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Effects of Action Observation on Physical Training after Stroke

P Celnik, M.D.^{1,2}, B Webster, BA¹, D Glasser, BA¹, and LG Cohen, M.D.¹

¹Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic, NINDS, NIH

²Dept. of Physical Medicine and Rehabilitation, and Dept. of Neurology, Johns Hopkins University

Abstract

Background and Purpose—In healthy humans, observation of another individual performing a motor training task (action observation, AO) facilitates, in the observer, the effects of physical training (PT) on motor memory formation. It is not known if this facilitatory process, of potential value for neurorehabilitation, occurs after stroke.

Methods—Eight chronic stroke patients completed this crossover-randomized investigation. A transcranial magnetic stimulation protocol that tests formation of motor memories was used to determine the effects of PT alone and in combination with AO in two different forms: congruent (PT+AO_{CONGRUENT}) and incongruent (PT+AO_{INCONGRUENT}) to the practiced task.

Results—The magnitude of motor memory formation was larger with PT+AO_{CONGRUENT} than with PT alone or PT+AO_{INCONGRUENT}. This effect was associated with a differential corticomotor excitability change in the muscles acting as agonist and antagonist of the trained/observed movements.

Conclusions—These results indicate that congruent AO in association with physical training can enhance the effects of motor training after stroke.

Keywords

stroke; action observation; mirror neurons system; rehabilitation

Introduction

Performing a motor task or observing another individual performing the same motor actions (Action Observation, AO) activates “mirror neurons” in the premotor and parietal cortex of macaque monkeys^{1,2}. In humans, AO results in increased cortical excitability of the primary motor cortex (M1)^{3,4}, and has been implicated in cognitive processes like understanding the actions and intentions of others⁵, imitation learning⁶, motor learning⁷, and motor memory formation⁸. Recently, we have shown that action observation combined with physical practice results in more prominent training effects relative to plain training in healthy volunteers, as reflected by formation of simple motor memories⁹. These findings suggested that AO could be a valuable strategy to improve motor rehabilitation following brain lesions like stroke^{10,11}. Additionally, recent evidence support the view that action observation could facilitate training of activities of daily living after stroke¹². Here, we

Correspondence to: Pablo Celnik, MD, Dept. of Physical Medicine and Rehabilitation, Johns Hopkins University, 600 N. Wolfe St. Baltimore, MD 21287, Tel.: +1-410-502-2438, Fax: +1-410-502-2419, pcelnik@jhmi.edu.

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tested specifically the hypothesis that AO could enhance the beneficial effects of physical training on motor memory formation in patients with chronic stroke.

Methods

Nine chronic stroke patients with single unilateral cortical or subcortical lesions (5 women, age range 40-74 years; online only Table) gave written informed consent to participate in the study. Eight of them completed the experimental protocol. One patient could not complete the protocol due to TMS-related headache. The National Institute of Neurological Disorders and Stroke, and Johns Hopkins School of Medicine Institutional Review Boards approved the protocol.

Experimental Design

Formation of a motor memory—The experimental design has been previously described in detail⁹. Transcranial magnetic stimulation (TMS, Magstim 200 (Jali Medical, Woburn, MA) was delivered through a figure-eight coil applied over the primary motor cortex (M1) to evoke contralateral thumb movements. Each TMS-evoked thumb movement direction was determined from the first-peak acceleration vector recorded using a small 2-dimensional accelerometer mounted on the thumb (Kistler Instrument, Amherst, NY; Fig. 1). Electromyographic (EMG) activity was recorded from surface electrodes placed over the extensor (EPB) and flexor (FPB) pollicis brevis muscles of the arm contralateral to the stimulated M1. EMG signals were digitized (sampling rate 4,000Hz) and fed into a computer for later analysis. Under this protocol, motor training consisting of voluntary thumb movements performed in a specific direction modifies the TMS-evoked movement directions in a way that indicates encoding of the kinematic details of the practiced movements^{8, 13, 14}.

