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Effects of the Alternate Combination of “Error-Enhancing” and “Active Assistive” Robot-Mediated Treatments on Stroke Patients

PEPPINO TROPEA^{1*}, BENEDETTA CESQUI^{2*}, VITO MONACO¹, SARA ALIBONI³,
FEDERICO POSTERARO⁴, AND SILVESTRO MICERA (Senior Member, IEEE)^{1,5}

¹The BioRobotics Institute, Scuola Superiore Sant’Anna, Pisa 56037, Italy

²Laboratory of Neuromotor Physiology, Santa Lucia Foundation, Rome 00133, Italy

³Department of Physical Medicine and Rehabilitation, Ospedale Versilia - Camaiore, Lucca 55041, Italy

⁴Neurological Rehabilitation Unit, Auxilium Vitae Rehabilitation Center, Volterra 56048, Italy

⁵Translational Neural Engineering Laboratory, Center for Neuroprosthetics, Swiss Federal Institute of Technology Lausanne, Lausanne 1015, Switzerland

CORRESPONDING AUTHOR: P. TROPEA (p.tropea@sss.up.it)

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*Equally contributed to this work.

ABSTRACT This paper aimed at investigating the effects of a novel robotic-aided rehabilitation treatment for the recovery of the upper limb related capabilities in chronic post stroke patients. Eighteen post-stroke patients were enrolled in a six-week therapy program and divided into two groups. They were all required to perform horizontal pointing movements both in the presence of a robot-generated divergent force field (DF) that pushed their hands proportional to the trajectory error and perpendicular to the direction of motion, and according to the typical active assistive (AA) approach used in robotic therapy. We used a crossover experimental paradigm where the two groups switched from one therapy treatment to the other. The hypothesis underlying this paper was that the use of the destabilizing scenario forced the patient to keep the end-point position as close as possible to the ideal path, hence requiring a more active control of the arm with respect to the AA approach. Our findings confirmed this hypothesis. In addition, when the DF treatment was provided in the first therapy cycle, patients also showed straighter and smoother paths during the subsequent AA therapy cycle, while this was not true in the opposite case. In conclusion, the results herein reported provide evidence that the use of an unstable DF field can lead to better recovery outcomes, and therefore it potentially more effective than solely active assistance therapy alone.

INDEX TERMS Rehabilitation robotics, stroke, assisted-as-needed, error-enhancing, upper arm.

I. INTRODUCTION

Stroke is a global health-care problem, and it is among the leading causes of disability in most western countries. The main goals of rehabilitation programs are: to promote the recovery of motor functions; to improve movement coordination; to guide learning of new compensatory strategies; and to prevent secondary complications such as undesired postures, spasticity, or atrophy [1], [2].

Several dedicated clinical studies have recently endorsed the use of robotic-based therapies to enhance the recovery of upper extremity motor functions following a stroke [3]–[8]. The standard treatment delivered by the available commercial devices (see [9] for a review) consists of guiding the

patient’s arm toward the intended target position, similar to what a therapist does in hand-over-hand assistance during conventional treatment. The force field acting on the patient’s arm is activated only if he/she is not able to complete the movement, while the deviation from the ideal path, usually represented by a straight line to target, or the minimum jerk [10], or the minimum torque-changes trajectory [11], is actively corrected by the robot. This approach has been observed to be highly effective since it reduces the spasticity of the affected arm, increases the strength of shoulder and elbow movements, promotes a better control of tone, and improves the kinematics in terms of velocity and movement smoothness [3], [12]–[15].

Actually, the potential benefits of robotic therapy are even more relevant. It could allow the treatment of a large number of patients under the supervision of only one therapist, with a significant reduction of costs for the health care system. Moreover, if combined with augmented haptic or visual feedback [4], [16]–[21], EMG biofeedback [4], [22]–[25] and functional muscles electrical stimulation [26], robotic platforms offer several types of interventions to enhance motor learning in ways not possible with traditional exercises.

Notwithstanding, we are still far from knowing what is the best treatment, its most effective duration and intensity, and even more important, how to customize it according to the patient's injury level [27], [28]. In this respect, recent literature highlights that the improvements related to the motor outcome obtained after a robotic-based treatment are not significantly different than those following a traditional, therapist-mediated, approach [29], [30].

One of the aspects of robotic-based therapy that needs further investigation is the identification of specific rehabilitative paradigms to improve the clinical outcomes of patients. Previous studies, dealing with the adaptation to mechanical [20], [31], [32] and visual [33]–[35] distortions, challenged the standard robotic treatment (i.e., therapy providing an assistive guidance of the arm) and showed that humans can learn how to make accurate movements in an unstable environment by controlling the magnitude, the shape and the orientation of the endpoint impedance [36]–[38]. Thus, these training exercises seem promising to force pathological subjects to strengthen the control of their arm [39] and to promote functional reorganization of the motor cortex.

