-CAT approach at home and to measure its efficacy in a clinical population of children, adolescents and young adults with UCP.
- The Tele-UPCAT platform allows individualised customization of the intervention according to the different manual functional levels and the different ages of participants.
- The sample size, even if calculated and powered on the previous clinical studies, is modest.
- The Tele-UPCAT platform does not obtain quantitative measurements of force and pressure hand measurements during AOT session.

BACKGROUND

Cerebral palsy (CP) is the most common cause of childhood chronic physical disability in Europe and in other industrialised societies. [1] The incident rate is between 2 and 3 per 1000 live births and increases to 40–100 per 1000 live births among very premature and very low birth-weight babies which represent the population with highest rate of neurodevelopmental disorders. Unilateral Cerebral Palsy (UCP) (i.e. a motor impairment impacting one side of the body) constitutes the most frequent form of CP, about 30-40% of all affected children. [2] Recent estimations of incidence and prevalence of CP have shown a significant increase in UCP in Europe over the last years. [3-4] The Upper Limb (UL) of children with UCP is generally more involved than the lower limb and the consequent disability affects their participation, quality of life, independence at home, school and community. Despite this large impact, the current clinical practice for UCP mainly include consultative intervention or time-limited therapy following pharmacological intervention. In the last decades, many intervention models targeting deficits in UL function have been developed to promote better use of impaired arm and hand for routine bimanual activities and to achieve functional independence. [5-8] In this field, one of the most recent models is the Action Observation Training (AOT), based on the discovery of the Mirror Neuron System, whose core regions are the ventral premotor and inferior parietal cortex. These areas are activated when individuals perform goal-directed motor acts (e.g. grasping an object) as well as if they simply observe the performance of the same or a similar action and trigger recruitment of the same network as the actual physical action. [9, 10] AOT is mainly based on observation of meaningful actions, and their successive imitation. AOT has been used as new intervention model in many adult studies for neurologic and non-neurologic diseases (such as Parkinson disease, stroke, orthopaedic surgery) and there is growing evidence of its effectiveness. [11-16] Recent studies carried out in children with CP indicate positive effects on UL function in younger population. [17-19] We have recently completed a clinical study called UP-CAT (UPper limb Children Action observation Training) with children with UCP based on 3 weeks of AOT, providing evidence of its efficacy in improving UL activity performance in daily activities. [19] To date, the UP-CAT study has only been carried out in a clinical rehabilitation setting with children who were living near the two clinical centres and whose parents are willing to commit to a 3-week intensive therapy program with consequently high costs for both health services and families. In addition, the parents, even if able to participate, found the need to attend every working day for three weeks too burdensome and suggested the delivery of the intervention at home. Biotechnologies, tele-rehabilitation and eHealth provide a promising approach to deliver tele-monitored home programs for a large number of participants at a relatively low cost. In this field our group has recently experienced the design, the build and the clinical validation of new technological Information and Communication Technologies (ICT) for providing in the first year of life tele-rehabilitation programs at home for infants at risk for developing neurodevelopmental disorders [20-23] In this context, similar approaches could represent a viable option in providing AOT programs at home, in a user-friendly, playful and rehabilitative setting in children. The present study protocol, designed as an exploratory Randomized Clinical Trial (RCT), has the purpose to investigate the feasibility of a new ICT platform, named Tele-UPCAT, to provide the UP-CAT approach at home. This pilot RCT aims to measure its efficacy in a group of children, adolescents and young adults with UCP comparing the effects of Tele-UPCAT approach (experimental group) with the standard care (control group).

The primary aim will be to evaluate the immediate effects (T1, in the week after the end of the treatment) of this new approach (home AOT) on bimanual hand function (Assisting Hand Assessment, AHA[24-26]) and to assess whether these effects will be retained at a medium and long term follow-up (i.e. 8 and 24 weeks after the end of treatment, T2 and T3). In addition, the feasibility of the Tele-UPCAT system as a comfortable, reliable and customizable tool for delivering an home AOT to UCP participants and their families will be assessed using semi-structured interviews.

Secondary aims will be to investigate the immediate (T1) and long-term clinical effects (T2, T3) on unimanual capacity (Melbourne Assessment 2, MA 2 [27] and Box and Block Test, BBT [28]) and on bimanual daily activities at home and in the community (ABILHAND-Kids [29]), participation (Participation and Environment Measure - Children and Youth, PEM-CY) [30, 31] and perception of quality of life (Cerebral Palsy Quality of Life Questionnaire, CP-QOL); [32-34]. Further aims will be the evaluation of feasibility of Tele-UPCAT platform on assessing, monitoring and detecting changes during and after the AOT program by comparing the data of the clinical outcome measures with those of quantitative measurement of manual activity, obtained using sensorized objects and Tele-UPCAT platform. Finally, a cost-effective analysis will be carried out using both the perspective of the patient/caregivers and the healthcare system.

METHODS/DESIGN

Study design

The Tele-UPCAT trial is an exploratory randomized, allocation concealed (waitlist-controlled), and evaluator-blinded clinical trial with two investigative arms using an AOT intensive rehabilitation program of home based AOT compared to standard care in children and young people with UCP. The study is a waitlist controlled trial, in order to allow all enrolled participants to perform AOT training either immediately or after a waitlist period. After obtaining informed consent, and completing baseline assessment (T0) participants will be block randomized into pairs according to the House functional classification system (HFCS) activity level (grades 2-3, 4-5 and 6-8) and age (5-14y, 15-20y), [35, 36] using a computer-generated set of random numbers. Randomization, sequence generation and preparation of group allocation materials will be carried out by an independent researcher who will be not involved in the trial. Pairs will be divided randomly into two groups with 1:1 experimental/standard care (waitlist) ratio. Participants allocated in the experimental group will immediately start AOT for a 3-weeks period, while those in the standard care group will continue with their usual care.

In both cases, AOT or standard care, participants and parents will be asked to take daily notes on a predefined diary of their daily activities, including therapies for their motor disability. In addition, to record the acceptability and feasibility of the training, participants and/or families allocated in the experimental group will fill in a multiple choice questionnaire (with box for notes) for ascertaining the perception about their experiences of using the Tele-UPCAT system.

All participants will be re-evaluated after the period of experimental training/standard care (T1) with standardized tests and questionnaires (see outcome measures). T1 will be the primary endpoint aimed at evaluating the short-term effects of AOT according to CONSORT Guidelines (see Figure 1). [37]

After this phase, participants previously allocated to the experimental group will continue standard care, while who's who started with standard care will then commence home based AOT. The participants of this SC group will be re-assessed at the end of training (T1 plus). Further assessment of all participants will be performed after 8 weeks (T2) and 24 weeks (T3) from the end of AOT training (T1 or T1 plus, for the experimental and waitlist group, respectively), to evaluate the medium and long term effects of AOT. All the assessments will be carried out at home by trained therapists.

In summary, assessments will be performed at:

- T0, baseline: the week before the period of AOT/Standard Care
- T1: at 1 week after period of AOT/Standard Care
- T1 plus: the week after period of AOT, for waitlist group
- T2: 8 weeks after end of AOT
- T3: 24 weeks after end of AOT.

The details of the study design are reported according to CONSORT guidelines [37] (Figure 1), SPIRIT (Standard Protocol Items: Recommendations for Intervention Trials) statement [38] and TIDier (Template for Intervention Description and Replication) Checklist [39, 40] (Supplement Material 1, 2 and 3). The programme of enrolment, interventions and assessments designed according to SPIRIT guidelines are shown in Figure 2.

Blinding

All the clinical outcome measures (AHA, [24-26] Melbourne Assessment 2 MA-2 [27] and Box & Block Test [28]) will be videotaped by a therapist blind to group assignment. Videotapes will be randomized and scored by assessors blind to group allocation and order of assessments. During each assessment all the participants will wear two Actigraphs (wGT3X-BT, wActiSleep-BT), one for each wrist.

Two independent researchers (two child neurologists) without competing interests will comprise the data monitoring committee for this study. They will review all adverse events (deciding to stop the trial if necessary), subject participant retention in each study arm and compliance with study protocol at 12 weekly intervals. Participants will have a study number in a dedicated data file. The file with study participants numbers and personal data will be stored in a password protected file, accessible only by the principal investigator. In order to promote participant's retention, all the assessment will be completed at home. The clinical primary and secondary outcome measures will be completed within one week of when expected. Enrolled participants are ethically able to withdraw from the study at any time, and have been notified there usual follow-up and clinical care would not be impacted.

Study sample and recruitment

Enrolment and clinical trial management will be carried out by child neurologists and physiatrists at the Department of Developmental Neuroscience of IRCCS Fondazione Stella Maris (FSM, Pisa, Italy), with the collaboration of the Unit of Children Rehabilitation of S.Maria Nuova Hospital (Reggio Emilia, Italy).

Potential participants will be identified according to inclusion criteria (see below), from UCP patients of the clinical departments. Suitable participants and their parents will be invited to participate and will be enrolled in the RCT only after written consent has been obtained.

Inclusion criteria are participants with:

- confirmed diagnosis of spastic motor type UCP; [2, 41]
- aged between 5 and 20 years at time of recruitment;
- predominant UL spasticity;
- House functional classification system, (HFCS) score ≥ 2 that is, able to passively hold an object in the hand or better [35, 36]
- cognitive level within normal limits i.e. Intelligence Quotient ≥ 70, as assessed in the last year prior to recruitment on the WPPSI-III, [42] WISC-IV [43] or WAIS [44]
- participants and parents willing to commit to the intensive therapy program for a 3-week period.

Participants will be excluded in case of:

- previous orthopaedic surgery or Botulinum Toxin A (BoNT-A) injection in the UL within 6 months prior to study entry.

Sample size

Even if planned as an exploratory study, a sample size estimates, according to CONSORT guidelines, [37, 38] have been based on projected treatment effect on the primary outcome measure, AHA. Taking account of the study design and the stratification, a minimum sample size of 10 per group will be required in order to detect a 1.40 effect size (value based on our preliminary data) at

significant level of 0.05 and 80% power. [18, 19] Considering a 20% of possible drop-outs a minimum of 12 participants per group will be recruited, total sample of 24 participants.

Study treatment

The Tele-UPCAT system has been designed through the close collaboration between the rehabilitation staff (child neurologists and child therapists) of IRCCS Fondazione Stella Maris and biomedical engineers of BioRobotics Institute Scuola Superiore Sant'Anna. Taking into account the previous clinical experience on UPCAT, the main components of the Tele-UPCAT system (e.g. the size of the screen, the need of a guide for alternating the time of observation and of execution, the key words for catching the attention, etc), the AOT library of exercises (e.g. the adapation of the objects for enlarging the exercises to more impaired hands) and the experimental training (e.g. time and duration) have been defined. In general, the training will be structured in one session per day, to be executed 5 working days for 3 consecutive weeks (i.e. 15 sessions in total). The duration of daily sessions will be about 60 minutes per day for a total of 15 hours. The participants undergoing the AOT intervention through the Tele-UPCAT system will watch 3 minutes first-person video sequences of unimanual or bimanual goal-directed actions followed by their execution for 3 minutes. Each day 3 different actions will be proposed twice.

Tele-UPCAT system

Tele-UPCAT system (see Figure 3) has been designed and built and will be provided at home by the BioRobotics Institute of Scuola Superiore Sant'Anna (Pontedera, Italy).
It is a dedicated platform for delivering AOT designed to be user-friendly, by subjects at home in a playful setting with integrated smart features.

The platform has been designed and developed by integrating two different modules:

- The Observation Module (OM) for the presentation of AOT videos and recording of participant's attention and exercise execution. This consists of a computer with 23" desktop, a dedicated software and a video camera. The Observation Module has been obtained by integrating a large all-in-one personal computer (All-in-One touch HP EliteOne 800 G2 - L3N93AV), a large switch and a video camera (GoPro HERO Session), which will record a whole field, including subject's face and hands and table with objects. The Observation Module is important to determine whether the participant is looking at the monitor during observation phase and has an overall view of the execution of actions. A dedicated software, designed after a deep and specific literature analysis, was developed for guiding and motivating participants through the phases of AOT (observation followed by execution). In addition, the software was customized for the wide age range of participants providing an interactive game with an engaging story different for every day of training for school aged children, and a slide-show with a voice-over for adolescents and young people. The general architecture of the software is based on the following sequence: observation of a 3-minute video followed by execution of the same action for 3 minutes. Subsequently, the same video will be replayed and then executed a second time. As stated before, a 60-minute session, including rest intervals, of three different goal-directed actions of increasing complexity are observed and imitated twice every day. At the end of each day the software will terminate the session and automatically update it for the next day.
- The Motor Performance Module (MPM) for the execution of actions. This will be mainly composed of a kit of exactly the same common objects and toys shown in the videos and two Actigraphs (wGT3X-BT, wActiSleep-BT, for more details see http://actigraphcorp.com/support/activity-monitors/gt3x/) worn one for each wrist. With this

design it will be possible to measure the upper limb activity during the AOT training while the lack of sensorized toys embedded in the MPM will not allow to measure quantitative measures of hand activity (e.g. force or pressure) during the AOT training.

The first prototype of Tele-UPCAT system has been widely tested before the beginning of the RCT in order to test the stability and reliability of the system.

AOT library

On the basis of the previous AOT exercises, [18, 19] rehabilitation staff (child neurologist and child therapists) has created a library of rehabilitation packages composed of three different series of AOT exercises suitable to be executed at home. They differ for complexity of action and range of UL capabilities conceived in relation to HFCS levels (≤ 4, 5-6, 7-8). [35, 36] Each series is organized into customized sequences designed to cover unimanual and bimanual UL goal-directed actions with a variety of objects and toys commonly used in routine life. For each series, experimental training is composed of 15 sets (8 unimanual followed by 7 bimanual) of routine UL activities, to be completed in 3 weeks (5 days per week). Each set has a general common goal (e.g. drinking a glass of water) composed of three sequential tasks of increasing complexity (e.g. from picking up a bottle of water, to opening the cap, to pouring the water into a glass). As previously indicated, in order to grade the activities according to the range of capabilities, three series of sets have been planned. The actions of each series have the same goal but the material and type of movement (i.e., range of movement, type of grasp) is customized in order to guarantee feasibility of the proposed activity while maintaining the same overall objective (see Table 1 and Figure 4). Each action of the three series performed by an actor is videotaped so that the videos show only the hand and arm from the first perspective; each video is then edited to last 3 minutes. A right-handed actor uses one or two hands for unimanual and bimanual exercises respectively for participants with right UCP. For the left UCP the previous videos where reversed if they maintained the same characteristic of the setting and of the hand movement, while the remaining videos where specifically videotaped.

Table 1. List of goal-directed actions planned for the AOT training grouped in unimanual (white cells) and bimanual (grey cells) actions

Days	Action a	Action b	Action c
1	Uncover a little ball by lifting a box	Place a little ball in a glass	Fill a glass with water
2	Pick coloured card and match it to the same colour	Move a coloured card and place it on a base	Pick a card and place it on the similar one
3	Pick up a rubber stamp and move from/to different positions	Pick up a rubber stamp and press it against horizontal plane to print a figure	Pick up a rubber stamp and press it against sloping plane to print a figure
4	Pick up coin, put it in piggy bank through the slot on the top OR Pick up a magnet and place it on a horizontal magnetic board	Pick up coin, put it in piggy bank through the vertical slot on the side OR Pick up a magnet and place it on a sloping magnetic board	Pick up coin, put it in piggy bank through the horizontal slot on the side OR Pick up a magnet and place it on a vertical magnetic board
5	Pick up a wooden rubber stamp and move to	Pick up a wooden rubber stamp and press it against	Pick up a wooden rubber stamp and press it against

	different positions	horizontal plane to print a figure	sloping plane to print a figure
6	Move a spray can OR Move the bottle with a little ball inside	Place the spray can on a support OR Remove a little ball from the bottle	Put the spray can into a cup OR Press the catapult and launch a little ball
7	Move a container filled with shimmy powder	Open the container	Sprinkle shimmery powder on a paper
8	Place magnetic fish on a paper	Pick up fishing rod and catch magnetic fish	Pick up magnetic fish and place them in a container
9	Move a hole punch	Insert a sheet of paper and make holes	Match holes on sticks
10	Wet a cloth placing it in a container with water	Wring cloth and place it in a plate	Open a toy washing machine and insert the cloth inside
11	Pick up a card and place it on a support	Pick up a card and insert it in a clothespin	Pick up a card and insert it in a clothespin in a different orientation
12	Pick up and handle a piece of Play-Doh	Divide it in two pieces	Open a toy oven and insert a saucepan (with Play Doh in it)
13	Search for coin in the bag and place it on a support	Take the coin and insert it in a wallet	Open a box and place the wallet inside
14	Open a tube of tempera paint	Wet a brush with tempera paint	Make figure using a stencil with the brush dipped in tempera paint
15	Move a glitter glue tube	Open it	Decorate a frame by pasting pieces of mosaic

Experimental training

Before delivering the Tele-UPCAT platform, the training will be customized individually for each participant. The rehabilitation staff will select, on the basis of age and HFCS level, from the library the most appropriated AOT rehabilitation packages for each participant, then the engineers will upload them in the Observational Module (OM). For the Motor Performance Module (MPM), the therapists will organize a container of all the objects identifying them with numbers relative to the training day (e.g. little ball number 1 which means day 1 of the training). In addition, a dedicated printed manual with instructions and guidelines related to the different steps of the training and for system management and the setup will be provided. The manual contains also all the contacts of both technical and rehabilitation staff for remote assistance in case of any problems during the training. Two Actigraphs (wGT3X-BT, wActiSleep-BT) will be initialized for the recording period (3 weeks) to be worn on each wrist.

The ICT platform will be delivered to the participant's home by the engineers that are in charge of the installation of the system. The families will identify a designated position with a table or a desk of about 80x100 cm near to a socket where the ICT platform will be placed. Engineers and rehabilitation staff will train both parents and participants about the correct use of the system, including safety aspects. During the first two training days, a therapist will visit each participant and their parents to confirm the set-up.

During the training sessions, each participant will sit on a chair with both arms placed on a table in front of a platform positioned at about 1 m. Especially when the participant will be a child, a parent will be seated on her/his more impaired side to prompt attention during task execution and assist if necessary. The software will guide the participant in the sequence of observations and executions.

Standard care
Participants previously allocated in the standard care group will continue their usual care for 3 weeks. Usual care for recruited participants could be consisted for physical or occupational therapy. The frequency and the type of all therapies will be recorded accurately by a diary in both groups.

Outcome measures

Description of sample

Children participating in the study will be classified according to HFCS, which assesses function of the impaired hand in children with CP.[35, 36] This classification consists of 9 grades ranging from a hand that is not used at all (grade 0) to one that is used spontaneously and independently from the other one (grade 8). Due to the general approach in classifying hand functional level, this scale can also be easily applied to young adults with UCP. HFCS will be used for all ages as a criterion for inclusion in this study (from grade 2 to grade 8). In addition, they will be classified according to the Manual Ability Classification System (MACS), a classification system of the child's ability to handle objects in daily activities on one of five levels. [45]

Primary outcome measure

On the basis of our scientific hypothesis and according to previous clinical experience, [18, 19] the primary outcome measure will be the AHA. The latest version 5.0 will be used. This assessment measures UL function during bimanual activities by evaluating spontaneous use of assisting hand during a semi-structured age-appropriated 10-15-minute session with specific toys or objects requiring bimanual handling. The school-kids form will be used for the assessment of UCP children 6-12 years old [24, 25] while the Adolescent version (Ad-AHA), using the board game "Go with the Floe", [26] will be completed with participants older than 13 years. This last version, even if validated up to 18 years, will be used with potential participants 18-20 years old to guarantee the same assessment across all participants regardless of age. Moreover, AHA has been already used, even if not validated, in young people with UCP [46, 47]. The scale uses a Rasch measurement model which is a method to convert raw scores into a linear measure located on a unidimensional scale and more specifically to convert them into 0 to 100 logit-based AHA units, that will be used for the statistical analyses. All AHA assessments will be videotaped in a standardised manner and the subsequent scoring will be carried out by a certified expert rater who will be masked to group allocation and assessment order [24-26].

Other outcome measures
Other secondary measures will include measures of unimanual capacity (MA-2, [27] and BBT [28]) and bimanual daily activities at home and in the community (ABILHAND-Kids). [29] Moreover, participation and quality of life will also be assessed. All assessment will be performed at T0, T1, T1 plus, T2 and T3 unless otherwise indicated. Questionnaires will be completed by parents and/or participants at home and if doubts will occur, child neurologists or therapists will be available to discuss face to face items not clear to them.

i. The Melbourne Assessment 2 (MA2) [27] measures unilateral UL function and it is a valid and reliable tool for evaluating quality of UL movement in children with neurological

conditions for ages between 2.5 and 15 years. MA2 is a criterion-referenced test that extends and refines the scale properties of the original Melbourne Assessment (MUUL) and like MUUL it can also be used for adolescents and young adults. MA2 measures four elements of UL movement quality: movement range, accuracy, dexterity and fluency. It comprises 14 test items of reaching, grasping, releasing and manipulating simple objects. The test is administered by video recording the child's performance for subsequent scoring (30 items score). A raw score is provided for each of the four sections (Movement Range, Accuracy, Dexterity and Fluency) that will be analysed separately. It predominantly includes concepts within the body function domain as well as in the activity domain. Even if the MUUL and also the MA-2 have been validated up to 15 years, the first one has been used in studies involving patients with CP older than 15 year and in adults. [46-47] We have chosen to use the MA-2 also for participants older than 15 years to guarantee the same assessment across all participants regardless of age instead of using other scales (e.g. the Fugl-Meyer Assessment or the Action Research Arm test). [48]

ii. Box and Block Test (BBT) is a quick (2-5 minutes), simple and inexpensive test which measures unimanual dexterity in the activity domain. BBT is composed of a test box with a partition in the middle and 150 wooden blocks (25mm). The patient had to transport as many blocks as possible in 1 minute from one compartment to another. Firstly, the patient is asked to perform the test with the unaffected hand and then with the affected hand. The number of blocks transported by affected hand in 1 minute will be counted and considered for the main analyses. It can be used for a wide range of populations from childhood to adulthood. [28]

iii. ABILHAND-Kids [29] is a semi-structured item-response questionnaire on a 3-point ordinal scale (impossible, difficult, easy) that measures daily manual activities referred to in the activity domain of ICF. Parents will be instructed to rate their child's perceived difficulty in performing each activity taking account the performance of their child when performing the activity without technical or human assistance, regardless of the limb(s) and the strategies used. It has been validate for children aged 6-15 years but it has been used for larger ranges (6-19 years). [49] The questionnaire has been developed using the Rasch measurement model which provides a method to convert the ordinal raw scores into a linear logit measures located on a unidimensional scale, that will be used for the analyses. This questionnaire will be used at all assessment periods.

iv. Participation and Environment Measure - Children and Youth (PEM-CY). [30, 31] It is a parent-reported instrument that evaluates participation and environment across home (ten items), school (five items) and community (ten items) settings. For each item, the parent is asked to identify how frequently (over the past four months) the child has participated (eight options: daily to never); how involved the child typically is while participating (five point scale: very involved to minimally involved); and whether the parent would like to see the child's participation in this type of activity change (no or yes, with five options for the type of change desired). For each setting, the parent is then asked to report on whether certain features of the environment make it easier or harder for the child to participate. The following summary scores will be obtained: total score and score for each of the three setting-specific environmental supportiveness (home, school, community). Moreover the total number of supports and the total number of barriers will be computed. This questionnaire will be used at T0 and T3.

v. Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years) evaluate quality of life in children and adolescents with CP. [32-34] A score on a 0-100 scale will be obtained for each of computed sub-domains. In particular the Children form filled in by the parents assesses 7 subdomains (Social well-being and acceptance, Feelings about functioning, Participation and physical health, Emotional well-being and self-esteem, Access to services, Pain and impact of disability and Family health) and five subdomains

(excluding Access to services and Family health to the previous) for the children version. The Teen form evaluates 7 subdomains (General well-being and participation, Communication and physical health, School well-being, Social well-being, Access to services, Family health and Feeling about functioning) for the form filled in by the parents and 5 (excluding Access to services and Family health to the previous) for those filled in by the caregivers. These questionnaires will be used at T0 and T3.

vi. Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks, is a new assessment tool that consists of observation, followed by execution of three tasks of increasing difficulty (unimanual lifting, bimanual placing near and bimanual cooperation, holding and pulling) by means of a sensorized object. New technological tools such as sensorized objects can help in assessing the manipulation capabilities (reaching and grasping) in a quantitative but ecological way and the sensitivity to a training. Previous studies of the authors were focused on the development of sensozied toys for measuring infant's manipulation [50-52]. Starting from this experience, a new sensorized object has been designed and developed by the engineers tuning the sensors sensitivity and working range to the needs of participants with UCP.
Two load-cells and a switch embedded in the sensorized object allow for the measurement of the following parameters: grasping time, maximum grasping force and delay time between unaffected and affected hand in reaching for the object. This set-up is out of Tele-UPCAT system even if it was designed and developed in parallel.

vii. Quantitative measurement of bimanual activities will be performed in all the participants enrolled in the study by means of Actigraph GXT3+, as components of Motor Performance Module of Tele-UPCAT system. Actigraphs wGT3X-BT and wActiSleep-BT, equipped with a Velcro strap bracelet, will be worn, one for each wrists. As general rule, the experimental group have to wear the actigraphs not only during the training sessions but also between T0 and T1 and between T1 and T2 (total 6 weeks, 24 hours per day or as much as possible) while the control group are requested to wear them between T0 and T1, between T1 and T1 plus and, if possible also between T1 plus and T2 (total 9 weeks, 24 hours per day or as much as possible). All the daily activities, experimental training or usual care, or removal will be recorded in a dedicated diary. The Actigraphs will also be worn, by all the participants, during each time point of clinical assessments with the outcome measures. Data will be mainly relative to the asymmetry index (AI), that is the difference between the mean activity of the dominant with those of the non dominant hand and it will be correlated with the clinical scores obtained in the clinical outcome measures (mainly AHA).

viii. Cost effectiveness: A within trial cost-utility analysis will be conducted to synthesise the costs and benefits of the training program. Resource use (staff time, equipment and facility use) associated with the program will be collected alongside the RCT. Health care utilisation will be collected using a resource use questionnaire previously used in CP studies. [53] Health utility will be derived from the adapted CHU-9D, [54] a quality of life measure designed specifically for economic evaluation and which has been validated in an Australian population. [55-57]

ix. A semi-guided face to face interview (Supplement material 4) about the acceptability of the training will be completed immediately after the training period (T1 or T1 plus). It will be performed by the rehabilitation staff with the aim of investigating participant's and parents' opinions about the training in terms of customization of exercises, suitability to UCP children, feasibility at home, required effort by the participants and acceptability of Actigraphs, suitability of the manual and of the software will be recorded.

Statistical analyses

Clinical data will be analysed by means of the Statistical Package for Social Sciences (SPSS). Means and standard deviation of clinical outcome scores for both groups will be calculated to identify potential baseline differences between groups. As a first step, normality of distributions will be verified by Shapiro-Wilk's test. Between-group differences for all selected outcome measures will be evaluated at T0, by means of t-test for unrelated samples or non-parametric Mann–Whitney U independent sample test, for normal or non-normal distributed data, respectively. To test our first hypothesis, an intention to treat analysis will be carried out, evaluating between-group differences (delta scores) for primary and secondary outcome measures at the primary endpoint (T1), compared with T0 (T1-T0), by means of parametric or non-parametric tests for unrelated samples. The age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver, acceptability of therapy (measured by semi structured interview) will be analysed for further secondary exploratory analyses (e.g. regression modelling) in order to determine if some of these variables are predictive of better responses to the Tele-UPCAT training. In addition, a matched-pairs test (t-tests or Wilcoxon) will be carried out in order to assess retention of effects at follow-up periods (T1 or T1 plus, T2 and T3) relative to assessment before AOT training (T0 or T1 for experimental or waitlist group respectively). Bonferroni corrections will not be carried out in relation to the exploratory nature of the current RCT study and the relative small number of the study sample. To detect if significant changes will correlate to HFCS levels, a correlation analysis between score changes after AOT training (T1 or T1 plus) and assessment before AOT training (T0 or T1) will be carried out. Finally, an exploratory within-group analysis will be performed for the waitlist group comparing changes during AOT with respect to those of the first standard care period.

ETHICS AND DISSEMINATION

This study protocol describes background, hypotheses, system, clinical and technological outcome measures for a RCT designed to evaluate the Tele-UPCAT system as a new approach to deliver AOT to children and young people with UCP at home.
Full ethical approval has been obtained from the Tuscany Paediatric Ethics Committee (169/2016, Protocol Version 5.0 of 10/11/2016) and any deviations from the protocol will be promptly notified to this Ethic Committee and applied only after its approval. The trial has been registered at http://www.clinicaltrials.gov (identifier NCT03094455). This study protocol is reported according to the SPIRIT statement (SPIRIT 2013) [38] and the TIDier guidelines [39, 40]. We anticipate that the results of this study will be disseminated through peer reviewed journals and national and international academic conferences only by the professionals directly involved in the clinical trial. The results of this study will be of interest for rehabilitation trials based on AOT paradigm. Referring to a previous RCT study, [18, 19] we suggest that the home setting might increase accessibility of rehabilitation to a large number of children and young people with UCP (e.g. participants that live far from the clinical centres) with a large range of hand impairments (including also participants with HFCS level lower than 6) and older age (5-20 years instead of 5-15). Moreover, if the Tele-UPCAT study, using a very simple ICT solution, demonstrates to be viable for delivering AOT at home with significant improvements in UL daily activities, it could lead to the application of new solution for cost efficient rehabilitation programs. Implementation of new smart technologies can i) provide user-friendly AOT programs at home; ii) remotely manage treatment by rehabilitation staff thus increasing the ratio 'number of patients per therapist'; iii) offer individualized and intensive training. It could become an economical and efficient rehabilitation program by achieving significant long-lasting effects in UL activity and participation through an easily implementable paradigm that could become an integral part of common clinical practice. Finally, this approach could become a rehabilitation tool and be applicable to broader populations of CP and other chronic disabilities.

PROJECT STATUS

This project began recruitment the 29 March 2017, and we expect to complete data collection for the last training the November 2017 and close the project in the April 2018.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHOR'S CONTRIBUTION

GS is the principal investigator of the project and mainly responsible of the clinical part of it while FC is the main responsible of the ICT platform. GS, EI, HF, KK, RB, AF and GC designed the research study. GS, EB, EI, SP and EB were responsible for the AOT library. GS, SP and ES were in charge for participants' recruitment in Pisa and identification of type of exercise and software and AF for Reggio Emilia. GS and EB will collect the data and will monitor the training. FC, IM, MM and FFP with the supervision of PD have designed and built the new platform. GS and GC will take the lead roles on preparation of publications on the clinical outcomes of the study.
All authors have read and approved the final manuscript.

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Figure 1. Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: -Participation and Environment Measure - Children and Youth

Figure 2. Schedule of enrolment, interventions, and assessments.

Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected in the Clinical Interface (2) by the clinical staff in relation to HFCS level (6-8, 4-5 or 2-3), Side of impaired hand and Type of interface. A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3) for Teenagers or little Boys and Girls. The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists and a Button. The integrated camera records subject's attention during the observation task and exercise execution.

