Temporal coupling due to illusory movements in bimanual actions: evidence from anosognosia for hemiplegia

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Research report

Temporal coupling due to illusory movements in bimanual actions: Evidence from anosognosia for hemiplegia

Lorenzo Pia , Lucia Spinazzola , Marco Rabuffetti , Maurizio Ferrarin , Francesca Garbarini , Alessandro Piedimonte , Jon Driver and Anna Berti

A B S T R A C T

In anosognosia for hemiplegia, patients may claim having performed willed actions with the paralyzed limb despite unambiguous evidence to the contrary. Does this false belief of having moved reflect the functioning of the same mechanisms that govern normal motor performance? Here, we examined whether anosognosics show the same temporal constraints known to exist during bimanual movements in healthy subjects. In these paradigms, when participants simultaneously reach for two targets of different difficulties, the motor programs of one hand affect the execution of the other. In detail, the movement time of the hand going to an easy target (i.e., near and large), while the other is going to a difficult target (i.e., far and small), is slowed with respect to unimanual movements (temporal coupling effect). One right-brain-damaged patient with left hemiplegia and anosognosia, six right-brain-damaged patients with left hemiplegia without anosognosia, and twenty healthy subjects were administered such a bimanual task. We recorded the movement times for easy and difficult targets, both in unimanual (one target) and bimanual (two targets) conditions. We found that, as healthy subjects, the anosognosic patient showed coupling effect. In bimanual asymmetric conditions (when one hand went to the easy target and the other went to the difficult target), the movement time of the non-paralyzed hand going to the easy target was slowed by the 'pretended' movement of the paralyzed hand going to the difficult target. This effect was not present in patients without anosognosia. We concluded that in anosognosic patients, the illusory movements of the paralyzed hand impose to the non-paralyzed hand the same motor constraints that emerge during the actual movements. Our data also support the view that coupling relies on central operations (i.e., activation of intention/programming system), rather than on online information from the periphery.

1. Introduction

Being aware of intending, controlling, and owning voluntary actions is at the root of humans' notion of self-awareness. Studying the abnormalities of the integration among the different aspects of motor behavior due to brain damages has a crucial role in addressing questions regarding the structure and functional signature of motor consciousness (Berti and Pia, 2006). Indeed, patients' counterintuitive behavior can unmask the inadequacies of theories on human brain functioning hidden from the view in the intact brain (see Churchland, 1986, for a discussion on this point). To this respect, one of the most informative neurological disorders is anosognosia for hemiplegia (hereinafter AHP), a condition in which movement cognition is dramatically distorted (see Bottini et al., 2010; Orfei et al., 2007; Pia et al., 2004 for reviews). AHP patients, affected by a complete paresis of the side of the body opposite to the brain damage (often the left side but see also Cocchini et al., 2009) deny that there is anything wrong with their contralesional limbs. The disturbance may range from emotional indifference (i.e., patients simply minimize the severity of the paralysis) to explicit denial. In this latter case, patients claim of being able to perform any kind of action with the paralyzed limb. If asked to perform a purposeful movement with the motionless limb, they may be convinced of having accomplished the action despite unambiguous evidence to the contrary coming from different sensory channels. However, it is noteworthy that explicit and implicit awareness for motor deficits can be dissociated. In other words, patients may explicitly deny a deficit despite having some insight into it, as they correctly approach bimanual tasks according to their motor impairment (Cocchini et al., 2010). Delusional beliefs concerning the affected side of the body, such as somatoparaphrenia (i.e., the ownership of the limb is ascribed to another person as, for instance, the doctor or a relative), misoplegia (e.g., hatred toward the affected limbs), or limb personifications (e.g., the plegic limb is considered as an entity with an own identity) are usually considered as additional, thought independent, abnormal manifestations (see Bottini et al., 2010 for a discussion on this point).