Despite this, the effects of a robotic aid rehabilitation program involving resistive or error augmentation force fields on stroke patients are still largely unknown for two main reasons. First, it is still controversial whether training with resistive forces could reinforce spasticity [40]. In addition, as already said, this approach differs from the standard level of hospital care (i.e., assistive approach) that is required when dealing with post stroke rehabilitation [9]. However, Patton and colleagues [20] have recently shown that stroke patients are able to adapt to a speed dependent force field perturbation, and suggested that the error amplification approach could provide a new pathway for augmenting motor learning in individuals with brain injuries. Accordingly, Abdollahi and colleagues reported further interesting results on the use of error augmentation in post stroke rehabilitation treatment [17].

The goal of the present study was to verify whether a robotic-based neurorehabilitative treatment involving practice with both the typical robot arm “active assistive” guidance approach (AA), and a “divergent force” field (DF) strategy, modifies the motor outcome of post stroke chronic patients. Two groups of subjects were enrolled in a rehabilitation program consisting of three blocks, each two weeks long, for a total of six weeks of treatment. To achieve our goal we designed a crossover experimental paradigm where the two groups of patients switched from one treatment modality to the other, to differently challenge patients, adapta-

tion to the training. In particular, patients belonging to the first group (Group I) were first trained in the DF modality, then they underwent a break in which no therapy was provided, and finally they were trained in the AA modality (i.e., DF-Break-AA). The second group (Group II) was involved in the same treatment with inverse ordering (i.e., AA-Break-DF).

Our analysis aimed at: 1) testing the hypothesis that the use of an unstable force field (i.e., DF) allows patients to finely control their arm achieving better motor outcomes than those obtained after the assistive treatment (i.e., AA); 2) investigating whether differences in motor outcome can be obtained by using a different therapy administration sequence (i.e., DF-Break-AA vs. AA-Break-DF).

II. METHODS

A. PARTICIPANTS

Eighteen post-stroke patients (9 male and 9 female; age 47.3 ± 17.0 years, range: 21-71 years; 4 right- and 12 left-handed) of different impairment levels were enrolled. They were all recruited from a cohort of outpatients of the Department of Physical Medicine and Rehabilitation, at Versilia Hospital, Camaiore, Italy. Inclusion criteria were: 1) diagnosis of a single, unilateral stroke, at least six month prior to the enrollment, verified by brain imaging; 2) sufficient cognitive and language abilities to understand and follow instructions; 3) absence of apraxia and severe concurrent medical problems (including shoulder pain). Patients were randomly arranged in two groups, gender and age matched.

The level of upper limb impairment was assessed using the “Stage of Arm” section of the Chedoke-McMaster (CM) Stroke Assessment Scale [41] at admission to the study. Table 1 summarizes the features of all involved participants and their clinical assessment.

This study was approved by the Ethical Committee of the Hospital. Patients gave their informed consent before starting the experimental sessions.

B. EXPERIMENTAL SETUP

Participants were seated in front of a screen and held the handle of the InMotion2 robotic system (Interactive Motion Technologies, Inc., Watertown, MA, USA), designed for clinical and neurological applications [5]. Restraining seatbelts were used to prevent compensation by trunk flexion during reaching.

The robot can move, guide, or perturb the movement of the upper limb of the subjects and can record the kinematics of the end-effector. It is also provided with an arm support device to compensate for gravity.

Each patient was instructed to make point-to-point movements (back and forth) on the horizontal plane from an initial position sited in the center of the workspace, toward one of the seven targets located on the periphery of a fan of 0.2 m radius (Figure 1).

TABLE 1. The table reports Chedoke-McMaster (CM) stroke assessment scale, Gender (G), Age, Motor Status Score (MSS), Modified Ashworth Scale (MAS) at Admission (Adm), at the Discharge (Dis) and in Between (iB), for all Patients (IDs) separated in Each Group (Gr).

