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Bi-hemispheric effects on corticospinal excitability induced by repeated sessions of imagery versus observation of actions

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Abstract. Purpose: To investigate whether repeated sessions of motor imagery and action observation modulate corticospinal excitability (CE) over time, whether these processes are susceptible of any training effect and if such effect might be different for the dominant and non dominant hemisphere.

Methods: 11 subjects underwent three sessions, spaced 5–7 days, of single-pulse Transcranial Magnetic Stimulation (TMS) of right and left primary motor cortex. Subjects were asked to imagine or observe pinch-grip actions with either hand. Motor evoked potentials (MEPs) were recorded bilaterally from the First Dorsal Interosseus muscle (FDI), acting as main agonist during precision grip.

Results: Motor imagery consistently enhanced CE with respect to action observation, regardless of hemispheric lateralization and of separate testing sessions. However, motor imagery increased CE only when measured over the non-dominant hemisphere, during the third session with respect to the first one. The increase of CE induced by action observation in the first session was not further modified throughout the remaining two sessions, in either hemisphere.

Conclusions: Results suggest that motor imagery is sustained by a cortical network susceptible to training effects only for the non-dominant hemisphere. Such an effect was lacking for action observation, likely because of the innateness of these mechanisms. Results might have implications for rehabilitative purposes.

Keywords: Transcranial magnetic stimulation, learning, motor imagery, actions observation, mirror neurons

1. Introduction

Current neuroimaging techniques indicate that neural mechanisms underlying motor imagery (the mental rehearsal of voluntary movements) and actions observation, partly share anatomical (Buccino et al., 2001;

Grezes and Decety, 2001) and neurophysiological substrates (Buccino et al., 2001; Grezes and Decety, 2001; Lui et al., 2008). These substrates form a wide premotor-parietal circuit, whose final common pathway is the primary motor cortex (M1). It has been hypothesized that such an “effector” area can be subliminally activated by both actions observation and motor imagery in a sort of covert action “execution” without a real production of an overt actual movement (Jeannerod, 2001).

While brain imaging techniques provide a semi-static picture of the activated brain regions (i.e., low

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temporal resolution), transcranial magnetic stimulation (TMS) can be used to measure the corticospinal excitability with a high temporal resolution, meanwhile fully reflecting physiological properties of the human motor system “at work” in different planned (Cattaneo, Caruana, Jezzini and Rizzolatti, 2009) or executed actions (Lemon, Johansson and Westling, 1995).

There are strong evidences that the size of motor evoked potentials (MEPs), following overthreshold single-pulse TMS of M1, increases when recorded in the muscles acting as *prime mover* within the dispatched -but not executed- motor program during motor imagery (Fadiga et al., 1999; Rossi, Pasqualetti, Tecchio, Pauri and Rossini, 1998; Rossini, Rossi, Pasqualetti and Tecchio, 1999). Similarly, movement observation produces a selective corticospinal facilitation, as reflected by the MEPs size increase in the muscles that the observer would use to actually reproduce the observed action (Aziz-Zadeh, Maeda, Zaidel, Mazziotta and Iacoboni, 2002; Brighina, La, V, Oliveri, Piazza and Fierro, 2000; Fadiga, Fogassi, Pavesi and Rizzolatti, 1995; Gangitano, Mottaghy and Pascual-Leone, 2001; Maeda, Kleiner-Fisman and Pascual-Leone, 2002; Urgesi, Candidi, Fabbro, Romani and Aglioti, 2006). This latter effect is probably due to facilitation of cortico-cortical circuits (Patuzzo, Fiaschi and Manganotti, 2003; Strafella and Paus, 2000) and seems particularly evident when observed actions are goal directed (Cattaneo et al., 2009; Maeda et al., 2002).

Due to these facilitatory effects on corticospinal output, the use of motor imagery and action observation, as strategies to improve motor functions, has been postulated (Mulder, 2007; Roosink and Zijdwind, 2010). For example, the cortical representation of finger flexor and extensor muscles - as revealed by a TMS mapping procedure - progressively enlarges in subjects who mentally performed five-days piano practice with one hand, as much as in those subjects who actually played it (Pascual-Leone et al., 1995).