The interpretation of AHP is not straightforward. Theories that explain AHP either as a psychological defense against the illness (e.g., Weinstein and Kahn, 1955), a secondary consequence of sensory feedback deficits (e.g., Cutting, 1978), or a combination of sensory deficits and higher-order cognitive impairments (e.g., Levine et al., 1991) are not thought to be exhaustive explanations. Indeed, double dissociations have been shown between AHP and each of the aforementioned impairments (Adair et al., 1995; Berti et al., 2005; Bisiach et al., 1986; Coslett, 2005; Heilman et al., 1998; Marcel, 2004; Starkstein et al., 1992). Recently, it has been proposed that AHP might be explained as a domain specific disorder of motor control (Berti and Pia, 2006; Berti et al., 2007; Gold et al., 1994; Jenkinson and Fotopoulou, 2010; Spinazzola et al., 2008). In line with several findings on intact brain showing that the conscious awareness of action and movement control shares several cortical areas (e.g., Desmurget and Sirigu, 2009), it has been demonstrated that AHP follows a brain damage located within the same cortical network that is responsible for motor monitoring in the lateral premotor and insular cortex (Berti et al., 2005; Fotopoulou et al., 2010; Garbarini et al., 2012; Karnath et al., 2005; Moro et al., 2011; Vocat et al., 2010). Consequently, the well-established framework of a forward model of normal motor control (Blakemore and Frith, 2003; Wolpert et al., 1995) has been employed to predict the pattern of intact and impaired neurocognitive mechanisms pinpointing the distorted motor awareness of AHP patients. The model posits that when a subject has the intention to move and the appropriate motor commands are selected and sent to the appropriate motor areas, a prediction (forward model) of the sensory consequences of the movement itself is formed on the efference copy of the programmed motor act. This would be subsequently matched (by a comparator system) to the actual sensory feedback (see also Gold et al., 1994), and constitutes the signal on which motor awareness is constructed. This model has two important implications. First, motor awareness would, counter-intuitively, precede movement execution, instead of following it. This entails that whenever a sensory prediction is formed, motor awareness emerges before the availability of any sensory feedback. Second, motor awareness is evaluated against the sensory feedback by the operation of the comparator system that, among other functions, can differentiate between movement/no-movement conditions. Within this framework, it has been proposed that, in AHP patients, a damage to the comparator processes would alter the monitoring of voluntary actions, thus preventing them from distinguishing between movement and no-movement states. Moreover, the (non-veridical) feeling of movement would arise from an intact motor intentionality assisted by the normal activity of the brain structures that implement the intention-programming system (Berti and Pia, 2006; Berti et al., 2007; Garbarini et al., 2012; Spinazzola et al., 2008).

Evidence of preserved movement intentionality in AHP patients comes from the fact that they may show normal proximal muscle electrical activity in the affected side when they believe they are moving the plegic limb (Berti et al., 2007; Hildebrandt and Zieger, 1995). Interestingly, such an intentional stance dominates their subjective experience of willed actions because patients falsely detect the movement of their plegic arm when they intend to move it, versus when they do not (Fotopoulou et al., 2008). To the best of our knowledge, however, only one study has directly analyzed the existence in AHP patients of the same motor programs for the affected limbs that govern normal movement execution. Garbarini et al. (2012), capitalized on evidence showing that the spatial constraints known to exist in healthy subjects during a classical bimanual movement paradigm (i.e., when people have to draw circles with one hand while drawing lines with the other tend to produce curved lines and line-like circles) arise also in amputee patients with vivid subjective experience of moving their 'phantom' limb (Franz and Ramachandran, 1998). Indeed, Franz and Ramachandran (1998) found that when amputees with vivid sensation of phantom limb movement have to draw linear segments in a continuous fashion with the intact arm while performing either lines or circles with the phantom arm produced spatial coupling. As clearly pointed out by the authors, those results suggest, for the first time, that spatial coupling strongly relies on internal motor program rather than on the online feedback coming from movement execution. Starting from this findings, Garbarini and coworkers reasoned that the circles–lines drawing task would have been the ideal paradigm to examine whether, despite the paralysis, the motor program of the affected hand is normally available in AHP patients. The results showed that when AHP patients are requested to simultaneously and continuously draw lines with the right (intact) hand and circles with the left (affected) hand the lines assume an oval shape. This effect, comparable to that of healthy subjects, indicated that voluntary actions performed by the moving hand can be spatially constrained by the intended (but not executed) movements of the paralyzed hand.