ID	Gr	CM	G	Age	MAS			MSS		
					Adm	iB	Dis	Adm	iB	Dis
P1	I	4	M	71	10	5	4	26	27	29
P2	I	6	F	67	1	1	0	29	32	34
P3	I	4	M	65	7	8	4	26	20	24
P4	I	6	M	24	1	1	0	29	36	36
P5	I	4	M	23	18	10	9	24	25	27
P6	I	4	F	63	10	10	7	24	23	25
P7	I	6	F	47	0	2	2	34	36	36
P8	I	5	F	34	1	1	0	36	36	36
P9	I	5	F	53	2	1	0	36	36	37
P10	II	4	M	43	9	9	7	26	27	30
P11	II	5	M	58	5	5	5	35	36	36
P12	II	4	M	48	9	3	8	25	27	27
P13	II	3	F	32	5	6	4	17	18	20
P14	II	4	M	66	8	4	4	23	26	27
P15	II	6	F	21	1	1	0	35	35	37
P16	II	4	M	34	12	8	6	28	30	31
P17	II	5	F	66	15	7	5	30	33	33
P18	II	3	F	36	13	7	5	13	21	22

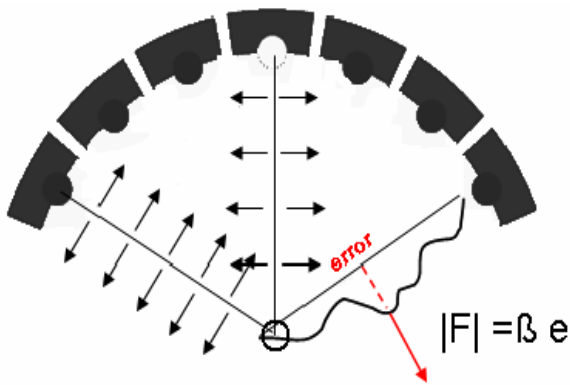


FIGURE 1. Rehabilitative scenario. The figure shows the fan paradigm adopted in this study and the assessment of the deviation (error) between the ideal (thin line) and the real (tick line) paths.

C. REHABILITATIVE TREATMENT

Patients were randomly assigned to the two groups of therapy treatments. The whole rehabilitation program lasts 6 weeks and was organized as follows: *i*) two weeks of training in one therapy modality (DF in the case of Group I and AA in the case of Group II), named Cycle I; *ii*) two weeks of break (no therapy); *iii*) two weeks of training with the other therapy modality (AA in the case of Group I and DF in the case of Group II), named Cycle II.

During the AA training the robot provided assistance-as-needed to move the hand from the actual position to the targets

if the patient was unable to independently achieve the movement, as described elsewhere [3]. Conversely, when patients were trained in the DF modality, the robot provided a perturbing force acting along the normal direction of the straight line connecting the initial and the goal targets [38], [42]. The intensity of the perturbing force was proportional to the distance between the ideal trajectory (i.e., the straight line between the start and the goal point) and the robot's end point actual position, according to:

$$F = \beta \cdot e \quad (1)$$

where e was the distance between the end point actual position and the target line direction and β was the coefficient representing the magnitude of the opposing force (Figure 1).

Each patient performed five training sessions per week. Each therapy session lasted one hour during which patients alternated 9 turns of the fan game (i.e., 126 movements), in either AA or DF training modes, followed by a turn in Null Field (NF) condition (i.e., 14 movements) where neither assistance nor perturbation was provided by the robot, for at least 3 times. When using the DF mode, the β value was changed at the beginning of each sub-session according to the following sequence: 50, 100, 75 N/m.

D. ANALYSIS OF FUNCTIONAL PERFORMANCE

The Motor Status Score (MSS) [43], [44] and the Modified Ashworth Scale (MAS) [45], [46] were used to assess patients' functional capability throughout the therapy. Each patient was evaluated by an experienced physical therapist, not involved in rehabilitation treatment team and blind with respect to the protocol, in three different phases of the treatment: at admission (Adm), at discharge (Dis), and in between (iB) the two therapy cycles.

E. ANALYSIS OF THE TRAJECTORY OF THE END-EFFECTOR

The trajectory of the end-effector was analyzed to assess the effectiveness of the ongoing therapy. For this purpose, the following kinematic parameters were computed:

- the mean (A_{xy}^m) and the maximum (A_{xy}^M) value of the tangential acceleration; the higher their values the greater the applied force;
- the maximum (D^M) absolute value of the distances between the ideal (i.e., the straight line connecting the starting point and the target) and the effective end point path; the lower the D^M value the straighter the trajectory.
- the ratio (MD) between mean and maximum values of the distances between the ideal and the effective path; MD is close to 1 when the trajectory is well-shaped;
- the number of peaks (N) of the speed profile [47]; the lower the value the smoother the trajectory;
- the jerk metric (J), calculated by dividing the negative mean jerk magnitude by the peak speed [14]; the higher the value the smoother the trajectory;
- the path length parameter (PL), as described by Colombo and colleagues [48].