On the other hand, action observation may form an elementary motor memory in M1 (Stefan et al., 2005) because it improves the learning of a simple motor practice in healthy humans (Stefan, Classen, Celnik and Cohen, 2008). Moreover, in association with physical training, it may represent an effective strategy to enhance the effects of rehabilitation after

stroke (Porro, Facchin, Fusi, Dri and Fadiga, 2007; Celnik, Webster, Glasser and Cohen, 2008). Despite these intriguing behavioral improvements, it remains to be neurophysiologically investigated the possibility that neural networks underlying motor imagery and action observation might undergo to similar changes after training.

Thus, we investigated, by single-pulse TMS of right or left M1 and electromyographic (EMG) recording of contralateral intrinsic hand muscles, if repeated sessions of motor imagery and action observation could further modulate the corticospinal excitability by increasing over time the Motor Evoked Potentials (MEPs) amplitude, as a consequence of a possible training effect. This might be relevant in view of possible rehabilitation strategies.

Moreover, by running the two tasks among three sessions spaced 5–7 days apart, the present experimental approach allowed us to serially compare intra-individual effects of motor imagery and action observation on corticospinal output in the dominant and non-dominant hemisphere.

2. Methods

2.1. Participants

Eleven healthy (5 females, 6 males; mean age: 31 ± 6.56) fully right-handed subjects (Oldfield, 1971), all naïve to the purpose of the experiment, were included after the approval of the procedure by the local Ethical Committee. They all gave a written informed consent to the study.

2.2. Task

Subjects sat comfortably in a reclining chair, keeping their arms fully relaxed in a natural position, with their hands pronated and resting on a pillow. Three recording sessions, lasting about 60 minutes each and spaced 5–7 days apart, were run. The first session started with a 10 minutes training period, to allow subjects to familiarize with TMS sensations on the scalp and evoked twitches in the hand, as well as to perform motor imagery and passive action observation tasks without activating their muscles. To this end, we continuously monitored the silence of the EMG activity in the muscles involved in the two tasks. Subjects were requested to visually imagine a

thumb-index finger pinch grip with the right or the left hand in order to better compare this condition with passive action observation. In this condition, subjects passively observed the same thumb-index finger pinch-grip performed by an experimenter. The experimenter presented the action from the visual hemifield contralateral to the stimulated M1, by using the right hand when TMS was applied on the left hemisphere and the left hand when TMS was applied on the right hemisphere (Aziz-Zadeh et al., 2002). In fact, a right-facing body view of human motion is better represented in the right visual hemifield of the observer, and vice-versa for the left-facing body motion observation (de Lussanet et al., 2008).

In each of the three experimental sessions, TMS was applied over the right or left M1 and MEPs were recorded from the contralateral FDI muscle. This choice was motivated by the central role played by this muscle during the pinch-grip actions that subjects had to imagine or to observe. Hence, there were different, randomly and counterbalanced administered conditions: rest, motor imagery and action observation for left and the right hand.

2.3. Stimulating and recording procedures

TMS was carried out via a standard eight-shaped focal coil connected to a monophasic Magstim 200 stimulator (Magstim Co., UK). The coil was positioned over the left or right hemiscalp, contralateral to the examined muscle, with the handle pointing backwards about 45° from the midline. The “hot spot” (i.e., the location on the scalp eliciting MEPs with the minimal TMS intensity) was marked by indelible ink in order to allow the same coil positioning during the entire study. Ag-AgCl adhesive electrodes were positioned over the muscle with the active electrode on the motor point and the reference electrode on the nearest finger joint. Then, the TMS intensity was adjusted to produce fairly stable MEPs of 600–800 μ V (peak to peak amplitude) in basal conditions (i.e., during the rest condition).