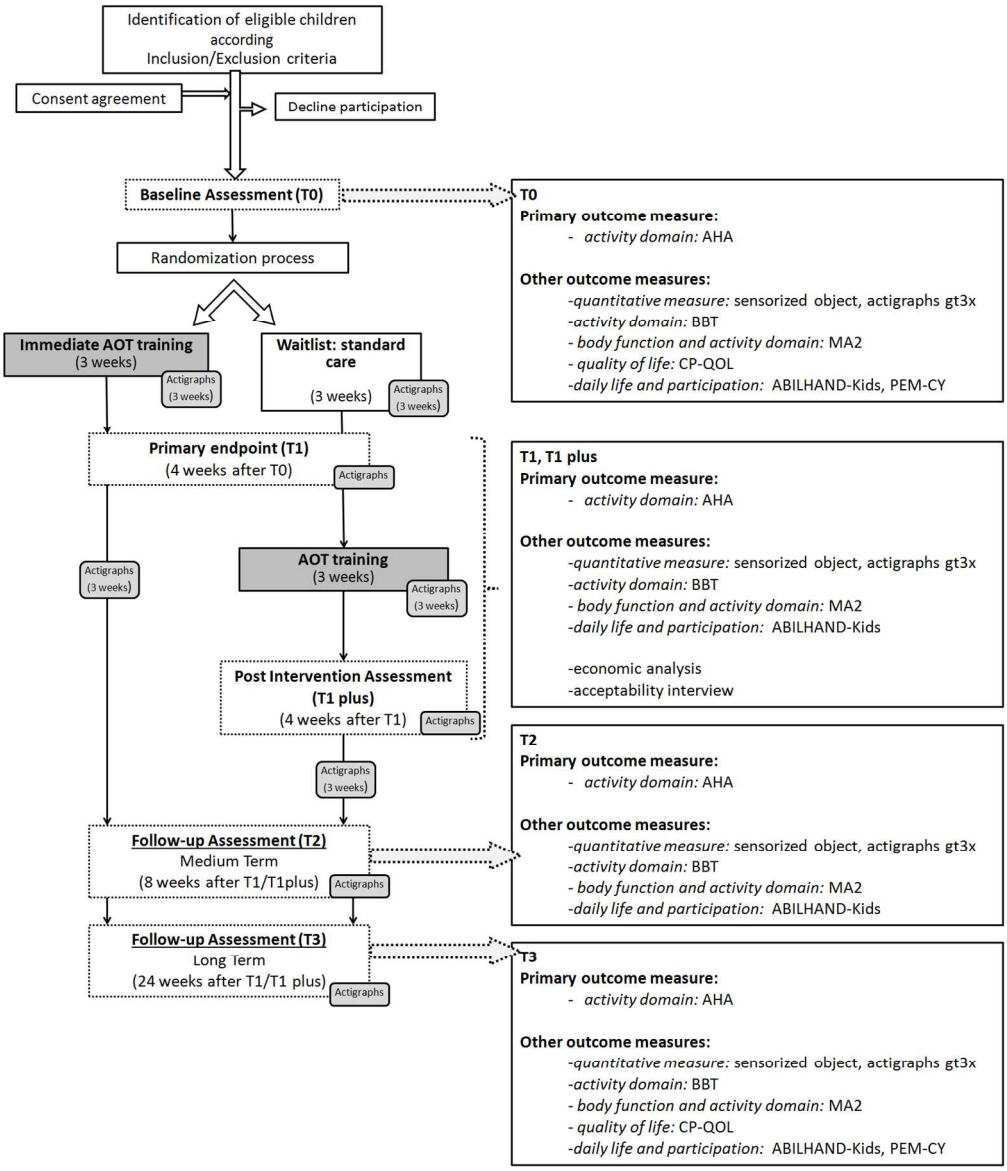
Figure 4. a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. **b)** Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

Supplement material 1. SPIRIT and TIDier checklists

Supplement material 2. Written informed consents (in Italian language)

Supplement material 3. Written informed consents (in English language)

Supplement material 4. Tele-UPCAT acceptability interview



Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: - Participation and Environment Measure - Children and Youth

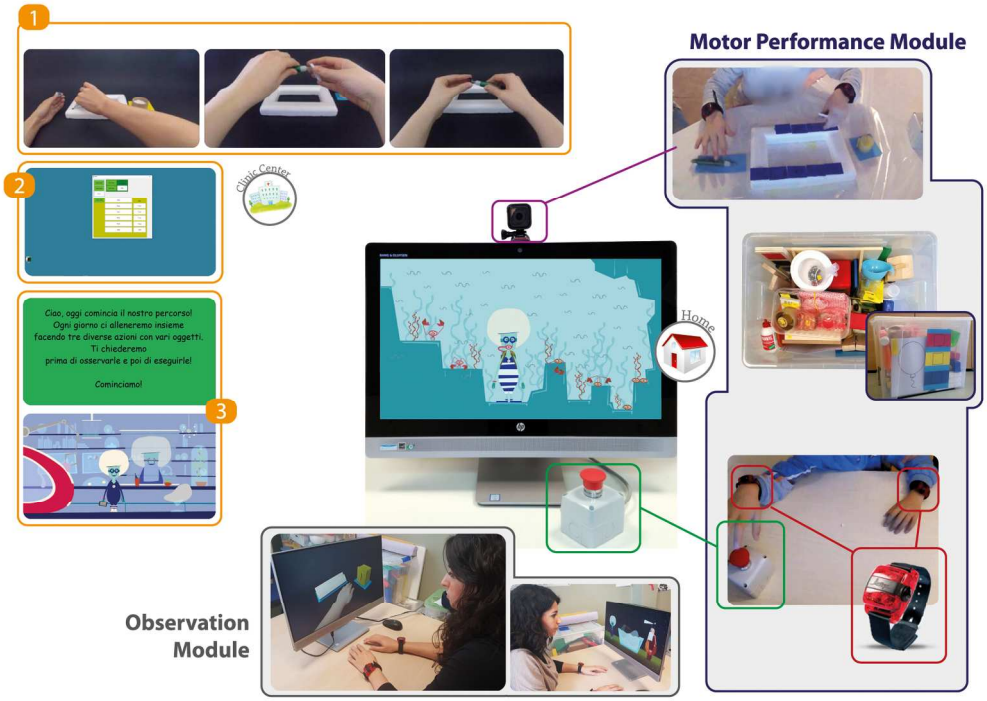
141x163mm (300 x 300 DPI)

	STUDY PERIOD				
	Enrollment	Post-allocation			
TIMEPOINT**	*T0*	*T_1*	*T_1 plus**	*T_2*	*T3*
ENROLLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation	X				
INTERVENTIONS:					
AOT intervention					
Wait list control group	←	→			
ASSESSMENTS:	←	→	←	→	
AHA	X	X	X	X	X
MA 2	X	X	X	X	X
BBT	X	X	X	X	X
ABILHAND-Kids	X	X	X	X	X
CP QoL	X				X
Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks	X	X	X	X	X
Quantitative measurement of bimanual upper limb activities by means of Actigraph GXT3+	X	X	X	X	X
Economic analysis		X	X		
Acceptability interview		X	X		

* only for wait-list group

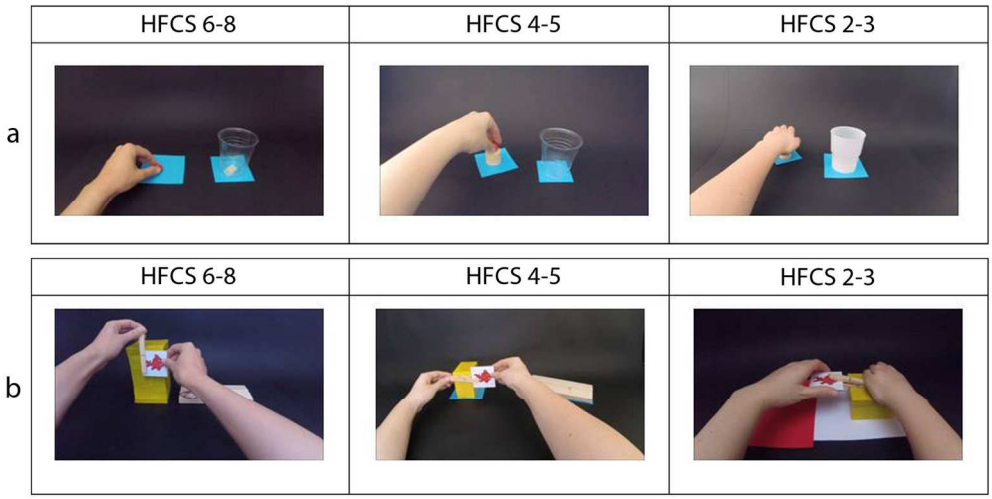
Schedule of enrolment, interventions, and assessments

60x88mm (300 x 300 DPI)



Caption : Caption : Caption : Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected in the Clinical Interface (2) by the clinical staff in relation to HFCS level (6-8, 4-5 or 2-3), Side of impaired hand and Type of interface. A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3) for Teenagers or little Boys and Girls. The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists and a Button. The integrated camera records subject's attention during the observation task and exercise execution.

170x120mm (300 x 300 DPI)



a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. b) Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal

170x83mm (300 x 300 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,13
	2b	All items from the World Health Organization Trial Registration Data Set	2,13
Protocol version	3	Date and version identifier	13
Funding	4	Sources and types of financial, material, and other support	2,13
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,13
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3,4
	6b	Explanation for choice of comparators	3,4
Objectives	7	Specific objectives or hypotheses	3,4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4,5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8,9
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	4
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5,6
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5,6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	4
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4,5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	5, 9-11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	5

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	5
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11, 12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11, 12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11, 12
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	5
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	5
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	5
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	12

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	5
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	5
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	12
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary material (2 and 3)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

TIDieR
Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	Page 2	_____
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	Pages 3-4	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	Pages 6-9	_____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	Pages 3-5	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	Pages 5-8	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	Pages 5, 8	_____
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	Page 8	_____

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	Page 6	_____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	Pages 6-8	_____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	_____N/A____	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____N/A____	_____
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	____N/A_____	_____

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

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MODULO INFORMATIVO
PER GENITORI/TUTORE LEGALE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentili Genitori/Tutore,
Le informazioni contenute nella scheda informativa seguente sono dettagliate e potrebbero risultare molto complesse.

Le chiediamo di accettare la partecipazione allo studio solo dopo avere letto con attenzione questo foglio informativo ed avere avuto un colloquio esauriente con il medico sperimentatore che le dovrà dedicare il tempo necessario per comprendere completamente ciò che le viene proposto.

Vostro/a figlio/a potrebbe essere idoneo a partecipare ad uno studio promosso dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni importanti riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non vi risultasse chiaro, potrete porre domande ai medici sperimentatori coinvolti dello studio. Prendetevi tutto il tempo necessario. La partecipazione di vostro/a figlio/a è volontaria e potrete ritirarla in qualsiasi momento.
Una volta che avrete letto questo modulo, avrete ricevuto risposta alle eventuali domande, e qualora decideste di far prendere parte vostro/a figlio/a allo studio, vi sarà chiesto di firmare un modulo di consenso, di cui riceverete una copia cartacea.

Cosa si propone lo studio

Vostro/a figlio/a è stato/a invitato/a a partecipare a questo studio per valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 bambini/adulti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei bambini che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 4 settimane; a termine delle quali i bambini di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i bambini saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T2). Per dettagli vedi Disegno dello studio Figura 1.

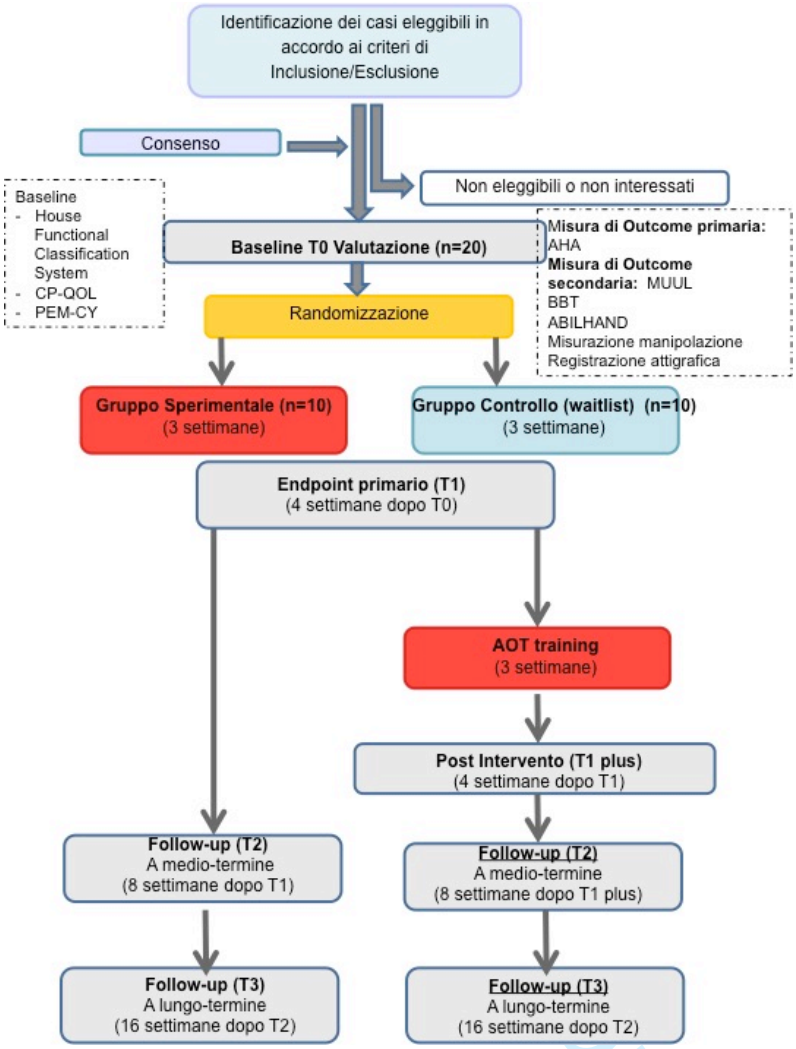


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i bambini arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolari di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I bambini che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i bambini allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la partecipazione allo studio

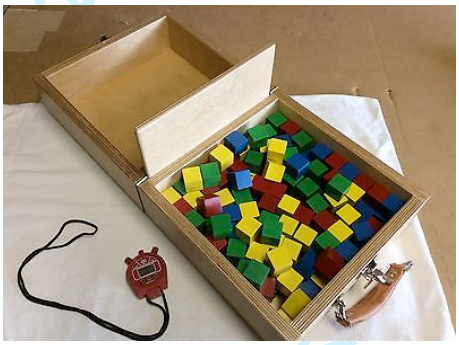
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



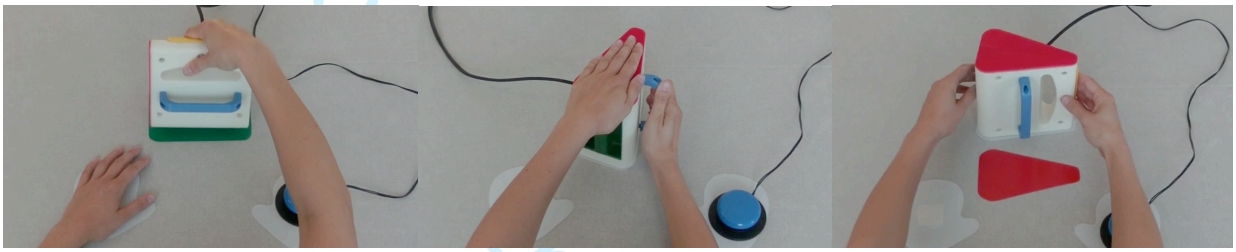
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND-Kids* è un breve questionario, validato in bambini con paralisi cerebrale infantile dai 6 ai 15 anni che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da un genitore in base alla difficoltà che ha il bambino a compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita nei bambini ed adolescenti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se doveste decidere di non prendere parte allo studio, o in caso doveste cambiare idea in seguito, vostro/a figlio/a non subirà alcuna penalità o perdita di benefici ai quali avrebbe altrimenti diritto. Le sue cure mediche attuali e future presso l'IRCCS

Fondazione Stella Maris non saranno compromesse dalla vostra decisione ed i medici continueranno a seguirlo/a con la dovuta attenzione.
Potrete ritirare l'adesione di vostro/a figlio/a allo studio in un qualsiasi momento dandone comunicazione al medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Procedure previste alla fine dello studio
Non è prevista alcuna procedura da attuarsi alla fine dello studio.

Informazione del medico di medicina generale /pediatra di libera scelta
Per la migliore tutela della salute di vostro/a figlio/a, vi verrà chiesto di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accettate di far partecipare vostro/a figlio/a.

Informazioni sui risultati dello studio
Qualora foste interessati, potrete chiedere al medico di comunicarvi i risultati generali dello studio ed in particolare quelli che riguardano vostro/a figlio/a.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i dati personali di Suo Figlio/a, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento

I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La partecipazione di Suo figlio/a allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione nella persona della Dr.ssa Giuseppina Sgandurra *, IRCCS Fondazione Stella Maris, Viale del Tirreno 331*. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la partecipazione di Suo figlio/a allo studio. In tal caso, i campioni biologici a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che riguardano Suo figlio/a, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi aggiuntivi a vostro carico derivanti dalla partecipazione allo studio. Non riceverete alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che vi è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data……..

Potrete segnalare qualsiasi fatto riteniate opportuno evidenziare, relativamente alla ricerca che riguarda vostro/a figlio/a, al Comitato Etico e/o alla Direzione sanitaria di questa struttura ospedaliera.

Per ulteriori informazioni e comunicazioni durante lo studio sarà a disposizione il seguente personale:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____

_____

Nome per esteso del medico che ha consegnato l'informativa | Data | Ora | Firma

CONSENSO INFORMATO PER GENITORI/TUTORE LEGALE

Versione 5.0 del 10/11/2016

Titolo Protocollo

Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Stella Maris, Prof. Giovanni Cioni IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 341/ ABC; 56128 Calambrone (Pisa), Italia Tel 050/886233.

e-mail: g.sgandurra@fsm.unipi.it

Io sottoscritta (madre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

Io sottoscritto (padre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

del minore _____ nato il ___/___/_____
residente a _____via/piazza _____

dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, della quale mi è stata consegnata una copia in data _____ alle ore _____ (indicare data e ora della consegna).

Dichiaro che mi sono stati chiaramente spiegati la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico.

DICHIARO inoltre che:

1. ho letto e compreso il foglio informativo fornito riguardo il progetto di ricerca e facente parte di questo consenso;
2. mi è stata data l'opportunità di porre qualsivoglia domanda allo sperimentatore dello studio e ho avuto risposte soddisfacenti;
3. mi è stato concesso il tempo sufficiente per riflettere sulle informazioni ricevute e per discuterne con terzi;
4. sono stato/a informato/a che il protocollo dello studio e tutti i moduli utilizzati hanno avuto il parere favorevole del Comitato Etico Pediatrico;
5. mi è stato chiaramente spiegato che posso decidere che il/la minore non prenda parte allo studio o ne esca in qualsiasi momento, senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
6. sono consapevole che la ricerca potrà essere interrotta in ogni momento, per decisione del responsabile della ricerca, senza pregiudizio per la salute del/della minore;
7. sono stato informato/a che sarò messo al corrente di qualsiasi nuovo dato che possa compromettere la sicurezza della ricerca e che, per ogni problema o per ulteriori domande, potrò rivolgermi ai medici presso i quali il/la minore è in cura;
8. per la migliore tutela della salute del/la minore, sono consapevole dell'importanza (e della mia responsabilità) di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accetto di far partecipare il/la minore; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici;

9. sono stato informato/a che i risultati dello studio saranno resi noti alla comunità scientifica, tutelando l'identità del minore secondo la normativa vigente sulla privacy.

10. sono consapevole che devo/dobbiamo ricevere una copia del presente modulo di consenso.

Sottoscrivendo questo modulo acconsento al trattamento dei dati personali di mio figlio/a e al loro trasferimento al di fuori dell'Unione europea (*da inserire se effettuato specificando gli estremi identificativi dei destinatari*) per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di:

□ **volere** □ **NON volere**
che il minore partecipi alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informati sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
informare il pediatra di libera scelta/medico di medicina generale della partecipazione allo studio (*è preferibile il suo coinvolgimento*)

_____ ___/___/_____ _____ _____
Nome per esteso del minore Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso Data Ora Firma
del genitore/tutore legale

_____ ___/___/_____ _____ _____
Nome per esteso Data Ora Firma
del genitore/tutore legal

Io sottoscritto Prof./Dr. …… (Cognome) …….. (Nome)

Dichiaro che i genitori/tutori legali del Paziente hanno firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle possibili alternative;
- aver verificato che i genitori/tutore legale abbiano sufficientemente compreso le informazioni fornitegli
- aver lasciato ai genitori/tutore legale il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato | Data | Ora | Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle "Modulo informativo per i genitori/tutore legale" dovrà essere consegnata ai genitori/tutori legali del Paziente

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
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MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

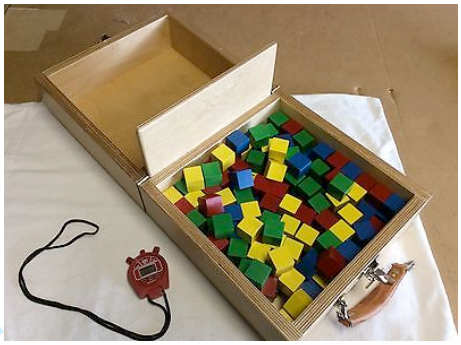
Perché facciamo questo studio?
La ricerca medica vuole migliorare la conoscenza sulle malattie.
Ti chiediamo di aiutarci a capire se l'uso di una terapia basata sull' osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato un' azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

Chi partecipa con me?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Che succede se partecipo?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo casuale ad uno dei due gruppi previsti nella prima fase dello studio: sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Inoltre ti saranno proposti, a dei tempi prestabiliti (quando ti arruoliamo, dopo che hai finito il trattamento o la fase di controllo, dopo che hai finito il trattamento se l'hai iniziato dopo, dopo 8 e dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!

Quanto durerà lo studio?
Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento). Ti verrà inoltre chiesto di effettuare i giochi e di compilare i questionari 3 o 4 volte.


Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?
Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?
Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio
Sei completamente libero di aderire o meno allo studio. Se deciderai di non partecipare, continuerai ad essere seguito periodicamente dalla tua equipe di riferimento del nostro centro clinico così come fatto fino ad ora.

Devo fornire il mio consenso per partecipare allo studio?
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare questo modulo di cui ti sarà data una copia.
Se decidi di non partecipare allo studio, o in caso dovessi cambiare idea in seguito, non succederà niente, continuerai a ricevere le cure a te necessarie presso questo ospedale.

E se dovessi avere delle domande?

Se hai delle domande puoi farle alla Dr.ssa Giuseppina Sgandurra durante il colloquio e potrai anche chiamarla al telefono al numero 050/886239: ti ascolterà e ti spiegherà tutto quello che desideri.

Data _____ ora _____ di consegna

_____Firma del medico che ha consegnato l'informativa

DICHIARAZIONE DI ASSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 6.0 del 29/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Il modulo informativo mi è stato consegnato il (data) _____ alle ore _____
Ho capito tutto quello che il medico mi ha spiegato.
Il Dottore ha ascoltato tutte le mie domande ed ha saputo rispondermi.
Se in futuro avrò bisogno di qualcos'altro i medici dello studio saranno a mia disposizione.

_____
Data e ora

_____
Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____
Firma del paziente. Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____ _____
Data/ora Firma del medico che ha informato il paziente

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
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ISO 9001 BUREAU VERITAS Certification

MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 17 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Caro/a ……,
potresti essere idoneo a partecipare ad uno studio proposto dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non ti risultasse chiaro, puoi porre domande ai medici dello studio. Prenditi tutto il tempo necessario. Non sei obbligato a partecipare. Se accetti, potrai decidere di ritirare la tua partecipazione in qualsiasi momento.
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue eventuali domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare il modulo di cui ti sarà data una copia.

Quale è lo scopo di questo studio?
Sei stato/a invitato/a a partecipare a questo studio perché pensiamo che puoi aiutarci a capire se l'uso di una terapia basata sulla osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato una azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

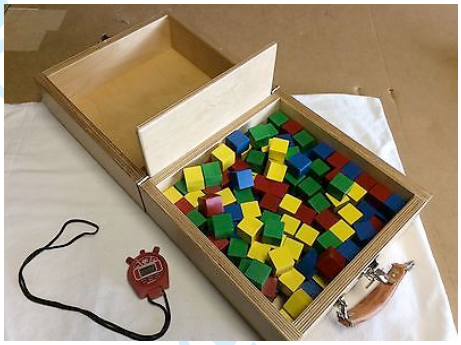
Quante persone parteciperanno?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Cosa comporta la partecipazione allo studio?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo random (casuale) ad uno dei due gruppi previsti nella prima fase dello studio:

sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre (durata 3 settimane) se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento).

Inoltre ti saranno proposti, a dei tempi prestabiliti (T0: quando ti arruoliamo, T1: dopo che hai finito il trattamento o la fase di controllo, T1 plus: dopo che hai finito il trattamento se l'hai iniziato dopo, T2: dopo 8 e T3: dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!



Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?

Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?

Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio o di ritirarmi dallo studio?

La tua partecipazione allo studio è volontaria.

Se decidi di non partecipare, o in caso dovessi cambiare idea in seguito, non subirai alcuna penalità o perdita di benefici ai quali avresti altrimenti diritto. Le tue cure mediche attuali e future presso l'IRCCS Fondazione Stella Maris non saranno compromesse dalla tua decisione ed i medici continueranno a seguirti con la dovuta attenzione.

Puoi ritirare la tua adesione allo studio in qualsiasi momento, comunicandolo al medico dello studio, la dottoressa *Giuseppina Sgandurra* senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che ti riguardano e potrai chiedere la cancellazione di quelli già raccolti. La tua partecipazione allo studio potrà essere interrotta se il medico valuterà che il nuovo trattamento non ha portato alcun giovamento o se si verificheranno effetti indesiderati. In questi

casi sarai tempestivamente informato dal medico e potrai discutere con lui circa ulteriori trattamenti validi per la tua patologia.

Cosa accadrà alle informazioni che sono state raccolte per lo studio?
Le informazioni mediche che ti riguardano come ad esempio l'età, il sesso, le caratteristiche della tua malattia, i risultati delle prove e il diario delle attività quotidiane saranno conservate presso un archivio della Fondazione Stella Maris.
I tuoi dati saranno archiviati in forma anonimizzata, il tuo nome sarà sostituito da un codice conosciuto solo da poche persone e quindi i tuoi dati saranno anonimi. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al tuo nominativo.
I dati dello studio potranno essere mostrati in occasione di convegni/congressi o pubblicati in riviste scientifiche per informare gli altri medici e i professionisti del settore sanitario.

Informazioni sui risultati dello studio
Alla fine dello studio sarai informato sui risultati della ricerca.

Ulteriori informazioni
Non sono previsti costi aggiuntivi a tuo carico derivanti dalla partecipazione allo studio.
Non riceverai alcun compenso economico per la partecipazione allo studio.
Il protocollo dello studio che ti è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data 22/11/2016.

Per ulteriori informazioni e comunicazioni potrai contattare il personale dello studio che sarà a tua disposizione:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha consegnato l'informativa — Data — Ora — Firma

MODULO DI CONSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 18 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Io sottoscritto (nome e cognome) _____
dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione allo studio in oggetto, secondo quanto riportato nel modulo informativo allegato, della quale mi è stata consegnata una copia in data _____ alle ore _____

Dichiaro che mi sono stati chiaramente spiegati la natura, lo scopo, i benefici attesi, i rischi e gli inconvenienti possibili dello studio clinico.

Dichiaro di aver potuto fare tutte le domande che ho ritenuto necessarie e di aver ricevuto risposte soddisfacenti, come pure di aver avuto la possibilità di informarmi in merito ai particolari dello studio con persona di mia fiducia.

Accetto dunque liberamente di partecipare alla ricerca, avendo compreso completamente il significato della richiesta e i rischi e benefici che possono derivare da questa partecipazione.

Acconsento al trattamento dei miei dati personali *e al loro trasferimento al di fuori dell'Unione europea (se applicabile)* per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

□ Desidero che mi siano comunicati i risultati dello studio.

__/__/____ _____ _____
Data Ora Firma del paziente

__/__/____ _____ _____
Data Ora Firma del medico che ha informato il paziente e registrato il suo consenso

FONDAZIONE
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Tel. 0571 419868

Gentile Sig.ra/Sig.re, le informazioni contenute nel seguente foglio informativo sono dettagliate e potrebbero risultare
MOLTO COMPLESSE

Le chiediamo di accettare la partecipazione allo studio SOLO dopo avere letto con attenzione questo foglio informativo ed avere avuto un COLLOQUIO ESAURIENTE con il medico sperimentatore che le dovrà dedicare il TEMPO NECESSARIO
per comprendere completamente ciò che le viene proposto

INFORMAZIONI SCRITTE
PER IL PAZIENTE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentile Signora / Egregio Signore,
Le è stato chiesto di partecipare ad uno studio clinico sperimentale e questo documento ha lo scopo di informarLa sulla natura dello studio, sul fine che esso si propone, su ciò che comporterà per Lei una tale partecipazione, sui suoi diritti e le sue responsabilità.
La prego di leggere attentamente queste informazioni scritte prima di prendere una decisione in merito ad una eventuale Sua partecipazione allo studio. Lei avrà a disposizione tutto il tempo necessario per decidere se partecipare o meno.
Potrà, inoltre, porre liberamente qualsiasi domanda di chiarimento e riproporre ogni quesito che non abbia ricevuto una risposta chiara ed esauriente.
Nel caso in cui, dopo aver letto e compreso tutte le informazioni ivi fornite, decidesse di voler partecipare allo studio clinico, Le chiederò di voler firmare e personalmente datare il modulo di Consenso Informato allegato a questo documento.

Che cosa si propone lo studio

Valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 soggetti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei soggetti che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 3 settimane a termine delle quali i soggetti di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i soggetti saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T3). Per dettagli vedi Disegno dello studio Figura 1.

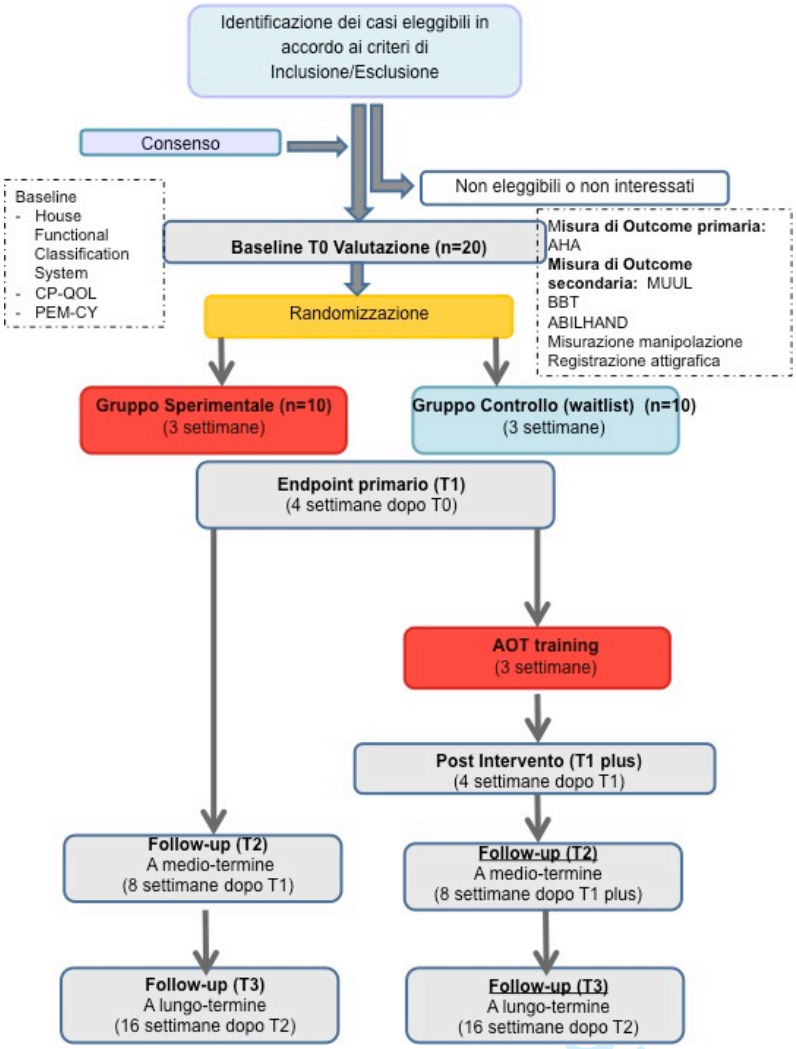


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i soggetti arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolati di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I soggetti che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i soggetti allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la Sua partecipazione allo studio

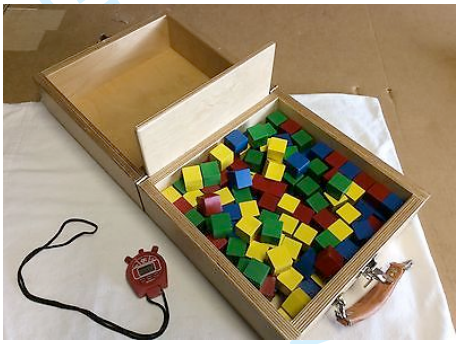
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



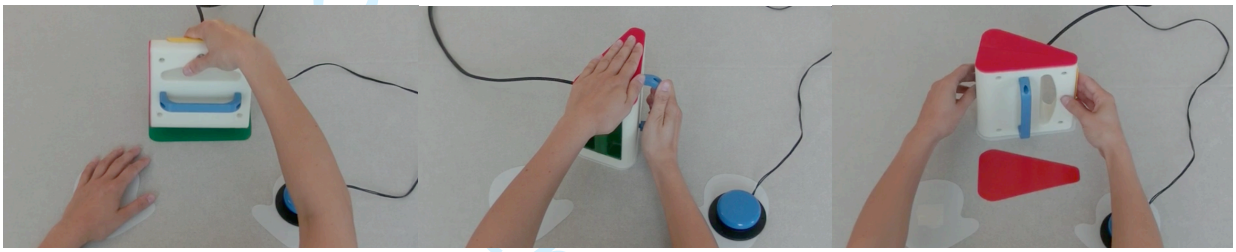
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni, ma utilizzati anche per l'età adulta. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND* è un breve questionario, validato in soggetti con paralisi cerebrale infantile che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da soggetto stesso in base alla difficoltà che esperimenta nel compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita in soggetti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se decide di partecipare, avrà il diritto di ritirarsi dallo studio in qualsiasi momento e senza l'obbligo di fornire spiegazioni, dandone tuttavia comunicazione al medico responsabile dello studio, la Dr.ssa Giuseppina Sgandurra.
Potrà ritirare la sua adesione allo studio in un qualsiasi momento dandone comunicazione al

medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Consenso ad informare il proprio medico di medicina generale
Per la migliore tutela della Sua salute, Le verrà chiesto di informare il Suo medico di medicina generale in merito alla sperimentazione alla quale accetta di partecipare.