For each experimental session, these parameters were calculated with data collected in the NF condition, and averaged to obtain a representative day-by-day evolution of patient performance.

Motor recovery was quantified comparing performances of the first and the last two days of each therapy cycle. Accordingly, four values (i.e., start – s_1 – and end – e_1 – of Cycle I, start – s_2 – and end – e_2 – of Cycle II) for each metric were recorded and then analyzed.

F. STATISTICS

The two-way ANalysis Of VAriance (ANOVA) of the between-subjects factor “group” (i.e., Group I vs. Group II) and the within-subjects factor “observation” (i.e., Adm vs. Dis vs. iB), was performed on MSS and MAS.

The three-way ANOVA of the between-subjects factor “group” (i.e., Group I vs. Group II) and the within-subjects factors “scenario” (i.e., AA vs. DF) and “phase” (i.e., start vs. end), was performed on all metrics describing the trajectory of the end-effector (i.e., A_{xy}^m , A_{xy}^M , D^M , MD, N, J and PL).

Data analysis was carried out off-line by means of customized Matlab (The MathWorks Inc., Cambridge, MA, US) scripts. Statistical analysis was performed in R environment (R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org/>), and the statistical significance was set at $p < 0.05$.

III. RESULTS

A. EVALUATION OF FUNCTIONAL PERFORMANCE

The statistical analysis on both MSS and MAS showed that the functional performance of the patients was significantly affected by the treatment (Table 2). Specifically, the phase of the rehabilitative treatment involved a reduction of the MAS and the increment of the MSS scores (Tables 1 and 3). No effect of the interaction of the two factors was observed (Table 2).

TABLE 2. The table reports p-values related to the two-way ANOVA performed on metrics describing the clinical evaluation outcomes (i.e., MAS Ad MSS). rows respectively refer to the group (i.e., Group I vs. Group II) and the phase of the treatment between the three testing points (i.e., Adm vs. Dis vs. iB). Values highlighted in bold are statistically significant.

	MAS	MSS
group	0.244	0.358
observation	<0.001	<0.001
group x observation	0.440	0.344

B. EFFECTIVENESS OF THE ONGOING THERAPY ON THE KINEMATICS OF THE END-EFFECTOR

All patients were able to perform the task in the DF condition (Figure 2). Moreover, as also observed for the functional

TABLE 3. The table reports all p-values related to the three-way ANOVA performed on metrics describing the kinematics of the end-effector. The first three rows respectively refer to between-subjects factor “Group” (i.e., Group I vs. Group II) and the within-subjects factors “scenario” (i.e., AA vs. DF) and “phase” (i.e., Start vs. End); the other rows report the interaction between previous factors. Values Highlighted in bold are statistically significant.

	A_{xy}^M	A_{xy}^m	D^M	MD	N	J	PL
group	0.188	0.252	0.168	0.378	0.936	0.520	0.391
scenario	0.028	0.031	<0.001	<0.001	0.155	0.143	0.007
phase	0.002	<0.001	0.111	0.093	<0.001	0.004	0.840
group x scenario	0.194	0.772	<0.001	0.002	<0.001	<0.001	<0.001
group x phase	0.453	0.302	0.712	0.372	0.042	0.643	0.566
scenario x phase	0.373	0.406	0.972	0.953	0.232	0.179	0.977
group x scenario x phase	0.681	0.677	0.970	0.758	0.113	0.742	0.430

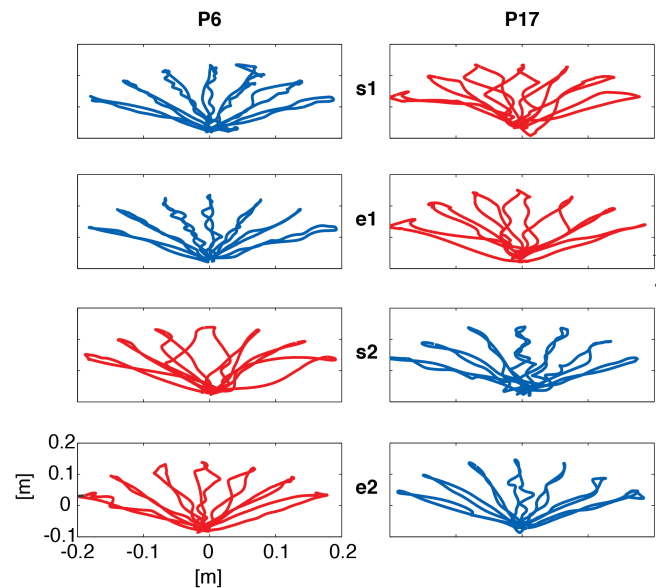


FIGURE 2. Trajectory of the end-effector. The figure shows the trajectory of the end-effector (one turn) for two representative subjects (P6 and P17) belonging respectively to Group I (on the left) and to Group II (on the right) during the 4 observations (i.e., s_1 , e_1 , s_2 and e_2). Curves in blue and red respectively refer to the DF and AA scenarios.

evaluation assessed by clinical scales, the phase of both treatments (i.e., start vs. end) significantly influenced the kinematics of the end-effector, mainly by increasing both acceleration and smoothness (see Figures 4 and 5, and Table 3).