MEPs were recorded with a four-channel electromyograph (Phasis, EBNeuro), with the bandpass filter set at 20 Hz–2 KHz, and the signal sampled at 20 KHz. TMS pulses were spaced 5–8 seconds to avoid any short-term conditioning effect (Classen et al., 2000; Terao et al., 1995), and were delivered 1–2 seconds after the initiation of the motor imagery task or during the closure phase of the pinch grip

during the action observation task. Such an ecological procedure has been already used to investigate corticospinal excitability changes related to action observation (Fadiga et al., 1995) and imagery (Rossi et al., 1998; Rossini et al., 1999).

Five MEPs centered on the median latency value, out of the seven-eight acquired for each condition (after exclusion of all trials contaminated by artifacts or EMG activity), were selected. This minimized the probability that MEPs belonging to different neural pools (i.e., with onset latency shorter than 1.5 ms from the mean) could be included in further analysis. Indeed, it is known that a latency shortening occurs even in case of subliminal voluntary contraction occurring in the 300 ms preceding the instant of TMS (Rossi et al., 2008; Starr, Caramia, Zarola and Rossini, 1988). Therefore, latency shortening represents a clear warning that even a subliminal contraction had eventually occurred.

2.4. Data analysis

Individual peak-to-peak MEPs size was calculated offline and averaged for each subject and for each condition. By taking into account the relative corticospinal variability due to testing in different days, stimulation intensity at rest was adjusted to produce a MEP of 600–800 μ V for each session in order to get a stable baseline along the entire experiment (Feurra et al., 2011). Such TMS intensity corresponded to about 110–115% of the individual motor threshold. Then, MEPs size of each session were calculated and analyzed as the percentage change of the mean peak-to-peak amplitude of the basal MEP measured at rest (Rossini et al., 1999).

In order to test the hypothesis of a training effect induced by repeated sessions of motor imagery and action observation, and possible differences of corticospinal facilitation between these two tasks throughout the three session, a three-way repeated measure ANOVA on MEPs percentage change, with two-levels factor Hemisphere (right and left M1), two-levels factor Condition (motor imagery and action observation) and the three-levels factor Experimental Session (1, 2 and 3) was performed. Huynh-Feldt correction was applied to compensate for the violation of the assumption of sphericity. In the presence of significant interactions, corrected pairwise comparisons (Bonferroni test) were performed. The level of significance was $p = 0.05$.

3. Results

The three-way ANOVA showed a significant main effect for Condition ($F_{1,10}=29.47$, $MSE=718502.1037$, $p=0.000$) which highlights that motor imagery significantly enhanced the MEPs size with respect to action observation. A two-way interaction Hemisphere \times Experimental Session ($F_{2,20}=4.142$, $MSE=95339,9090$, $p=0.031$) was observed. Post-hoc comparisons showed a near to be significant effect ($p=0.052$) with a generalized increase of the MEPs size during the third session with respect to the first one for the non dominant hemisphere. Finally, a three way interaction ($F_{2,20}=3.582$, $MSE=27305,4057$, $p=0.047$, observed power=0.620) was observed. Figure 1 summarizes changes in MEPs size across the different experimental conditions. Post-hoc comparisons are described in details in the following sub-paragraphs.

3.1. Motor imagery versus action observation

Post-hoc comparisons showed that motor imagery significantly increased the MEPs size with respect to action observation when TMS was applied on both hemispheres (Fig. 1): this occurred on session 1 ($p=0.024$), session 2 ($p=0.000$) and session 3 ($p=0.030$) for the left hemisphere, and on session 1 ($p=0.045$), session 2 ($p=0.002$) and session 3

($p=0.006$) for the right hemisphere. This demonstrates that corticospinal facilitation induced by motor imagery was constantly higher than that induced by action observation, regardless of eventual training effects due to the repetition of the tasks.

3.2. Training effect induced by motor imagery and action observation

The most interesting finding was the significant enhancement ($p=0.006$) of MEPs size during the third session versus the first one, exclusively for the motor imagery task. Such an effect was observed only when TMS was delivered over the right, non-dominant, M1. No significant effects emerged by comparing session 3 with session 2 ($p=0.159$). No training effects due to motor imagery emerged when TMS was delivered on the dominant hemisphere (Fig. 1).