Informazioni circa i risultati dello studio
Se Lei lo richiederà, alla fine dello studio potranno esserLe comunicati i risultati generali dello studio ed in particolare quelli che La riguardano.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:
Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all'età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento
I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti
Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi

direttamente al centro di sperimentazione nella persona della Dott.ssa Giuseppina Sgandurra. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. In tal caso, i dati acquisiti a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi a Suo carico derivanti dalla partecipazione allo studio. Non riceverà alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che Le è stato proposto è stato approvato dal Comitato Etico Pediatrico Toscano in data…… Il Comitato Etico ha tra le altre cose verificato la conformità dello studio alle Norme di Buona Pratica Clinica della Unione Europea ed ai principi etici espressi nelle Dichiarazione di Helsinki.

Lei potrà segnalare qualsiasi fatto ritenga opportuno evidenziare, relativamente alla ricerca che La riguarda, al Comitato Etico e/o alla Direzione Sanitaria di questa struttura ospedaliera.

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	g.sgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha consegnato l'informativa | Data | Ora | Firma

MODULO DI CONSENSO INFORMATO

V 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Io sottoscritto/a _____ nato/a il ___/___/_____ residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza) _____

DICHIARO

- di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, facente parte di questo consenso, della quale mi è stata consegnata una copia in data _____ alle ore _____ (*indicare data e ora della consegna*);
- che mi sono stati chiaramente spiegati e di aver compreso la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico;
- di aver avuto l'opportunità di porre domande chiarificatrici e di aver avuto risposte soddisfacenti;
- di aver avuto tutto il tempo necessario prima di decidere se partecipare o meno;
- di non aver avuto alcuna coercizione indebita nella richiesta del Consenso;
- che mi è stato chiaramente spiegato di poter decidere liberamente di non prendere parte allo studio o di uscirne in qualsiasi momento senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
- di essere consapevole dell'importanza (e della mia responsabilità) di informare il mio medico di medicina generale della sperimentazione alla quale accetto di partecipare; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici.

Sottoscrivendo questo modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di

□ **volere** □ **NON volere**
partecipare alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informato sui risultati di questa ricerca dal medico dello studio

□ **volere** □ **NON volere**
essere informato sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
Informare il medico di medicina generale della partecipazione allo studio

_____ ___/___/_____ _____ _____
Nome per esteso del paziente (adulto, minore maturo) Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso rappresentante legale Data Ora Firma

Io sottoscritto Prof./Dr. …… ……
Cognome Nome

Dichiaro che il Paziente ha firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito al Paziente esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle sue possibili alternative;
- aver verificato che il Paziente abbia sufficientemente compreso le informazioni fornitegli
- aver lasciato al Paziente il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato
Data Ora Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle “Informazioni Scritte per il Paziente” dovrà essere consegnata al Paziente stesso

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

PRESIDENTE
Avv. Giuliano Maffei
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DIRETTORE GENERALE
Dott. Roberto Cutajar
segreteria: Tel. 050 886271

DIRETTORE SCIENTIFICO
Prof. Giovanni Cioni
segreteria: Tel. 050 886233

DIRETTORE SANITARIO
Dott. Giuseppe De Vito
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INFORMATIVA E MANIFESTAZIONE DEL CONSENSO
AL TRATTAMENTO DEI DATI PERSONALI

Titolo Protocollo
Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233.
e-mail: g.sgandurra@fsm.unipi.it

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris in accordo alle responsabilità previste dalle norme della buona pratica clinica (decreto-legge n. 211/2003), tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine esclusivamente in funzione della realizzazione dello studio.
Il trattamento dei dati personali relativi tra cui età, sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano, raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati unitamente a tale codice, alla Sua data di nascita, al sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento
I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che, il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione. Sperimentatore principale Dr.ssa Giuseppina Sgandurra , IRCCS Fondazione Stella Maris. Viale del Tirreno 331, 56128 Calambrone (Pisa), *g.sgandurra@fsm.unipi.it.*

Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca.

Consenso

Sottoscrivendo tale modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

Nome e Cognome dell'interessato (in stampatello) _____

Firma dell'interessato _____

Data _____

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
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ISO 9001
BUREAU VERITAS
Certification

INFORMATIVE MODULE FOR PARENTS/LEGAL TUTORS

Version 5.0 of 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 5.0 V **and date** of 10/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear parents/legal tutor,
the information contained in this informative document are detailed and can be very complex. We ask you to accept the participation in the trial only after you have carefully read this document and have had an exhaustive conversation with the investigator that must devote the necessary time to fully understand what it is proposed.

Your son/daughter may be eligible to participate in a study of the IRCCS Fondazione Stella Maris. This module provides important information on the purposes, risks and possible benefits of this study. If some aspect of this module are not clear, you can ask questions to doctors researchers involved in the study. Take all the time necessary. Your son/daughter's participation is voluntary and you may withdraw it at any time. Once you have read this form, you will receive answers to any questions, and if you decide to take your son/daughter to study, you will be asked to sign a consent form, which you will receive a printed copy.

Which are the aims of the study

The study aims to evaluate the feasibility and effectiveness of the Action Observation Training (AOT) with regard to the standard care in home-based rehabilitation in children and adults with hemiplegia.

A second goal will be to measure and monitor the movements of the upper limbs through the use of actigraphs, simple commercial instruments such as watches (see below), whose data will be compared with the clinical results.

What is AOT?

The recent discovery of the Mirror Neuron System (SNS) has promoted the development of the Action-Observation Training (AOT), a therapy based on the observation of goal-directed actions followed by their motor replication as a model for motor learning.
AOT has been used with promising results in some studies in adult with stroke and recently also in children with Cerebral Palsy showing positive effects on the upper limb function. In particular, the IRCCS Fondazione Stella Maris (FSM) has carried out in a group of 24 children with hemiplegia Preliminary data support the hypothesis that AOT can improve the upper limbs function in children with hemiplegia. Based on these promising results, this study has been proposed.

The recruitment will be made by the FSM . We propose to select 20 participants aged between 5-20 years with unilateral cerebral palsy with a predominant spasticity pattern that interferes with the upper limb function; sufficient cooperation in the activities to be proposed; parents or legal tutor or adult with hemiplegia available to collaborate in 3- consecutive weeks of intensive home training program.

Recruitment will take place after the signing of informed consent by the subjects and/or by the parents or the legal tutor. The enrolled subjects will be divided randomly into two groups: experimental and standard care (control) groups. Subjects assigned to the experimental group will begin with the AOT for a period of 3 weeks, while those in the control or standard care will continue as they normally do by making a diary of any rehabilitation activities they conduct.
All subjects will be evaluated before (T0) and after (T1) the experimental / standard care period with standardized scales and tests. At the end of this period to those individuals who have not carried out the experimental training have the opportunity to carry out the training. The training will be offered with the same details and it will last three weeks at the end of which the subjects of this group will be re-evaluated with standardized scales and test (T1 plus). All subjects will be re-evaluated after 8 weeks from T1/T1 plus (T2) and after 16 weeks of T1 (T3).
These evaluations will be performed in order to evaluate the effects of training at short term (T1 and T1 plus) and at medium (T2) and long term (T3). For details see Study Design Figure 1.

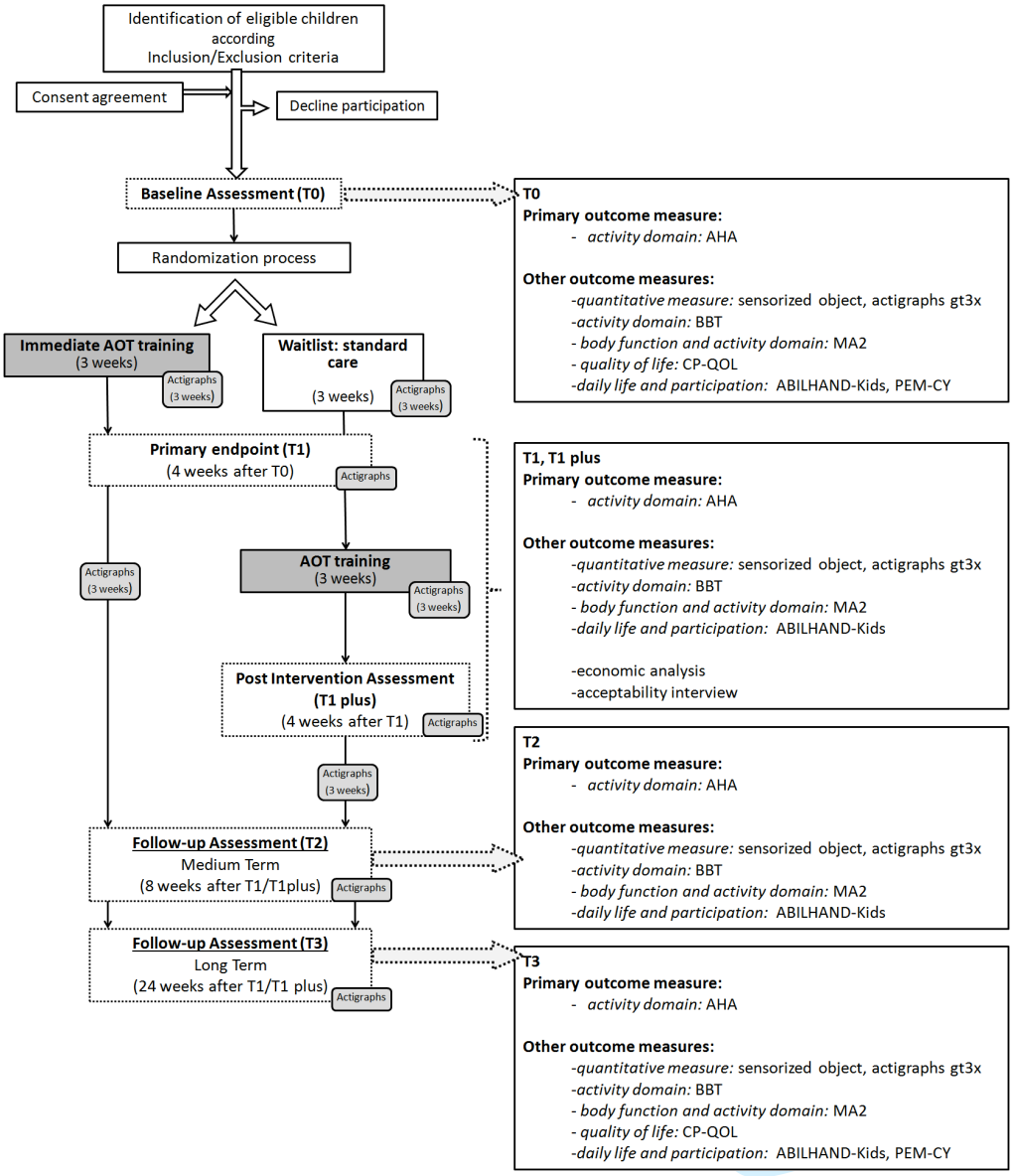


Figure 1: Flow-chart of Clinical Study

Summarizing all subjects will be assessed using standardized scales and tests at different times: T0, T1, T2, T3.

- T0: in the week before the beginning of the AOT training / standard care period
- T1: in the week after the AOT training / standard care
- T1 plus: in the week after the AOT training. This evaluation will be carried out only in the group of subjects who will undergo training in the second phase.
- T2: 8 weeks after the end of experimental training
- T3: 16 weeks after T2.

AOT training will be performed through a dedicated and personalized platform that will be delivered at home along with the useful material for training. The treatment will be performed by the participants, with the supervision of the parents, it will last about one hour per day, for 5 days a week for 3 weeks (total of 15 days). During the first two / three days of training, a therapist will support parents or adult hemiplegic subjects in the management of the training.

During the 3-week training sessions, the subjects will wear two actigraphs on the wrists (Figure 1) every day as long as possible. Subjects who will initially be allocated to the control group will be asked to keep a diary of any rehabilitation activities that they normally conduct and will be asked to wear actigraphs every day as long as possible, such as subjects assigned to the experimental group. It will be required to keep the actigraphs also in the 3 weeks following the end of the training.

The actigraph is a non-invasive motion accelerometer sensor that is worn on the wrist like a watch, is comfortable and water resistant. Today the actigraph is a trendy tool in use by youth and adults for fitness tracking and daily calorie consumption. The model used in this study is shown in the picture below.

Figure 2: wGT3X-BT

Recruitment will take place only after the informed consent has been given.
During the recruitment some clinical data (including age, gender, brain injury characteristics, affected side, manual functional level at the Home Functional Classification System) will be recorded and a dedicated database will be created.
To protect privacy and anonymity, to each subject will be assigned a numeric code that will be kept in separate form, so the database will not contain any identifying data. Access to such data will be restricted to the only staff directly involved in the study and all data will be processed in anonymous form.

What does your participation in the study involve?

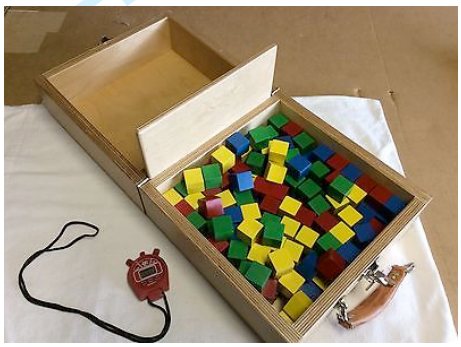
The study lasts 12 months, during this period a group of at least 20 children and young adults (5-20 years) with congenital hemiplegia will be enrolled at the IRCCS Fondazione Stella Maris . Participation will be voluntary on the basis of informed consent. The study will include a specific rehabilitation training, home-based AOT, through an ad hoc platform that will allow to conduct a personalized AOT training.

The clinical assessment (tests and questionnaires) is normally used for the functional evaluation in subjects with congenital hemiplegia:

The protocol will consist of the following tests:

1- Assisting Hand Assessment (AHA) is a scale that allows to evaluate manual and bimanual functionality.

2- Box and Block Test (BBT) is used to evaluate manual dexterity in which it is required to grasp, one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute.



3- *Melbourne Assessment of Upper Limb Function (MA2)*. It is a standardized instrument for measuring the capacity and quality of movement of the 'upper limb in children with Cerebral Palsy aged between 2 and 15 years, but it is also used for adults. It will be used at all evaluation times.

4- *ABILHAND* is a short questionnaire, validated in patients with cerebral palsy that measures 21 daily bimanual activities. The rating is assigned by the subject or the parent based on the experiences in daily accomplish, each task has a score of 3 points (impossible, difficult, easy). It will be used at all evaluation times.

5- *Participation and Environment Measure - Children and Youth (PEM-CY)*. This is a measure of participation and environmental factors at home, at school and in the community. It will be used at T0 and T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL -child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL -Teen, 13-18 years)*. These questionnaires are used to assess the quality of life in people with cerebral palsy. It will be used at T0 and T3.

7- *instrumental measurement of the manipulation during uni and bimanual tasks executed after observation.* It is an object containing two load cells to measure the force exerted (compression or traction) when grasped by the plegic hand and an on-off switch to evaluate the contact of the unaffected hand. An additional switch is placed at the starting point on the table under the more affected hand to record the moment when it starts moving toward the object. The instrument is used immediately after viewing three manipulation tasks carried out with three different types of grip: a one-hand task performed with the more affected hand, a two-hand bimanual task for the two hands, and a two-hand co-operation task for the two hands.

TASK 1. TASK 2. TASK 3.

The entire evaluation will last approximately one hour.

8- The use of the a*ctigraph in daily life.* The recruited subjects wear two actigraphs (Figure 2) outside of the clinical evaluation on his wrists (one for each wrist) for three-week periods (AOT experimental phase, phase control, phase follow-up). At the end of the registration period, the actigraph will turn off themselves and will be returned directly or by mail service to the examiner.

Benefits from participation in the study

Based on the literature and the preliminary results obtained in our previous studies, we expected that AOT training could improve the use of the upper limb in everyday life activities.

Possible risks

There are no direct risks or side effect related to the participation.

Possible alternatives

The alternative is not participate in the study.

What happen if you decide to do not take part in the study or retire from the study

The participation is voluntary. If you decide to attend, you will be able to withdraw from the study at any time and without the obligation to provide explanations, however, by notifying the doctor responsible for the study, Dr. Giuseppina Sgandurra.
If this is the case, no additional data will be collected and you can ask for the deletion of those already collected.

Information of General practitioner /pediatrician
For the best protection of the health of your child, you will be asked to inform the family doctor/paediatrician of the participation on the trial.

Information about the results of the study
If you require it, at the end of the study, results of the study and, in particular, those concerning you may be provided.

INFORMATION RELATING TO PERSONAL DATA PROCESSING:
Treatment holders and their purpose
The IRCCS Fondazione Stella Maris in accordance with the responsibilities provided by the rules of good practice, will process your personal data, particularly on health essential to the objective of the study, other data related to your origin and to the characteristics of your medical condition only solely on the basis of your study. For this purpose, the data provided will be collected by the Testing Center and processed in anonymity and in the privacy of the data. The processing of personal data related to 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphic records are essential for conducting the study: the refusal to provide will keep you from participating.

Nature of data
The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored for at least 7 (seven) years from the end of the study in this code, to your date of birth, the 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphs records are necessary for carrying out the study. Only the physician and authorized clinicians will be able to link this code to your name.

Treatment Mode
Data, whether processed by electronic means, will only be published in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, in such a way as to guarantee the confidentiality of your identity.

Exercise of rights
You may exercise your rights under art. 7 of the Code (eg. Access to your personal data, integrate, update, correct and object to their treatment for legitimate reasons, etc.) Applying directly to the testing center in the person of Dr. Giuseppina Sg andurra. You may terminate your participation at any time without giving any justification. In this case, the acquired data related to you will be destroyed. Further data will not be collected for you, without prejudice to the use of those already collected to determine, without altering the results of the search: even for the data already collected, you may ask for the cancellation.

Further information

There are no charge costs due to participation in the study. You will not receive any financial compensation for participating in the study.

The protocol of the study proposed to you has been approved by the Tuscan Ethics Pediatric Committee on 22/11/2016. The Ethics Committee has, among other things, verified the compliance of the study with the European Good Clinical Practice and the ethical principles expressed in the Helsinki Declaration.

You may report any matter you may find relevant to the Ethics Committee and / or the Health Care Department of this hospital structure regarding the research you are concerned with.

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	g. Sgandurra @ fsm.unipi.it	

_____ ___ / ___ / _____ _____ _____

Name of Doctor's who delivered the information | Date | Time | Signature

INFORMED CONSENT FOR PARENTS/LEGAL TUTOR
Version 5.0 of 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*

Version 5.0 V **and date** of 10/11 / 2016

Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella M aris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

I signed (mother/guardian) _ born on ___/___/___ ___ living in _ Street _ phone _ address (if different from the residence) _ I, the undersigned (parent/guardian) _ born on ___/___/___ ___ living in _ Street _ phone _ address (if different from residence) _ of the child _ born on ___/___/___ ___ living in _ Street _

I acknowledge that I have received from Dr. _ the explanations regarding the request to participate in the research, according to the informative document, which I had a copy dated _ _ _ _ _ _ _ _ _ _ _ _ _ _ at _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ (indicate date and time of delivery). I declare that it have been clearly explained the nature, purpose, procedures, expected benefits, risks and possible drawbacks and alternatives of the trial.

DECLARE in addition that:

1. I have read and understood the information provided about the research project and the informative part of this document;
2. it was given the opportunity to ask any questions to the investigator of the study and I had satisfactory answers;;
3. it was allowed enough time to reflect on the information received and to discuss with third parties;
4. I have been informed that the study protocol and all the modules that are used have had a favourable opinion of the Ethics Committee;
5. It was clearly explained that I can decide that the child cannot s not participate in the study or can withdraw at any time, without providing justification, and that these

decisions will not change in any way the relationships with physicians and with the structure that are treating him;

6. I am aware that the research can be interrupted at any time by decision of the head of research, without prejudice to the health of the child;
7. I have been informed that I will be informed of any new information which might affect the safety of the research and that, for every problem or if I have additional questions, I can ask to doctors;
8. for the best protection of the health of the minor, are aware of the importance (and responsibility) to inform the family doctor/paediatrician of the trial to which I agree to involve the child
9. I was informed that the study results will be made available to the scientific community, while protecting the identitication of the child in accordance with current legislation on privacy
10. I am aware that I/we must receive a copy of this consent form

By submitting this form I consent to the processing of personal data of my child and to their transfer outside the European Union (to be entered if performed by specifying the identity of recipients) for the purposes of research in limits and in the manner specified in the information provided hereby.

DECLARE therefore that I:

□ **want** □ **DON'T WANT**
that my child participate
□ in one under clinical evaluation
□ both under clinical evaluation and at home

□ **want** □ **DON'T WANT**
I will be informed about the results of research by the doctor of the study, also in relation to the unexpected news that might be accidentally encountered with the investigations required by the study

□ **want** □ **DON'T WANT**
inform your paediatrician/general practitioner of your involvement in the study

_____ ___/___/_____ _____ _____

Complete name of the child Date Time Signature

_____ ___/___/_____ _____ _____

Complete name of the parent/caregiver Date Time Signature

_____ ___/___/_____ _____ _____

Complete name of the parent/caregiver Date Time Signature

I signed Prof./Dr. …… (Surname) ……..… (Name)

I declare that the parents/guardians of Patient signed spontaneously his participation in the study

I also declare to:

- providing comprehensive explanations of the purpose of the study, the procedures, the potential risks and benefits and possible alternatives;
- I have verified that the parents/legal guardian have sufficiently understood the information provided
- Having left to the parents/legal tutor the necessary time and opportunity to ask questions about the study
- I am not exercising any coercion or unjustified influence in the Consent's request

_____ ___/___/_____ _____

_____

Name of doctor whom deliver consensus Date Time Signature

NOTA BENE

a copy of this form, signed and dated, attached to "information form for parents/legal guardian" should be delivered to parents/legal guardians of Patient

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
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Tel. 0571 419868

ISO 9001 BUREAU VERITAS Certification

INFORMATIVE MODULE
FOR PATIENTS AGED 7-13 YEARS
Version 6 .0 of 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

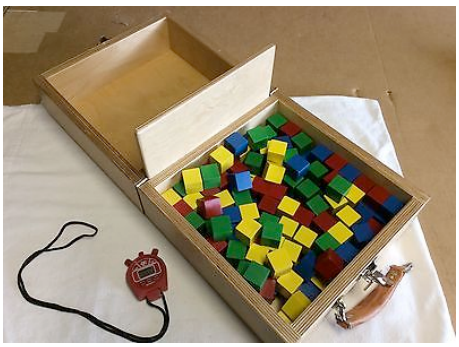
Why do we do this study?
Medical research wants to improve knowledge about diseases. We ask you to help us to understand whether the use of an "action observation-based therapy" may be helpful to improve the functionality of your affected arm. The observational therapy involves the viewing of short videos, to be observed carefully, which showed an 'action done with the hands and soon after you will be asked to perform the same movement trying to imitate as much as possible.
In addition we will ask you to wear bracelets, similar to a watch, to better measure and monitor the movements of your arms.

Who participates with me?
They will attend 20 children / teenagers and young adults aged 5-20 years. Everyone will be with similar motor difficulties like yours.

What happens if I participate?
If you decide to take part in the study at the beginning you will randomly assigned to one of two groups: experimental or control. If you will be assigned to the experimental group immediately you will begin a training based on action observation at home while if you will assigned to the control group you will be offered to wait about 4 weeks before starting the same type of therapy and in the meantime you will continue to do what you are doing now. So in each case you will do an action observation training immediately or after 4 weeks. In both cases you will be asked to wear bracelets, similar to a watch, on your wrists.
The therapy that you will do before or after is basically based on a computer program where "Ubi", an extra-terrestrial, will help you step by step in doing the exercises.

Additionally at a pre-set time (T0: when we enrol you, T1: T1: after the treatment or the control phase, T1 plus: after the treatment if you have started after, T2: after 8 weeks and T3: after 16 weeks from the end of the treatment) specific scales and questionnaires will be proposed to you and your parents that help us to understand how you use your hands!

How long will the study last?
The study will last one year. If you agree to join the study your participation lasts 3 weeks (treatment duration). You will also be asked to do the tests and fill out the questionnaires 3 or 4 times.



Some examples of games

There are benefits expected from my participation in the study?
We expect that this therapy could help you in improving the use of your hands

What are the risks of the study?
There are no risks because it is a very simple treatment which can be done safely at home and the assessments are those that normally you carry our during the clinical evaluation in the clinical centre.

What happen if I decide to do not take part in the study
You are completely free to join or not to the study. If you decide to do not participate, you will continue to be periodically monitored by your clinical team as well as done so far.

Do I have to give my consent to participate in the study?
Once you have read this information form and have asked your questions, you will decide if take part in the study. If you want to participate, you will need to sign this form for which you will be given a copy for you.
If you decide to do not take part in the study, or if you change your mind afterwards, nothing will happen, you will continue to receive the necessary care at this hospital.

And should I have any questions?
If you have any questions you can ask them to Dr. Giuseppina Sgandurra at the interview and can also call on the telephone number 050/886239: listens to you and explain to you everything you want.

Date _____ time _____ delivery

Signature of the Doctor who delivered the information

DECLARATION OF CONSENT
FOR PATIENTS AGED 7-13 YEARS
Version 6 .0 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

The information form was delivered to me on (date) _____ at _____
I understood everything the doctor explained to me.
The Doctor has listened to all my questions and has answered me.
If in the future I'll need something else, the doctors of the study will be at my disposal.

_____
Date and time

_____
Write your name here if you would like to take part in the study

_____
Signing the patient. Enter your name in the block here if you would like to take part in the study

_____ _____
Date hour Doctor's signature that informed the patient

FONDAZIONE
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ISO 9001 BUREAU VERITAS Certification

INFORMATIVE MODULE
FOR PATIENTS AGED 14 - 17 YEARS
Version 6 .0 of 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear ……..,
may be eligible to participate in this clinical study proposed by IRCCS Fondazione Stella Maris.
This module provides information on the purposes, risks and potential benefits of this study. If some aspect of this form does not make you clear, you can ask questions to doctors of the study. Take all the time you need. You are not obligated to participate. If you accept, you may choose to withdraw your participation at any time.
Once you have read this form and answered your questions, you will be asked to decide if you would like to participate in the study. If you want to participate, you will need to sign the form for which you will be given a copy to you.

What is the purpose of this study?
We are inviting you to participate in this study because we think that you can help us to understand if the use of action observation therapy can be helpful in improving the functionality of your arm. The action observation therapy involves the viewing of short videos, to be observed carefully, which shows an 'action done with the hands" and soon after you will be asked to perform the same movement trying to imitate them as much as possible. In addition we will ask you to wear bracelets, similar to a watch, to better measure and monitor the movements of your arms.

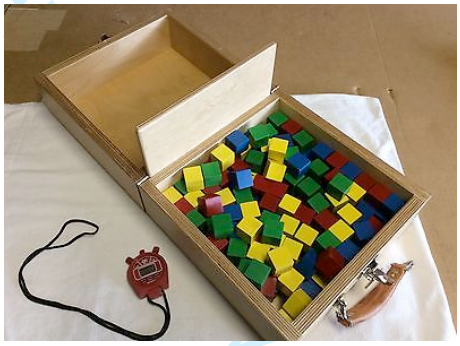
How many people will participate?
They will attend 20 children / teenagers and young adults aged 5-20 years. Everyone will be with similar motor difficulties like yours.

What does participating in the study mean?
If you decide to take part in the study at the beginning you will randomly assigned to one of two groups: experimental or control. If you will be assigned

to the experimental group immediately you will begin a training based on action observation at home (3 weeks) while if you will be assigned to the control group you will be offered to wait about 4 weeks before starting the same type of therapy and in the meantime you will continue to do what you are doing now. So in each case you will do an action observation training immediately or after 4 weeks. In both cases you will be asked to wear bracelets, similar to a watch, on your wrists. The therapy that you will do before or after is based on a computer program where "Ubi", an extra-terrestrial, will help you step by step in the exercises you do.

The study will last one year. If you accept to take part in the study your participation is 3 weeks (duration of treatment).

Additionally at a pre-set time (T0: when we enrol you, T1: T1: after the treatment or the control phases, T1 plus: after the treatment if you have started after, T2: after 8 weeks and T3: after 16 weeks from the end of the treatment) will be proposed specific scales and questionnaires that help us to understand how you use your hands!



Some examples of games

There are benefits expected from my participation in the study?
We expect that this therapy could help you in improving the use of your hands

What are the risks of the study?
There are no risks involved because it is a very simple treatment that you can done safely at home and assessments are those that normally our during the clinical evaluation in the clinical center.

What if I decide not to take part in the study or withdraw from the study?
Your participation in the study is voluntary.
If you decide to do not participate, or if you change your mind afterwards, you will not have any penalty or loss of benefits that you would otherwise have been entitled to. Your current and future medical care in the Fondazione IRCCS Stella Maris will not be affected by your decision, and doctors continue to follow you with due attention.
You can withdraw your participation in the study at any time communicating with Dr. *Giuseppina Sgandurra* providing any justification. In this case no additional data will be collected about you and you will be able to request the deletion of those already collected. Your participation in the study may be interrupted if your doctor evaluates that the new treatment has not benefited or if you

experience any side effects. In these cases, you will be promptly informed by your doctor and you will be able to discuss with him about further treatments that are valid for your condition.

What will happen to the information that was collected for the study?
The medical information about you such as age, sex, characteristics of your diseases, the results of the tests and the diary of daily activities will be kept in an archive of Fondazione Stella Maris.
Your data will be archived in anonym form, your name will be replaced by a code known only to a few people and your data will be anonymous. Only the physician and authorized persons will be able to link this code to your name.
Study data can be displayed at conferences/congresses or published in scientific journals to inform other doctors and health professionals.

Information on the results of the study
At the end of the study you will be informed on the results of the research.

Further information
There are no additional costs incurred from your participation in the study. You will not receive any financial compensation for participating in the study.
The study protocol have been written in accordance with the requirements of Good Clinical Practice and the Declaration of Helsinki, and was approved by the Ethics Committee of the Pediatric Tuscany Region on 22/11/2016.

For more information and communications, you can contact the study staff who will be at your disposal:

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	gsgandurra@fsm.unipi.it	

_____ ___ / ___ / _____ _____ _____
Name of Doctor's Date Time Signature
who delivered the information

INFORMED CONSENT
FOR PATIENTS AGED 14 -17 YEARS
Version 6 .0 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

I am signed (name and surname) _____ I declare that I have received information from Dr. _____ full explanations regarding the request for participation in the study in question, as indicated in the attached information form, of which I was given a copy on _____ at _____

I state that I have clearly understood the nature, purpose, expected benefits, risks and disadvantages of the clinical trial.

I declare that I have been able to do all the questions I have found necessary and have received satisfactory answers, as well as having been able to tell me about the details of the study with a person of my confidence.

I therefore agree to participate in the research, having fully understood the meaning of the request and the risks and benefits that may result from this participation.

I agree that my personal data *and their transfer outside the European Union (if applicable)* for research purposes to the extent and in the manner indicated in this document.
□ I wish the results of the study were communicated to me.