Results (Table 3) showed that the end point trajectories appeared straighter after the training in the DF than in the AA modalities (see Figure 2) in conjunction with lower accelerations (see A_{xy}^m , A_{xy}^M in Figure 5). In this context, the statistical analysis revealed significant influence of the “scenario” factor on almost all parameters (see Table 3, “scenario” row), documenting that in the DF condition the D^M , MD and PL parameters were on average lower than in the AA one (see Figures 3 and 4). This suggested that the training with the DF-based treatment promoted the reduction of the deviation of the end-effector from the ideal path (i.e., the straight line linking

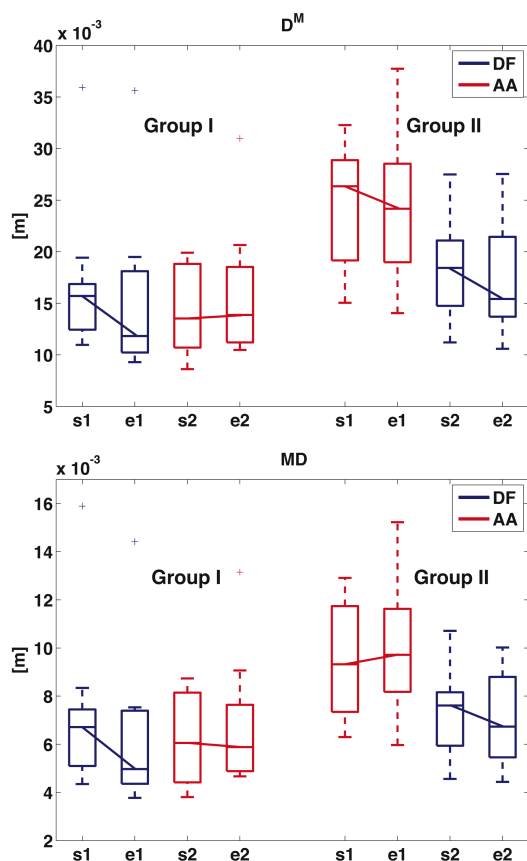


FIGURE 3. Changes in D^M and MD metrics parameters over the course of the therapy. Top panel: Box plot of D^M parameter (mean across subjects) of the beginning of the treatment type therapy (s) and at the end of the treatment type (e) for both Group I and Group II. Red boxes are relative to the active assistive therapy, and blue boxes represent results from the divergent field therapy. Bottom panel: Box plot of MD parameter.

the start and the goal targets) resulting in a fine control of the end-effector.

Finally, it was interesting to notice that the statistical analysis did not reveal any significant difference between the groups in all parameters describing the trajectory of the end-effector confirming that patients were subdivided in comparable sub-groups from the functional viewpoint. On the other hand, the interaction between factors “group” (i.e., Group I vs. Group II) and “scenario” (i.e., AA vs. DF) was significant in the case of the D^M , MD, N, J and PL end point trajectory parameters (see Figures 3, 4 and 5, and Table 3). In fact:

- D^M , MD and PL related to Group I remained almost unaltered between the first (i.e., DF) and the second (i.e., AA) therapy cycles, while those referring to Group II decreased through the whole treatment (i.e., AA and DF);
- J and N decreased between the first and the second treatment sessions in both groups, the variation was wider in the Group I.

These results indicated that when patients were first involved in the DF scenario they continued to adopt a fine control of the handle during the AA treatment as well.