It is also noteworthy that other constraints in the production of bimanual movements can be observed on purely temporal measures. For instance, whereas in unimanual reaching movements exists a reliable temporal relationship between distance and time, when movements are combined in a bimanual task with different target distances, the two hands initiated and (approximately) terminated in a more coupled fashion (Kelso et al., 1979). Interestingly, temporal coupling is dissociable from spatial coupling on both functional and anatomical grounds (e.g., Franz et al., 1996; Heuer, 1993). Therefore, if AHP patients' motor behavior is driven by the same motor computations that govern normal movement execution, the temporal aspects of motor preparation of the paralyzed hand should be also preserved. One of the most employed paradigm to study temporal coupling has been proposed by Kelso et al. (1979). The authors developed a bimanual version of the classical Fitt's task, which originally showed that in unimanual movements the time required for reaching a target is a function of the task difficulty, that is distance and target width (Fitt's law, Fitts, 1954). Accordingly, these authors found that when people have to reach for an easy target (i.e., near-large), the movement times (hereinafter MTs) are shorter than when they have to reach for difficult (i.e., far-small) targets, both in unimanual (one hand at a time reaches for the target), and in bimanual symmetric conditions (both hands go either to the easy or to the difficult targets). However, Kelso and coworkers found a violation of Fitt's law in the bimanual asymmetric condition (one hand goes to the easy target and the other goes to the difficult target). Here, the movements of the two hands were coupled so that they were initiated and terminated synchronously, mainly because the hand moving to the easy target slowed. In other words, the temporal aspect of the motor programming/execution of one hand was affected by the simultaneous motor programming/execution of the other hand (temporal coupling effect).

We capitalized on this evidence to test whether in AHP patients the illusory movements of the plegic arm impose on the healthy arm the same temporal constraints that are observed in healthy subjects during the actual movements in the asymmetric condition. If so, any effects on the motor parameters of the healthy hand would be the consequence of normally activated motor representations of the plegic hand. Kelso's paradigm (Kelso et al., 1979) was administered to right-brain-damaged patients with complete left upper limb hemiplegia (with and without anosognosia) and to healthy subjects. We predicted that when AHP patients are asked to move one hand to the easy target and the other to the difficult target (i.e., bimanual asymmetric condition), the non-paralyzed arm going to the easy target would show a normal interference effect (slowing down of the MT) from the paralyzed arm requested to go to the difficult target. In hemiplegic patients without anosognosia (hereinafter HP), we predicted that, being these patients perfectly aware of their deficit, they should not attempt any movement with the plegic hand. Therefore, no temporal coupling effect should be observed (Garbarini et al., 2012).

2. Materials and methods

2.1. Participants

One AHP patient, five HP patients (HP group), and twenty healthy subjects (hereinafter C group) were included in the study after having given written informed consent. The research was approved by the local ethic committee. Both age and education did not differ (two tailed *t*-test $p < .05$) among the participants (C group: mean age = 54.3, standard deviation − SD = 14.59; mean educational level = 8.25, SD = 3.16. HP group: mean age = 66, SD = 12; mean educational level = 8, SD = 4. AHP: age = 41, educational level = 8). The AHP patient comparisons were performed with a modified *t*-test for individual scores versus a control sample (Crawford and Howell, 1998; Cavallo et al., 2011). The patients had a complete left upper limb plegia (if the affected limb has some degrees of weakness but can still move, the claim of still being able to move cannot be considered absolutely wrong and the anosognosia score is not completely reliable; see Berti et al., 2005; Berti and Pia, 2006). The patients were also tested with the Mini Mental State Examination (MMSE) (Measso et al., 1993) to evaluate the possible presence of severe general cognitive impairment. Contralesional somatosensory, motor, visual field defects as well as AHP and neglect were assessed according to Spinazzola et al. (2008). The awareness of movements was also tested during the experimental task, at the end of each trial: participants were required to report whether or not the requested movements had been performed. Demographic and clinical data are reported in Table 1. Patients' lesion reconstructions are reported in Fig. 1.