Action observation tasks did not exert a significant training effect on the corticospinal output on both hemispheres.

3.3. Laterality of motor imagery and action observation

No significant effects by comparing left and right M1 emerged along the three sessions of motor imagery and action observation.

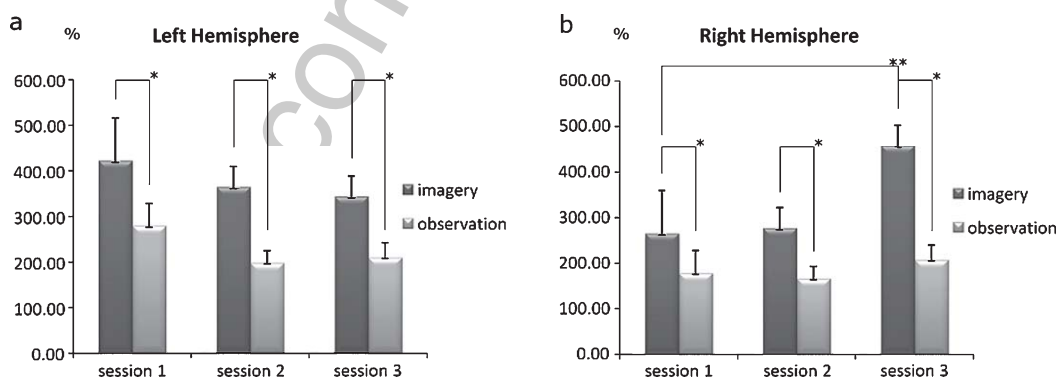


Fig. 1. Percentage changes versus basal (always expressed as 100%) of mean amplitude values (\pm SE) of MEPs recorded in the contralateral FDI muscle after TMS of the dominant and non-dominant hemisphere, across the three different sessions, during motor imagery and actions observation. Note that the corticospinal output is always increased versus the basal condition (rest): from 150% to 250% during the observation of actions, and from 210% to 400% during motor imagery. Motor imagery significantly increased the MEPs size with respect to action observation both for the left (panel a) and for the right (panel b) hemisphere. The significant increase of MEPs' size at the third session during motor imagery in the right hemisphere (panel b) suggests that a training effect occurred. A similar, but not significant, trend was observed in the third session of observation, again in the right hemisphere.

4. Discussion

Corticospinal facilitatory effects during motor imagery and action observation tasks, in terms of increased MEPs' size in the muscles acting as prime mover in the imagined or observed actions, is a solid neurophysiological result (Urgesi et al., 2006; Rossini et al., 1999; Rossi et al., 1998; Maeda et al., 2002; Gangitano et al., 2001; Fadiga et al., 1995; Brighina et al., 2000; Aziz-Zadeh et al., 2002). This is not surprising, since these two processes recruit a consistent and partly shared network of cortical areas, including ventral premotor cortex (vPMC), supplementary motor area (SMA), inferior and superior parietal lobe and, finally, the primary motor cortex as the common final pathway (Munzert, Lorey and Zentgraf, 2009; Fadiga, Craighero and Olivier, 2005; Rizzolatti and Craighero, 2004).

4.1. Motor imagery versus actions observation

There are only a few neurophysiological studies directly comparing effects of motor imagery and action observation in the same group of subjects. In most of them, no differences between these processes, in terms of corticospinal output changes, were found: imagery and observation led to comparable corticospinal facilitation towards hand muscles (Clark, Tremblay and Ste-Marie, 2004; Leonard and Tremblay, 2007; Patuzzo et al., 2003) and synergistic ones (Marconi, Pecchioli, Koch and Caltagirone, 2007), unless subjects were engaged in observation tasks of different complexity. In these cases, the corticospinal excitability is higher during active observation (i.e., observation for imitation) or observation of goal-directed actions (Cattaneo et al., 2009) with respect to passive observation (i.e., observation without instructions, as in the current study) and imagery (Roosink and Zijdwind, 2010). However, in all these studies, only the left dominant hemisphere had been investigated.