__ / __ / ____ _____
_____ Signature of the patient
Date hour
__ / __ / ____ _____ _____
_____ Doctor's signature that informed the patient and registered his consent
Date hour

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

PRESIDENTE
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56128)
Viale del Tirreno, 341/A-B-C angolo
Via dei Frassini, 1
Partita Iva 0012624 050 6
Centralino:
Tel. 050 886111

Dear Mrs / Mrs, the information contained in the following informative module is detailed and could be very complex

we ask you to accept the participation in the study ONLY after reading this carefully document and interviewing the investigator who will dedicate to you all the time necessary to fully understand what we are proposing to you

INFORMATIVE MODULE FOR THE PATIENT

Version 5.0 of the 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 5.0 V **and date** of 10/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear ____ ,
we ask you to take part in this clinical study, this document is intended to provide you all the information about the study: the purpose, what you will be asked, which are your rights and responsibilities. Read the information carefully before making a decision about your participation in the study. You will have all the time you need to decide whether you want participate or not.
You will be free to ask any questions until you have received a clear and comprehensive answer for yourself.
If, after reading and understanding all the information you decide to participate in the clinical trial, you will need to sign the Consensus Information Form attached to this document.

Which are the aims of the study

The study aims to evaluate the feasibility and effectiveness of the Action Observation Training (AOT) with regard to the standard care in home-based rehabilitation in children and adults with hemiplegia.

A second goal will be to measure and monitor the movements of the upper limbs through the use of actigraphs, simple commercial instruments such as watches (see below), whose data will be compared with the clinical results.

What is AOT?

The recent discovery of the Mirror Neuron System (SNS) has promoted the development of the Action-Observation Training (AOT), a therapy based on the observation of goal-directed actions followed by their motor replication as a model for motor learning.

AOT has been used with promising results in some studies in adult with stroke and recently also in children with Cerebral Palsy showing positive effects on the upper limb function. In particular, the IRCCS Fondazione Stella Maris (FSM) has carried out in a group of 24 children with hemiplegia Preliminary data support the hypothesis that AOT can improve the upper limbs function in children with hemiplegia. Based on these promising results, this study has been proposed.

The recruitment will be made by the FSM . We propose to select 20 participants aged between 5-20 years with unilateral cerebral palsy with a predominant spasticity pattern that interferes with the upper limb function; sufficient cooperation in the activities to be proposed; parents or legal tutor or adult with hemiplegia available to collaborate in 3- consecutive weeks of intensive home training program.

Recruitment will take place after the signing of informed consent by the subjects and/or by the parents or the legal tutor. The enrolled subjects will be divided randomly into two groups: experimental and standard care (control) groups. Subjects assigned to the experimental group will begin with the AOT for a period of 3 weeks, while those in the control or standard care will continue as they normally do by making a diary of any rehabilitation activities they conduct.

All subjects will be evaluated before (T0) and after (T1) the experimental / standard care period with standardized scales and tests. At the end of this period to those individuals who have not carried out the experimental training have the opportunity to carry out the training. The training will be offered with the same details and it will last three weeks at the end of which the subjects of this group will be re-evaluated with standardized scales and test (T1 plus). All subjects will be re-evaluated after 8 weeks from T1/T1 plus (T2) and after 16 weeks of T1 (T3).

These evaluations will be performed in order to evaluate the effects of training at short term (T1 and T1 plus) and at medium (T2) and long term (T3). For details see Study Design Figure 1.

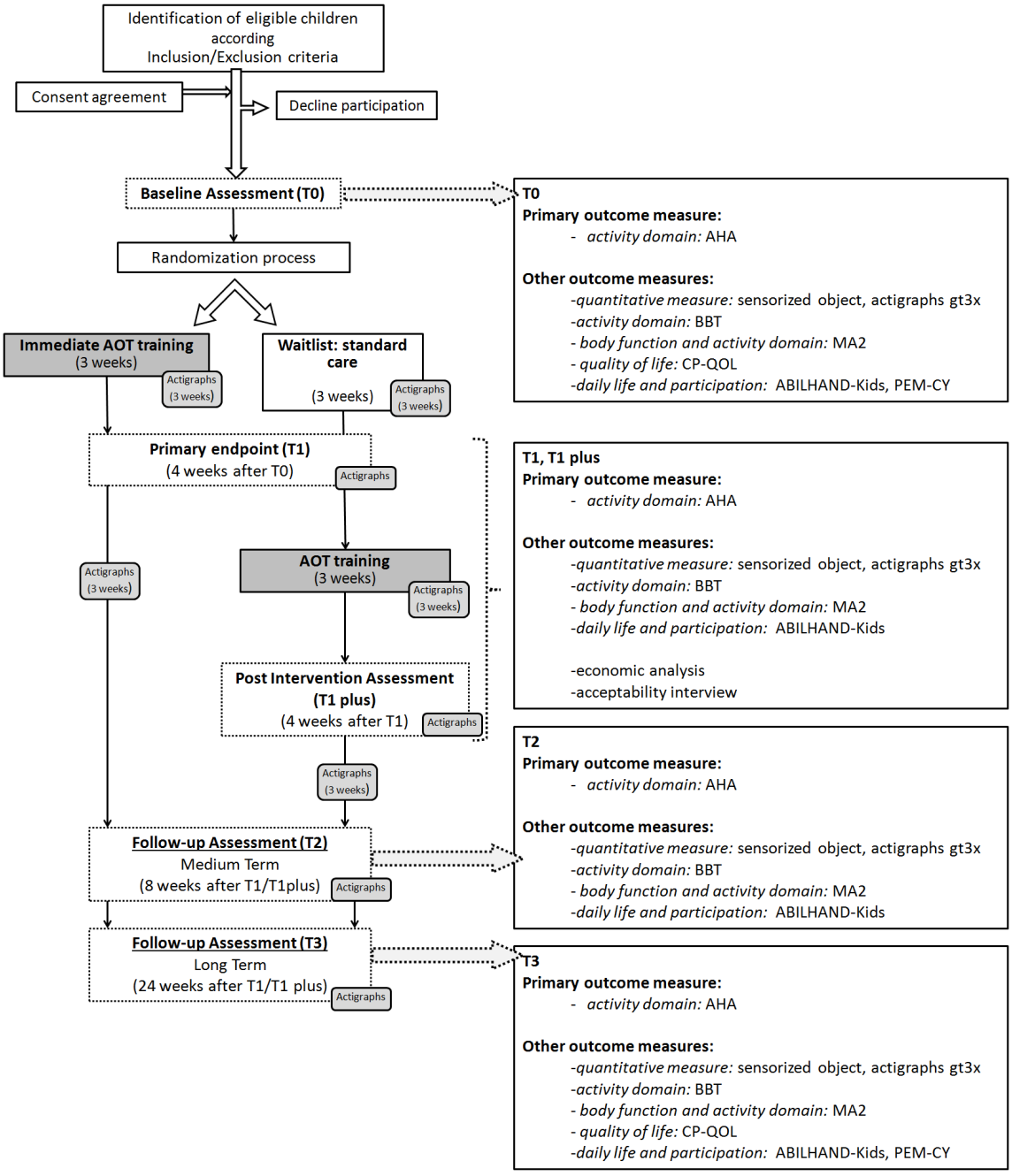


Figure 1: Flow-chart of Clinical Study

Summarizing all subjects will be assessed using standardized scales and tests at different times:
T0, T1, T2, T3.

- T0: in the week before the beginning of the AOT training / standard care period
- T1: in the week after the AOT training / standard care
- T1 plus: in the week after the AOT training. This evaluation will be carried out only in the group of subjects who will undergo training in the second phase.
- T2: 8 weeks after the end of experimental training
- T3: 16 weeks after T2.

AOT training will be performed through a dedicated and personalized platform that will be delivered at home along with the useful material for training. The treatment will be performed by the participants, with the supervision of their parents, it will last about one hour per day, for 5 days a week for 3 weeks (total of 15 days). During the first two / three days of training, a therapist will support parents or adult hemiplegic subjects in the management of the training.

During the 3-week training sessions, the subjects will wear two actigraphs on the wrists (Figure 1) every day as long as possible. Subjects who will initially be allocated to the control group will be asked to keep a diary of any rehabilitation activities that they normally conduct and will be asked to wear actigraphs every day as long as possible, such as subjects assigned to the experimental group. It will be required to keep the actigraphs also in the 3 weeks following the end of the training.

The actigraph is a non-invasive motion accelerometer sensor that is worn on the wrist like a watch, is comfortable and water resistant. Today the actigraph is a trendy tool in use by youth and adults for fitness tracking and daily calorie consumption. The model used in this study is shown in the picture below.

Figure 2: wGT3X-BT

Recruitment will take place only after the informed consent has been given.
During the recruitment some clinical data (including age, gender, brain injury characteristics, affected side, manual functional level at the Home Functional Classification System) will be recorded and a dedicated database will be created.
To protect privacy and anonymity, to each subject will be assigned a numeric code that will be kept in separate form, so the database will not contain any identifying data. Access to such data will be restricted to the only staff directly involved in the study and all data will be processed in anonymous form.

What does your participation in the study involve?
The study lasts 12 months, during this period a group of at least 20 children and young adults (5-20 years) with congenital hemiplegia will be enrolled at the IRCCS Fondazione Stella Maris. Participation will be voluntary on the basis of informed

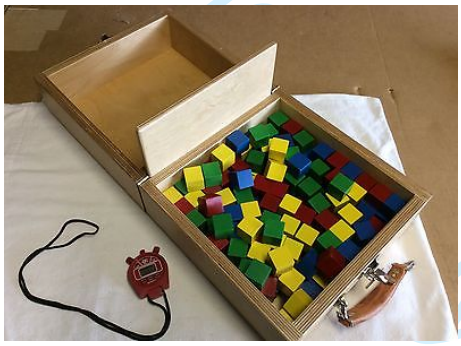
consent. The study will include a specific rehabilitation training, home-based AOT, through an ad hoc platform that will allow to conduct a personalized AOT training.

The clinical assessment (tests and questionnaires) is normally used for the functional evaluation in subjects with congenital hemiplegia:

The protocol will consist of the following tests:

1- Assisting Hand Assessment (AHA) is a scale that allows to evaluate manual and bimanual functionality.

2- Box and Block Test (BBT) is used to evaluate manual dexterity in which it is required to grasp, one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute.



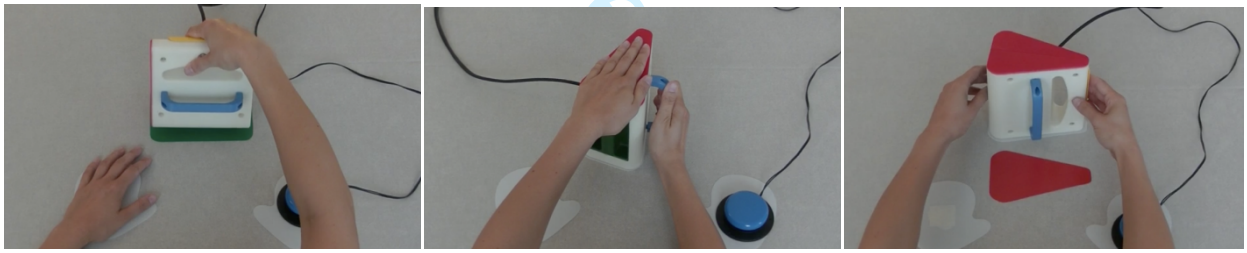
3- *Melbourne Assessment of Upper Limb Function (MA2)*. It is a standardized instrument for measuring the capacity and quality of movement of the 'upper limb in children with Cerebral Palsy aged between 2 and 15 years, but it is also used for adults. It will be used at all evaluation times.

4- *ABILHAND* is a short questionnaire, validated in patients with cerebral palsy that measures 21 daily bimanual activities. The rating is assigned by the subject or the parent based on the experiences in daily accomplish, each task has a score of 3 points (impossible, difficult, easy). It will be used at all evaluation times.

5- *Participation and Environment Measure - Children and Youth (PEM-CY).* This is a measure of participation and environmental factors at home, at school and in the community. It will be used at T0 and T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL - child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL -Teen, 13-18 years).* These questionnaires are used to assess the quality of life in people with cerebral palsy. It will be used at T0 and T3.

7- *instrumental measurement of the manipulation during uni and bimanual tasks executed after observation.* It is an object containing two load cells to measure the force exerted (compression or traction) when grasped by the plegic hand and an on-off switch to evaluate the contact of the unaffected hand. An additional switch is placed at the starting point on the table under the more affected hand to record the moment when it starts moving toward the object. The instrument is used immediately after viewing three manipulation tasks carried out with three different types of grip: a one-hand task performed with the more affected hand, a two-hand bimanual task for the two hands, and a two-hand co-operation task for the two hands.



TASK 1. TASK 2. TASK 3.

The entire evaluation will last approximately one hour.

8- The use of the a*ctigraph in daily life.* The recruited subjects wear two actigraphs (Figure 2) outside of the clinical evaluation on his wrists (one for each wrist) for three-week periods (AOT experimental phase, phase control, phase follow-up). At the end of the registration period, the actigraph will turn off themselves and will be returned directly or by mail service to the examiner.

Benefits from participation in the study

Based on the literature and the preliminary results obtained in our previous studies, we expected that AOT training could improve the use of the upper limb in everyday life activities.

Possible risks
There are no direct risks or side effect related to the participation.

Possible alternatives
The alternative is to do not participate in the study.

What happen if you decide to do not take part in the study or retire from the study
The participation is voluntary. If you decide to attend, you will be able to withdraw from the study at any time and without the obligation to provide explanations, however, by notifying the doctor responsible for the study, Dr. Giuseppina Sgandurra.
If this is the case, no additional data will be collected and you can ask for the deletion of those already collected.

I consent to informing your general practitioner
For the best protection of your health, you will be asked to inform your doctor of the experiment you are willing to attend.

Information about the results of the study
If you require it, at the end of the study, results of the study and, in particular, those concerning you may be provided.

INFORMATION RELATING TO PERSONAL DATA PROCESSING:
Treatment holders and their purpose
The IRCCS Fondazione Stella Maris in accordance with the responsibilities provided by the rules of good practice, will process your personal data, particularly on health essential to the objective of the study, other data related to your origin and to the characteristics of your medical condition only solely on the basis of your study. For this purpose, the data provided will be collected by the Testing Center and processed in anonymity and in the privacy of the data. The processing of personal data related to 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphic records are essential for conducting the study: the refusal to provide will keep you from participating.

Nature of data
The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored for at least 7 (seven) years from the end of the study in this code, to your date of birth, the 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphs records are necessary for carrying out

the study. Only the physician and authorized clinicians will be able to link this code to your name.

Treatment Mode

Data, whether processed by electronic means, will only be published in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, in such a way as to guarantee the confidentiality of your identity.

Exercise of rights

You may exercise your rights under art. 7 of the Code (eg. Access to your personal data, integrate, update, correct and object to their treatment for legitimate reasons, etc.) Applying directly to the testing centre in the person of Dr. Giuseppina Sgandurra. You may terminate your participation at any time without giving any justification. In this case, the acquired data related to you will be destroyed. Further data will not be collected for you, without prejudice to the use of those already collected to determine, without altering the results of the search: even for the data already collected, you may ask for the cancellation.

Further information

There are no charge costs due to participation in the study. You will not receive any financial compensation for participating in the study.

The protocol of the study proposed to you has been approved by the Tuscan Ethics Paediatric Committee on 22/11/2016. The Ethics Committee has, among other things, verified the compliance of the study with the European Good Clinical Practice and the ethical principles expressed in the Helsinki Declaration.

You may report any matter you may find relevant to the Ethics Committee and / or the Health Care Department of this hospital structure regarding the research you are concerned with.

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	g. Sgandurra @ fsm.unipi.it	

_____ ___ / ___ / _____ _____

_____

Name of Doctor's Date
Time Signature
who delivered the information

INFORMED FORM OF CONSENT

V 5.0 of the 10/11 / 2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*

Version 5.0 V **and date** of 10/11 / 2016

Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella M aris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

I signed _____ born ___ / ___ / _____ resident to _____ via / square _____ Tel ._____ domicile (if different from residence) _____

DECLARE

- had received from Dr. _____ exhaustive explanations about the request to participate in the present research, as reported in the information document, part of this agreement, which I was given a copy on _____ at _____ *(insert date time of delivery);*
- that I have been clearly explained and I have understood the nature, purpose, procedures, the expected benefits, risks and possible inconveniences and alternatives of the clinical study;
- that I have had the opportunity to ask questions and to have had satisfactory answers;
- that you have had all the time you need before deciding whether to participate or not;

- that I have not had any unjustified coercion in the request for Consent;
- that I was clearly asked that I could freely decide to do not take part in the study or to leave at any time without giving any justification, and that those decisions will not in any way modify the relationship with the physicians and the structure that are treating me ;
- I am aware of the importance (and of my responsibility) to inform my general practitioner of the experiment I am willing to attend
-

By subscribing to this form, I consent to the processing of my personal data for the purposes of the search within the limits and with the methods indicated in the information provided to me with this document.

I therefore declare of

□ **want** □ **NOT want**
□ participate in one under clinical evaluation
□ both under clinical evaluation and at home

□ **want** □ **NOT want**
be informed of the results of this research by the medical practitioner

□ **want** □ **NOT want**
be informed on the results of the research by the medical practitioner, also in relation to unexpected news that should be accidentally encountered with the investigations provided by the study

□ **want** □ **NOT want**
Inform your doctor of general practitioner in study participation

_____ ___ / ___ / _____ _____
_____
Full patient name (adult, lower mature) Date
Time Signature

_____ ___ / ___ / _____ _____
_____
Name for Extended Legal Representative Date
Time Signature

I signed Prof./Dr. ....
Surname Name

I declare that the Patient has spontaneously signed his participation in the study

I also declare:

- providing the patient with comprehensive explanations regarding the purposes of the study, the procedures, possible risks and benefits and possible alternatives there are to;
- have verified that the patient has sufficiently understood the information provided to him / her
- having left to the Patient the time needed and the opportunity to ask questions about the study
- not exercising any coercion or unjustified influence in the Consent's request

_____ ___/___/_____ _____
_____
Name of Doctor's Date Date Time Signature
who provided the information and
gathered informed consent

Please note

a copy of this form, signed and dated, enclosed with the "Written Information for the Patient" must be delivered to the Patient

Semi-structured qualitative interview about acceptability of AOT training

Answer to these questions with your parents, feel free to add your comments

Customization of exercises				
1	Did the exercises seem suitable for you (materials, type of actions...)?	yes, at all	yes, in part	no
2	Were exercises difficult for you (required perfomance)?	yes, all of them	yes, many of them	no
3	Did you notice an increasing difficulty (from the easiest the first day to the most difficult)?	yes		no
4	Did exercises seems like other typical activities/daily life actions?	yes, all of them	yes, many of them	no
5	Do you think that AOT activities had a role in promoting your ability?	yes, at all	yes, in part	no
Suitability of children with UCP for the Tele-UPCAT system in their own home				
6	Did you like to do the training at home?	yes		no
7	Did you like to perform exercises without a therapist?	yes, at all	yes, in part	no
8	Who helped you for the training?			
Feasibility at home				
9	Did you have a suitable table where the system was placed?	yes		no
10	If no, did you need to re-organize your home space?	yes, at all	yes, in part	
11	Do you judge the whole system bulky?	yes		no
12	Was the management of the system difficult?	yes, at all	yes, in part	no
Required effort by the participants				
13	Was the effort (about 1 hour per day) feasible for you?	yes, at all	yes, in part	no
14	Did you change your daily routine to do the training?	yes, at all	yes, in part	no
15	Did you have to renounce to something (sport, freetime, holidays..)?	yes, at all	yes, in part	no
16	Did you like to have a fixed time for the training each day?	yes, at all	yes, in part	no
17	Do you think that you could proceed the training for more days?	yes, at all	yes, in part	no
18	Were the exercises too hard (difficult, long..) for you?	yes, at all	yes, in part	no

Semi-structured qualitative interview about acceptability of AOT training

Answer to these questions with your parents, feel free to add your comments

Acceptability of Actigraphs				
19	Did you like to wear Acrigraphs?	yes		no
20	Did Actigraphs annoy you?	yes	yes, sometimes	no
21	Did you wear them for the whole day?	yes, at all	yes, in part	no
22	Did you remember how to wear them (orientation)?	yes		no
23	Did you remember to fill in your diary?	yes	yes, sometimes	no
Suitability of the manual				
24	Was the manual enough clear?	yes, at all	yes, in part	no
25	Did you have any difficulties in finding/preparing the material?	yes	yes, sometimes	no
26	Were the instructions for the managining of the system complete and clear?	yes	yes, sometimes	no
Software				
27	Did you like Ubi (for children)/slides (for adolescents)?	yes, at all	yes, in part	no
28	Do you think that something need to be changed?	yes		no
29	Was the managing of the software difficult?	yes, at all	yes, in part	no
30	Did you have technical issues/troubles?	yes	yes, sometimes	no
31	Did you need technical assistance?	yes	yes, sometimes	no

BMJ Open

Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPperLimb Children Action observation Training for Participants with Unilateral Cerebral Palsy

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Date Submitted by the Author:	22-Jan-2018
Complete List of Authors:	Sgandurra, Giuseppina; IRCCS Fondazione Stella Maris, ; Universita degli Studi di Pisa, Dipartimento di Medicina Clinica e Sperimentale Cecchi, Francesca; The BioRobotics Institute, Polo Sant'Anna Valdera Beani, Elena; Stella Maris Scientific Institute, Department of Developmental Neuroscience Mannari, Irene; The BioRobotics Institute, Polo Sant'Anna Valdera Maselli, Martina; The BioRobotics Institute, Polo Sant'Anna Valdera Falotico, Francesco; The BioRobotics Institute, Polo Sant'Anna Valdera Inguaggiato, Emanuela; Stella Maris Scientific Institute, Department of Developmental Neuroscience Perazza, Silvia; Stella Maris Scientific Institute, Department of Developmental Neuroscience Sicola, Elisa; Stella Maris Scientific Institute, Department of Developmental Neuroscience Feys, Hilde; KU Leuven - University of Leuven, Department of Rehabilitation Sciences Klingels, Katrijn; KU Leuven - University of Leuven, Department of Rehabilitation Sciences; Hasselt University Ferrari, Adriano; IRCCS S. Maria Nuova Hospital Dario, Paolo; The BioRobotics Institute, Polo Sant'Anna Valdera Boyd, Roslyn; The University of Queensland, Queensland Cerebral Palsy and Rehabilitation Research Centre; The University of Queensland, Queensland Children's Medical Research Institute Cioni, Giovanni; Stella Maris Scientific Institute, Department of Developmental Neuroscience; University of Pisa, Department of Clinical and Experimental Medicine
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Neurology, Paediatrics
Keywords:	action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Tele-UPCAT: Study Protocol of a Randomized Controlled Trial of a Home-Based Tele-monitored UPperLimb Children Action observation Training for Participants with Unilateral Cerebral Palsy

Giuseppina Sgandurra[1,2], Francesca Cecchi[3], Elena Beani[1], Irene Mannari[3], Martina Maselli[3], Francesco Paolo Falotico[3], Emanuela Inguaggiato[1], Silvia Perazza[1], Elisa Sicola[1], Hilde Feys[4], Katrijn Klingels[4,5], Adriano Ferrari[6,7], Paolo Dario[3], Roslyn Boyd[8], Giovanni Cioni[1,2]*

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E-mail: gcioni@fsm.unipi.it

Word Count: 5971

Abstract

Introduction:

A new rehabilitative approach, called UPperLimb Children Action Observation Training (UP-CAT), based on the principles of Action Observation Training (AOT), has provided promising results for Upper Limb rehabilitation in children with Unilateral Cerebral Palsy (UCP). This study will investigate if a new Information and Communication Technology (ICT) platform, named Tele-UPCAT, is able to deliver AOT in a home setting and will test its efficacy on children and young people with UCP.

Methods and Analysis:

A randomized, allocation concealed (waitlist-control) and evaluator-blinded clinical trial with two investigative arms will be carried out. The experimental group will perform AOT at home for 3-weeks using a customized Tele-UPCAT system where they will watch video sequences of goal-directed actions and then complete the motor training of the same actions. The control group will receive usual care for 3 weeks which may include upper limb training. They will be offered AOT at home after 3 weeks. Twenty-four children with UCP will be recruited for 12 participants per group. The primary outcome will be measured using Assisting Hand Assessment. The Melbourne Assessment 2, ABILHAND, Participation and Environment Measure-Children and Youth and Cerebral Palsy Quality of Life Questionnaire will be included as secondary measures. Quantitative measures from sensorized objects and participants worn Actigraphs GXT3+ will be analysed. The assessment points will be the week before (T0) and after (T1) the period of AOT/Standard Care. Further assessments will be at T1 plus, the week after the AOT period for the waitlist group and at 8 (T2) and 24 weeks (T3) after AOT training.

Ethics and Dissemination:

The trial has been approved by the Tuscany Paediatric Ethics Committee (169/2016). Publication of all outcomes will be in peer-reviewed journals and conference presentations.

Trial registration: ClinicalTrials.gov: NCT03094455 (16 March 2017). The trial was funded by Italian Ministry of Health grant:GR-2011-02350053

Abstract words: 300

Key words: action observation training, unilateral cerebral palsy, tele-rehabilitation, upper limb, randomized controlled trial, Information and Communication Technologies

Strengths and limitation of this study

- This is the first protocol study where an ICT platform is proposed, called Tele-UPCAT, to deliver the Action Observation Therapy (AOT) at home.
- The study is a well-designed RCT aimed to investigate the UP-CAT approach at home and to measure its efficacy in children, adolescents and young adults with UCP.
- The Tele-UPCAT platform allows individualised customization of the intervention according to the different levels of upper limb severity and the different ages of participants.
- The sample size, even if it will be calculated and powered on the previous clinical studies, is modest.
- The Tele-UPCAT platform does not obtain quantitative measurements of force and pressure hand measurements during AOT session.

BACKGROUND

Cerebral palsy (CP) is the most common cause of childhood chronic physical disability in Europe and in other industrialised societies. [1] The incident rate is between 2 and 3 per 1000 live births and increases to 40–100 per 1000 live births among very premature and very low birth-weight babies which represent the population with highest rate of neurodevelopmental disorders. [2] Unilateral Cerebral Palsy (UCP) (i.e. a motor impairment impacting one side of the body more than the other side) constitutes the most frequent form of CP, about 30-40% of all affected children. [3] Recent estimations of incidence and prevalence of CP have shown a significant increase in UCP in Europe over the last years. [4-5] The Upper Limb (UL) of children with UCP is generally more involved than the lower limb and the consequent disability affects their participation, quality of life, independence at home, school and community. Despite this large impact, the current clinical practice for UCP mainly includes consultative intervention or time-limited therapy following pharmacological intervention.

In the last decades, targeted UL therapies such as constraint-induced movement therapy (CIMT), hand-arm bimanual intensive training (HABIT) and combined approaches have emerged. Reviews on these models have clearly shown that intensive models of therapy achieves modest to strong effects to improve UL function compared to standard care and that bimanual and unimanual training demonstrate similar gains in UL outcomes [6-10].

In this field, one of the most recent models is the Action Observation Training (AOT), based on the discovery of the Mirror Neuron System, whose core regions are the ventral premotor and inferior parietal cortex. These areas are activated when individuals perform goal-directed motor acts (e.g. grasping an object) as well as if they simply observe the performance of the same or a similar action and trigger recruitment of the same network as the actual physical action. [11, 12] AOT is mainly based on observation of meaningful actions, and their successive imitation. AOT has been used as new intervention model in many adult studies for neurologic and non-neurologic diseases (such as Parkinson disease, stroke, orthopaedic surgery) and there is growing evidence of its effectiveness. [13-18] Recent studies carried out in children with CP indicate positive effects on UL function in younger population. [19-21] We have recently completed a clinical study called UP-CAT (UPper limb Children Action observation Training) with children with UCP based on 3 weeks of AOT, providing evidence of its efficacy in improving UL activity performance in daily activities. [21]To date, the UP-CAT study has only been carried out in a clinical rehabilitation setting with children who were living near the two clinical centres and whose parents are willing to commit to a 3-week intensive therapy program with consequently high costs for both health services and families. In addition, the parents, even if able to participate, found the need to attend every working day for three weeks too burdensome and suggested the delivery of the intervention at home.

Biotechnologies, tele-rehabilitation and eHealth provide a promising approach to deliver tele-monitored home programs for a large number of participants at a relatively low cost. In this field our group has recently experienced the design, the build and the clinical validation of new technological Information and Communication Technologies (ICT) for providing in the first year of life tele-rehabilitation programs at home for infants at risk for developing neurodevelopmental disorders [22-25] In this context, similar approaches could represents viable option in providing AOT programs at home, in a user-friendly, playful and rehabilitative setting in children. The core of AOT relies on the content of actions to be observed and on the patients' motivation in carefully observing to imitate and actively replicate them. For these reasons the AOT can be easily carried out at home. The present study protocol, designed as an exploratory Randomized Clinical Trial (RCT), has the purpose to investigate the feasibility of a new ICT platform, named Tele-UPCAT, to provide the UP-CAT approach at home. This RCT aims to measure its efficacy in a group of children, adolescents and young adults with UCP comparing the effects of Tele-UPCAT approach (experimental group) with the standard care (control group).

The primary aim will evaluate the immediate effects (T1, in the week after the end of the treatment) of this new approach (home AOT) on bimanual hand function (Assisting Hand Assessment, AHA [26-28]) and assess whether these effects will be retained at a medium and long term follow-up (i.e. 8 and 24 weeks after the end of treatment, T2 and T3). In addition, the feasibility of the Tele-UPCAT system as a comfortable, reliable and customizable tool for delivering a home AOT to UCP participants and their families will be assessed using semi-structured interviews.
Secondary aims will investigate the immediate (T1) and long-term clinical effects (T2, T3) on unimanual capacity (Melbourne Assessment 2, MA 2 [29] and Box and Block Test, BBT [30]) and on bimanual daily activities at home and in the community (ABILHAND-Kids [31]), participation (Participation and Environment Measure - Children and Youth, PEM-CY) [32, 33] and perception of quality of life (Cerebral Palsy Quality of Life Questionnaire, CP-QOL); [34-36]. Further aims will assess the feasibility of Tele-UPCAT platform on assessing, monitoring and detecting changes during and after the AOT program by comparing the data of the clinical outcome measures with those of quantitative measurement of manual activity, obtained using sensorized objects and Tele-UPCAT platform. Finally, a cost-effective analysis will be carried out using both the perspective of the patient/caregivers and the healthcare system.

METHODS/DESIGN

Study design

The Tele-UPCAT trial is an exploratory randomized, allocation concealed (waitlist-controlled), and evaluator-blinded clinical trial with two investigative arms using an AOT intensive rehabilitation program of home based AOT compared to standard care in children and young people with UCP. This study is a waitlist controlled trial, in order to allow all enrolled participants to perform AOT training either immediately or after a waitlist period. After obtaining informed consent, and completing baseline assessment (T0) participants will be block randomized into pairs according to the House functional classification system (HFCS) activity level (grades 2-3, 4-5 and 6-8) and age (5-14y, 15-20y), [37, 38] using a computer-generated set of random numbers. Randomization, sequence generation and preparation of group allocation materials will be carried out by an independent researcher who will be not involved in the trial. Pairs will be divided randomly into two groups with 1:1 experimental/standard care (waitlist) ratio. Participants allocated in the experimental group will immediately start AOT for a 3-weeks period, while those in the standard care group will continue with their usual care.
A predefined diary for recording all daily activities (e.g. times of sleep, weak-up, meals, school, therapies for upper limb or for lower limb and their dose) will be filled in by all the participants and their parents. In addition, to record the acceptability and feasibility of the training, participants and/or families allocated in the experimental group will fill in a multiple choice questionnaire (with box for notes) for ascertaining the perception about their experiences of using the Tele-UPCAT system.
All participants will be re-evaluated after the period of experimental training/standard care (T1) with standardized tests and questionnaires (see outcome measures). T1 will be the primary endpoint aimed at evaluating the short-term effects of AOT according to CONSORT Guidelines (see Figure 1). [39]
After this phase, participants previously allocated to the experimental group will continue standard care, while who's who started with standard care will then commence home based AOT. The participants of this SC group will be re-assessed at the end of training (T1 plus). Further assessment of all participants will be performed after 8 weeks (T2) and 24 weeks (T3) from the end of AOT training (T1 or T1 plus, for the experimental and waitlist group, respectively), to evaluate the medium and long term effects of AOT. All the assessments will be carried out at home by trained therapists.

In summary, assessments will be performed at:

- T0, baseline: the week before the period of AOT/Standard Care
- T1: at 1 week after period of AOT/Standard Care
- T1 plus: the week after period of AOT, for waitlist group
- T2: 8 weeks after end of AOT
- T3: 24 weeks after end of AOT.

The details of the study design are reported according to CONSORT guidelines [39] (Figure 1), SPIRIT (Standard Protocol Items: Recommendations for Intervention Trials) statement [40] and TIDier (Template for Intervention Description and Replication) Checklist [41, 42] (Supplement Material 1, 2 and 3). The programme of enrolment, interventions and assessments designed according to SPIRIT guidelines are shown in Figure 2.