2.2. Stimuli and apparatus

The apparatus consisted of a rectangular board equipped with two sets of three keys each; a home key, near-large key (easy target), and far-small key (difficult target) longitudinally displaced with respect to the subjects' body and within reaching distance (40, 70, and 180 mm from the edge, respectively). One set of key was on the left side of the board, whereas the other was on the right (see Fig. 2 for a picture of the board and for quotes and technical details).

2.3. Procedures

Participants were seated at a table on which the board was centered on the body midline. At the beginning of each trial,

Table 1 – Demographic and clinical data of patients.

Case number	Group	Sex	Age	Schooling (y)	Duration (d)	Etiology	Lesion site	Visual field defect	HP	AHP	Hemianesthesia		MMSE	Neglect		
											Tactile	Proprioceptive		Extrapersonal		Personal
														Star cancellation	Sentence reading	
1	AHP^{pre}	M	41	8	71	I	ITG, MTG, STG, Tpwm, AG, SG, PCG, Ppwm, PSTG, IFG, MFG, ic, pt	3–3	3–3	3–3	2–2	2–2	23.62	17	9/9	1
2	AHP^{post}	M	41	8	323	I	n.a.	3–3	3–3	0–0	n.a.	n.a.	n.a.	1	0/9	0
3	HP	M	65	8	62	I	STG, Tpwm, SG, AG, Ppwm, PCG, Ppwm, PSTG, ic, pt, cn	3–3	3–3	0–0	2–2	2–2	30	8	0/9	1
4	HP	M	67	8	137	I	ITG, MTG, STG, Tpwm, ins, pt, ic, Ppwm	1–1	3–2	0–0	1–0	0–0	26	1	0/9	0
5	HP	F	70	8	60	H	cn, th, ic, Tpwm	0–0	3–3	0–0	2–2	2–1	30	0	1/9	1
6	HP	M	82	3	75	I	STG, SG, ins, PSTG, ic, ec	0–0	3–3	0–0	0–0	0–0	25.5	4	0/9	0
7	HP	M	48	13	101	I	IFG, ins, ic, ec, pt	0–0	3–3	0–0	0–0	0–0	30	0	0/9	0

Case number: patient's code (^{pre} = pre-session; ^{post} = post-session). Group: presence (AHP) or absence (HP) of anosognosia for hemiplegia. Sex: M = Male, F = Female. Schooling: years (y) of formal education. Duration of the disease: number of days (d) between the onset of the disease and the first assessment. Etiology: H = hemorrhage, I = ischemia. Lesion site: ITG = inferior temporal gyrus, MTG = middle temporal gyrus, STG = superior temporal gyrus, Tpwm = temporal periventricular white matter; SG = supramarginal gyrus, AG = angular gyrus, Ppwm = parietal periventricular white matter, ins = insula, PCG = precentral gyrus, PSTS = postcentral gyrus, pt = putamen, cn = caudate nucleus, ic = internal capsule, ec = external capsule, th = thalamus, Fpwm = frontal periventricular white matter. Visual field defect: visual half-field neurological deficits (the two values refer to the upper and lower quadrants, respectively); scores ranged from normal (0) to severe defects (3). HP: motor neurological deficits for the contralesional arms (the two values refer to the upper and lower limbs respectively); scores ranged from normal (0) to severe defects (3). Hemianesthesia: tactile and proprioceptive neurological deficits for the contralesional arms (the two values refer to the upper and lower limbs, respectively); scores ranged from normal (0) to severe defects (2). . AHP: unawareness of the motor neurological deficits (the two values refer to the upper and lower limb respectively); scores ranged from normal (0) to severe defects (2). Neglect (extrapersonal): left minus right-sided omissions in the star cancellation task and number of wrong reported sentences in the sentence-reading task. Neglect (personal): scores ranged from normal (0) to severe defects (3).