Experimental protocol—Each patient participated in three testing sessions separated by at least 7 days in a crossover design. The order of the sessions was counterbalanced. Each session started by recording the direction of 60 TMS-evoked thumb movements (approximately a 10min period, **baseline**, Fig. 1a). Immediately after baseline determinations, subjects underwent one of the following 30mins interventions in each separate session (Session 1, 2 or 3 in a random order, Fig. 1b): *Physical Training (PT, n=8)*, consisting of performance of voluntary thumb movements, visually paced at 1Hz, performed in a direction opposite to the Baseline TMS-evoked movement direction (3 blocks of 10 min each separated by 2 min rest); *Physical Training and Congruent Action Observation (PT +AO_{CONGRUENT}, n=8)*. In this session, PT was carried out as in the previous session simultaneously with observation of a video displaying the hand of a healthy volunteer performing the training task in the same direction to that physically practiced. Patients were instructed to perform the thumb training motions simultaneously with the observed thumb movements, both in the same direction for 30 min. This training mode is referred to as **PT +AO_{CONGRUENT}** to reflect the fact that trained and observed thumb movements were in the same direction. *Physical Training and Incongruent Action Observation (PT +AO_{INCONGRUENT}, n=8)*. Motor training in this session was performed in the same way as in the previous two. The only difference with the previous session was that patients observed a video-displaying thumb training motions in a direction opposite to that physically trained. We called this training type **PT+AO_{INCONGRUENT}** to reflect the fact that trained and observed movements were in approximately opposite directions. The hand orientation in the video of both sessions was as if the observer was looking at their own hand (first person observation), since it has been shown that the degree of corticomotor excitability modulation is maximal when the action is observed from the prospective of the observer⁴. To ensure proper attentional focus on the video observation component of the training, patients were

instructed to count silently the number of rare movements (6% of the total) that occurred in the direction opposite to the majority of observed motions (94%) in each of the training sessions containing action observation. When physical practice was performed in combination with action observation, patients were instructed to perform the movements at the same time as in the video. Relaxation of uninvolved muscles was monitored on-line by EMG. Verbal feedback was provided along the training to ensure training consistency and synchronization to the observed movements, and relaxation of the uninvolved muscles or in between thumb motions. After each intervention, we determined the direction of 60 TMS-evoked thumb movements (**post-intervention**), as previously done during baseline (Fig. 1c).

The primary endpoint measure was the percentage of TMS-evoked movements that fell within the training target zone (TTZ), defined as a window of $\pm 20^\circ$ centered on the mean training direction^{8,9} (see Fig. 1b). The training direction was determined using data originated in the accelerometer attached to the finger, as done also for determination of pre and post intervention TMS-evoked movement directions (see *Formation of a motor memory*).

Consistency of motor training performance was monitored in all sessions by measuring three kinematic parameters: (1) the angular difference between TMS-evoked movement directions at baseline and during training, (2) the angular dispersion of training movement directions, and (3) the magnitude of the first peak acceleration of the trained movements. All patients reported their level of attention and fatigue during the interventions using visual analogue scales (range 1–7; 1=worst possible response, 7=best response). Motor cortical excitability was measured recording motor evoked potentials (MEP) amplitudes from muscles mediating movements in the trained (MEP_{AGONIST}) and baseline (MEP_{ANTAGONIST}) directions. In this setting, agonist refers to the muscle agonistic to the physically trained motions, while antagonist refers to muscles antagonistic to the physically trained motions. To calculate the effects of each training intervention (sessions 1, 2 and 3) on the motor cortical excitability of both muscle groups (agonist and antagonist), we calculated the post/pre (baseline) MEP amplitude ratio, referred to along the manuscript as MEP_{POST-/PRE-INTERVENTION}. This measure provides information on the effects of each intervention on the relative weight of corticospinal influences on muscles agonistic and antagonistic to the TMS-evoked movement directions.

Data analysis

An investigator blinded to the intervention type performed data analysis. The primary end point measure of the study, the percent of TMS-evoked movement falling in the TTZ before and after each session training type (dependent variable, a measure of motor memory formation^{14, 15}), was analyzed using repeated measures analysis of variance (ANOVA_{RM}) with independent factors TIME (BASELINE, POST-INTERVENTION) and SESSION (MT, MT+AOcongruent, MT+AOincongruent). Separate ANOVAs were used to evaluate changes in MEP amplitudes in each muscle group, attention, fatigue, each of the motor training kinematic parameters and MEP_{POST-/PRE-INTERVENTION} ratio. Post hoc analysis was done when appropriate using Fisher's PLSD. All data is presented as mean \pm standard error of the mean (SEM) unless otherwise stated.

Results

Patients reported comparable levels of attention and fatigue across sessions (Table 1). Kinematic monitoring showed comparable angular difference between TMS-evoked movement directions at baseline and during training and angular dispersion of training movement directions across interventions (Table 2). First peak acceleration of the trained movements was slightly higher in PT+AO_{CONGRUENT} than in PT+AO_{INCONGRUENT}

(ANOVA_{RM INTERVENTION}: $F[2,8]=4.02$, $p<0.05$; Fisher's PLSD Post Hoc $p<0.02$, an effect more prominent in 3 subjects that may reflect a relatively higher difficulty in training in one direction while observing movements in the opposite direction).