Here, we found that the corticospinal facilitation induced by visual motor imagery was consistently higher if compared to the one induced by passive action observation (Fig. 1). As the main ANOVA showed, this occurred in all the three recording sessions and regardless of the stimulated hemisphere was dominant or not. Such a discrepancy with the study of Roosink and Zijdwind (2010), which showed a more consistent corticospinal facilitation during active action observation compared to kinesthetic and visual

imagery, may rely on a combination of biophysical and task-related factors: the former concerns the use of a focal rather than an unselective circular coil; the latter concerns the fact that we adopted a passive observation task (i.e., without instructions) which, at least for the left hemisphere, commonly induces a lower corticospinal facilitation with respect to the active observation one (Roosink and Zijdwind, 2010). The use of a focal coil and a near-threshold intensity of TMS might have definitely been more efficient for the activation of the neural pools recruited by the experimental tasks, avoiding the simultaneous activation of additional (possibly inhibitory) cortical interneurons, as usually happens with non-focal round coils (Rossi, 2009).

Finally, we adopted a fully ecological setting requiring a self-triggered imaging and a simple passive action observation task, without goal-directed actions or simulation of actions on a computer screen (Leonard and Tremblay, 2007). Therefore, our data suggest that the adult human motor system, under these experimental circumstances, may be susceptible to neuroplasticity effects for motor imagery rather than for action observation.

4.2. Laterality of motor imagery and action observation

When tested by single-pulse TMS, the left and right motor cortices of normal right-handed adults "at rest", usually do not show significant asymmetries in terms of threshold of activation (or MEPs' size) measured from hand muscles (Rossini, Desiato and Caramia, 1992; Wassermann, McShane, Hallett and Cohen, 1992; Cicinelli, Traversa, Bassi, Scivoletto and Rossini, 1997; Civardi, Cavalli, Naldi, Varrasi and Cantello, 2000; Semmler and Nordstrom, 1998; Quartarone et al., 2005; Battaglia et al., 2006; Rossi et al., 2009), with few exceptions (Triggs, Calvanio, Macdonell, Cros and Chiappa, 1994; Matsunaga, Uozumi, Tsuji and Murai, 1998). A certain degree of left/right asymmetry can be observed in intracortical inhibitory and excitatory circuitry, when tested with paired-pulse TMS (Civardi et al., 2000; Rossi et al., 2009).

Only a few studies addressed the asymmetry of corticospinal output between the dominant and the non-dominant hemisphere during motor imagery. Results are not unanimous: while most of the investigations did not find any differences between the two

375 hemispheres (Battaglia et al., 2006; Facchini, Muell-
376 bacher, Battaglia, Boroojerdi and Hallett, 2002; Filippi
377 et al., 2001; Quartarone et al., 2005), only one study
378 suggested that an asymmetry effect is due to the lack
379 of facilitation in the non-dominant hemisphere (Stinear
380 2006). Finally, the corticospinal excitability of the left,
381 dominant hemisphere, increased when subjects were
382 engaged in imagery of ipsilateral and contralateral
383 hand movements (Fadiga et al., 1999; Stinear, Flem-
384 ing and Byblow, 2006), while the right hemisphere
385 was susceptible to a corticospinal excitability enhance-
386 ment, only during imagery of contralateral movements
387 (Fadiga, 1999).

388 The lack of MEPs changes in the non-dominant
389 hemisphere for action observation and imagery could
390 be interpreted with the notion that the right hemi-
391 sphere seems to be engaged only in a later stage of
392 action recognition therefore, when there is an under-
393 standing of the required intention (Ortigue, Sinigaglia,
394 Rizzolatti and Grafton, 2010). The current experi-
395 mental setting did not require the recognition of a
396 goal-directed action.