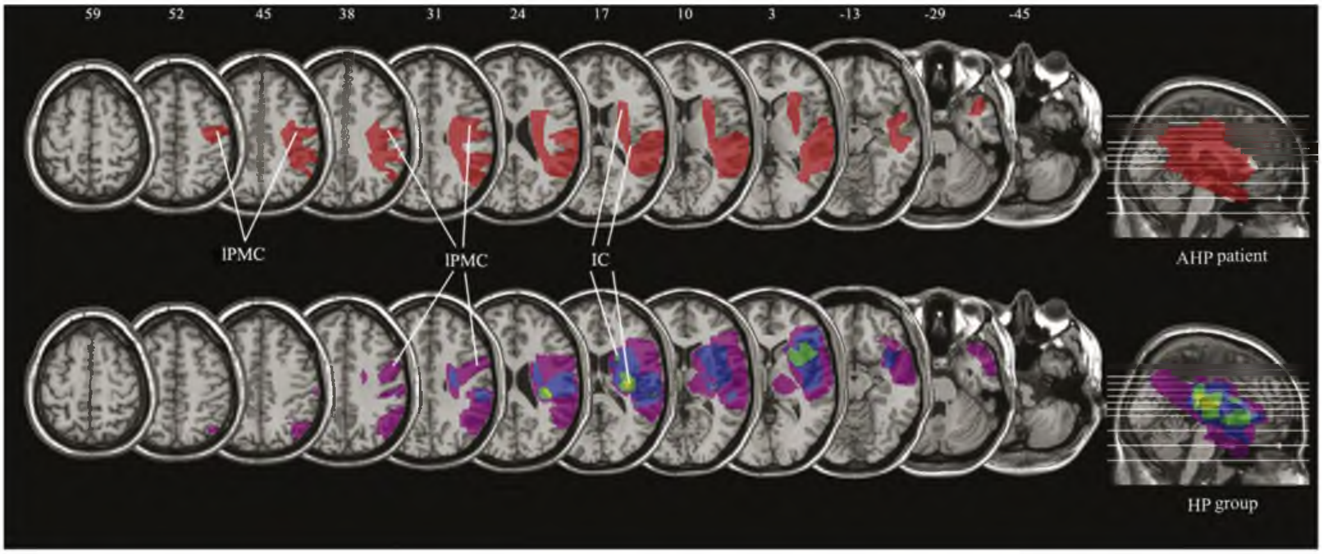

Fig. 1 – Lesion plot of the AHP patient and overlay lesion plot of the HP group. Lesions were mapped in the stereotaxic space of Talairach and Tournoux (Talairach and Tournoux, 1988) using a standard MRI volume that conformed to that space as redefined by the Montreal Neurological Institute. Image manipulations were performed with MRIcro software (Rorden and Brett, 2000). The number of overlapping lesions is illustrated by different colors coding increasing the frequencies from violet ($n = 1$) to red ($n = 5$). Talairach *z*-coordinates of each transverse section are given.

their index finger(s) were placed on the home key(s). Then, they were asked to move their index finger(s) from the home key(s) to specific target key(s) as fast and as accurately as possible after a start tone. In unimanual conditions, participants had to reach for one target (either on the left or on the right side of the board), whereas in bimanual conditions they had to reach for two targets (one on the left side and one on the right side of the board). C group performed four unimanual conditions (left index finger to left easy target, LE; left index finger to left difficult target, LD; right index finger to right easy target, RE; right index finger to right difficult target, RD), and four bimanual conditions (either symmetric, when both fingers went to the same target, that is LE–RE, LD–RD, or asymmetric when one finger went to the easy and the other went to the difficult target, namely LD–RE, LE–RD). The AHP patient and HP group performed two unimanual conditions (RE and RD) and four bimanual conditions (LE–RE, LD–RE, LE–RD, LD–RD). Each condition was composed of 10 trials. After each trial, participants were asked whether they had performed the requested movement (the yes/no answer was recorded in an experiment log). The AHP patent was administered the experiment twice: in a pre-session (hereinafter AHP^{pre}), namely when the clinical assessment revealed anosognosia for hemiplegia, and in a post-session (hereinafter AHP^{post}), that is when the assessment did not revealed it anymore.