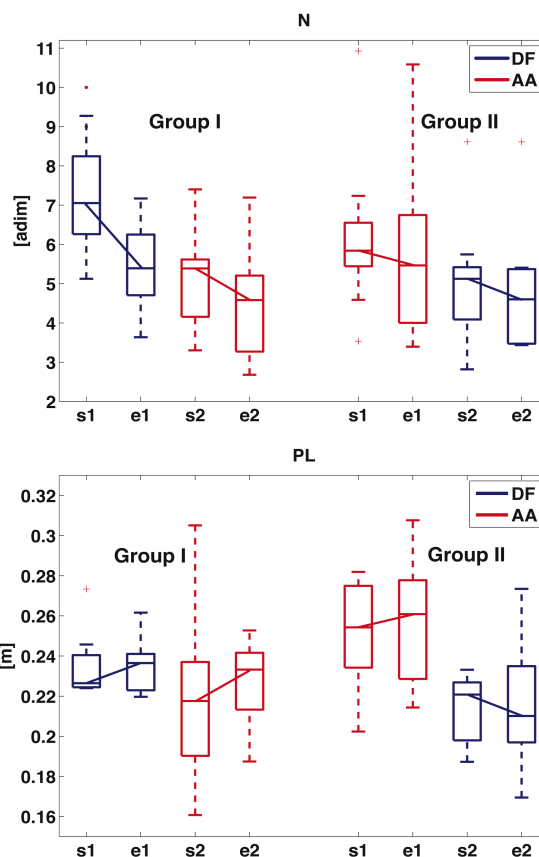


FIGURE 4. Changes in N and PL metrics parameters over the course of the therapy. Top panel: Box plot of N parameter (mean across subjects) of the beginning of the treatment type therapy (s) and at the end of the treatment type (e) for both Group I and Group II. Red boxes are relative to the active assistive therapy, and blue boxes represent results from the divergent field therapy. Bottom panel: Box plot of PL parameter.

Conversely, when patients firstly practiced in the AA field, their initial explorative approach was only later replaced with a fine control strategy when treated in the DF one.

The interaction between factors “group” (i.e., Group I vs. Group II) and “phase” (i.e., start vs. end) slightly affected only N (see Figure 4 and Table 3). In particular, although this parameter decreased in both groups and during each treatment, a more consistent reduction was present in Group I, during both DF and AA approaches. This result confirmed that the preliminary treatment in the DF field involved a faster increment of movement smoothness along the whole 6-week long treatment.

IV. DISCUSSION

The aim of this study was to investigate the effects of the combination of unstable force field and assistive guidance based exercises as neurorehabilitative treatments for the recovery of upper limb related capabilities of post stroke chronic patients.

To investigate this issue we enrolled two groups of patients in a rehabilitation program in which both therapies were administrated in alternated fashion. Specifically, Group I

underwent the DF treatment followed by the AA one. Group II underwent the same rehabilitative treatments provided in the inverse training sequence. The level of motor recovery was assessed considering both the evolution of several kinematic characteristics of the end effector trajectories, and using clinical scales throughout the therapy.

Our results mainly showed significant improvements in the functional outcomes of both Group I and Group II (see Figures 3 and 4, and Tables 1, 2, 3). In addition, all patients undergoing the DF therapy showed a straighter end-effector path than when trained with the AA modality (Figure 3).

Finally, when patients were first trained in the unstable force field, they continued to adopt a fine control of the handle during the AA treatment, as well.

A. EFFECTS OF THE TREATMENTS

One of the main issues related to the use of active assistive approach (i.e., AA) is the patient slacking in response to assistance [49]. Typically, patients are allowed to move freely in the workspace and to develop their own compensatory motor strategy to accomplish the task. The robot assisting controller is then designed to gently guide the patient's arm whenever she/he is not able to initiate the movement or reach the aimed target. While this training program was found to be certainly an effective tool in the case of highly impaired patients who can barely move the arm, it could not challenge the patient further if she/he is already able to reach the target. Accordingly, we also observed in our experiments that patients undergoing the AA training (in particular those of Group II) showed more spread trajectories of the end-effector (see Figure 2).

The DF training exercise instead forced patients to control their arm in order to achieve end point paths closer to the ideal one than the AA approach (Figure 3), in conjunction with a significant reduction of the number of on-line corrections throughout the whole treatment (see N in Figure 4).

These results suggest that the AA treatment could have led patients to adopt a more explorative strategy during training, whereas in the case of the DF therapy cycle, an early and stronger control of the patient's arm was required to limit the disturbance. In this respect, it is important to observe that when the DF treatment was provided in the first therapy cycle, patients showed straighter and smoother paths also during the AA scenario, while this was not true in the opposite case. These issues revealed that the DF training might have influenced motor strategies for the control of the robot's handle more than the assistive approach. Therefore, the sequence of delivery of the treatments could influence the outcome of a robotic-based rehabilitative program.