397 4.3. Training of motor imagery and action 398 observation

399 To the best of our knowledge, no previous stud-
400 ies longitudinally compared the neurophysiological
401 effects of repeated sessions of motor-imagery and
402 action observation in the same subjects. This is a
403 crucial point, in view of the emerging possibility to
404 exploit these procedures as add-on strategies to con-
405 ventional rehabilitation plans. The facilitation of the
406 corticospinal output is a logical pre-requisite to make
407 an approach potentially useful for neuro-rehabilitative
408 purposes. Previous studies compared already the effect
409 of motor imagery and observation on learning (Mul-
410 der, 2007; Holmes and Calmels, 2008) or on strength
411 increase (Yue and Cole, 1992; Smith, 2003; Zijdwind,
412 2003), but without looking at concurrent corticospinal
413 changes directly.

414 Our results show that motor imagery induces an
415 increase of MEPs amplitude throughout sessions com-
416 patible with a sort of training effect. This effect was
417 observed only in the non-dominant hemisphere, prob-
418 ably because we used a simple motor imagery task.
419 Indeed, it has been already demonstrated that increas-
420 ing the complexity of the imagery task may trigger
421 training processes even in the dominant hemisphere,
422 as happened in subjects performing repeated daily

423 sessions of imagined finger movements, which led to
424 the same plastic changes induced by the actual execu-
425 tion (Pascual-Leone et al., 1995).

426 On the other hand, action observation, which
427 induced corticospinal facilitation only in the left hemi-
428 sphere, did not change tonically the corticospinal
429 output in either hemispheres as training progresses.
430 This finding was somehow unexpected, since some
431 evidence indicates that action observation may form
432 an elementary motor memory in M1 (Stefan et al.,
433 2005) by improving the learning of a simple motor
434 practice in healthy humans (Stefan et al., 2008). We
435 speculate that the absence of “training effects” after
436 observation tasks, besides the absence of complexity of
437 the observed actions, might depend on the more auto-
438 matic and innate nature of these processes mediated by
439 the mirror neurons system (Rizzolatti and Craighero,
440 2004) which mainly act to dynamically couple action
441 observation and action execution (Newman-Norlund,
442 van Schie, van Zuijlen and Bekkering, 2007). How-
443 ever, it is still possible, and matter to be verified,
444 that by adopting more complex tasks of observation,
445 as well as different demands for examined subjects
446 (i.e., observation to imitate rather than simple passive
447 observation) could favour a progressive training effect
448 of corticospinal output. For example, Catmur (2007)
449 showed that an incompatible sensorimotor training
450 between observed and executed actions can reverse
451 the perceptual-motor matching properties of the mir-
452 ror system. Positive effects of training on corticospinal
453 output during motor imagery but not during action
454 observation well parallel the notion that sport athletes
455 may use imagery strategies to improve their actual
456 motor skills, whereas they would use observational
457 learning for practice only (Hall et al., 2009).

458 Some limitations of this study need to be consid-
459 ered: the subjects sample should have been larger with
460 respect to the number of measured variables. Indeed,
461 despite the task was relatively short lasting, it was dif-
462 ficult to recruit subjects (all volunteers) available for a
463 three sessions study run in different days. So we tried
464 to suit subjects needs and to guarantee regular intervals
465 between sessions. Moreover, in order to better quantify
466 and classify the increase of the MEPs size as a “training
467 effect” we should have used a subjective rating scale
468 as the Vividness of Movement Imagery Questionnaire-
469 2 (VMIQ-2) (Williams, Pearce, Lopoporto, Morris and
470 Holmes, 2012). The absence of any significant effects
471 on the non dominant hemisphere between session 1
472 and 2 during the motor imagery task, may be due to

the small number of sessions (only three). It could not been excluded that by testing more sessions spaced by different time periods (i.e., days, months) (Page, Levine, Sisto and Johnston, 2001), as in memory studies (Klingberg et al., 2005), we could have obtained a clearer time-line of the “training effect” postulated here.

5. Conclusions

In summary, this is the first report in which motor imagery and action observation effects on the human motor system have been compared in a longitudinal manner. Findings suggest that motor imagery is sustained by a cortical network susceptible to a training effect only in the non-dominant hemisphere. The corticospinal facilitation induced by motor imagery on the left hemisphere, which is generally higher than that induced by action observation, seems to be not susceptible of any further modulation, at least with this easy task commonly performed in the everyday life activities.

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