Reaction time (calculated as the time from the start tone onset to the finger leaving from the starting position, hereinafter RT) and the MT (from the fingertip take off to the contact with the chosen stimulus) were measured and recorded. Trials with RTs shorter than 150 ms were excluded as anticipations (0%). RTs and MTs more than two SDs from each participant's condition means were discarded as outliers (7%). The remaining data were analyzed by means of separate repeated measures ANOVAs with RT or MT as dependent variables.

3. Results

While both the C and HP groups, and the AHP^{post} patient were 100% correct in judging whether they achieved a given movement, the AHP^{pre} patient always misjudged his performance in the self-evaluation test: in bimanual conditions, he always claimed having performed the bimanual action. This result suggests that the patient experienced a vivid subjective sensation of the movements that he did not actually perform.

3.1. *RTs*

In the C group, a repeated measures ANOVA with 'movement' (unimanual/bimanual asymmetric/bimanual symmetric), 'difficulty level' (easy/difficult), and 'hand' (left/right) was performed. Neither the main factors nor the interactions were significant ($p > .05$).

In the HP group, a repeated measures ANOVA with the 'movement' (unimanual/bimanual asymmetric/bimanual symmetric) and 'difficulty level' (easy/difficult) was performed. Neither the main factors nor the interactions were significant ($p > .05$). Single case analysis in each HP patient replicated the group results ($p > .05$).

In the AHP patient, a repeated measures ANOVA with the 'movement' (unimanual/bimanual asymmetric/bimanual symmetric), 'difficulty level' (easy/difficult), and 'session' (pre/post) was performed. Neither the main factors nor the interactions were significant ($p > .05$).

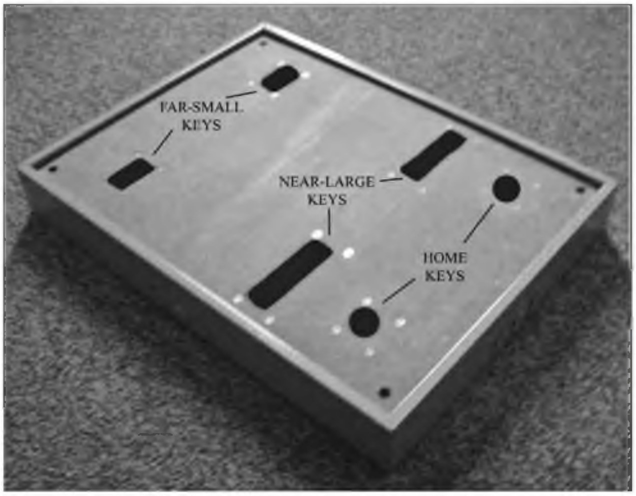

Fig. 2 – A picture of the board. Home keys were circular (ø = 20 mm), whereas the target keys were rectangular (near-large = 70 × 20 mm, far-small = 36 × 20). Each key was crafted by fixing a rectangular plastic shape of the same size to a couple of hinge lever micro switch (OMRON, Japan) that can be operated by a force of .6 N. The six keys/switch were low-voltage wired in order to switch the output of each key from 0 V (OFF status) to 1.5 V (ON). These six channels, associated to the six keys, were input in an A/D conversion board (Pico Technology, UK), sampled at 2000 Hz, and the digital input transferred, via USB port, to a self developed software (Microsoft Visual Basic, USA). This software detects the ON/OFF status for all channels, computes, and stores the occurred actions and the related time delays.

These data show that the different conditions of the experiment did not affect movement initiation. In particular, for the bimanual movement of healthy subjects these results indicate that right and left hand movements were initiated simultaneously.