Baseline determination of TMS-evoked thumb movements in the TTZ were comparable across sessions (ANOVA_{RM SESSION}: $F[2,7]=1.5$, $p=0.26$). PT, and PT+AO_{INCONGRUENT} training sessions did not elicit increases in the percentage of TMS-evoked thumb movements in the TTZ (Fig 2). On the other hand, the PT+AO_{CONGRUENT} training type resulted in a marked increase in the percentage of TMS-evoked thumb movements falling in the TTZ (Paired t-Test: $t[7]=-2.7$, $p<0.04$). This change in the PT+AO_{CONGRUENT} condition was larger than those observed with PT+AO_{INCONGRUENT} or PT alone (ANOVA_{RM TIME}: $F[1,7]=9.5$, $p<0.02$; $S_{SESSION}$: $F[2,7]=5.4$, $p<0.02$; T_{TIME} by $S_{SESSION}$ interaction: $F[2,14]=5.2$, $p<0.02$; Fisher's PLSD Post Hoc for PT+AO_{INCONGRUENT}, PT+AO_{CONGRUENT}: $p<0.02$; Post Hoc for PT alone, PT+AO_{CONGRUENT}: <0.02). The PT+AO_{CONGRUENT} effect was present in 7 of the 8 patients that completed the experimental protocol (Fig. 2, light gray lines). Of note, two participants had a dramatic effect after PT+AO_{CONGRUENT}. However, removing these subjects from the main statistical analysis did not modify the significance (ANOVA_{RM TIME} $F[1,5]=10.7$, $p<0.03$; $S_{SESSION}$: $F[2,5]=3.8$, $p=0.05$; T_{TIME} by $S_{SESSION}$ interaction: $F[2,10]=4.1$, $p=0.05$; Fisher's PLSD Post Hoc for PT+AO_{INCONGRUENT}, PT+AO_{CONGRUENT}: $p<0.03$; Post Hoc for PT alone, PT+AO_{CONGRUENT}: $p=0.05$).

At baseline, MEP amplitudes were comparable across sessions in both muscle groups (ANOVA_{RM MUSCLE} $F[1,7]=0.005$ $p=0.94$, $I_{INTERVENTION}$ $F[1,7]=1.85$ $p=0.19$, M_{MUSCLE} by $S_{SESSION}$ Interaction $F[1,7]=1.02$ $p=0.38$; Table 3). At post-intervention, MEP_{AGONIST} and MEP_{ANTAGONIST} amplitudes did not change significantly (ANOVA_{RM MUSCLE} $F[1,7]=0.06$ $p=0.80$, $I_{INTERVENTION}$ $F[1,7]=0.49$ $p=0.62$, M_{MUSCLE} by $I_{INTERVENTION}$ Interaction $F[1,7]=1.89$ $p=0.83$, Fig 3a). Both muscles MEP amplitudes slightly decreased in PT and increased in the PT+AO_{INCONGRUENT} sessions. However, in the PT+AO_{CONGRUENT} session MEP_{ANTAGONIST} had a slight increase while MEP_{ANTAGONIST} decreased. This differential change in excitability is reflected by a statistically significant change in the MEP_{POST-PRE-INTERVENTION} ratio (ANOVA_{RM MUSCLE}: $F[1,7]=8.71$, $p=0.03$; $S_{SESSION}$: $F[2,7]=0.24$, $p=0.79$; M_{MUSCLE} by $S_{SESSION}$ Interaction: $F[2,14]=5.73$, $p<0.02$; Fig. 3b).

Discussion

This study shows that action observation can enhance the beneficial effects of motor training on motor memory formation in patients with chronic stroke. Interestingly, the kinematic details of the observed action influence these modulatory effects: they are present when the observed action matches the direction of the physical training, and absent when they do not match. This effect was associated with an increase in corticomotor excitability of the muscle representations mediating movements in the trained and observed direction, whereas the excitability of the antagonist muscles decreased.

Previous investigations in the macaque monkey brain demonstrated the existence of “mirror neurons” that discharge both, with performance of a motor action and with observation of another individual performing similar motor actions^{1, 2}. Human studies have described a “mirror neuron system” with similar characteristics¹⁶, involved in action understanding¹⁷, imitation⁶, motor learning⁷, socialization¹⁸, and capable of modulating training effects in healthy individuals⁹. Given these properties and the capacity to engage the motor execution network it has been proposed that action observation could contribute to enhance the effects of motor rehabilitation after stroke^{10, 11}. A recent small clinical trial in fifteen stroke patients investigating this strategy reported beneficial effects of observation of other individuals performing tasks involving activities of daily living on recovery of the ability to

perform certain motor tasks. These observational training elicited fMRI activation of areas in which mirror neurons have been found¹². However, performance of action observation and training exercises were not done simultaneously, which may have reduced the effects of action observation, as it is known that modulation of action observation on corticomotor excitability is stronger when high degree of specificity between phase³ and direction is present⁴.