Blinding

All the clinical outcome measures (AHA,[26-28] Melbourne Assessment 2 MA-2[29] and Box & Block Test [30]) will be videotaped by a therapist blind to group assignment. Videotapes will be randomized and scored by assessors blind to group allocation and order of assessments. During each assessment, all the participants will wear two Actigraphs (wGT3X-BT, wActiSleep-BT), one for each wrist.

Two independent researchers (two paediatric neurologists) without competing interests will comprise the data monitoring committee for this study. They will review all adverse events (deciding to stop the trial if necessary), the retention of participant in each study arm and the compliance of study protocol at 12 weekly intervals. Each participant will have a study number in a dedicated data file. The file with participant's numbers and personal data will be stored in a password protected file, accessible only by the principal investigator. In order to promote participant's retention, all the assessment will be completed at home. The clinical primary and secondary outcome measures will be completed within one week. Enrolled participants are ethically able to withdraw from this study any time and have been notified that their usual follow-up and clinical care would not be impacted.

Study sample and recruitment

Enrolment and clinical trial management will be carried out by paediatric neurologists and physiatrists at the Department of Developmental Neuroscience of IRCCS Fondazione Stella Maris (FSM, Pisa, Italy), with the collaboration of the Unit of Children Rehabilitation of S.Maria Nuova Hospital (Reggio Emilia, Italy).

Potential participants will be identified according to inclusion criteria (see below), from UCP patients of the clinical departments. Suitable participants and their parents will be invited to participate and will be enrolled in the RCT only after written consent has been obtained.

Inclusion criteria are participants with:

- confirmed diagnosis of spastic motor type UCP; [3, 43]
- aged between 5 and 20 years at time of recruitment;
- predominant UL spasticity;
- House functional classification system, (HFCS) score $\geq$ 2 that is, able to passively hold an object in the hand or better [37, 38]
- cognitive level within normal limits i.e. Intelligence Quotient $\geq$ 70, as assessed in the last year prior to recruitment on the WPPSI-III, [44] WISC-IV [45] or WAIS [46]
- participants and parents willing to commit to the intensive therapy program for a 3-week period.

Participants will be excluded in case of:

- previous orthopaedic surgery or Botulinum Toxin A (BoNT-A) injection in the UL within 6 months prior to the enrolment of this study.

Sample size

Even if this study will be planned as an exploratory study, a sample size estimates, according to CONSORT guidelines, [38, 40] have been based on projected treatment effect on the primary outcome measure, AHA. Taking account of the study design and the stratification, a minimum sample size of 10 per group will be required in order to detect a 1.40 effect size (value based on our preliminary data) at significant level of 0.05 and 80% power. [20, 21] Considering a 20% of possible drop-outs a minimum of 12 participants per group will be recruited, total sample of 24 participants.

Study treatment

The Tele-UPCAT system has been designed through the close collaboration between the rehabilitation staff (child neurologists and child therapists) of IRCCS Fondazione Stella Maris and biomedical engineers of BioRobotics Institute Scuola Superiore Sant'Anna. Taking into account the previous clinical experience on UPCAT, the main components of the Tele-UPCAT system (e.g. the size of the screen, the need of a guide for alternating the time of observation and of execution, the key words for catching the attention, etc.), the AOT library of exercises (e.g. the adaptation of the objects for enlarging the exercises to more impaired hands) and the experimental training (e.g. time and duration) have been defined. In general, the training will be structured in one session per day, to be executed 5 working days for 3 consecutive weeks (i.e. 15 sessions in total). The duration of daily sessions will be about 1 hour per day for a total of 15 hours. The participants undergoing the AOT intervention through the Tele-UPCAT system will watch 3 minutes first-person video sequences of unimanual or bimanual goal-directed actions followed by their execution for 3 minutes. Three different actions will be proposed twice each day.

Tele-UPCAT system

Tele-UPCAT system (see Figure 3) has been designed and built and will be provided at home by the BioRobotics Institute of Scuola Superiore Sant'Anna (Pontedera, Italy).
It is a dedicated platform for delivering AOT designed to be user-friendly, by subjects at home in a playful setting with integrated smart features.

The platform has been designed and developed by integrating two different modules:

- The Observation Module (OM) for the presentation of AOT videos and recording of participant's attention and exercise execution. This consists of a computer with 23" desktop, a dedicated software and a video camera. The Observation Module has been obtained by integrating a large all-in-one personal computer (All-in-One touch HP Elite One 800 G2 - L3N93AV), a large switch and a video camera (GoPro HERO Session), which will record a whole field, including subject's face and hands and table with objects. The Observation Module is important to determine whether the participant is looking at the monitor during observation phase and has an overall view of the execution of actions. A dedicated software, designed after a deep and specific literature analysis, was developed for guiding and motivating participants through the phases of AOT (observation followed by execution). In addition, the software was customized for the wide age range of participants providing an interactive game with an engaging story different for every day of training for school aged children, and a slide-show with a voice-over for adolescents and young people. The general architecture of the software is based on the following sequence: observation of a 3-minute video followed by execution of the same action for 3 minutes. Subsequently, the same video will be replayed and then executed a second time. As stated before, a 60-minute session, including rest intervals, of three different goal-directed actions of increasing complexity are observed and imitated twice every day. At

the end of each day the software will terminate the session and automatically update it for the next day.

- The Motor Performance Module (MPM) for the execution of actions. This will be mainly composed of a kit of exactly the same common objects and toys shown in the videos and two Actigraphs (wGT3X-BT, wActiSleep-BT, for more details see http://actigraphcorp.com/support/activity-monitors/gt3x/) worn one for each wrist. With this design it will be possible to measure the upper limb activity during the AOT training while the lack of sensorized toys embedded in the MPM will not allow to measure quantitative measures of hand activity (e.g. force or pressure) during the AOT training.

The first prototype of Tele-UPCAT system has been widely tested before the beginning of the RCT in order to test the stability and reliability of the system.

AOT library

On the basis of the previous AOT exercises, [20, 21] rehabilitation staff (child neurologist and child therapists) has created a library of rehabilitation packages composed of three different series of AOT exercises suitable to be executed at home. They differ for complexity of action and range of UL capabilities conceived in relation to HFCS levels (≤4, 5-6, 7-8). [37, 38] Each series is organized into customized sequences designed to cover unimanual and bimanual UL goal-directed actions with a variety of objects and toys commonly used in routine life. For each series, experimental training is composed of 15 sets (8 unimanual followed by 7 bimanual) of routine UL activities, to be completed in 3 weeks (5 days per week). Each set has a general common goal (e.g. drinking a glass of water) composed of three sequential tasks of increasing complexity (e.g. from picking up a bottle of water, to opening the cap, to pouring the water into a glass). As previously indicated, in order to grade the activities according to the range of capabilities, three series of sets have been planned. The actions of each series have the same goal but the material and type of movement (i.e., range of movement, type of grasp) is customized in order to guarantee feasibility of the proposed activity while maintaining the same overall objective (see Table 1 and Figure 4). Each action of the three series performed by an actor is videotaped so that the videos show only the hand and arm from the first perspective; each video is then edited to last 3 minutes. A right-handed actor uses one or two hands for unimanual and bimanual exercises respectively for participants with right UCP. For the left UCP the previous videos where reversed if they maintained the same characteristic of the setting and of the hand movement, while the remaining videos where specifically videotaped.

Table 1. List of goal-directed actions planned for the AOT training grouped in unimanual (white cells) and bimanual (grey cells) actions

Days	Action a	Action b	Action c
1	Uncover a little ball by lifting a box	Place a little ball in a glass	Fill a glass with water
2	Pick coloured card and match it to the same colour	Move a coloured card and place it on a base	Pick a card and place it on the similar one
3	Pick up a rubber stamp and move from/to different positions	Pick up a rubber stamp and press it against horizontal plane to print a figure	Pick up a rubber stamp and press it against sloping plane to print a figure
4	Pick up coin, put it in piggy bank through the slot on the top	Pick up coin, put it in piggy bank through the vertical slot on the side	Pick up coin, put it in piggy bank through the horizontal slot on the side

	OR Pick up a magnet and place it on a horizontal magnetic board	OR Pick up a magnet and place it on a sloping magnetic board	OR Pick up a magnet and place it on a vertical magnetic board
5	Pick up a wooden rubber stamp and move to different positions	Pick up a wooden rubber stamp and press it against horizontal plane to print a figure	Pick up a wooden rubber stamp and press it against sloping plane to print a figure
6	Move a spray can OR Move the bottle with a little ball inside	Place the spray can on a support OR Remove a little ball from the bottle	Put the spray can into a cup OR Press the catapult and launch a little ball
7	Move a container filled with shimmy powder	Open the container	Sprinkle shimmery powder on a paper
8	Place magnetic fish on a paper	Pick up fishing rod and catch magnetic fish	Pick up magnetic fish and place them in a container
9	Move a hole punch	Insert a sheet of paper and make holes	Match holes on sticks
10	Wet a cloth placing it in a container with water	Wring cloth and place it in a plate	Open a toy washing machine and insert the cloth inside
11	Pick up a card and place it on a support	Pick up a card and insert it in a clothespin	Pick up a card and insert it in a clothespin in a different orientation
12	Pick up and handle a piece of Play-Doh	Divide it in two pieces	Open a toy oven and insert a saucepan (with Play Doh in it)
13	Search for coin in the bag and place it on a support	Take the coin and insert it in a wallet	Open a box and place the wallet inside
14	Open a tube of tempera paint	Wet a brush with tempera paint	Make figure using a stencil with the brush dipped in tempera paint
15	Move a glitter glue tube	Open it	Decorate a frame by pasting pieces of mosaic

Experimental training

Before delivering the Tele-UPCAT platform, the training will be customized individually for each participant. The rehabilitation staff will select, on the basis of age and HFCS level, from the library the most appropriated AOT rehabilitation packages for each participant, then the engineers will upload them in the Observational Module (OM). For the Motor Performance Module (MPM), the therapists will organize a container of all the objects identifying them with numbers relative to the training day (e.g. little ball number 1 which means day 1 of the training). In addition, a dedicated printed manual with instructions and guidelines related to the different steps of the training and for system management and the setup will be provided. The manual contains also all the contacts of both technical and rehabilitation staff for remote assistance in case of any problems during the training. Two Actigraphs (wGT3X-BT, wActiSleep-BT) will be initialized for the recording period (3 weeks) to be worn on each wrist.

The ICT platform will be delivered to the participant's home by the engineers that are in charge of the installation of the system. The families will identify a designated position with a table or a desk of about 80x100 cm near to a socket where the ICT platform will be placed. Engineers and rehabilitation staff will train both parents and participants about the correct use of the system, including safety aspects. During the first two training days, a therapist will visit each participant and their parents to confirm the set-up.
During the training sessions, each participant will sit on a chair with both arms placed on a table in front of a platform positioned at about 1 m. Especially when the participant will be a child, a parent will be seated on her/his more impaired side to prompt attention during task execution and assist if necessary. The software will guide the participant in the sequence of observations and executions.

Standard care
Participants previously allocated in the standard care group will continue their usual care for 3 weeks. Usual care for recruited participants could be consisted for physical or occupational therapy.

The frequency, dose and the type of all therapies will be recorded accurately by a diary in both groups.

Outcome measures

Description of sample

Children participating in the study will be classified according to HFCS, which assesses function of the impaired hand in children with CP.[37, 38] This classification consists of 9 grades ranging from a hand that is not used at all (grade 0) to one that is used spontaneously and independently from the other one (grade 8). Due to the general approach in classifying hand functional level, this scale can also be easily applied to young adults with UCP. HFCS will be used for all ages as a criterion for inclusion in this study (from grade 2 to grade 8). In addition, they will be classified according to the Manual Ability Classification System (MACS), a classification system of the child's ability to handle objects in daily activities on one of five levels. [47]

Primary outcome measure

On the basis of our scientific hypothesis and according to previous clinical experience, [20, 21] the primary outcome measure will be the AHA. The latest version 5.0 will be used. This assessment measures UL function during bimanual activities by evaluating spontaneous use of assisting hand during a semi-structured age-appropriated 10-15-minute session with specific toys or objects requiring bimanual handling. The school-kids form will be used for the assessment of UCP children 6-12 years old [26, 27] while the Adolescent version (Ad-AHA), using the board game "Go with the Floe", [28] will be completed with participants older than 13 years. This last version, even if validated up to 18 years, will be used with potential participants 18-20 years old to guarantee the same assessment across all participants regardless of age. Moreover, AHA has been already used, even if not validated, in young people with UCP [48, 49]. The scale uses a Rasch measurement model which is a method to convert raw scores into a linear measure located on a unidimensional scale and more specifically to convert them into 0 to 100 logit-based AHA units, that will be used for the statistical analyses. All AHA assessments will be videotaped in a standardised manner and the subsequent scoring will be carried out by a certified expert rater who will be masked to group allocation and assessment order[26-28].

Other outcome measures

Other secondary measures will include measures of unimanual capacity (MA-2,[29] and BBT [30]) and bimanual daily activities at home and in the community (ABILHAND-Kids).[31] Moreover, participation and quality of life will also be assessed. All assessment will be performed at T0, T1, T1 plus, T2 and T3 unless otherwise indicated. Questionnaires will be completed by parents and/or participants at home and if doubts will occur, child neurologists or therapists will be available to discuss face to face items not clear to them.

i. The Melbourne Assessment 2 (MA2) [29] measures unilateral UL function and it is a valid and reliable tool for evaluating quality of UL movement in children with neurological conditions for ages between 2.5 and 15 years. MA2 is a criterion-referenced test that extends and refines the scale properties of the original Melbourne Assessment (MUUL) and like MUUL it can also be used for adolescents and young adults. MA2 measures four elements of UL movement quality: movement range, accuracy, dexterity and fluency. It comprises 14 test items of reaching, grasping, releasing and manipulating simple objects. The test is administered by videorecording the child's performance for subsequent scoring (30 items score). A raw score is provided for each of the four sections (Movement Range, Accuracy, Dexterity and Fluency) that will be analysed separately. It predominantly includes concepts within the body function domain as well as in the activity domain. Even if the MUUL and also the MA-2 have been validated up to 15 years, the first one has been used in studies involving patients with CP older than 15 year and in adults. [48-49] We have chosen to use the MA-2 also for participants older than 15 years to guarantee the same assessment across all participants regardless of age instead of using other scales (e.g. the Fugl-Meyer Assessment or the Action Research Arm test). [50]

ii. Box and Block Test (BBT) is a quick (2-5 minutes), simple and inexpensive test which measures unimanual dexterity in the activity domain. BBT is composed of a test box with a partition in the middle and 150 wooden blocks (25mm). The patient had to transport as many blocks as possible in 1 minute from one compartment to another. Firstly, the patient is asked to perform the test with the unaffected hand and then with the affected hand. The number of blocks transported by affected hand in 1 minute will be counted and considered for the main analyses. It can be used for a wide range of populations from childhood to adulthood.[30]

iii. ABILHAND-Kids[31] is a semi-structured item-response questionnaire on a 3-point ordinal scale (impossible, difficult, easy) that measures daily manual activities referred to in the activity domain of ICF. Parents will be instructed to rate their child's perceived difficulty in performing each activity taking account the performance of their child when performing the activity without technical or human assistance, regardless of the limb(s) and the strategies used. It has been validate for children aged 6-15 years but it has been used for larger ranges (6-19 years). [51] The questionnaire has been developed using the Rasch measurement model which provides a method to convert the ordinal raw scores into a linear logit measures located on a unidimensional scale, that will be used for the analyses. This questionnaire will be used at all assessment periods.

iv. Participation and Environment Measure - Children and Youth (PEM-CY). [32, 33] It is a parent-reported instrument that evaluates participation and environment across home (ten items), school (five items) and community (ten items) settings. For each item, the parent is asked to identify how frequently (over the past four months) the child has participated (eight options: daily to never); how involved the child typically is while participating (five point scale: very involved to minimally involved); and whether the parent would like to see the child's participation in this type of activity change (no or yes, with five options for the type of change desired). For each setting, the parent is then asked to report on whether certain features of the environment make it easier or harder for the child to participate. The following summary scores will be obtained: total score and score for each of the three setting-specific environmental supportiveness (home, school, community). Moreover the

total number of supports and the total number of barriers will be computed. This questionnaire will be used at T0 and T3.

v. Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years) evaluate quality of life in children and adolescents with CP. [34-36] A score on a 0-100 scale will be obtained for each of computed sub-domains. In particular the Children form filled in by the parents assesses 7 subdomains (Social well-being and acceptance, Feelings about functioning, Participation and physical health, Emotional well-being and self-esteem, Access to services, Pain and impact of disability and Family health) and five subdomains (excluding Access to services and Family health to the previous) for the children version. The Teen form evaluates 7 subdomains (General well-being and participation, Communication and physical health, School well-being, Social well-being, Access to services, Family health and Feeling about functioning) for the form filled in by the parents and 5 (excluding Access to services and Family health to the previous) for those filled in by the caregivers. These questionnaires will be used at T0 and T3.

vi. Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks, is a new assessment tool that consists of observation, followed by execution of three tasks of increasing difficulty (unimanual lifting, bimanual placing near and bimanual cooperation, holding and pulling) by means of a sensorized object. New technological tools such as sensorized objects can help in assessing the manipulation capabilities (reaching and grasping) in a quantitative but ecological way and the sensitivity to a training. Previous studies of the authors were focused on the development of sensozied toys for measuring infant's manipulation [52-54]. Starting from this experience, a new sensorized object has been designed and developed by the engineers tuning the sensors sensitivity and working range to the needs of participants with UCP.
Two load-cells and a switch embedded in the sensorized object allow for the measurement of the following parameters: grasping time, maximum grasping force and delay time between unaffected and affected hand in reaching for the object. This set-up is out of Tele-UPCAT system even if it was designed and developed in parallel.

vii. Quantitative measurement of bimanual activities will be performed in all the participants enrolled in the study by means of Actigraph GXT3+, as components of Motor Performance Module of Tele-UPCAT system. Actigraphs wGT3X-BT and wActiSleep-BT, equipped with a Velcro strap bracelet, will be worn, one for each wrists. As general rule, the experimental group have to wear the actigraphs not only during the training sessions but also between T0 and T1 and between T1 and T2 (total 6 weeks, 24 hours per day or as much as possible) while the control group are requested to wear them between T0 and T1, between T1 and T1 plus and, if possible also between T1 plus and T2 (total 9 weeks, 24 hours per day or as much as possible). All the daily activities, experimental training or usual care, or removal will be recorded in a dedicated diary. The Actigraphs will also be worn, by all the participants, during each time point of clinical assessments with the outcome measures. Data will be mainly relative to the asymmetry index (AI), that is the difference between the mean activity of the dominant with those of the non dominant hand and it will be correlated with the clinical scores obtained in the clinical outcome measures (mainly AHA).

viii. Cost effectiveness: A within trial cost-utility analysis will be conducted to synthesise the costs and benefits of the training program. Resource use (staff time, equipment and facility use) associated with the program will be collected alongside the RCT. Health care utilisation will be collected using a resource use questionnaire previously used in CP studies. [55] Health utility will be derived from the adapted CHU-9D, [56] a quality of life measure designed specifically for economic evaluation and which has been validated in an Australian population. [57-59]

ix. A semi-guided face to face interview (Supplement material 4) about the acceptability of the

training will be completed immediately after the training period (T1 or T1 plus). It will be performed by the rehabilitation staff with the aim of investigating participant's and parents' opinions about the training in terms of customization of exercises, suitability to UCP children, feasibility at home, required effort by the participants and acceptability of Actigraphs, suitability of the manual and of the software will be recorded.

Statistical analyses

Clinical data will be analysed by means of the Statistical Package for Social Sciences (SPSS). Means and standard deviation of clinical outcome scores for both groups will be calculated to identify potential baseline differences between groups. As a first step, normality of distributions will be verified by Shapiro-Wilk's test. Between-group differences for all selected outcome measures will be evaluated at T0, by means of t-test for unrelated samples or non-parametric Mann–Whitney U independent sample test, for normal or non-normal distributed data, respectively. To test our first hypothesis, an intention to treat analysis will be carried out, evaluating between-group differences (delta scores) for primary and secondary outcome measures at the primary endpoint (T1), compared with T0 (T1-T0), by means of parametric or non-parametric tests for unrelated samples. The age, HFCS level, characteristics of usual care (in both groups), supervision of caregiver, acceptability of therapy (measured by semi structured interview) will be analysed for further secondary exploratory analyses (e.g. regression modelling) in order to determine if some of these variables are predictive of better responses to the Tele-UPCAT training. In addition, a matched-pairs test (t-tests or Wilcoxon) will be carried out in order to assess retention of effects at follow-up periods (T1 or T1 plus, T2 and T3) relative to assessment before AOT training (T0 or T1 for experimental or waitlist group respectively). Bonferroni corrections will not be carried out in relation to the exploratory nature of the current RCT study and the relative small number of the study sample. To detect if significant changes will correlate to HFCS levels, a correlation analysis between score changes after AOT training (T1 or T1 plus) and assessment before AOT training (T0 or T1) will be carried out. Finally, an exploratory within-group analysis will be performed for the waitlist group comparing changes during AOT with respect to those of the first standard care period.

ETHICS AND DISSEMINATION

This study protocol describes background, hypotheses, system, clinical and technological outcome measures for a RCT designed to evaluate the Tele-UPCAT system as a new approach to deliver AOT to children and young people with UCP at home.
Full ethical approval has been obtained from the Tuscany Paediatric Ethics Committee (169/2016, Protocol Version 5.0 of 10/11/2016) and any deviations from the protocol will be promptly notified to this Ethic Committee and applied only after its approval. The trial has been registered at http://www.clinicaltrials.gov (identifier NCT03094455). This study protocol is reported according to the SPIRIT statement (SPIRIT 2013)[40] and the TIDier guidelines [41, 42]. We anticipate that the results of this study will be disseminated through peer reviewed journals and national and international academic conferences only by the professionals directly involved in the clinical trial. The results of this study will be of interest for rehabilitation trials based on AOT paradigm. Referring to a previous RCT study, [20, 21] we suggest that the home setting might increase accessibility of rehabilitation to a large number of children and young people with UCP (e.g. participants that live far from the clinical centres) with a large range of hand impairments (including also participants with HFCS level lower than 6) and older age (5-20 years instead of 5-15). Moreover, if the Tele-UPCAT study, using a very simple ICT solution, demonstrates to be viable for delivering AOT at home with significant improvements in UL daily activities, it could lead to the application of new solution for cost efficient rehabilitation programs. Implementation of new smart technologies can i) provide user-friendly AOT programs at home; ii) remotely manage

treatment by rehabilitation staff thus increasing the ratio 'number of patients per therapist'; iii) offer individualized and intensive training. It could become an economical and efficient rehabilitation program by achieving significant long-lasting effects in UL activity and participation through an easily implementable paradigm that could become an integral part of common clinical practice. Finally, this approach could become a rehabilitation tool and be applicable to broader populations of CP and other chronic disabilities.

PROJECT STATUS

This project began recruitment the 29 March 2017, and we expect to complete data collection for the last training the November 2017 and close the project in the April 2018.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This trial has been funded by the Italian Ministry of Health to GS and FC (GR-2011-02350053).

AUTHOR'S CONTRIBUTION

GS is the principal investigator of the project and mainly responsible of the clinical part of it while FC is the main responsible of the ICT platform. GS, EI, HF, KK, RB, AF and GC designed the research study. GS, EB, EI, SP and EB were responsible for the AOT library. GS, SP and ES were in charge for participants' recruitment in Pisa and identification of type of exercise and software and AF for Reggio Emilia. GS and EB will collect the data and will monitor the training. FC, IM, MM and FFP with the supervision of PD have designed and built the new platform. GS and GC will take the lead roles on preparation of publications on the clinical outcomes of the study.
All authors have read and approved the final manuscript.

ACKNOWLEDGMENTS

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Figure 1. Flow-chart of Tele-UPCAT study according to CONSORT guidelines. Abbreviations: AHA: Assisting Hand Assessment, BBT: Box and Block Test, MA2: Melbourne Assessment 2; CP-QOL: Cerebral Palsy – Quality of Life, PEM-CY: -Participation and Environment Measure - Children and Youth

Figure 2. Schedule of enrolment, interventions, and assessments.

Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected in the Clinical Interface (2) by the clinical staff in relation to HFCS level (6-8, 4-5 or 2-3), Side of impaired hand and Type of interface. A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3) for Teenagers or little Boys and Girls. The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists and a Button. The integrated camera records subject's attention during the observation task and exercise execution.

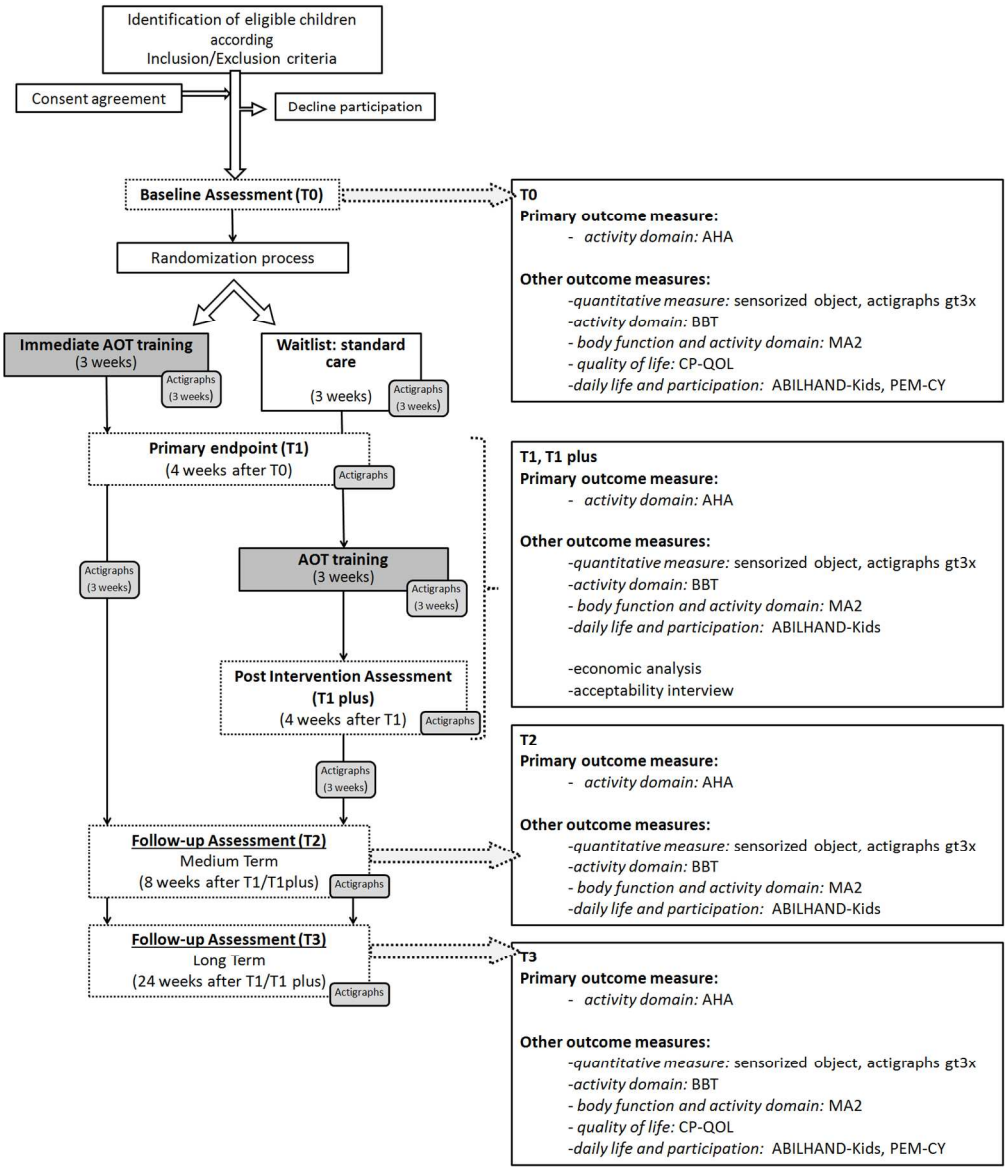
Figure 4.a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. **b)** Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal.

Supplement material 1. SPIRIT and TIDier checklists

Supplement material 2. Written informed consents (in Italian language)

Supplement material 3. Written informed consents (in English language)

Supplement material 4. Tele-UPCAT acceptability interview



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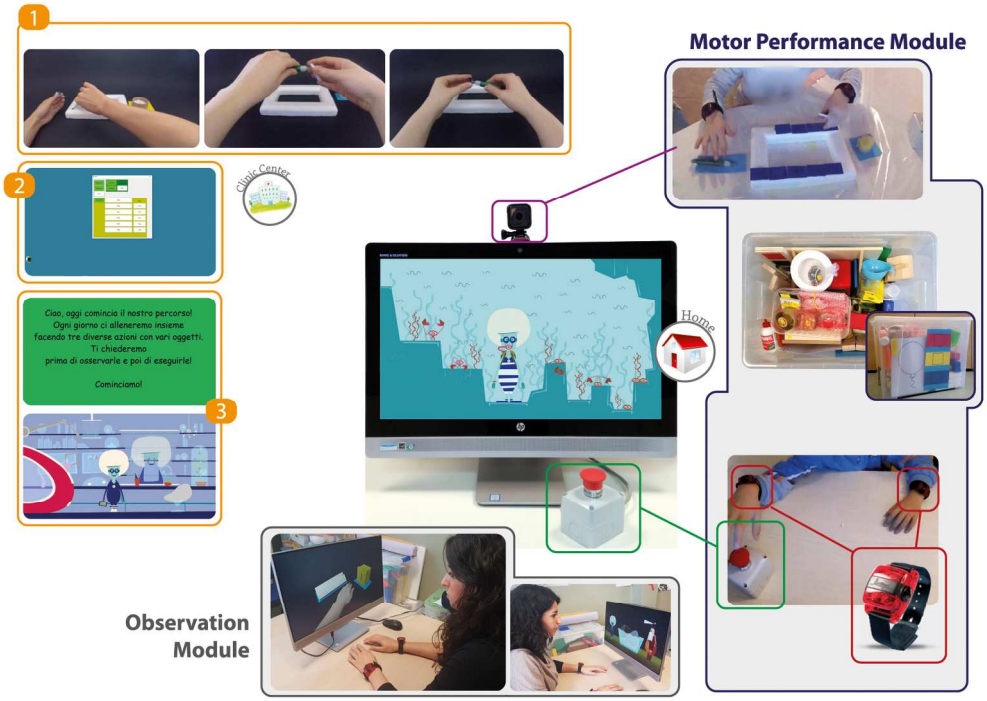
141x163mm (300 x 300 DPI)

	STUDY PERIOD				
	Enrollment	Post-allocation			
TIMEPOINT**	*T0*	*T_1*	*T_1 plus**	*T_2*	*T3*
ENROLLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation	X				
INTERVENTIONS:					
AOT intervention					
Wait list control group	←	→			
ASSESSMENTS:	←	→	←	→	
AHA	X	X	X	X	X
MA 2	X	X	X	X	X
BBT	X	X	X	X	X
ABILHAND-Kids	X	X	X	X	X
CP QoL	X				X
Quantitative measurement during unimanual and bimanual manipulation tasks, executed after the observation of the same tasks	X	X	X	X	X
Quantitative measurement of bimanual upper limb activities by means of Actigraph GXT3+	X	X	X	X	X
Economic analysis		X	X		
Acceptability interview		X	X		

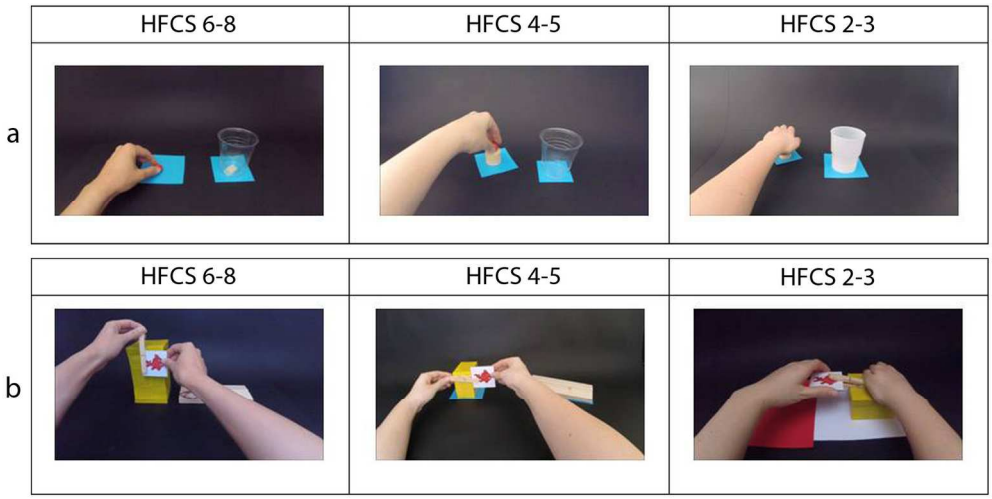
* only for wait-list group

Schedule of enrolment, interventions, and assessments

60x88mm (300 x 300 DPI)



Caption : Caption : Caption : Figure 3. Tele-UPCAT platform. Set-up of the Tele-UPCAT platform for delivering the AOT at home. It includes an Observation Module for the presentation of AOT videos (1) selected in the Clinical Interface (2) by the clinical staff in relation to HFCS level (6-8, 4-5 or 2-3), Side of impaired hand and Type of interface. A dedicated software, aimed at guiding and motivating subjects to perform AOT is also provided with age related features (3) for Teenagers or little Boys and Girls. The Motor Performance Module for the execution of actions is composed of a kit of common objects and toys, identical to those shown in the videos and a couple of Actigraphs (wGT3X-BT, wActiSleep-BT) worn on both wrists and a Button. The integrated camera records subject's attention during the observation task and exercise execution.



a) Example of the unimanual action b of day 1 for the left hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal. b) Example of the bimanual action b of day 11 for the right hand, with a different pattern of movement, based on subject HFCS level, maintaining the same goal

170x83mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,13
	2b	All items from the World Health Organization Trial Registration Data Set	2,13
Protocol version	3	Date and version identifier	13
Funding	4	Sources and types of financial, material, and other support	2,13
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,13
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13

Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3,4
	6b	Explanation for choice of comparators	3,4
Objectives	7	Specific objectives or hypotheses	3,4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4,5

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8,9
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	4
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5,6
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5,6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	4
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4,5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	5, 9-11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	5

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	5
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11, 12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11, 12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11, 12
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	5
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	5
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	5
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	12

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	5
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	5
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	12
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary material (2 and 3)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

TIDieR
Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	Page 2	_____
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	Pages 3-4	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	Pages 6-9	_____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	Pages 3-5	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	Pages 5-8	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	Pages 5, 8	_____
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	Page 8	_____

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	Page 6	_____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	Pages 6-8	_____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	_____N/A____	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____N/A____	_____
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	____N/A_____	_____

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

FONDAZIONE
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OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
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MODULO INFORMATIVO
PER GENITORI/TUTORE LEGALE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentili Genitori/Tutore,
Le informazioni contenute nella scheda informativa seguente sono dettagliate e potrebbero risultare molto complesse.