Some further considerations on the rehabilitation protocol are needed. The results herein reported could be affected by two main factors: i) patients were in the chronic stage of the pathology such that the treatment might only moderately rely on the plasticity of the central nervous system [50]–[52]; ii) treatments were not customized according to the

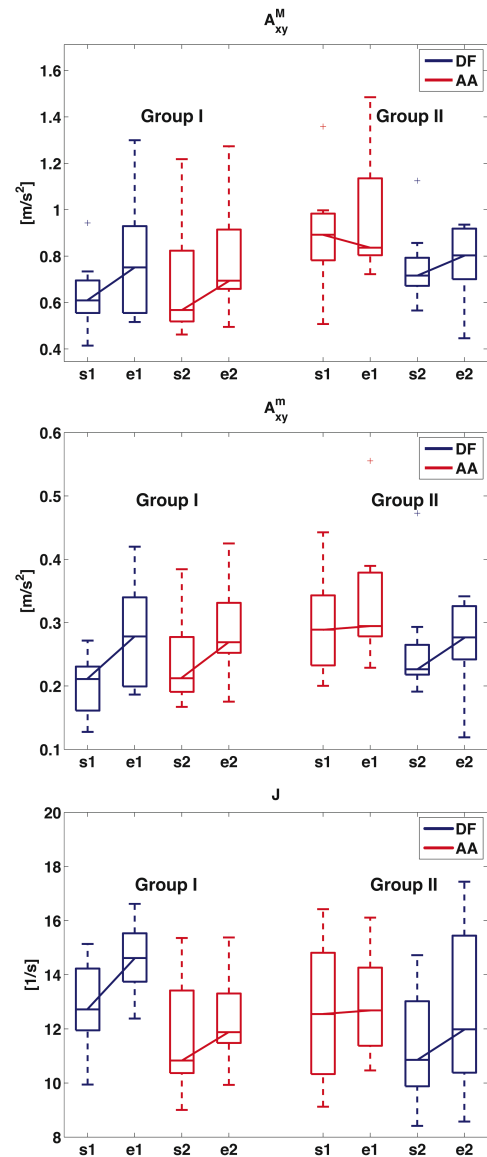


FIGURE 5. Changes in A_{xy}^M , A_{xy}^m , and J metrics parameters over the course of the therapy. Top panel: Box plot of A_{xy}^M parameter (mean across subjects) of the beginning of the treatment type therapy (s) and at the end of the treatment type (e) for both Group I and Group II. Red boxes are relative to the active assistive therapy, and blue boxes represent results from the divergent field therapy. Middle panel: Box plot of A_{xy}^m parameter. Bottom panel: Box plot of J parameter.

severity of each patient and the degree of recovery [53], [54]. Nonetheless, the purpose of our study was to investigate how the adopted paradigms affected patients' motor outcomes and whether the order they were provided influenced the performance. In this respect, our results suggest that the use of a destabilizing force field, such as that used in the present study (i.e. DF), seems to promote early fine control of the movement.

Noticeably, we did not observe any significant difference either in clinical scales or in kinematics performance between the groups. Therefore, no conclusion could be drawn on the effectiveness of the use of one treatment with respect to the

other. Further experiments are required to confirm that the DF paradigm affects patients' behavior while undergoing the treatment in the AA scenario.

V. CONCLUSION

The results herein reported suggest that the use of the DF training exercise forces the patient to keep the end-point position as close as possible to the ideal path, hence promoting a more active control of the arm with respect to the standard active assistive approach. Indeed a preliminary treatment based on the DF scenario can affect the performance during AA therapy, while this was not true in the opposite case. Our findings point to the need for novel neuro-rehabilitative treatments using highly-motivating environments that allow greater patient control over the movement to be performed. Further analysis will be soon carried out to investigate this issue in detail.

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PEPPINO TROPEA received the master's degree in biomedical engineering from the University of Pisa, Pisa, Italy, in 2007, and the Ph.D. degree in biorobotics from Scuola Superiore Sant'Anna, Pisa, in 2011. In 2010, he was a Visiting Student with the Spaulding Rehabilitation Hospital – Harvard Medical School, Boston, MA, USA.

He is currently a Post-Doctoral Associate with the Neural Engineering Group, The BioRobotics Institute, Scuola Superiore Sant'Anna. His current research interests include neuro-motor control mechanisms and the motor recovery process following a stroke to develop new control algorithms, functional assessment methods, and robotic-based rehabilitative strategies.



BENEDETTA CESQUI received the University degree in mechanical engineering from the University of Rome, Roma, Italy, in 2004, and the Ph.D. degree in biorobotics from IMT- Alti Studi Lucca, Lucca, Italy, in 2008. In 2007, she was a Visiting Student with the Department of Mechanical Engineering, MIT Massachusetts Institute of Technology, Boston, MA, USA, working on the design of an EMG based control to be used in roboticaided upper limb rehabilitation in stroke therapy. Since

2006, she has been with the Department of Neurorehabilitation, Viareggio Hospital – Lido di Camaiore, Lucca, Italy, for the validation of new stroke rehabilitation techniques with the help of robotic devices.