In the present study we found that observation of another subject performing training motions in the same direction and in phase with those physically trained enhanced motor memory formation relative to physical training alone. This effect cannot be explained by differences in baseline corticomotor excitability, motor training kinematics, attention or fatigue during the different interventional sessions (tables 1, 2 and 3).

The finding that 30 minutes physical training alone under our experimental conditions was not enough to encode a motor memory is consistent with prior studies in chronic stroke patients^{19, 20}. This relative inability of 30 min training to elicit the desired effect on motor memory formation represents an excellent model against which to compare various strategies designed to boost training effects. It has been shown that dopaminergic agents could enhance training effects on motor memory formation in older adults²¹ and in patients with stroke¹⁹. Interestingly, action observation in older healthy volunteers can also enhance training effects to elicit motor memory encoding similar to that induced in younger healthy volunteers by physical training alone⁹. Action observation enhanced training effects to a similar extent in elderly healthy volunteers⁹ and in our present results in stroke patients.

Changes in cortical excitability identified here provide information on the underlying mechanisms associated to these behavioral effects. The differential modulation of corticomotor excitability of the agonist and antagonist muscles involved in the performed and observed movements suggests a change in the balance of inhibition and excitation within the cortical representation of the thumb. It is likely that Hebbian-like confluence of inputs arriving to the corticospinal neurons within the hand representation of M1 from the ventral premotor cortex^{22, 23}, where mirror-like activity is found^{5, 24}, and non-primary motor regions^{25, 26}, associated to performance of motor tasks, is the mechanism underlying the corticomotor excitability change. Interestingly, similar brain regions activated by hand movements after stroke may contribute to recovery of motor function²⁷⁻²⁹. Therefore, it is possible that using action observation to activate premotor areas and in turn modulate motor neuronal output may be particularly suited in stroke patients.

In summary, our results indicate that action observation could contribute to neurorehabilitation by enhancing the beneficial effects of training on motor function in a partially paralyzed hand, an issue of relevance for approximately 50 to 70% of patients post stroke³⁰. The influence of AO in patients with more severe motor impairment has not been investigated. These preliminary results support a role for action observation in neurorehabilitative treatments after stroke and suggest that it would be worthwhile to investigate this hypothesis in double-blind, controlled multicenter clinical trials.

Summary

This preliminary study shows that simultaneous observation of another individual performing the same action as that physically trained can enhance the effects of motor training on motor memory formation. This effect, accompanied by specific and differential changes in corticomotor excitability within the hand motor representation of the primary motor cortex, suggests the potential use of action observation as a strategy to enhance motor rehabilitation in patients with chronic stroke.