Le chiediamo di accettare la partecipazione allo studio solo dopo avere letto con attenzione questo foglio informativo ed avere avuto un colloquio esauriente con il medico sperimentatore che le dovrà dedicare il tempo necessario per comprendere completamente ciò che le viene proposto.

Vostro/a figlio/a potrebbe essere idoneo a partecipare ad uno studio promosso dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni importanti riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non vi risultasse chiaro, potrete porre domande ai medici sperimentatori coinvolti dello studio. Prendetevi tutto il tempo necessario. La partecipazione di vostro/a figlio/a è volontaria e potrete ritirarla in qualsiasi momento.
Una volta che avrete letto questo modulo, avrete ricevuto risposta alle eventuali domande, e qualora decideste di far prendere parte vostro/a figlio/a allo studio, vi sarà chiesto di firmare un modulo di consenso, di cui riceverete una copia cartacea.

Cosa si propone lo studio

Vostro/a figlio/a è stato/a invitato/a a partecipare a questo studio per valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 bambini/adulti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei bambini che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 4 settimane; a termine delle quali i bambini di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i bambini saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T2). Per dettagli vedi Disegno dello studio Figura 1.

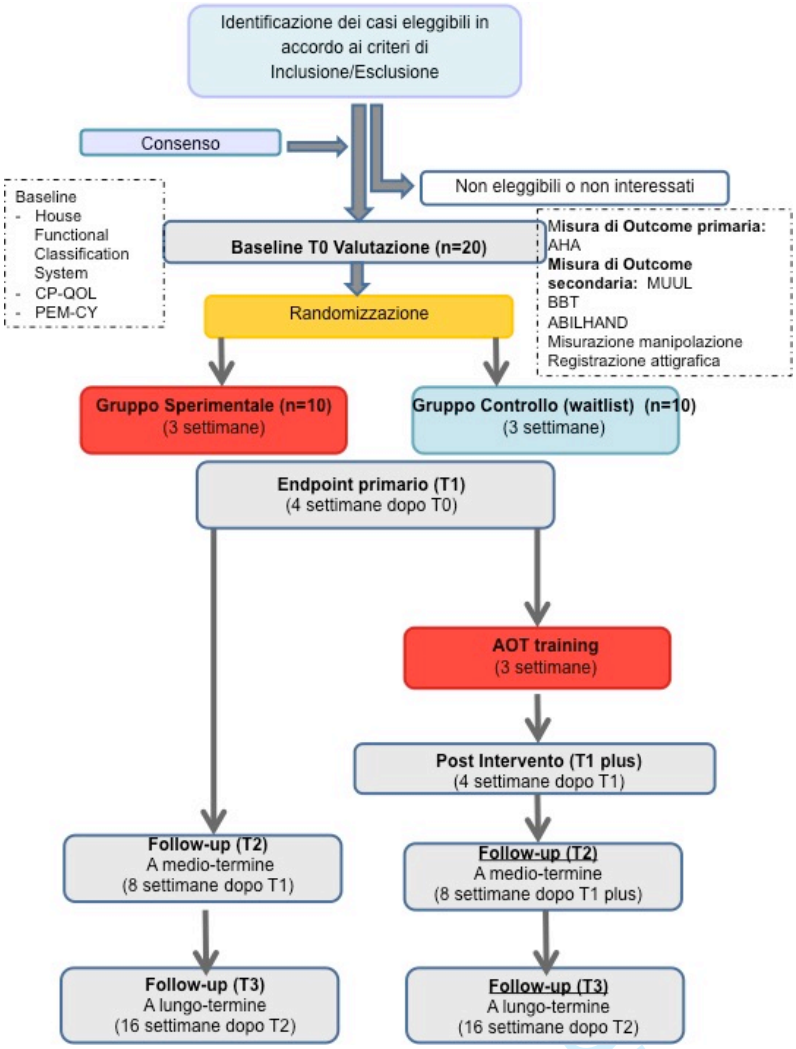


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i bambini arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolari di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I bambini che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i bambini allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la partecipazione allo studio

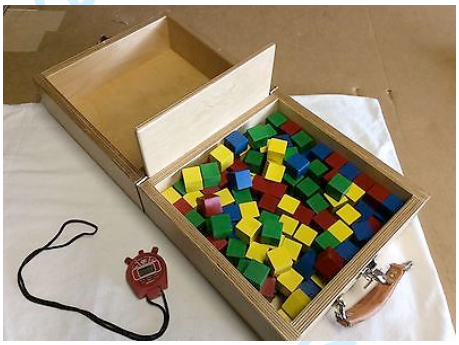
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



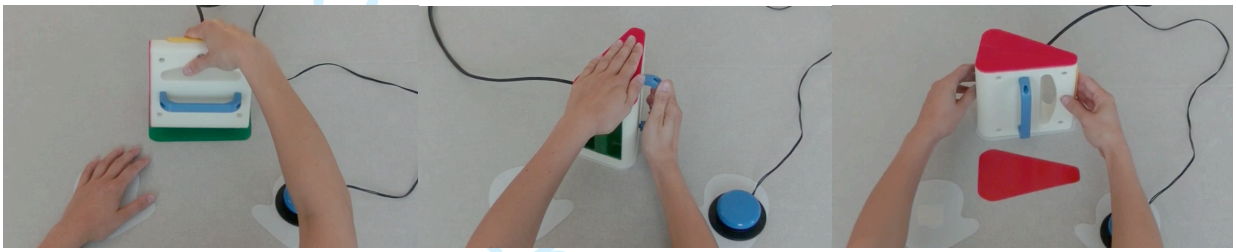
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND-Kids* è un breve questionario, validato in bambini con paralisi cerebrale infantile dai 6 ai 15 anni che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da un genitore in base alla difficoltà che ha il bambino a compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita nei bambini ed adolescenti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se doveste decidere di non prendere parte allo studio, o in caso doveste cambiare idea in seguito, vostro/a figlio/a non subirà alcuna penalità o perdita di benefici ai quali avrebbe altrimenti diritto. Le sue cure mediche attuali e future presso l'IRCCS

Fondazione Stella Maris non saranno compromesse dalla vostra decisione ed i medici continueranno a seguirlo/a con la dovuta attenzione.
Potrete ritirare l'adesione di vostro/a figlio/a allo studio in un qualsiasi momento dandone comunicazione al medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Procedure previste alla fine dello studio
Non è prevista alcuna procedura da attuarsi alla fine dello studio.

Informazione del medico di medicina generale /pediatra di libera scelta
Per la migliore tutela della salute di vostro/a figlio/a, vi verrà chiesto di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accettate di far partecipare vostro/a figlio/a.

Informazioni sui risultati dello studio
Qualora foste interessati, potrete chiedere al medico di comunicarvi i risultati generali dello studio ed in particolare quelli che riguardano vostro/a figlio/a.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i dati personali di Suo Figlio/a, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento

I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La partecipazione di Suo figlio/a allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione nella persona della Dr.ssa Giuseppina Sgandurra *, IRCCS Fondazione Stella Maris, Viale del Tirreno 331*. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la partecipazione di Suo figlio/a allo studio. In tal caso, i campioni biologici a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che riguardano Suo figlio/a, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi aggiuntivi a vostro carico derivanti dalla partecipazione allo studio. Non riceverete alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che vi è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data……..

Potrete segnalare qualsiasi fatto riteniate opportuno evidenziare, relativamente alla ricerca che riguarda vostro/a figlio/a, al Comitato Etico e/o alla Direzione sanitaria di questa struttura ospedaliera.

Per ulteriori informazioni e comunicazioni durante lo studio sarà a disposizione il seguente personale:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____
_____
Nome per esteso del medico Data Ora Firma
che ha consegnato l'informativa

CONSENSO INFORMATO PER GENITORI/TUTORE LEGALE

Versione 5.0 del 10/11/2016

Titolo Protocollo

Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Stella Maris, Prof. Giovanni Cioni IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 341/ ABC; 56128 Calambrone (Pisa), Italia Tel 050/886233.
e-mail: g.sgandurra@fsm.unipi.it

Io sottoscritta (madre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

Io sottoscritto (padre/tutore) _____ nata il ___/___/_____residente a_____ via/piazza _____ Tel._____ domicilio (se diverso dalla residenza)_____

del minore _____ nato il ___/___/_____
residente a _____via/piazza _____

dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, della quale mi è stata consegnata una copia in data _____ alle ore _____ (indicare data e ora della consegna).

Dichiaro che mi sono stati chiaramente spiegati la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico.

DICHIARO inoltre che:

1. ho letto e compreso il foglio informativo fornito riguardo il progetto di ricerca e facente parte di questo consenso;
2. mi è stata data l'opportunità di porre qualsivoglia domanda allo sperimentatore dello studio e ho avuto risposte soddisfacenti;
3. mi è stato concesso il tempo sufficiente per riflettere sulle informazioni ricevute e per discuterne con terzi;
4. sono stato/a informato/a che il protocollo dello studio e tutti i moduli utilizzati hanno avuto il parere favorevole del Comitato Etico Pediatrico;
5. mi è stato chiaramente spiegato che posso decidere che il/la minore non prenda parte allo studio o ne esca in qualsiasi momento, senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
6. sono consapevole che la ricerca potrà essere interrotta in ogni momento, per decisione del responsabile della ricerca, senza pregiudizio per la salute del/della minore;
7. sono stato informato/a che sarò messo al corrente di qualsiasi nuovo dato che possa compromettere la sicurezza della ricerca e che, per ogni problema o per ulteriori domande, potrò rivolgermi ai medici presso i quali il/la minore è in cura;
8. per la migliore tutela della salute del/la minore, sono consapevole dell'importanza (e della mia responsabilità) di informare il medico di medicina generale/pediatra di libera scelta della sperimentazione alla quale accetto di far partecipare il/la minore; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici;

9. sono stato informato/a che i risultati dello studio saranno resi noti alla comunità scientifica, tutelando l'identità del minore secondo la normativa vigente sulla privacy.

10. sono consapevole che devo/dobbiamo ricevere una copia del presente modulo di consenso.

Sottoscrivendo questo modulo acconsento al trattamento dei dati personali di mio figlio/a e al loro trasferimento al di fuori dell'Unione europea (*da inserire se effettuato specificando gli estremi identificativi dei destinatari*) per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di:

□ **volere** □ **NON volere**
che il minore partecipi alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informati sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
informare il pediatra di libera scelta/medico di medicina generale della partecipazione allo studio (*è preferibile il suo coinvolgimento*)

_____ ___/___/_____ _____ _____
Nome per esteso del minore Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso Data Ora Firma
del genitore/tutore legale

_____ ___/___/_____ _____ _____
Nome per esteso Data Ora Firma
del genitore/tutore legal

Io sottoscritto Prof./Dr. …… (Cognome) …….. (Nome)

Dichiaro che i genitori/tutori legali del Paziente hanno firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle possibili alternative;
- aver verificato che i genitori/tutore legale abbiano sufficientemente compreso le informazioni fornitegli
- aver lasciato ai genitori/tutore legale il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato | Data | Ora | Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle "Modulo informativo per i genitori/tutore legale" dovrà essere consegnata ai genitori/tutori legali del Paziente

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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Sede Legale:
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CENTRO DIURNO DI
RIABILITAZIONE PSICHIATRICA
La Scala di San Miniato (PI)
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MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

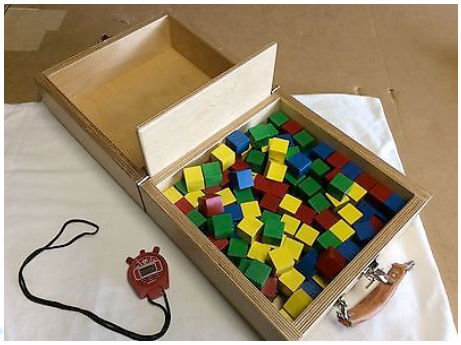
Perché facciamo questo studio?
La ricerca medica vuole migliorare la conoscenza sulle malattie.
Ti chiediamo di aiutarci a capire se l'uso di una terapia basata sull' osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato un' azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

Chi partecipa con me?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Che succede se partecipo?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo casuale ad uno dei due gruppi previsti nella prima fase dello studio: sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Inoltre ti saranno proposti, a dei tempi prestabiliti (quando ti arruoliamo, dopo che hai finito il trattamento o la fase di controllo, dopo che hai finito il trattamento se l'hai iniziato dopo, dopo 8 e dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!

Quanto durerà lo studio?
Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento). Ti verrà inoltre chiesto di effettuare i giochi e di compilare i questionari 3 o 4 volte.


Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?
Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?
Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio
Sei completamente libero di aderire o meno allo studio. Se deciderai di non partecipare, continuerai ad essere seguito periodicamente dalla tua equipe di riferimento del nostro centro clinico così come fatto fino ad ora.

Devo fornire il mio consenso per partecipare allo studio?
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare questo modulo di cui ti sarà data una copia.
Se decidi di non partecipare allo studio, o in caso dovessi cambiare idea in seguito, non succederà niente, continuerai a ricevere le cure a te necessarie presso questo ospedale.

E se dovessi avere delle domande?

Se hai delle domande puoi farle alla Dr.ssa Giuseppina Sgandurra durante il colloquio e potrai anche chiamarla al telefono al numero 050/886239: ti ascolterà e ti spiegherà tutto quello che desideri.

Data _____ ora _____ di consegna

_____Firma del medico che ha consegnato l'informativa

DICHIARAZIONE DI ASSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 7 E 13 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 6.0 del 29/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Il modulo informativo mi è stato consegnato il (data) _____ alle ore _____
Ho capito tutto quello che il medico mi ha spiegato.
Il Dottore ha ascoltato tutte le mie domande ed ha saputo rispondermi.
Se in futuro avrò bisogno di qualcos'altro i medici dello studio saranno a mia disposizione.

_____
Data e ora

_____
Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____
Firma del paziente. Scrivi il tuo nome in stampatello qui se desideri partecipare allo studio

_____ _____
Data/ora Firma del medico che ha informato il paziente

FONDAZIONE
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ISO 9001 BUREAU VERITAS Certification

MODULO INFORMATIVO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 17 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Caro/a ……,
potresti essere idoneo a partecipare ad uno studio proposto dall'IRCCS Fondazione Stella Maris.
Questo modulo fornisce informazioni riguardanti gli scopi, i rischi e i possibili benefici di questo studio. Se qualche aspetto di questo modulo non ti risultasse chiaro, puoi porre domande ai medici dello studio. Prenditi tutto il tempo necessario. Non sei obbligato a partecipare. Se accetti, potrai decidere di ritirare la tua partecipazione in qualsiasi momento.
Una volta che avrai letto questo modulo e avrai ricevuto risposta alle tue eventuali domande, ti sarà chiesto di decidere se desideri partecipare allo studio. Se vorrai partecipare, dovrai firmare il modulo di cui ti sarà data una copia.

Quale è lo scopo di questo studio?
Sei stato/a invitato/a a partecipare a questo studio perché pensiamo che puoi aiutarci a capire se l'uso di una terapia basata sulla osservazione può essere utile a migliorare la funzionalità del tuo braccio. La terapia basata sull'osservazione prevede la visione di brevi filmati, da osservare attentamente, che mostrato una azione fatta con le mani e subito dopo ti verrà chiesto di eseguire lo stesso movimento cercando di imitarlo il più possibile.
Inoltre ti chiederemo di indossare ai polsi dei braccialetti simili ad un orologio per meglio misurare e monitorare i movimenti delle tue braccia.

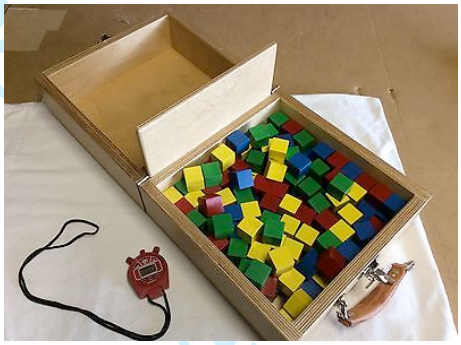
Quante persone parteciperanno?
Parteciperanno allo studio 20 bambini/ragazzi e giovani adulti di età compresa tra 5-20 anni. Tutti con difficoltà motorie simili alle tue.

Cosa comporta la partecipazione allo studio?
Se decidi di partecipare allo studio verrai all'inizio assegnato in modo random (casuale) ad uno dei due gruppi previsti nella prima fase dello studio:

sperimentale o controllo. Se verrai assegnato al gruppo sperimentale ti sarà proposto di iniziare subito un ciclo di terapia basata sull'osservazione a casa mentre (durata 3 settimane) se verrai assegnato al gruppo controllo ti sarà proposto di aspettare circa 4 settimane prima di iniziare lo stesso ciclo di terapia e nel frattempo continuerai a fare quello che stai facendo ora. Dunque farai in ogni caso la terapia basata sull'osservazione ma o la farai subito o dovrai solo aspettare. In entrambi i casi ti sarà chiesto di indossare ai polsi dei braccialetti simili ad un orologio. La terapia che farai prima o dopo in pratica si basa su un programma al computer in cui "Ubi", un extraterrestre, ti aiuterà passo passo negli esercizi da fare.

Lo studio durerà un anno. Se accetterai di prendere parte allo studio la tua partecipazione è di 3 settimane (durata del trattamento).

Inoltre ti saranno proposti, a dei tempi prestabiliti (T0: quando ti arruoliamo, T1: dopo che hai finito il trattamento o la fase di controllo, T1 plus: dopo che hai finito il trattamento se l'hai iniziato dopo, T2: dopo 8 e T3: dopo 16 settimane dalla fine del trattamento) dei giochi e dei questionari che ci aiutano a capire come usi le mani!



Alcuni esempi di giochi

Sono previsti benefici derivanti dalla mia partecipazione allo studio?

Ci aspettiamo che questa terapia possa aiutarti a migliorare l'uso delle tue mani

Quali sono i rischi dello studio?

Non sono previsti rischi in quanto si tratta di un trattamento molto semplice che potrai eseguire tranquillamente a casa e le valutazioni sono quelle che normalmente svolgi quanto vieni presso il nostro centro clinico.

Che cosa succede se decido di non prendere parte allo studio o di ritirarmi dallo studio?

La tua partecipazione allo studio è volontaria.

Se decidi di non partecipare, o in caso dovessi cambiare idea in seguito, non subirai alcuna penalità o perdita di benefici ai quali avresti altrimenti diritto. Le tue cure mediche attuali e future presso l'IRCCS Fondazione Stella Maris non saranno compromesse dalla tua decisione ed i medici continueranno a seguirti con la dovuta attenzione.

Puoi ritirare la tua adesione allo studio in qualsiasi momento, comunicandolo al medico dello studio, la dottoressa *Giuseppina Sgandurra* senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che ti riguardano e potrai chiedere la cancellazione di quelli già raccolti. La tua partecipazione allo studio potrà essere interrotta se il medico valuterà che il nuovo trattamento non ha portato alcun giovamento o se si verificheranno effetti indesiderati. In questi

casi sarai tempestivamente informato dal medico e potrai discutere con lui circa ulteriori trattamenti validi per la tua patologia.

Cosa accadrà alle informazioni che sono state raccolte per lo studio?
Le informazioni mediche che ti riguardano come ad esempio l'età, il sesso, le caratteristiche della tua malattia, i risultati delle prove e il diario delle attività quotidiane saranno conservate presso un archivio della Fondazione Stella Maris.
I tuoi dati saranno archiviati in forma anonimizzata, il tuo nome sarà sostituito da un codice conosciuto solo da poche persone e quindi i tuoi dati saranno anonimi. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al tuo nominativo.
I dati dello studio potranno essere mostrati in occasione di convegni/congressi o pubblicati in riviste scientifiche per informare gli altri medici e i professionisti del settore sanitario.

Informazioni sui risultati dello studio
Alla fine dello studio sarai informato sui risultati della ricerca.

Ulteriori informazioni
Non sono previsti costi aggiuntivi a tuo carico derivanti dalla partecipazione allo studio.
Non riceverai alcun compenso economico per la partecipazione allo studio.
Il protocollo dello studio che ti è stato proposto è stato redatto in conformità alle Norme di Buona Pratica Clinica e alla Dichiarazione di Helsinki, ed è stato approvato dal Comitato Etico Pediatrico della Regione Toscana in data 22/11/2016.

Per ulteriori informazioni e comunicazioni potrai contattare il personale dello studio che sarà a tua disposizione:

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	gsgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha consegnato l'informativa — Data — Ora — Firma

MODULO DI CONSENSO
PER PAZIENTI DI ETA' COMPRESA TRA 14 E 18 ANNI
Versione 6.0 del 29/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data *V 6.0 del 29/11/2016*
Promotore dello studio: *IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)*
Sperimentatore Principale: *Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it*

Io sottoscritto (nome e cognome) _____
dichiaro di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione allo studio in oggetto, secondo quanto riportato nel modulo informativo allegato, della quale mi è stata consegnata una copia in data _____ alle ore _____

Dichiaro che mi sono stati chiaramente spiegati la natura, lo scopo, i benefici attesi, i rischi e gli inconvenienti possibili dello studio clinico.

Dichiaro di aver potuto fare tutte le domande che ho ritenuto necessarie e di aver ricevuto risposte soddisfacenti, come pure di aver avuto la possibilità di informarmi in merito ai particolari dello studio con persona di mia fiducia.

Accetto dunque liberamente di partecipare alla ricerca, avendo compreso completamente il significato della richiesta e i rischi e benefici che possono derivare da questa partecipazione.

Acconsento al trattamento dei miei dati personali *e al loro trasferimento al di fuori dell'Unione europea (se applicabile)* per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

□ Desidero che mi siano comunicati i risultati dello studio.

__/__/____ _____ _____
Data Ora Firma del paziente

__/__/____ _____ _____
Data Ora Firma del medico che ha informato il paziente e registrato il suo consenso

FONDAZIONE
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Gentile Sig.ra/Sig.re, le informazioni contenute nel seguente foglio informativo sono dettagliate e potrebbero risultare
MOLTO COMPLESSE

Le chiediamo di accettare la partecipazione allo studio SOLO dopo avere letto con attenzione questo foglio informativo ed avere avuto un COLLOQUIO ESAURIENTE con il medico sperimentatore che le dovrà dedicare il TEMPO NECESSARIO
per comprendere completamente ciò che le viene proposto

INFORMAZIONI SCRITTE
PER IL PAZIENTE
Versione 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Gentile Signora / Egregio Signore,
Le è stato chiesto di partecipare ad uno studio clinico sperimentale e questo documento ha lo scopo di informarLa sulla natura dello studio, sul fine che esso si propone, su ciò che comporterà per Lei una tale partecipazione, sui suoi diritti e le sue responsabilità.
La prego di leggere attentamente queste informazioni scritte prima di prendere una decisione in merito ad una eventuale Sua partecipazione allo studio. Lei avrà a disposizione tutto il tempo necessario per decidere se partecipare o meno.
Potrà, inoltre, porre liberamente qualsiasi domanda di chiarimento e riproporre ogni quesito che non abbia ricevuto una risposta chiara ed esauriente.
Nel caso in cui, dopo aver letto e compreso tutte le informazioni ivi fornite, decidesse di voler partecipare allo studio clinico, Le chiederò di voler firmare e personalmente datare il modulo di Consenso Informato allegato a questo documento.

Che cosa si propone lo studio

Valutare la fattibilità e l'efficacia dell' Action Observation Training (AOT) rispetto alla standard care nella riabilitazione a domicilio dell'arto superiore in bambini con emiplegia.

Un secondo obiettivo sarà quello di misurare e monitorare i movimenti degli arti superiori tramite l'uso di attigrafi, strumenti semplici commerciali tipo orologi (vedi oltre), i cui dati verranno comparati con i risultati clinici.

Che cosa è l'AOT

La recente scoperta del Sistema dei Neuroni Specchio (SNS) ha favorito lo sviluppo dell' Action-Observation Training (AOT), una terapia che si basa sul ruolo dell'osservazione di azioni significative seguita dalla loro esecuzione come modello per l'apprendimento.

L'AOT è stato utilizzato con risultati promettenti in alcuni studi su pazienti adulti colpiti da ictus, recenti studi su bambini affetti da Paralisi Cerebrale Infantile indicano alcuni effetti positivi sulla funzione dell' arto superiore. In particolare, l'IRCCS Fondazione Stella Maris (FSM) ha negli anni scorsi effettuato in un gruppo di 24 bambini con emiplegia uno studio sull' AOT, **Errore. L'origine riferimento non è stata trovata.**I dati preliminari di tale studio supportano l'ipotesi che una riabilitazione intensiva basata sull' AOT è in grado di migliorare le attività con gli arti superiori dei bambini con emiplegia. Sulla base di tali promettenti risultati è stato proposto il presente studio.

La selezione dei soggetti e la sperimentazione clinica dei casi avverrà a cura della FSM.
Si intende selezionare 20 soggetti di età compresa tra 5-20 anni affetti da paralisi cerebrale infantile a tipo emiplegia con predominante quadro di spasticità che interferisce con la funzione dell'arto superiore; sufficiente capacità di cooperazione e di comprensione nelle attività da proporre; genitori o tutori legali o soggetti adulti con emiplegia disponibili a collaborare ad un programma riabilitativo intensivo domiciliare di 3 settimane consecutive.

Il reclutamento avverrà solo dopo firma del consenso alla partecipazione da parte dei soggetti e se minorenni anche dei genitori o tutori.
I soggetti arruolati saranno divisi in modo random (ossia casuale) in due gruppi: sperimentale e standard care/controllo. I soggetti allocati nel gruppo sperimentale inizieranno subito con l'AOT per un periodo di 3 settimane, mentre quelli del controllo o standard care proseguiranno quanto normalmente eseguono facendo un diario delle eventuali attività riabilitative che conducono.
Tutti i bambini saranno valutati prima (T0) e dopo (T1) il periodo di training sperimentale/standard care con scale e test standardizzati. Al termine di tale periodo a quei soggetti che non hanno effettuato il training sperimentale sarà data l'opportunità di effettuare il training. Il training sarà proposto con le stesse modalità del precedente e durerà 3 settimane a termine delle quali i soggetti di questo gruppo saranno rivalutati con scale e test standardizzati (T1 plus). Tutti i soggetti saranno rivalutati anche dopo 8 settimane da T1 (T2) e dopo 16 settimane da T1 (T3).
La valutazioni saranno effettuate allo scopo di valutare gli effetti del training nel breve tempo (T1 e T1 plus) e nel medio (T2) e lungo tempo (T3). Per dettagli vedi Disegno dello studio Figura 1.

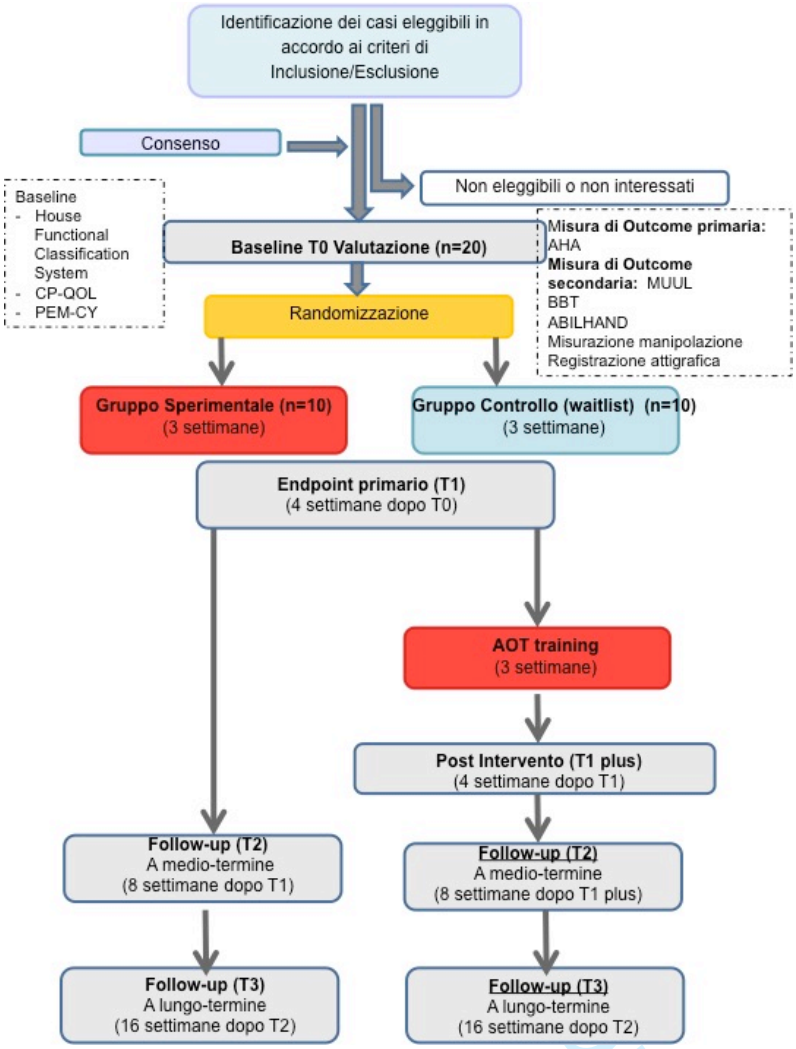


Figura 1: Disegno dello studio Clinico

Riassumendo tutti i soggetti arruolati saranno valutati con scale e test standardizzati in tempi differenti:
T0, T1, T2, T3.

- T0: nella settimana precedente all'avvio del training/standard care
- T1: nella settimana successiva al primo periodo di training sperimentale/standard care
- T1 plus: nella settimana successiva al training sperimentale. Questa valutazione sarà effettuata solo dal gruppo di soggetti che effettuerà il training nella seconda fase.
- T2: 8 settimane dalla fine del training sperimentale
- T3: 16 settimane dopo T2.

Il training di AOT sarà effettuato tramite piattaforma dedicata e personalizzata che verrà consegnata a casa insieme al materiale da utilizzare. Il trattamento verrà effettuato dai bambini, con la supervisione dei genitori, durerà circa un'ora al giorno per 5 giorni alla settimana per 3 settimane successive (totale di 15 giorni). I primi due/tre giorni del training un terapista coadiuverà a domicilio i genitori o i soggetti emiplegici adulti nella gestione del training.