She is currently a Post-Doctoral Associate with the Department of Neuro-motor Physiology, Santa Lucia Foundation, Rome. Her current research interests include upper limb motor control strategies, both in the framework of interceptive actions, and neurorehabilitation, eye movements, and virtual reality systems.



VITO MONACO received the master's degree in electrical engineering from Politecnico di Bari, Bari, Italy, in 2003, and the Ph.D. degree in biorobotics, science, and engineering from IMT Lucca in conjunction with the Scuola Superiore Sant' Anna, Pisa, Italy, in 2008.

He is currently an Assistant Professor with The Biorobotics Institute, Scuola Superiore Sant'Anna. His current research interests include the analysis of the modifications of motor control during daily activity due to aging and neuro-musculo-skeletal disorders, the biomechanics of falls, and the development of robotic platforms aimed at delivering neuro-rehabilitative treatments for the recovery of locomotion in post-stroke patients.



SARA ALIBONI received the University degree in medicine from the University of Parma, Parma, Italy, in 2002, and the specialist in Physical Medicine and Rehabilitation from the University of Parma in 2005. Since 2006, she has been collaborating with D. F. Posteraro in the study of the robotic therapy for the upper limb in chronic hemiplegic patients with a MIT Manus device.

She is currently a Medical Doctor in the Department of Neurorehabilitation, Viareggio Hospital, Lucca, Italy. Her current research interests include upper limb motor control strategies, spasticity and treatment with botulinum toxin and orthosis, brain injury, and pediatric rehabilitation.



FEDERICO POSTERARO graduated as a Medical Doctor in 1987. He received the Degree (*cum laude*) in child neurology and psychiatry in 1993 and the Physical Medicine and Rehabilitation (Hons.) degree from the University of Pisa, Pisa, Italy, in 2001.

His research activities are with child rehabilitation at IRCCS Stella Maris, Pisa. From 2002 to 2008, he was a Medical Doctor with the Rehabilitation Medicine Unit, Versilia Hospital, since 2008, he has been the Director of Neurological Unit and Severe Brain Injury Unit of Auxilium Vitae Volterra. He has been working on the use of advanced technologies for many years with specific reference to neurological-derived disability.

Dr. Posteraro has been a Principal Investigator for three EU research projects and other several national research projects. He has authored 25 international scientific publications, ten of them published on indexed journals, 15 national publications, six chapters of books. He has attended more than 100 international and national congresses. Since 1996, he has been involved in teaching activities with the University of Pisa. From 2003 to 2009, he was a member of the board of the Italian Society of Neurological Rehabilitation. Since 2011, he has been a member of the board of the Italian Society of Neurological Rehabilitation.



SILVESTRO MICERA is currently an Associate Professor of biomedical engineering with the Scuola Superiore Sant'Anna, Pisa, Italy, and the Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland. He received the University degree (Laurea) in electrical engineering from the University of Pisa, Pisa, in 1996, and the Ph.D. degree in biomedical engineering from Scuola Superiore Sant'Anna in 2000. From 2000 to 2009, he has been an Assistant Professor of biorobotics

with the Scuola Superiore Sant'Anna, where he is currently an Associate Professor and the Head of the Neural Engineering group. In 2007, he was a Visiting Scientist with the Massachusetts Institute of Technology, Cambridge, MA, USA, with a Fulbright Scholarship. From 2008 to 2011, he was the Head of the Neuroprosthesis Control Group and an Adjunct Assistant Professor with the Institute for Automation, Swiss Federal Institute of Technology (EPFL), Zurich, Switzerland. In 2009, he was a recipient of the "Early Career Achievement Award" of the IEEE Engineering in Medicine and Biology Society. Since 2011, he has been an Associate Professor and the Head of the Translational Neural Engineering Laboratory, EPFL.

His current research interests include the development of hybrid neuro-prosthetic systems (interfacing the central and peripheral nervous systems with artificial systems) and of mechatronic and robotic systems for function and assessment restoration in disabled and elderly persons. He is the author of more than 80 ISI scientific papers and several international patents. He is currently an Associate Editor of the IEEE Transactions on Biomedical Engineering and the IEEE Transactions on Neural Systems and Rehabilitation Engineering. He is an Editorial Board Member of the *Journal of Neuroengineering and Rehabilitation*, the *Journal of Neural Engineering*, and the IEEE Journal of Translational Engineering in Health and Medicine.