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References

1. Gallese V, Fadiga L, Fogassi L, Rizzolatti G. Action recognition in the premotor cortex. *Brain*. 1996; 119(Pt 2):593–609. [PubMed: 8800951]
2. Fogassi L, Ferrari PF, Gesierich B, Rozzi S, Chersi F, Rizzolatti G. Parietal lobe: From action organization to intention understanding. *Science*. 2005; 308:662–667. [PubMed: 15860620]
3. Gangitano M, Mottaghy FM, Pascual-Leone A. Phase-specific modulation of cortical motor output during movement observation. *Neuroreport*. 2001; 12:1489–1492. [PubMed: 11388435]
4. Maeda F, Kleiner-Fisman G, Pascual-Leone A. Motor facilitation while observing hand actions: Specificity of the effect and role of observer's orientation. *J Neurophysiol*. 2002; 87:1329–1335. [PubMed: 11877507]
5. Iacoboni M, Molnar-Szakacs I, Gallese V, Buccino G, Mazziotta JC, Rizzolatti G. Grasping the intentions of others with one's own mirror neuron system. *PLoS Biol*. 2005; 3:e79. [PubMed: 15736981]
6. Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G. Cortical mechanisms of human imitation. *Science*. 1999; 286:2526–2528. [PubMed: 10617472]
7. Mattar AA, Gribble PL. Motor learning by observing. *Neuron*. 2005; 46:153–160. [PubMed: 15820701]
8. Stefan K, Cohen LG, Duque J, Mazzocchio R, Celnik P, Sawaki L, Ungerleider L, Classen J. Formation of a motor memory by action observation. *J Neurosci*. 2005; 25:9339–9346. [PubMed: 16221842]
9. Celnik P, Stefan K, Hummel F, Duque J, Classen J, Cohen LG. Encoding a motor memory in the older adult by action observation. *Neuroimage*. 2006; 29:677–684. [PubMed: 16125417]
10. Pomeroy VM, Clark CA, Miller JS, Baron JC, Markus HS, Tallis RC. The potential for utilizing the “Mirror neurone system” To enhance recovery of the severely affected upper limb early after stroke: A review and hypothesis. *Neurorehabil Neural Repair*. 2005; 19:4–13. [PubMed: 15673838]
11. Buccino G, Solodkin A, Small SL. Functions of the mirror neuron system: Implications for neurorehabilitation. *Cogn Behav Neurol*. 2006; 19:55–63. [PubMed: 16633020]
12. Ertelt D, Small S, Solodkin A, Dettmers C, McNamara A, Binkofski F, Buccino G. Action observation has a positive impact on rehabilitation of motor deficits after stroke. *Neuroimage*. 2007; 36(2):T164–173. [PubMed: 17499164]
13. Butefisch CM, Davis BC, Wise SP, Sawaki L, Kopylev L, Classen J, Cohen LG. Mechanisms of use-dependent plasticity in the human motor cortex. *Proc Natl Acad Sci U S A*. 2000; 97:3661–3665. [PubMed: 10716702]
14. Classen J, Liepert J, Wise SP, Hallett M, Cohen L. Rapid plasticity of human cortical movement representation induced by practice. *J Neurophysiol*. 1998; 79:1117–1123. [PubMed: 9463469]
15. Butefisch CM, Khurana V, Kopylev L, Cohen LG. Enhancing encoding of a motor memory in the primary motor cortex by cortical stimulation. *J Neurophysiol*. 2004; 91:2110–2116. [PubMed: 14711974]
16. Rizzolatti G, Craighero L. The mirror-neuron system. *Annu Rev Neurosci*. 2004; 27:169–192. [PubMed: 15217330]
17. Flanagan JR, Johansson RS. Action plans used in action observation. *Nature*. 2003; 424:769–771. [PubMed: 12917683]
18. Wolpert DM, Doya K, Kawato M. A unifying computational framework for motor control and social interaction. *Philos Trans R Soc Lond B Biol Sci*. 2003; 358:593–602. [PubMed: 12689384]
19. Floel A, Hummel F, Breitenstein C, Knecht S, Cohen LG. Dopaminergic effects on encoding of a motor memory in chronic stroke. *Neurology*. 2005; 65:472–474. [PubMed: 16087920]

20. Sawaki L, Wu CW, Kaelin-Lang A, Cohen LG. Effects of somatosensory stimulation on use-dependent plasticity in chronic stroke. *Stroke*. 2006; 37:246–247. [PubMed: 16322491]
21. Floel A, Breitenstein C, Hummel F, Celnik P, Gingert C, Sawaki L, Knecht S, Cohen LG. Dopaminergic influences on formation of a motor memory. *Ann Neurol*. 2005; 58:121–130. [PubMed: 15984008]
22. Shimazu H, Maier MA, Cerri G, Kirkwood PA, Lemon RN. Macaque ventral premotor cortex exerts powerful facilitation of motor cortex outputs to upper limb motoneurons. *J Neurosci*. 2004; 24:1200–1211. [PubMed: 14762138]
23. Cerri G, Shimazu H, Maier MA, Lemon RN. Facilitation from ventral premotor cortex of primary motor cortex outputs to macaque hand muscles. *J Neurophysiol*. 2003; 90:832–842. [PubMed: 12904495]
24. Buccino G, Binkofski F, Fink GR, Fadiga L, Fogassi L, Gallese V, Seitz RJ, Zilles K, Rizzolatti G, Freund HJ. Action observation activates premotor and parietal areas in a somatotopic manner: An fmri study. *Eur J Neurosci*. 2001; 13:400–404. [PubMed: 11168545]
25. Dum RP, Strick PL. Motor areas in the frontal lobe of the primate. *Physiol Behav*. 2002; 77:677–682. [PubMed: 12527018]
26. Mima T, Sadato N, Yazawa S, Hanakawa T, Fukuyama H, Yonekura Y, Shibasaki H. Brain structures related to active and passive finger movements in man. *Brain*. 1999; 122(Pt 10):1989–1997. [PubMed: 10506099]
27. Calautti C, Baron JC. Functional neuroimaging studies of motor recovery after stroke in adults: A review. *Stroke*. 2003; 34:1553–1566. [PubMed: 12738893]
28. Ward NS. The neural substrates of motor recovery after focal damage to the central nervous system. *Arch Phys Med Rehabil*. 2006; 87:30–35.
29. Yozbatiran N, Cramer SC. Imaging motor recovery after stroke. *NeuroRx*. 2006; 3:482–488. [PubMed: 17012062]
30. Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y. Heart disease and stroke statistics--2007 update: A report from the american heart association statistics committee and stroke statistics subcommittee. *Circulation*. 2007; 115:e69–171. [PubMed: 17194875]