Durante le tre le settimane di training verrà inoltre chiesto ai soggetti arruolati di indossare degli attigrafi commerciali (Figura 1) tutti i giorni per il maggior tempo possibile.
I soggetti che inizialmente verranno allocati nel gruppo controllo o standard care sarà chiesto di mantenere un diario delle eventuali attività riabilitative che conducono normalmente e sarà chiesto di indossare gli attigrafi tutti i giorni per il maggior tempo possibile, come i soggetti allocati al gruppo sperimentale.
Sarà chiesto di mantenere gli attigrafi anche nelle 3 settimane successive alla fine del training.

L'attigrafo è un sensore accelerometrico di movimento non invasivo che si indossa al polso come un orologio, è confortevole e resistente all'acqua. Oggigiorno gli attigrafi commerciali sono diventati strumenti di tendenza in uso da giovani ed adulti per il monitoraggio dell'attività fisica e del consumo calorico quotidiano. Il modello utilizzato nel presente studio è riportato nella foto di seguito.

Figura 2: wGT3X-BT

Il reclutamento avverrà solo dopo la firma del consenso informato.
Al reclutamento saranno acquisiti alcuni dati clinici (tra cui età, sesso, caratteristiche della lesione cerebrale, lato plegico, livello di funzionalità manuale all'House Functional Classification System) e sarà creato un apposito database.
A tutela della privacy e dell'anonimato a ciascun soggetto sarà assegnato un codice numerico che verrà conservato in forma separata, in questo modo il database non conterrà nessun dato identificativo del soggetto. L'accesso a tali dati sarà limitato al solo personale direttamente coinvolto nello studio e tutti i dati verranno trattati in forma anonima.

Cosa comporta la Sua partecipazione allo studio

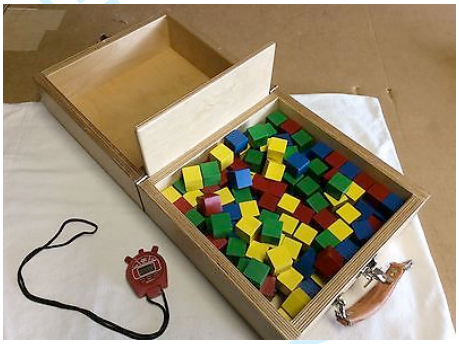
Lo studio avrà una durata totale di 12 mesi, durante tale periodo saranno arruolati presso l'IRCCS Fondazione Stella Maris un gruppo di 20 bambini/adolescenti e giovani adulti (5-20 anni) con emiplegia congenita. La partecipazione sarà su base volontaria, previa firma del consenso informato. Lo studio prevederà un intervento riabilitativo della funzione manuale a domicilio tramite una piattaforma costruita ad hoc che consentirà di effettuare un training personalizzato di AOT.

Lo studio prevede lo svolgimento di test e questionari clinici, normalmente impiegati per la valutazione funzionale dell'emiplegia congenita:

Il protocollo consisterà nei seguenti test:

1- Assisting Hand Assessment (AHA) una scala, che attraverso la proposta di attività ludico-ricreative, consente di valutare la funzionalità manuale e bimanuale.

2- Box and Block Test (BBT) E' una misura per la valutazione della destrezza manuale in cui viene richiesto prima con una mano poi con l'altra di spostare i cubi da un lato della scatola all'altro in 60 secondi.



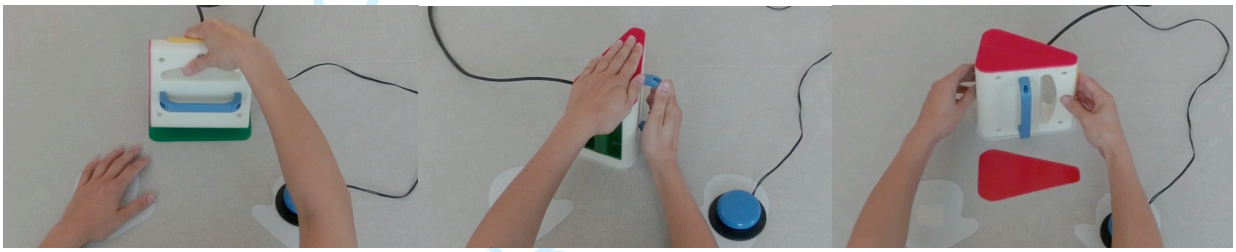
3- *Melbourne Assessment of Upper Limb Function (MUUL)*. Si tratta di uno strumento standardizzato per la misurazione della capacità e qualità di movimento dell' arto superiore nei bambini con Paralisi Cerebrale Infantile di età compresa tra i 2 e i 15 anni, ma utilizzati anche per l'età adulta. Verrà utilizzato a tutti i tempi di valutazione.

4- L'*ABILHAND* è un breve questionario, validato in soggetti con paralisi cerebrale infantile che misura 21 principali attività quotidine bimanuali. Il punteggio viene assegnato da soggetto stesso in base alla difficoltà che esperimenta nel compiere quotidianamente l'attività richiesta con un punteggio su 3 punti (impossibile, difficile, facile). Verrà utilizzato a tutti i tempi di valutazione.

5- *Participation and Environment Measure - Children and Youth (PEM-CY*). Si tratta di una misura di participation e di fattori ambientali a casa, a scuola e nella comunità. Verrà utilizzato a T0 e a T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL –Child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL –Teen, 13-18 years)*. Si tratta di questionari per la valutazione della qualità della vita in soggetti con paralisi cerebrale infantile. Verrà utilizzato a T0 e a T3.

7- *Misurazione strumentale della manipolazione durante task uni e bimanuali eseguiti dopo osservazione.* Si tratta di un oggetto contenente due celle di carico per misurare la forza esercitata (in compressione o trazione) quando viene afferrato dalla mano plegica e uno switch on-off per valutare il contatto della mano sana. Un ulteriore switch è posizionato sul punto di partenza sul tavolo sotto la mano plegica per registrare il momento in cui inizia il suo movimento verso l'oggetto. Lo strumento viene utilizzato subito dopo la visione di tre task di manipolazione effettuati con tre diversi tipi di presa: un task unimanuale effettuato con la mano plegica, un task bimanuale sincrono tra le due mani ed un task bimanuale di cooperazione tra le due mani.



TASK 1. TASK 2. TASK 3.

L'intera valutazione durerà circa un'ora.

8- *Uso dell'attigrafo nella vita quotidiana.* I soggetti reclutati che saranno disponibili ad indossare l'attigrafo (Figura 2) al di fuori della valutazione clinica sarà chiesto di indossare 2 attigrafi ai polsi (uno per ciascun polso) per periodi di tre settimane (fase sperimentale AOT, fase controllo, fase di follow-up). Al termine del periodo di registrazione gli attigrafi si spegneranno da soli e saranno riconsegnati direttamente o tramite posta allo sperimentatore.

Benefici derivanti dalla partecipazione allo studio

Sulla base dei dati della letteratura e sui risultati preliminari ottenuti presso il Ns Istituto si prevede, grazie al training di AOT, un possibile miglioramento funzionale nell'utilizzo dell'arto superiore nelle attività di vita quotidiana.

Possibili rischi

Non si prevedono rischi diretti dalla partecipazione allo studio.

Possibili alternative

L'alternativa è non partecipare allo studio.

Che cosa succede se decidete di non prendere parte allo studio o di ritirarvi dallo studio

La partecipazione allo studio è volontaria. Se decide di partecipare, avrà il diritto di ritirarsi dallo studio in qualsiasi momento e senza l'obbligo di fornire spiegazioni, dandone tuttavia comunicazione al medico responsabile dello studio, la Dr.ssa Giuseppina Sgandurra.
Potrà ritirare la sua adesione allo studio in un qualsiasi momento dandone comunicazione al

medico dello studio, alla Dr.ssa Giuseppina Sgandurra, senza fornire alcuna giustificazione. In tal caso non saranno raccolti ulteriori dati che lo/a riguardano e potrete chiedere la cancellazione di quelli già raccolti.

Consenso ad informare il proprio medico di medicina generale
Per la migliore tutela della Sua salute, Le verrà chiesto di informare il Suo medico di medicina generale in merito alla sperimentazione alla quale accetta di partecipare.

Informazioni circa i risultati dello studio
Se Lei lo richiederà, alla fine dello studio potranno esserLe comunicati i risultati generali dello studio ed in particolare quelli che La riguardano.

INFORMAZIONI IN MERITO AL TRATTAMENTO DEI DATI PERSONALI:
Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris e in accordo alle responsabilità previste dalle norme della buona pratica, tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine ed alle caratteristiche della sua condizione medica solo esclusivamente in funzione della realizzazione dello studio. A tal fine i dati indicati saranno raccolti dal Centro di sperimentazione e trattati in modo anonimo e a tutela della privacy. Il trattamento dei dati personali relativi all'età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono indispensabili allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati, per almeno 7 (sette) anni dalla conclusione dello studio, unitamente a tale codice, alla Sua data di nascita, l' età, sesso, lato plegico/dominanza manuale, funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento
I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti
Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi

direttamente al centro di sperimentazione nella persona della Dott.ssa Giuseppina Sgandurra. Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. In tal caso, i dati acquisiti a Lei correlati verranno distrutti. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca: anche per i dati già raccolti potrà eventualmente chiedere la cancellazione.

Ulteriori informazioni

Non sono previsti costi a Suo carico derivanti dalla partecipazione allo studio. Non riceverà alcun compenso economico per la partecipazione allo studio.

Il protocollo dello studio che Le è stato proposto è stato approvato dal Comitato Etico Pediatrico Toscano in data…… Il Comitato Etico ha tra le altre cose verificato la conformità dello studio alle Norme di Buona Pratica Clinica della Unione Europea ed ai principi etici espressi nelle Dichiarazione di Helsinki.

Lei potrà segnalare qualsiasi fatto ritenga opportuno evidenziare, relativamente alla ricerca che La riguarda, al Comitato Etico e/o alla Direzione Sanitaria di questa struttura ospedaliera.

Dr.ssa .	Sgandurra	Giuseppina
Telefono	050/886233	
E.mail	g.sgandurra@fsm.unipi.it	

_____ ___/___/_____ _____ _____

Nome per esteso del medico che ha consegnato l'informativa | Data | Ora | Firma

MODULO DI CONSENSO INFORMATO

V 5.0 del 10/11/2016

Titolo Protocollo: *Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia*

Versione e data V 5.0 del 10/11/2016

Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

Io sottoscritto/a _____ nato/a il ___/___/_____
residente a_____ via/piazza _____
Tel._____ domicilio (se diverso dalla residenza) _____

DICHIARO

- di aver ricevuto dal Dottor _____ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, facente parte di questo consenso, della quale mi è stata consegnata una copia in data _____ alle ore _____ (*indicare data e ora della consegna*);
- che mi sono stati chiaramente spiegati e di aver compreso la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili e le alternative dello studio clinico;
- di aver avuto l'opportunità di porre domande chiarificatrici e di aver avuto risposte soddisfacenti;
- di aver avuto tutto il tempo necessario prima di decidere se partecipare o meno;
- di non aver avuto alcuna coercizione indebita nella richiesta del Consenso;
- che mi è stato chiaramente spiegato di poter decidere liberamente di non prendere parte allo studio o di uscirne in qualsiasi momento senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i medici curanti e con la struttura presso la quale sono in cura;
- di essere consapevole dell'importanza (e della mia responsabilità) di informare il mio medico di medicina generale della sperimentazione alla quale accetto di partecipare; nel caso decida di non informarlo, esonero sia il mio medico curante che i medici che mi seguono nella sperimentazione dalla responsabilità per i danni che possano derivare dall'incompatibilità tra il(i) farmaco(i) in studio ed altri trattamenti medici.

Sottoscrivendo questo modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

DICHIARO pertanto di

□ **volere** □ **NON volere**
partecipare alla □ sola fase di valutazione clinica
□ sia alla fase di valutazione clinica che a domicilio

□ **volere** □ **NON volere**
essere informato sui risultati di questa ricerca dal medico dello studio

□ **volere** □ **NON volere**
essere informato sui risultati della ricerca dal medico dello studio, anche in relazione alle notizie inattese che dovessero essere accidentalmente riscontrate con le indagini previste dallo studio

□ **volere** □ **NON volere**
Informare il medico di medicina generale della partecipazione allo studio

_____ ___/___/_____ _____ _____
Nome per esteso del paziente (adulto, minore maturo) Data Ora Firma

_____ ___/___/_____ _____ _____
Nome per esteso rappresentante legale Data Ora Firma

Io sottoscritto Prof./Dr. …… ……
Cognome Nome

Dichiaro che il Paziente ha firmato spontaneamente la sua partecipazione allo studio

Dichiaro inoltre di:

- aver fornito al Paziente esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, ai possibili rischi e benefici e alle sue possibili alternative;
- aver verificato che il Paziente abbia sufficientemente compreso le informazioni fornitegli
- aver lasciato al Paziente il tempo necessario e la possibilità di fare domande in merito allo studio
- non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso

_____ ___/___/_____ _____ _____
Nome per esteso del medico che ha fornito le informazioni e raccolto il consenso informato
Data Ora Firma

NOTA BENE

una copia del presente modulo, firmato e datato, allegato alle “Informazioni Scritte per il Paziente” dovrà essere consegnata al Paziente stesso

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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Dott. Roberto Cutajar
segreteria: Tel. 050 886271

DIRETTORE SCIENTIFICO
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DIRETTORE SANITARIO
Dott. Giuseppe De Vito
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RIABILITAZIONE PSICHIATRICA
La Scala di San Miniato (PI)
Tel. 0571 419868

INFORMATIVA E MANIFESTAZIONE DEL CONSENSO
AL TRATTAMENTO DEI DATI PERSONALI

Titolo Protocollo
Action-Observation Training (AOT) per la riabilitazione a domicilio di soggetti con emiplegia
Versione e data V 5.0 del 10/11/2016
Promotore dello studio: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Sperimentatore Principale: Dr.ssa Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italia Tel 050/886233.
e-mail: g.sgandurra@fsm.unipi.it

Titolari del trattamento e relative finalità
Il Centro di sperimentazione IRCCS Fondazione Stella Maris in accordo alle responsabilità previste dalle norme della buona pratica clinica (decreto-legge n. 211/2003), tratteranno i Suoi dati personali, in particolare quelli sulla salute e, soltanto nella misura in cui sono indispensabili in relazione all'obiettivo dello studio, altri dati relativi alla Sua origine esclusivamente in funzione della realizzazione dello studio.
Il trattamento dei dati personali relativi tra cui età, sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

Natura dei dati
Il medico che La seguirà nello studio La identificherà con un codice: i dati che La riguardano, raccolti nel corso dello studio, ad eccezione del Suo nominativo, saranno registrati, elaborati e conservati unitamente a tale codice, alla Sua data di nascita, al sesso, lato plegico/dominanza manuale, livello di funzionalità manuale, misure ottenuti dai test di funzionalità manuale, attività quotidiane svolte, dati provenienti dalle registrazioni attigrafiche sono necessari allo svolgimento dello studio. Soltanto il medico e i soggetti autorizzati potranno collegare questo codice al Suo nominativo.

Modalità del trattamento
I dati, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici. La Sua partecipazione allo studio implica che, il Comitato etico e le autorità sanitarie italiane e straniere potranno conoscere i dati che La riguardano, contenuti anche nella Sua documentazione clinica originale, con modalità tali da garantire la riservatezza della Sua identità.

Esercizio dei diritti

Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente al centro di sperimentazione. Sperimentatore principale Dr.ssa Giuseppina Sgandurra , IRCCS Fondazione Stella Maris. Viale del Tirreno 331, 56128 Calambrone (Pisa), *g.sgandurra@fsm.unipi.it.*

Potrà interrompere in ogni momento e senza fornire alcuna giustificazione la Sua partecipazione allo studio. Non saranno inoltre raccolti ulteriori dati che La riguardano, ferma restando l'utilizzazione di quelli eventualmente già raccolti per determinare, senza alterarli, i risultati della ricerca.

Consenso

Sottoscrivendo tale modulo acconsento al trattamento dei miei dati personali per gli scopi della ricerca nei limiti e con le modalità indicate nell'informativa fornitami con il presente documento.

Nome e Cognome dell'interessato (in stampatello) _____

Firma dell'interessato _____

Data _____

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INFORMATIVE MODULE FOR PARENTS/LEGAL TUTORS

Version 5.0 of 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 5.0 V **and date** of 10/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear parents/legal tutor,
the information contained in this informative document are detailed and can be very complex. We ask you to accept the participation in the trial only after you have carefully read this document and have had an exhaustive conversation with the investigator that must devote the necessary time to fully understand what it is proposed.

Your son/daughter may be eligible to participate in a study of the IRCCS Fondazione Stella Maris. This module provides important information on the purposes, risks and possible benefits of this study. If some aspect of this module are not clear, you can ask questions to doctors researchers involved in the study. Take all the time necessary. Your son/daughter's participation is voluntary and you may withdraw it at any time. Once you have read this form, you will receive answers to any questions, and if you decide to take your son/daughter to study, you will be asked to sign a consent form, which you will receive a printed copy.

Which are the aims of the study

The study aims to evaluate the feasibility and effectiveness of the Action Observation Training (AOT) with regard to the standard care in home-based rehabilitation in children and adults with hemiplegia.

A second goal will be to measure and monitor the movements of the upper limbs through the use of actigraphs, simple commercial instruments such as watches (see below), whose data will be compared with the clinical results.

What is AOT?

The recent discovery of the Mirror Neuron System (SNS) has promoted the development of the Action-Observation Training (AOT), a therapy based on the observation of goal-directed actions followed by their motor replication as a model for motor learning.
AOT has been used with promising results in some studies in adult with stroke and recently also in children with Cerebral Palsy showing positive effects on the upper limb function. In particular, the IRCCS Fondazione Stella Maris (FSM) has carried out in a group of 24 children with hemiplegia Preliminary data support the hypothesis that AOT can improve the upper limbs function in children with hemiplegia. Based on these promising results, this study has been proposed.

The recruitment will be made by the FSM . We propose to select 20 participants aged between 5-20 years with unilateral cerebral palsy with a predominant spasticity pattern that interferes with the upper limb function; sufficient cooperation in the activities to be proposed; parents or legal tutor or adult with hemiplegia available to collaborate in 3- consecutive weeks of intensive home training program.

Recruitment will take place after the signing of informed consent by the subjects and/or by the parents or the legal tutor. The enrolled subjects will be divided randomly into two groups: experimental and standard care (control) groups. Subjects assigned to the experimental group will begin with the AOT for a period of 3 weeks, while those in the control or standard care will continue as they normally do by making a diary of any rehabilitation activities they conduct.
All subjects will be evaluated before (T0) and after (T1) the experimental / standard care period with standardized scales and tests. At the end of this period to those individuals who have not carried out the experimental training have the opportunity to carry out the training. The training will be offered with the same details and it will last three weeks at the end of which the subjects of this group will be re-evaluated with standardized scales and test (T1 plus). All subjects will be re-evaluated after 8 weeks from T1/T1 plus (T2) and after 16 weeks of T1 (T3).
These evaluations will be performed in order to evaluate the effects of training at short term (T1 and T1 plus) and at medium (T2) and long term (T3). For details see Study Design Figure 1.

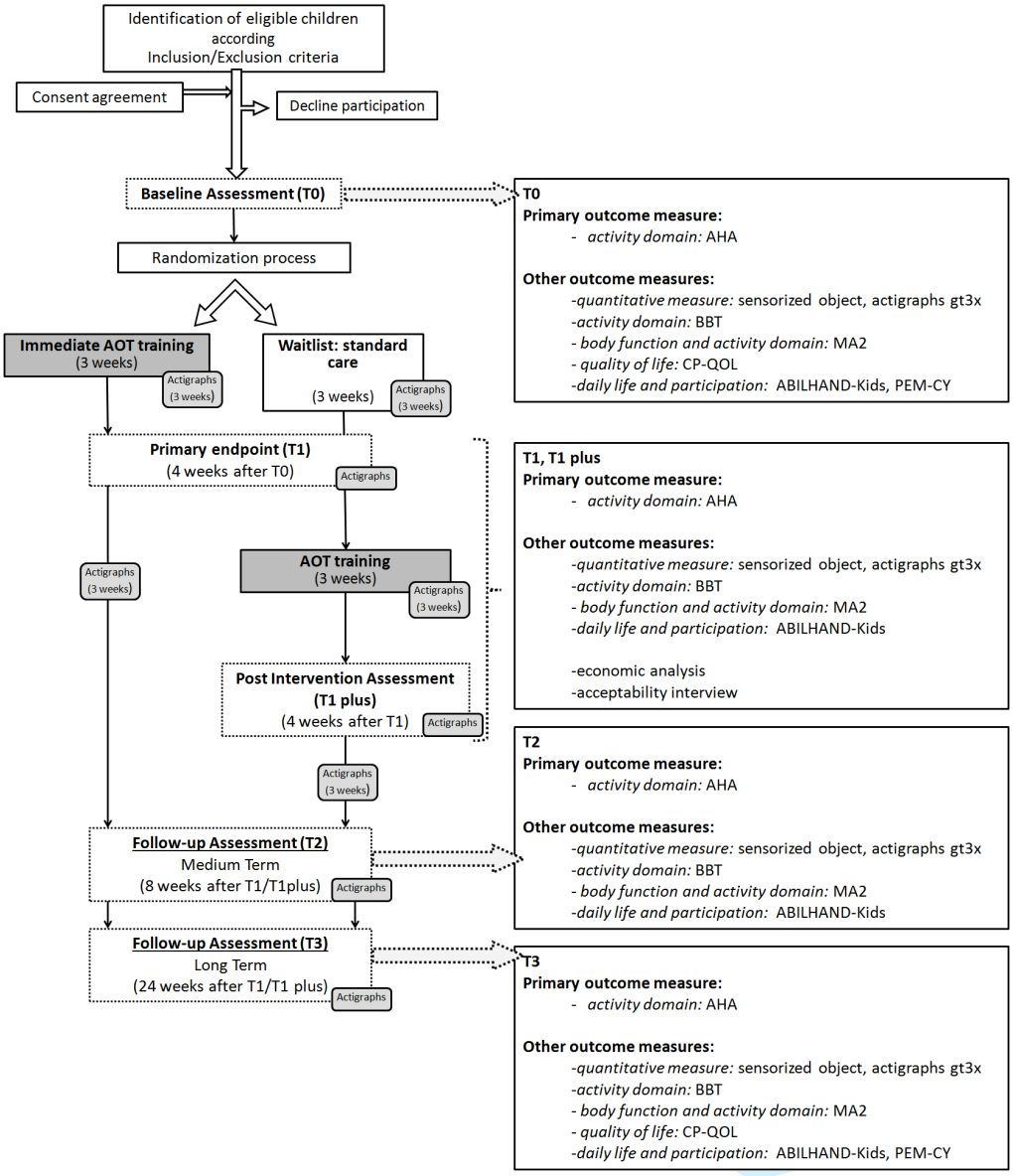


Figure 1: Flow-chart of Clinical Study

Summarizing all subjects will be assessed using standardized scales and tests at different times: T0, T1, T2, T3.

- T0: in the week before the beginning of the AOT training / standard care period
- T1: in the week after the AOT training / standard care
- T1 plus: in the week after the AOT training. This evaluation will be carried out only in the group of subjects who will undergo training in the second phase.
- T2: 8 weeks after the end of experimental training
- T3: 16 weeks after T2.

AOT training will be performed through a dedicated and personalized platform that will be delivered at home along with the useful material for training. The treatment will be performed by the participants, with the supervision of the parents, it will last about one hour per day, for 5 days a week for 3 weeks (total of 15 days). During the first two / three days of training, a therapist will support parents or adult hemiplegic subjects in the management of the training.

During the 3-week training sessions, the subjects will wear two actigraphs on the wrists (Figure 1) every day as long as possible. Subjects who will initially be allocated to the control group will be asked to keep a diary of any rehabilitation activities that they normally conduct and will be asked to wear actigraphs every day as long as possible, such as subjects assigned to the experimental group. It will be required to keep the actigraphs also in the 3 weeks following the end of the training.

The actigraph is a non-invasive motion accelerometer sensor that is worn on the wrist like a watch, is comfortable and water resistant. Today the actigraph is a trendy tool in use by youth and adults for fitness tracking and daily calorie consumption. The model used in this study is shown in the picture below.

Figure 2: wGT3X-BT

Recruitment will take place only after the informed consent has been given.
During the recruitment some clinical data (including age, gender, brain injury characteristics, affected side, manual functional level at the Home Functional Classification System) will be recorded and a dedicated database will be created.
To protect privacy and anonymity, to each subject will be assigned a numeric code that will be kept in separate form, so the database will not contain any identifying data. Access to such data will be restricted to the only staff directly involved in the study and all data will be processed in anonymous form.

What does your participation in the study involve?

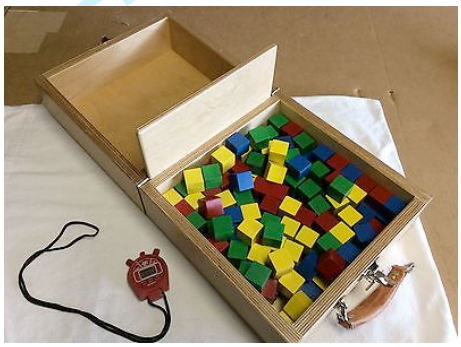
The study lasts 12 months, during this period a group of at least 20 children and young adults (5-20 years) with congenital hemiplegia will be enrolled at the IRCCS Fondazione Stella Maris . Participation will be voluntary on the basis of informed consent. The study will include a specific rehabilitation training, home-based AOT, through an ad hoc platform that will allow to conduct a personalized AOT training.

The clinical assessment (tests and questionnaires) is normally used for the functional evaluation in subjects with congenital hemiplegia:

The protocol will consist of the following tests:

1- Assisting Hand Assessment (AHA) is a scale that allows to evaluate manual and bimanual functionality.

2- Box and Block Test (BBT) is used to evaluate manual dexterity in which it is required to grasp, one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute.



3- *Melbourne Assessment of Upper Limb Function (MA2)*. It is a standardized instrument for measuring the capacity and quality of movement of the 'upper limb in children with Cerebral Palsy aged between 2 and 15 years, but it is also used for adults. It will be used at all evaluation times.

4- *ABILHAND* is a short questionnaire, validated in patients with cerebral palsy that measures 21 daily bimanual activities. The rating is assigned by the subject or the parent based on the experiences in daily accomplish, each task has a score of 3 points (impossible, difficult, easy). It will be used at all evaluation times.

5- *Participation and Environment Measure - Children and Youth (PEM-CY)*. This is a measure of participation and environmental factors at home, at school and in the community. It will be used at T0 and T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL -child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL -Teen, 13-18 years)*. These questionnaires are used to assess the quality of life in people with cerebral palsy. It will be used at T0 and T3.

7- *instrumental measurement of the manipulation during uni and bimanual tasks executed after observation.* It is an object containing two load cells to measure the force exerted (compression or traction) when grasped by the plegic hand and an on-off switch to evaluate the contact of the unaffected hand. An additional switch is placed at the starting point on the table under the more affected hand to record the moment when it starts moving toward the object. The instrument is used immediately after viewing three manipulation tasks carried out with three different types of grip: a one-hand task performed with the more affected hand, a two-hand bimanual task for the two hands, and a two-hand co-operation task for the two hands.

TASK 1. TASK 2. TASK 3.

The entire evaluation will last approximately one hour.

8- The use of the a*ctigraph in daily life.* The recruited subjects wear two actigraphs (Figure 2) outside of the clinical evaluation on his wrists (one for each wrist) for three-week periods (AOT experimental phase, phase control, phase follow-up). At the end of the registration period, the actigraph will turn off themselves and will be returned directly or by mail service to the examiner.

Benefits from participation in the study

Based on the literature and the preliminary results obtained in our previous studies, we expected that AOT training could improve the use of the upper limb in everyday life activities.

Possible risks

There are no direct risks or side effect related to the participation.

Possible alternatives

The alternative is not participate in the study.

What happen if you decide to do not take part in the study or retire from the study

The participation is voluntary. If you decide to attend, you will be able to withdraw from the study at any time and without the obligation to provide explanations, however, by notifying the doctor responsible for the study, Dr. Giuseppina Sgandurra.
If this is the case, no additional data will be collected and you can ask for the deletion of those already collected.

Information of General practitioner /pediatrician
For the best protection of the health of your child, you will be asked to inform the family doctor/paediatrician of the participation on the trial.

Information about the results of the study
If you require it, at the end of the study, results of the study and, in particular, those concerning you may be provided.

INFORMATION RELATING TO PERSONAL DATA PROCESSING:
Treatment holders and their purpose
The IRCCS Fondazione Stella Maris in accordance with the responsibilities provided by the rules of good practice, will process your personal data, particularly on health essential to the objective of the study, other data related to your origin and to the characteristics of your medical condition only solely on the basis of your study. For this purpose, the data provided will be collected by the Testing Center and processed in anonymity and in the privacy of the data. The processing of personal data related to 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphic records are essential for conducting the study: the refusal to provide will keep you from participating.

Nature of data
The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored for at least 7 (seven) years from the end of the study in this code, to your date of birth, the 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphs records are necessary for carrying out the study. Only the physician and authorized clinicians will be able to link this code to your name.

Treatment Mode
Data, whether processed by electronic means, will only be published in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, in such a way as to guarantee the confidentiality of your identity.

Exercise of rights
You may exercise your rights under art. 7 of the Code (eg. Access to your personal data, integrate, update, correct and object to their treatment for legitimate reasons, etc.) Applying directly to the testing center in the person of Dr. Giuseppina Sg andurra. You may terminate your participation at any time without giving any justification. In this case, the acquired data related to you will be destroyed. Further data will not be collected for you, without prejudice to the use of those already collected to determine, without altering the results of the search: even for the data already collected, you may ask for the cancellation.

Further information

There are no charge costs due to participation in the study. You will not receive any financial compensation for participating in the study.

The protocol of the study proposed to you has been approved by the Tuscan Ethics Pediatric Committee on 22/11/2016. The Ethics Committee has, among other things, verified the compliance of the study with the European Good Clinical Practice and the ethical principles expressed in the Helsinki Declaration.

You may report any matter you may find relevant to the Ethics Committee and / or the Health Care Department of this hospital structure regarding the research you are concerned with.

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	g. Sgandurra @ fsm.unipi.it	

_____ ___/___/_____ _____ _____

Name of Doctor's who delivered the information | Date | Time | Signature

INFORMED CONSENT FOR PARENTS/LEGAL TUTOR
Version 5.0 of 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*

Version 5.0 V **and date** of 10/11 / 2016

Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella M aris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

I signed (mother/guardian) _ born on ___/___/___ ___ living in _ Street _ phone _ address (if different from the residence) _ I, the undersigned (parent/guardian) _ born on ___/___/___ ___ living in _ Street _ phone _ address (if different from residence) _ of the child _ born on ___/___/___ ___ living in _ Street _
I acknowledge that I have received from Dr. _ the explanations regarding the request to participate in the research, according to the informative document, which I had a copy dated _ _ _ _ _ _ _ _ _ _ _ _ _ _ at _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ (indicate date and time of delivery). I declare that it have been clearly explained the nature, purpose, procedures, expected benefits, risks and possible drawbacks and alternatives of the trial.

DECLARE in addition that:

1. I have read and understood the information provided about the research project and the informative part of this document;
2. it was given the opportunity to ask any questions to the investigator of the study and I had satisfactory answers;;
3. it was allowed enough time to reflect on the information received and to discuss with third parties;
4. I have been informed that the study protocol and all the modules that are used have had a favourable opinion of the Ethics Committee;
5. It was clearly explained that I can decide that the child cannot s not participate in the study or can withdraw at any time, without providing justification, and that these

decisions will not change in any way the relationships with physicians and with the structure that are treating him;

6. I am aware that the research can be interrupted at any time by decision of the head of research, without prejudice to the health of the child;
7. I have been informed that I will be informed of any new information which might affect the safety of the research and that, for every problem or if I have additional questions, I can ask to doctors;
8. for the best protection of the health of the minor, are aware of the importance (and responsibility) to inform the family doctor/paediatrician of the trial to which I agree to involve the child
9. I was informed that the study results will be made available to the scientific community, while protecting the identification of the child in accordance with current legislation on privacy
10. I am aware that I/we must receive a copy of this consent form

By submitting this form I consent to the processing of personal data of my child and to their transfer outside the European Union (to be entered if performed by specifying the identity of recipients) for the purposes of research in limits and in the manner specified in the information provided hereby.