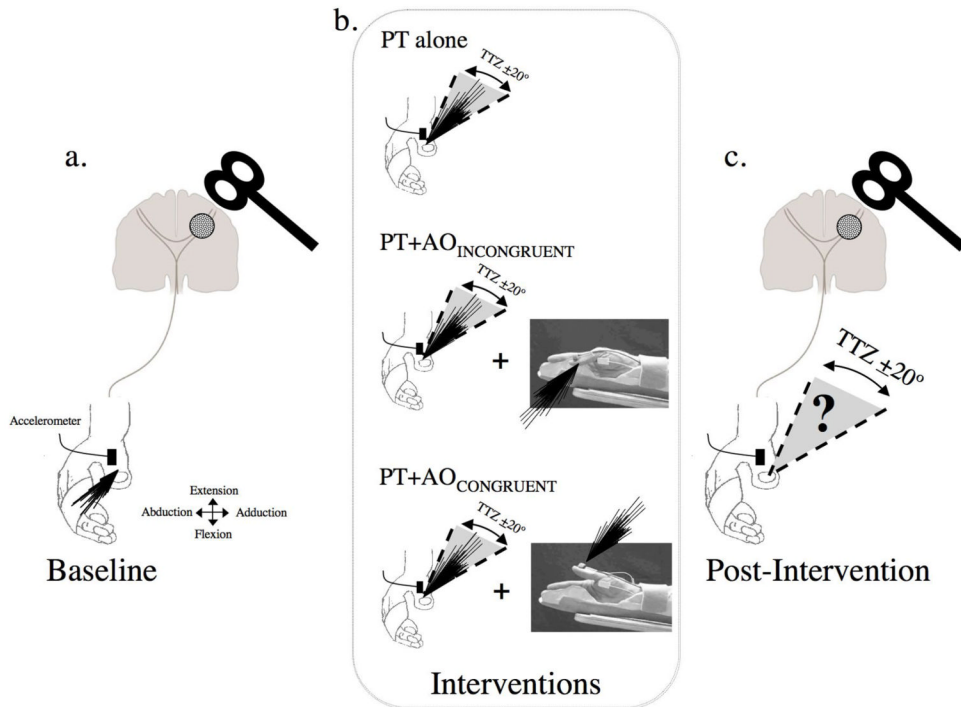


Fig. 1.

Graphic representation of the experimental set up. a) Baseline. Black lines depict the direction of individual TMS-evoked thumb movements, in this example a combination of flexion and abduction. b) Interventions. Patients perform: (1) physical training (PT) alone (represented by a drawing of a thumb and black lines showing the direction of the practice movements), (2) PT+AO_{INCONGRUENT} (same drawing as in PT plus a still picture obtained from the video presented during the experiments showing the thumb in flexion position and black lines depicting the observed movements direction, opposite to the physically trained motions), and (3) PT+AO_{CONGRUENT} (shown by the same drawing as in PT plus a still picture with the thumb in extension position and black lines depicting the direction of the observed movements). In the 3 experimental sessions, the physical training component consisted of thumb movements practiced in a direction opposite to the baseline TMS-evoked movement direction (in the sketch this is represented by the TTZ, a training target zone defined as a window of $\pm 20^\circ$ centered on the mean training direction). c) Post-intervention. The percent of TMS-evoked thumb movements falling within the TTZ, the primary outcome measure, was calculated.