DECLARE therefore that I:

□ **want** □ **DON'T WANT**
that my child participate
□ in one under clinical evaluation
□ both under clinical evaluation and at home

□ **want** □ **DON'T WANT**
I will be informed about the results of research by the doctor of the study, also in relation to the unexpected news that might be accidentally encountered with the investigations required by the study

□ **want** □ **DON'T WANT**
inform your paediatrician/general practitioner of your involvement in the study

_____ ___/___/_____ _____ _____

Complete name of the child Date Time Signature

_____ ___/___/_____ _____ _____

Complete name of the parent/caregiver Date Time Signature

_____ ___/___/_____ _____ _____

Complete name of the parent/caregiver Date Time Signature

I signed Prof./Dr. …… (Surname) ……..… (Name)

I declare that the parents/guardians of Patient signed spontaneously his participation in the study

I also declare to:

- providing comprehensive explanations of the purpose of the study, the procedures, the potential risks and benefits and possible alternatives;
- I have verified that the parents/legal guardian have sufficiently understood the information provided
- Having left to the parents/legal tutor the necessary time and opportunity to ask questions about the study
- I am not exercising any coercion or unjustified influence in the Consent's request

_____ ___/___/_____ _____

_____

Name of doctor whom deliver consensus Date Time Signature

NOTA BENE

a copy of this form, signed and dated, attached to "information form for parents/legal guardian" should be delivered to parents/legal guardians of Patient

FONDAZIONE
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ISO 9001 BUREAU VERITAS Certification

INFORMATIVE MODULE
FOR PATIENTS AGED 7-13 YEARS
Version 6 .0 of 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

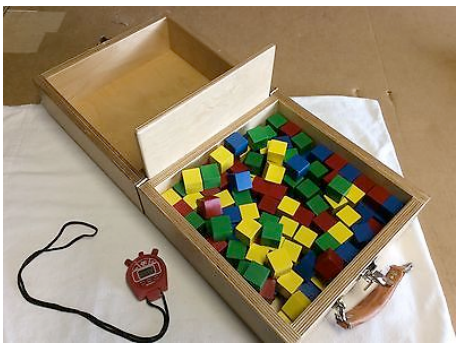
Why do we do this study?
Medical research wants to improve knowledge about diseases. We ask you to help us to understand whether the use of an "action observation-based therapy" may be helpful to improve the functionality of your affected arm. The observational therapy involves the viewing of short videos, to be observed carefully, which showed an 'action done with the hands and soon after you will be asked to perform the same movement trying to imitate as much as possible.
In addition we will ask you to wear bracelets, similar to a watch, to better measure and monitor the movements of your arms.

Who participates with me?
They will attend 20 children / teenagers and young adults aged 5-20 years. Everyone will be with similar motor difficulties like yours.

What happens if I participate?
If you decide to take part in the study at the beginning you will randomly assigned to one of two groups: experimental or control. If you will be assigned to the experimental group immediately you will begin a training based on action observation at home while if you will assigned to the control group you will be offered to wait about 4 weeks before starting the same type of therapy and in the meantime you will continue to do what you are doing now. So in each case you will do an action observation training immediately or after 4 weeks. In both cases you will be asked to wear bracelets, similar to a watch, on your wrists.
The therapy that you will do before or after is basically based on a computer program where "Ubi", an extra-terrestrial, will help you step by step in doing the exercises.

Additionally at a pre-set time (T0: when we enrol you, T1: T1: after the treatment or the control phase, T1 plus: after the treatment if you have started after, T2: after 8 weeks and T3: after 16 weeks from the end of the treatment) specific scales and questionnaires will be proposed to you and your parents that help us to understand how you use your hands!

How long will the study last?
The study will last one year. If you agree to join the study your participation lasts 3 weeks (treatment duration). You will also be asked to do the tests and fill out the questionnaires 3 or 4 times.



Some examples of games

There are benefits expected from my participation in the study?
We expect that this therapy could help you in improving the use of your hands

What are the risks of the study?
There are no risks because it is a very simple treatment which can be done safely at home and the assessments are those that normally you carry our during the clinical evaluation in the clinical centre.

What happen if I decide to do not take part in the study
You are completely free to join or not to the study. If you decide to do not participate, you will continue to be periodically monitored by your clinical team as well as done so far.

Do I have to give my consent to participate in the study?
Once you have read this information form and have asked your questions, you will decide if take part in the study. If you want to participate, you will need to sign this form for which you will be given a copy for you.
If you decide to do not take part in the study, or if you change your mind afterwards, nothing will happen, you will continue to receive the necessary care at this hospital.

And should I have any questions?
If you have any questions you can ask them to Dr. Giuseppina Sgandurra at the interview and can also call on the telephone number 050/886239: listens to you and explain to you everything you want.

Date _____ time _____ delivery

Signature of the Doctor who delivered the information

DECLARATION OF CONSENT
FOR PATIENTS AGED 7-13 YEARS
Version 6 .0 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

The information form was delivered to me on (date) _____ at _____
I understood everything the doctor explained to me.
The Doctor has listened to all my questions and has answered me.
If in the future I'll need something else, the doctors of the study will be at my disposal.

_____
Date and time

_____
Write your name here if you would like to take part in the study

_____
Signing the patient. Enter your name in the block here if you would like to take part in the study

_____ _____
Date hour Doctor's signature that informed the patient

FONDAZIONE
STELLA MARIS - *IRCCS*
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
OSPEDALE DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
PER LA NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA
ISTITUTO DI RIABILITAZIONE PER PATOLOGIE NEUROPSICHIATRICHE

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CENTRO DIURNO DI
RIABILITAZIONE PSICHIATRICA
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Tel. 0571 419868

ISO 9001 BUREAU VERITAS Certification

INFORMATIVE MODULE
FOR PATIENTS AGED 14 - 17 YEARS
Version 6 .0 of 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear ……..,
may be eligible to participate in this clinical study proposed by IRCCS Fondazione Stella Maris.
This module provides information on the purposes, risks and potential benefits of this study. If some aspect of this form does not make you clear, you can ask questions to doctors of the study. Take all the time you need. You are not obligated to participate. If you accept, you may choose to withdraw your participation at any time.
Once you have read this form and answered your questions, you will be asked to decide if you would like to participate in the study. If you want to participate, you will need to sign the form for which you will be given a copy to you.

What is the purpose of this study?
We are inviting you to participate in this study because we think that you can help us to understand if the use of action observation therapy can be helpful in improving the functionality of your arm. The action observation therapy involves the viewing of short videos, to be observed carefully, which shows an 'action done with the hands" and soon after you will be asked to perform the same movement trying to imitate them as much as possible. In addition we will ask you to wear bracelets, similar to a watch, to better measure and monitor the movements of your arms.

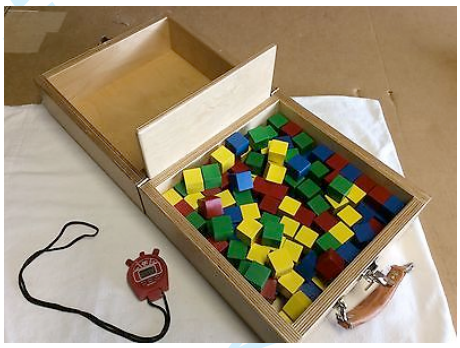
How many people will participate?
They will attend 20 children / teenagers and young adults aged 5-20 years. Everyone will be with similar motor difficulties like yours.

What does participating in the study mean?
If you decide to take part in the study at the beginning you will randomly assigned to one of two groups: experimental or control. If you will be assigned

to the experimental group immediately you will begin a training based on action observation at home (3 weeks) while if you will be assigned to the control group you will be offered to wait about 4 weeks before starting the same type of therapy and in the meantime you will continue to do what you are doing now. So in each case you will do an action observation training immediately or after 4 weeks. In both cases you will be asked to wear bracelets, similar to a watch, on your wrists. The therapy that you will do before or after is based on a computer program where "Ubi", an extra-terrestrial, will help you step by step in the exercises you do.

The study will last one year. If you accept to take part in the study your participation is 3 weeks (duration of treatment).

Additionally at a pre-set time (T0: when we enrol you, T1: T1: after the treatment or the control phases, T1 plus: after the treatment if you have started after, T2: after 8 weeks and T3: after 16 weeks from the end of the treatment) will be proposed specific scales and questionnaires that help us to understand how you use your hands!



Some examples of games

There are benefits expected from my participation in the study?
We expect that this therapy could help you in improving the use of your hands

What are the risks of the study?
There are no risks involved because it is a very simple treatment that you can done safely at home and assessments are those that normally our during the clinical evaluation in the clinical center.

What if I decide not to take part in the study or withdraw from the study?
Your participation in the study is voluntary.
If you decide to do not participate, or if you change your mind afterwards, you will not have any penalty or loss of benefits that you would otherwise have been entitled to. Your current and future medical care in the Fondazione IRCCS Stella Maris will not be affected by your decision, and doctors continue to follow you with due attention.
You can withdraw your participation in the study at any time communicating with Dr. *Giuseppina Sgandurra* providing any justification. In this case no additional data will be collected about you and you will be able to request the deletion of those already collected. Your participation in the study may be interrupted if your doctor evaluates that the new treatment has not benefited or if you

experience any side effects. In these cases, you will be promptly informed by your doctor and you will be able to discuss with him about further treatments that are valid for your condition.

What will happen to the information that was collected for the study?
The medical information about you such as age, sex, characteristics of your diseases, the results of the tests and the diary of daily activities will be kept in an archive of Fondazione Stella Maris.
Your data will be archived in anonym form, your name will be replaced by a code known only to a few people and your data will be anonymous. Only the physician and authorized persons will be able to link this code to your name.
Study data can be displayed at conferences/congresses or published in scientific journals to inform other doctors and health professionals.

Information on the results of the study
At the end of the study you will be informed on the results of the research.

Further information
There are no additional costs incurred from your participation in the study. You will not receive any financial compensation for participating in the study.
The study protocol have been written in accordance with the requirements of Good Clinical Practice and the Declaration of Helsinki, and was approved by the Ethics Committee of the Pediatric Tuscany Region on 22/11/2016.

For more information and communications, you can contact the study staff who will be at your disposal:

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	gsgandurra@fsm.unipi.it	

_____ ___ / ___ / _____ _____ _____
Name of Doctor's Date Time Signature
who delivered the information

INFORMED CONSENT
FOR PATIENTS AGED 14 -17 YEARS
Version 6 .0 29/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 6.0 **and date** of 29/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

I am signed (name and surname) _____ I declare that I have received information from Dr. _____ full explanations regarding the request for participation in the study in question, as indicated in the attached information form, of which I was given a copy on _____ at _____

I state that I have clearly understood the nature, purpose, expected benefits, risks and disadvantages of the clinical trial.

I declare that I have been able to do all the questions I have found necessary and have received satisfactory answers, as well as having been able to tell me about the details of the study with a person of my confidence.

I therefore agree to participate in the research, having fully understood the meaning of the request and the risks and benefits that may result from this participation.

I agree that my personal data *and their transfer outside the European Union (if applicable)* for research purposes to the extent and in the manner indicated in this document.
□ I wish the results of the study were communicated to me.

__ / __ / ____ _____
_____ Signature of the patient
Date hour

__ / __ / ____ _____ _____
_____ Doctor's signature that informed the patient and registered his consent
Date hour

FONDAZIONE
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56128)
Viale del Tirreno, 341/A-B-C angolo
Via dei Frassini, 1
Partita Iva 0012624 050 6
Centralino:
Tel. 050 886111

Dear Mrs / Mrs, the information contained in the following informative module is detailed and could be very complex

we ask you to accept the participation in the study ONLY after reading this carefully document and interviewing the investigator who will dedicate to you all the time necessary to fully understand what we are proposing to you

INFORMATIVE MODULE FOR THE PATIENT
Version 5.0 of the 10/11/2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*
Version 5.0 V **and date** of 10/11 / 2016
Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)
Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella Maris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Phone 050/886233. e-mail: gsgandurra@fsm.unipi.it

Dear ____ ,
we ask you to take part in this clinical study, this document is intended to provide you all the information about the study: the purpose, what you will be asked, which are your rights and responsibilities. Read the information carefully before making a decision about your participation in the study. You will have all the time you need to decide whether you want participate or not.
You will be free to ask any questions until you have received a clear and comprehensive answer for yourself.
If, after reading and understanding all the information you decide to participate in the clinical trial, you will need to sign the Consensus Information Form attached to this document.

Which are the aims of the study

The study aims to evaluate the feasibility and effectiveness of the Action Observation Training (AOT) with regard to the standard care in home-based rehabilitation in children and adults with hemiplegia.

A second goal will be to measure and monitor the movements of the upper limbs through the use of actigraphs, simple commercial instruments such as watches (see below), whose data will be compared with the clinical results.

What is AOT?

The recent discovery of the Mirror Neuron System (SNS) has promoted the development of the Action-Observation Training (AOT), a therapy based on the observation of goal-directed actions followed by their motor replication as a model for motor learning.

AOT has been used with promising results in some studies in adult with stroke and recently also in children with Cerebral Palsy showing positive effects on the upper limb function. In particular, the IRCCS Fondazione Stella Maris (FSM) has carried out in a group of 24 children with hemiplegia Preliminary data support the hypothesis that AOT can improve the upper limbs function in children with hemiplegia. Based on these promising results, this study has been proposed.

The recruitment will be made by the FSM . We propose to select 20 participants aged between 5-20 years with unilateral cerebral palsy with a predominant spasticity pattern that interferes with the upper limb function; sufficient cooperation in the activities to be proposed; parents or legal tutor or adult with hemiplegia available to collaborate in 3- consecutive weeks of intensive home training program.

Recruitment will take place after the signing of informed consent by the subjects and/or by the parents or the legal tutor. The enrolled subjects will be divided randomly into two groups: experimental and standard care (control) groups. Subjects assigned to the experimental group will begin with the AOT for a period of 3 weeks, while those in the control or standard care will continue as they normally do by making a diary of any rehabilitation activities they conduct.

All subjects will be evaluated before (T0) and after (T1) the experimental / standard care period with standardized scales and tests. At the end of this period to those individuals who have not carried out the experimental training have the opportunity to carry out the training. The training will be offered with the same details and it will last three weeks at the end of which the subjects of this group will be re-evaluated with standardized scales and test (T1 plus). All subjects will be re-evaluated after 8 weeks from T1/T1 plus (T2) and after 16 weeks of T1 (T3).

These evaluations will be performed in order to evaluate the effects of training at short term (T1 and T1 plus) and at medium (T2) and long term (T3). For details see Study Design Figure 1.

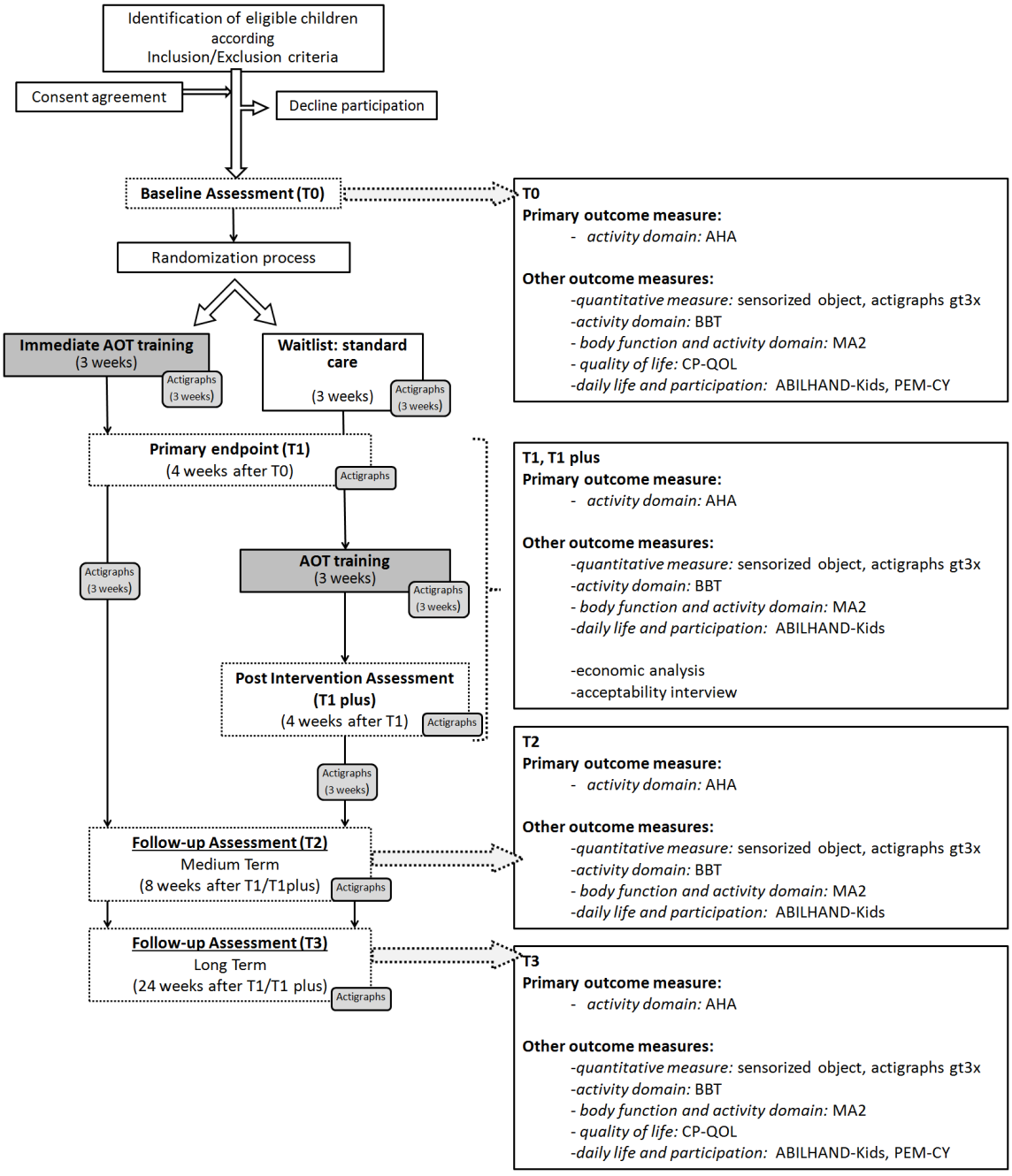


Figure 1: Flow-chart of Clinical Study

Summarizing all subjects will be assessed using standardized scales and tests at different times:
T0, T1, T2, T3.

- T0: in the week before the beginning of the AOT training / standard care period
- T1: in the week after the AOT training / standard care
- T1 plus: in the week after the AOT training. This evaluation will be carried out only in the group of subjects who will undergo training in the second phase.
- T2: 8 weeks after the end of experimental training
- T3: 16 weeks after T2.

AOT training will be performed through a dedicated and personalized platform that will be delivered at home along with the useful material for training. The treatment will be performed by the participants, with the supervision of their parents, it will last about one hour per day, for 5 days a week for 3 weeks (total of 15 days). During the first two / three days of training, a therapist will support parents or adult hemiplegic subjects in the management of the training.

During the 3-week training sessions, the subjects will wear two actigraphs on the wrists (Figure 1) every day as long as possible. Subjects who will initially be allocated to the control group will be asked to keep a diary of any rehabilitation activities that they normally conduct and will be asked to wear actigraphs every day as long as possible, such as subjects assigned to the experimental group. It will be required to keep the actigraphs also in the 3 weeks following the end of the training.

The actigraph is a non-invasive motion accelerometer sensor that is worn on the wrist like a watch, is comfortable and water resistant. Today the actigraph is a trendy tool in use by youth and adults for fitness tracking and daily calorie consumption. The model used in this study is shown in the picture below.

Figure 2: wGT3X-BT

Recruitment will take place only after the informed consent has been given.
During the recruitment some clinical data (including age, gender, brain injury characteristics, affected side, manual functional level at the Home Functional Classification System) will be recorded and a dedicated database will be created.
To protect privacy and anonymity, to each subject will be assigned a numeric code that will be kept in separate form, so the database will not contain any identifying data. Access to such data will be restricted to the only staff directly involved in the study and all data will be processed in anonymous form.

What does your participation in the study involve?
The study lasts 12 months, during this period a group of at least 20 children and young adults (5-20 years) with congenital hemiplegia will be enrolled at the IRCCS Fondazione Stella Maris. Participation will be voluntary on the basis of informed

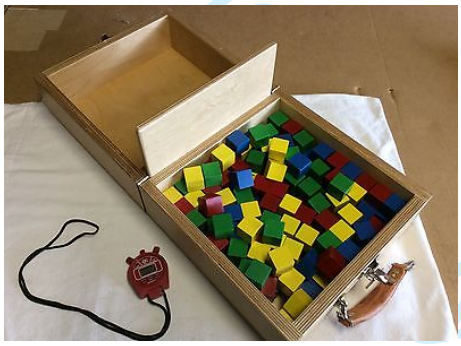
consent. The study will include a specific rehabilitation training, home-based AOT, through an ad hoc platform that will allow to conduct a personalized AOT training.

The clinical assessment (tests and questionnaires) is normally used for the functional evaluation in subjects with congenital hemiplegia:

The protocol will consist of the following tests:

1- Assisting Hand Assessment (AHA) is a scale that allows to evaluate manual and bimanual functionality.

2- Box and Block Test (BBT) is used to evaluate manual dexterity in which it is required to grasp, one block at a time with one hand, transport the block over the partition, and release it into the opposite compartment within 1 minute.



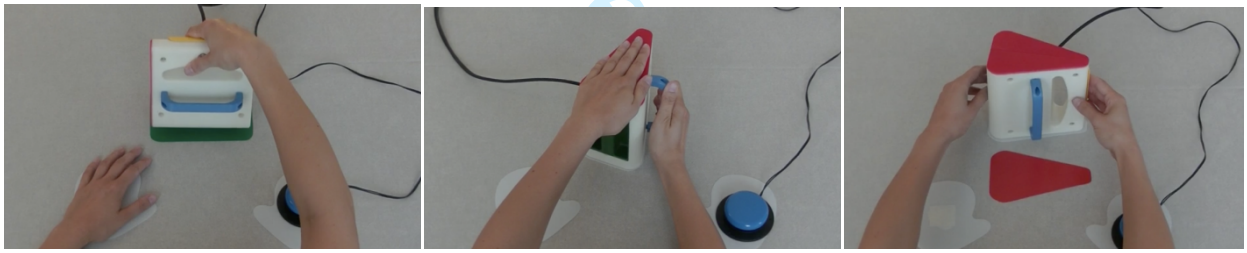
3- *Melbourne Assessment of Upper Limb Function (MA2)*. It is a standardized instrument for measuring the capacity and quality of movement of the 'upper limb in children with Cerebral Palsy aged between 2 and 15 years, but it is also used for adults. It will be used at all evaluation times.

4- *ABILHAND* is a short questionnaire, validated in patients with cerebral palsy that measures 21 daily bimanual activities. The rating is assigned by the subject or the parent based on the experiences in daily accomplish, each task has a score of 3 points (impossible, difficult, easy). It will be used at all evaluation times.

5- *Participation and Environment Measure - Children and Youth (PEM-CY).* This is a measure of participation and environmental factors at home, at school and in the community. It will be used at T0 and T3.

6- *Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL - child, 4-12 years) and Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL -Teen, 13-18 years).* These questionnaires are used to assess the quality of life in people with cerebral palsy. It will be used at T0 and T3.

7- *instrumental measurement of the manipulation during uni and bimanual tasks executed after observation.* It is an object containing two load cells to measure the force exerted (compression or traction) when grasped by the plegic hand and an on-off switch to evaluate the contact of the unaffected hand. An additional switch is placed at the starting point on the table under the more affected hand to record the moment when it starts moving toward the object. The instrument is used immediately after viewing three manipulation tasks carried out with three different types of grip: a one-hand task performed with the more affected hand, a two-hand bimanual task for the two hands, and a two-hand co-operation task for the two hands.



TASK 1. TASK 2. TASK 3.

The entire evaluation will last approximately one hour.

8- The use of the a*ctigraph in daily life.* The recruited subjects wear two actigraphs (Figure 2) outside of the clinical evaluation on his wrists (one for each wrist) for three-week periods (AOT experimental phase, phase control, phase follow-up). At the end of the registration period, the actigraph will turn off themselves and will be returned directly or by mail service to the examiner.

Benefits from participation in the study

Based on the literature and the preliminary results obtained in our previous studies, we expected that AOT training could improve the use of the upper limb in everyday life activities.

Possible risks
There are no direct risks or side effect related to the participation.

Possible alternatives
The alternative is to do not participate in the study.

What happen if you decide to do not take part in the study or retire from the study
The participation is voluntary. If you decide to attend, you will be able to withdraw from the study at any time and without the obligation to provide explanations, however, by notifying the doctor responsible for the study, Dr. Giuseppina Sgandurra.
If this is the case, no additional data will be collected and you can ask for the deletion of those already collected.

I consent to informing your general practitioner
For the best protection of your health, you will be asked to inform your doctor of the experiment you are willing to attend.

Information about the results of the study
If you require it, at the end of the study, results of the study and, in particular, those concerning you may be provided.

INFORMATION RELATING TO PERSONAL DATA PROCESSING:
Treatment holders and their purpose
The IRCCS Fondazione Stella Maris in accordance with the responsibilities provided by the rules of good practice, will process your personal data, particularly on health essential to the objective of the study, other data related to your origin and to the characteristics of your medical condition only solely on the basis of your study. For this purpose, the data provided will be collected by the Testing Center and processed in anonymity and in the privacy of the data. The processing of personal data related to 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphic records are essential for conducting the study: the refusal to provide will keep you from participating.

Nature of data
The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored for at least 7 (seven) years from the end of the study in this code, to your date of birth, the 'age, sex, hemiplegic side / handedness, hand function, daily activities, data from actigraphs records are necessary for carrying out

the study. Only the physician and authorized clinicians will be able to link this code to your name.

Treatment Mode

Data, whether processed by electronic means, will only be published in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, in such a way as to guarantee the confidentiality of your identity.

Exercise of rights

You may exercise your rights under art. 7 of the Code (eg. Access to your personal data, integrate, update, correct and object to their treatment for legitimate reasons, etc.) Applying directly to the testing centre in the person of Dr. Giuseppina Sgandurra. You may terminate your participation at any time without giving any justification. In this case, the acquired data related to you will be destroyed. Further data will not be collected for you, without prejudice to the use of those already collected to determine, without altering the results of the search: even for the data already collected, you may ask for the cancellation.

Further information

There are no charge costs due to participation in the study. You will not receive any financial compensation for participating in the study.

The protocol of the study proposed to you has been approved by the Tuscan Ethics Paediatric Committee on 22/11/2016. The Ethics Committee has, among other things, verified the compliance of the study with the European Good Clinical Practice and the ethical principles expressed in the Helsinki Declaration.

You may report any matter you may find relevant to the Ethics Committee and / or the Health Care Department of this hospital structure regarding the research you are concerned with.

Dr.	Sgandurra	Giuseppina
Phone	050/886233	
E-mail	g. Sgandurra @ fsm.unipi.it	

_____ ___ / ___ / _____ _____

_____

Name of Doctor's Date
Time Signature
who delivered the information

INFORMED FORM OF CONSENT

V 5.0 of the 10/11 / 2016

Protocol Title: *Action-Observation Training (AOT) for home rehabilitation of patients with hemiplegia*

Version 5.0 V **and date** of 10/11 / 2016

Study promoter: IRCCS Fondazione Stella Maris, Viale del Tirreno, 331. Calambrone (PI)

Principal Investigator: Dr. Giuseppina Sgandurra, IRCCS Fondazione Stella M aris; Viale del Tirreno 331; 56128 Calambrone (Pisa), Italy Tel 050/886233. e-mail: gsgandurra@fsm.unipi.it

I signed _____ born ___ / ___ / _____ resident to _____ via / square _____ Tel ._____ domicile (if different from residence) _____

DECLARE

- had received from Dr. _____ exhaustive explanations about the request to participate in the present research, as reported in the information document, part of this agreement, which I was given a copy on _____ at _____ *(insert date time of delivery);*
- that I have been clearly explained and I have understood the nature, purpose, procedures, the expected benefits, risks and possible inconveniences and alternatives of the clinical study;
- that I have had the opportunity to ask questions and to have had satisfactory answers;
- that you have had all the time you need before deciding whether to participate or not;

- that I have not had any unjustified coercion in the request for Consent;
- that I was clearly asked that I could freely decide to do not take part in the study or to leave at any time without giving any justification, and that those decisions will not in any way modify the relationship with the physicians and the structure that are treating me ;
- I am aware of the importance (and of my responsibility) to inform my general practitioner of the experiment I am willing to attend
-

By subscribing to this form, I consent to the processing of my personal data for the purposes of the search within the limits and with the methods indicated in the information provided to me with this document.

I therefore declare of

□ **want** □ **NOT want**
□ participate in one under clinical evaluation
□ both under clinical evaluation and at home

□ **want** □ **NOT want**
be informed of the results of this research by the medical practitioner

□ **want** □ **NOT want**
be informed on the results of the research by the medical practitioner, also in relation to unexpected news that should be accidentally encountered with the investigations provided by the study

□ **want** □ **NOT want**
Inform your doctor of general practitioner in study participation

_____ ___ / ___ / _____ _____
_____
Full patient name (adult, lower mature) Date
Time Signature

_____ ___ / ___ / _____ _____
_____
Name for Extended Legal Representative Date
Time Signature

I signed Prof./Dr. ....
Surname Name

I declare that the Patient has spontaneously signed his participation in the study

I also declare:

- providing the patient with comprehensive explanations regarding the purposes of the study, the procedures, possible risks and benefits and possible alternatives there are to;
- have verified that the patient has sufficiently understood the information provided to him / her
- having left to the Patient the time needed and the opportunity to ask questions about the study
- not exercising any coercion or unjustified influence in the Consent's request

_____ ___/___/_____ _____
_____
Name of Doctor's Date Date Time Signature
who provided the information and
gathered informed consent

Please note

a copy of this form, signed and dated, enclosed with the "Written Information for the Patient" must be delivered to the Patient

Semi-structured qualitative interview about acceptability of AOT training

Answer to these questions with your parents, feel free to add your comments

Customization of exercises				
1	Did the exercises seem suitable for you (materials, type of actions...)?	yes, at all	yes, in part	no
2	Were exercises difficult for you (required perfomance)?	yes, all of them	yes, many of them	no
3	Did you notice an increasing difficulty (from the easiest the first day to the most difficult)?	yes		no
4	Did exercises seems like other typical activities/daily life actions?	yes, all of them	yes, many of them	no
5	Do you think that AOT activities had a role in promoting your ability?	yes, at all	yes, in part	no
Suitability of children with UCP for the Tele-UPCAT system in their own home				
6	Did you like to do the training at home?	yes		no
7	Did you like to perform exercises without a therapist?	yes, at all	yes, in part	no
8	Who helped you for the training?			
Feasibility at home				
9	Did you have a suitable table where the system was placed?	yes		no
10	If no, did you need to re-organize your home space?	yes, at all	yes, in part	
11	Do you judge the whole system bulky?	yes		no
12	Was the management of the system difficult?	yes, at all	yes, in part	no
Required effort by the participants				
13	Was the effort (about 1 hour per day) feasible for you?	yes, at all	yes, in part	no
14	Did you change your daily routine to do the training?	yes, at all	yes, in part	no
15	Did you have to renounce to something (sport, freetime, holidays..)?	yes, at all	yes, in part	no
16	Did you like to have a fixed time for the training each day?	yes, at all	yes, in part	no
17	Do you think that you could proceed the training for more days?	yes, at all	yes, in part	no
18	Were the exercises too hard (difficult, long..) for you?	yes, at all	yes, in part	no

Semi-structured qualitative interview about acceptability of AOT training

Answer to these questions with your parents, feel free to add your comments

Acceptability of Actigraphs				
19	Did you like to wear Acrigraphs?	yes		no
20	Did Actigraphs annoy you?	yes	yes, sometimes	no
21	Did you wear them for the whole day?	yes, at all	yes, in part	no
22	Did you remember how to wear them (orientation)?	yes		no
23	Did you remember to fill in your diary?	yes	yes, sometimes	no
Suitability of the manual				
24	Was the manual enough clear?	yes, at all	yes, in part	no
25	Did you have any difficulties in finding/preparing the material?	yes	yes, sometimes	no
26	Were the instructions for the managining of the system complete and clear?	yes	yes, sometimes	no
Software				
27	Did you like Ubi (for children)/slides (for adolescents)?	yes, at all	yes, in part	no
28	Do you think that something need to be changed?	yes		no
29	Was the managing of the software difficult?	yes, at all	yes, in part	no
30	Did you have technical issues/troubles?	yes	yes, sometimes	no
31	Did you need technical assistance?	yes	yes, sometimes	no