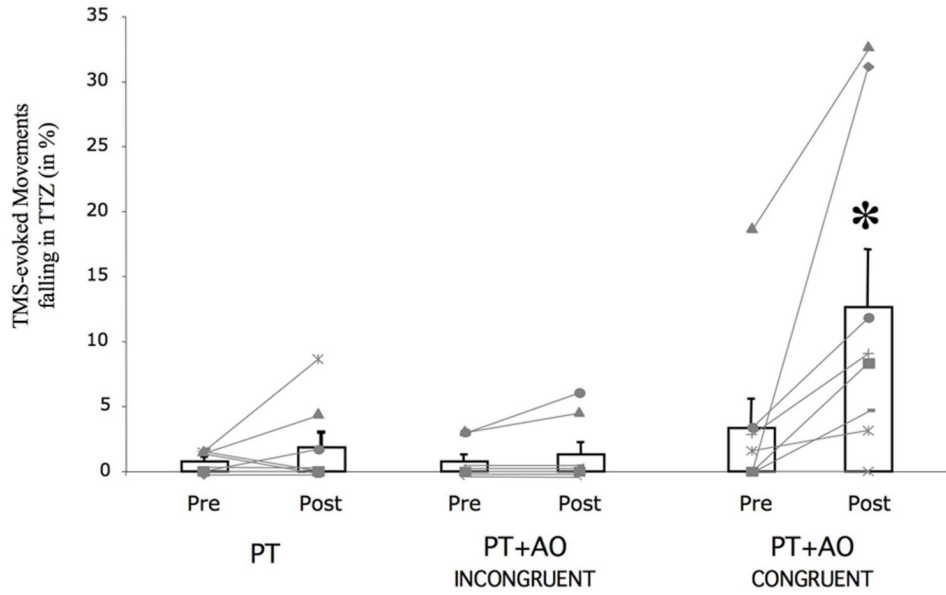


Fig 2. Percent of intervention-dependent TMS-evoked thumb movements falling in the TTZ (bar graph, n=8; mean \pm SEM). Note the increase in the percentage of TMS-evoked thumb movements falling in the TTZ when MT+AO_{CONGRUENT} is performed. *, p < 0.02. In light gray, the percent of movements in TTZ for each subject is shown. Seven of eight subjects experience an increased in TMS-evoked motions following the trained and observed directions in the PT+AO_{CONGRUENT} condition.

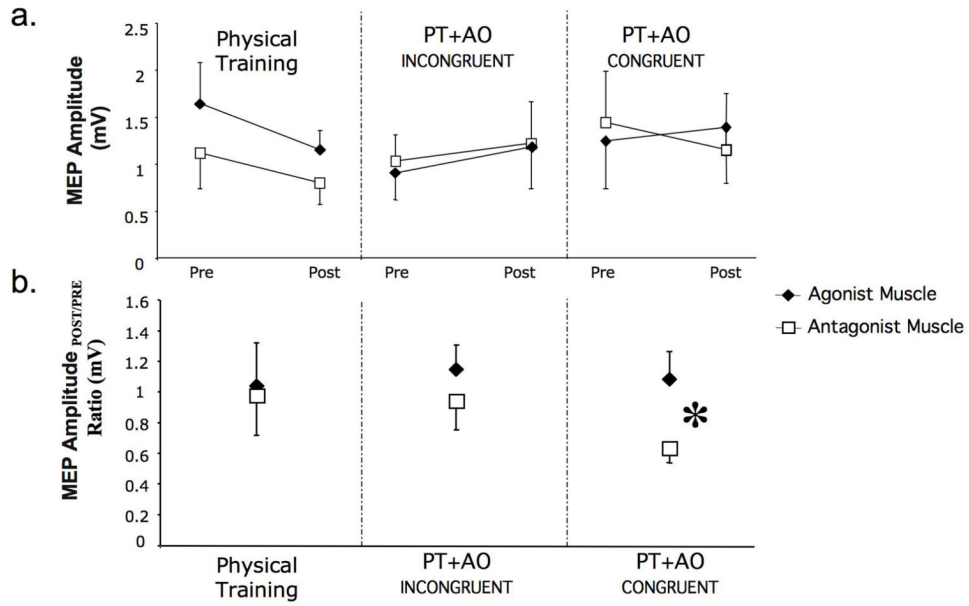


Fig. 3. Corticomotor excitability changes as measured by motor evoked potential amplitudes (MEP). In 3a, absolute MEP amplitudes for the agonist and antagonist muscles to the physically practice direction is shown at baseline (pre) and after (post) each intervention in the 3 sessions. After PT alone MEP amplitude decreased similarly for both muscles and have minimal changes after PT+AO_{INCONGRUENT}. In the PT+AO_{CONGRUENT} condition, MEP amplitude for the agonist muscle had a slight increased whereas the antagonist muscle decreased. This differential modulation of excitability is evidenced in the MEP_{POST/PRE}-INTERVENTION ratio (3b). Here, only PT+AO_{CONGRUENT} elicited a significant different ratio. *, p < 0.03.

Table 1

Subjective reports in visual analogue scales.

	Pt1	Pt2	Pt3	Pt4	Pt5	Pt6	Pt7	Pt8	Mean±SEM	Stats
Fatigue	PT	5	5	6	6	7	5	5	5.5±0.3	F=0.97 p=0.40
	PT+A _O INCONGRUENT	6	5	4	5	6	5	5	5.2±0.3	
	PT+A _O CONGRUENT	5	5	5	3	5	6	2	4.5±0.4	
Attention	PT	5	4	6	5	5	5	6	5.2±0.3	F=2.01 p=0.17
	PT+A _O INCONGRUENT	4.5	5	5	5	5	5	3	4.7±0.3	
	PT+A _O CONGRUENT	5	5	6	5	5	2	3	4.5±0.4	

Subjective reports of fatigue and attention as rated by the participants in a visual analogue scale (fatigue and attention: 1= worst, 7= least fatigue or best attention). Data for individual patients (Pt1, Pt2, ... Pt8) and the group mean±SEM is presented. *p* and *F* values were calculated from independent ANOVARM.

Table 2

Physical training kinematics.

	Pt1	Pt2	Pt3	Pt4	Pt5	Pt6	Pt7	Pt8	Avg±SEM	Stats
Peak Acceleration (m/s²)	PT	3.5	0.2	2.2	4.3	0.9	0.1	10.3	1.6	F=4.02 p<0.05
	PT+AO _{INCONGRUENT}	2.8	0.2	2.0	3.9	0.9	0.1	8.2	1.4	
	PT+AO _{CONGRUENT}	3.9	0.1	3.0	5.9	0.8	0.1	12.2	1.5	
Angular Difference (°)	PT	6.3	183.5	105.7	116.4	24.2	91.9	236.4	118.1±28	F=0.43 p= 0.65
	PT+AO _{INCONGRUENT}	46.5	201.0	19.4	127.1	75.0	111.6	147.9	116.5±23	
	PT+AO _{CONGRUENT}	16.6	237.6	76.5	82.1	52.5	126.0	231.5	129.9±30	
Angular Dispersion	PT	0.8	0.9	0.5	0.8	0.7	1.0	0.9	0.8±0.1	F=1.63 p= 0.23
	PT+AO _{INCONGRUENT}	0.7	0.9	0.5	0.7	0.8	0.9	0.9	0.8±0.1	
	PT+AO _{CONGRUENT}	0.8	0.9	0.8	0.7	0.9	1.0	1.0	0.9±0.1	

The magnitude of the first peak acceleration during training movements is presented in m/s², degrees for angular difference between the mean training angle and the mean baseline angle, and length of unit vector for angular dispersion. Data for individual patients (Pt1, Pt2, ..., Pt8) and the group mean±SEM is presented. *p* and *F* values originate from separate ANOVARM.

Table 3

Baseline corticomotor excitability and stimulation parameters.

	Pt1	Pt2	Pt3	Pt4	Pt5	Pt6	Pt7	Pt8	Avg±SEM	Stats
Motor Threshold (Agonist muscle; % of stimulator output)	PT	34.0	69.0	56.0	60.0	55.0	49.0	58.0	57.5±1.3	F= 1.47 p= 0.27
	PT+TO _{INCONGRUENT}	35.0	63.0	55.0	61.0	53.0	56.0	57.0	56.8±1.2	
	PT+TO _{CONGRUENT}	34.0	61.0	52.0	61.0	52.0	48.0	59.0	55.3±1.2	
Stimulation Intensity (used to elicit TMS- movements; % of stimulator output)	PT	43.0	74.0	68.0	70.0	78.0	74.0	74.0	70.8±1.2	F= 1.23 p= 0.32
	PT+TO _{INCONGRUENT}	42.0	74.0	68.0	72.0	84.0	80.0	72.0	72.1±1.3	
	PT+TO _{CONGRUENT}	42.0	74.0	68.0	68.0	85.0	72.0	74.0	70.4±1.3	
Agonist MEP (mV)	PT	2.0	0.1	3.2	1.0	3.2	0.4	1.2	0.6	Muscle F= 0.005 p= 0.94 Intervention F=1.85 p=0.19 Interaction F=1.02 p=0.38
	PT+TO _{INCONGRUENT}	1.0	0.2	0.9	0.2	2.4	0.2	1.4	0.8±0.03	
	PT+TO _{CONGRUENT}	1.3	0.4	1.0	0.1	4.5	0.2	1.2	1.1±0.4	
Antagonist MEP (mV)	PT	3.5	0.1	1.2	0.3	1.2	0.6	0.7	0.7	
	PT+TO _{INCONGRUENT}	1.8	0.2	2.4	0.9	0.9	0.3	0.6	0.9±0.3	
	PT+TO _{congruent}	2.9	0.2	4.5	0.5	1.0	0.5	0.7	1.3±0.4	

Data for individual patients (Pt1, Pt2, ...Pt8) and the group mean±SEM is presented. p and F values originate from independent ANOVARM.