3.2. MTs

In the C group, a repeated measures ANOVA with the 'movement' (unimanual/bimanual asymmetric/bimanual symmetric), 'difficulty level' (easy/difficult), and 'hand' (left/right) was performed. There was a significant effect of the 'movement' [F (2, 34) = 57.65, $p < .00001$], 'difficulty level' [F (1, 17) = 317.49, $p < .00001$], and 'movement' × 'difficulty level' interaction [F (2, 34) = 55.33, $p < .00001$]. MTs were shorter (Duncan's two tailed t-test $p < .0005$) in unimanual (mean = 392, standard error – SE = 19) than bimanual symmetric (mean = 463, SE = 27) and in the bimanual asymmetric (mean = 535, SE = 29) conditions. In addition, MTs were shorter in easy (mean = 410, SE = 24) than in difficult (mean = 516, SE = 25) conditions. However, this difference disappeared in the bimanual asymmetric condition (Duncan's two tailed t-test $p = .74$) when one hand went to the easy target (mean = 533, SE = 31) and the other to the difficult one (mean = 537, SE = 29) mainly because the hand moving to the easy target slowed (see Fig. 3). This data in healthy subjects replicated the Kelso and coworkers results (Kelso et al., 1979).

In the HP group, a repeated measures ANOVA with the 'movement' (unimanual/bimanual asymmetric/bimanual symmetric) and 'difficulty level' (easy/difficult) was performed. There was a significant effect of the 'difficulty level' [F (1, 4) = 226.85, $p < .001$] but no 'movement' × difficulty level' interaction. MTs were shorter in easy (mean = 374.31, SE = 28.01) versus difficult (mean = 548.99, SE = 34.07). Single case analysis in each patient replicated the group results (see Fig. 4).

In the AHP patient, a repeated measures ANOVA with the 'movement' (unimanual/bimanual asymmetric/bimanual symmetric), 'difficulty level' (easy/difficult), and 'session' (pre/post) was performed. The patient showed a significant effect of the main factors 'session' [F (1, 13) = 12.52, $p = .004$] and 'difficulty level' [F (1, 13) = 41.41, $p < .0001$], and of the interactions 'movement' × 'session' [F (2, 26) = 8.04, $p = .002$] and 'movement' × 'difficulty level' × 'session'[F (2, 26) = 3.65, $p = .04$]. MTs were shorter in pre (mean = 1043, SE = 25) versus post (mean = 913, SE = 27) sessions and, in the pre-session, in unimanual (mean = 936, SE = 50) than in bimanual symmetric (mean = 1059, SE = 35) and bimanual asymmetric (mean = 1135, SE = 34) conditions. MTs were also shorter in easy (mean = 861, SE = 29) versus difficult (mean = 1096, SE = 22) conditions. However, in the pre-session, the difference disappeared in the bimanual asymmetric condition (Duncan's two tailed t-test $p = .669$) when the right hand went to the easy target (mean = 1160, SE = 63) and the left had to go to the difficult target (mean = 1109, SE = 52) but did not accomplish the task due to the paralysis. Again, this effect was due to the slowing of the right hand (Fig. 5). It is noteworthy that despite the AHP patient in the pre-session being overall slower than the C group, their MTs pattern was not significantly different ($p > .05$). The AHP patient comparisons were performed with a modified t-test for individual scores versus a control sample (Crawford and Howell, 1998; Cavallo et al., 2011).

Summing up, these results show that, in the bimanual asymmetric condition, a coupling effect was found for both the C group, where the subjects actually moved both hands, and for the AHP patient, who could only move their right hand.

4. Discussion

The main aim of this study was to test whether, in those hemiplegic patients who have a false belief of being still able to move, the temporal aspects of motor programming for the affected hand is spared and normally functioning. Hence, we adapted a motor task known to induce temporal coupling (Kelso et al., 1979). We predicted that if AHP patients' illusion of movement is not a mere confabulation but is grounded on normal intention/programming activation, we should find coupling effects also in the AHP patient of our study.

We first replicated the original results obtained by Kelso et al. (1979). In the C group, the MTs of both hands increased as a function of task difficulty in unimanual and bimanual symmetric conditions (i.e., the Fitt's law was met). We also found a violation of Fitt's law in the bimanual asymmetric

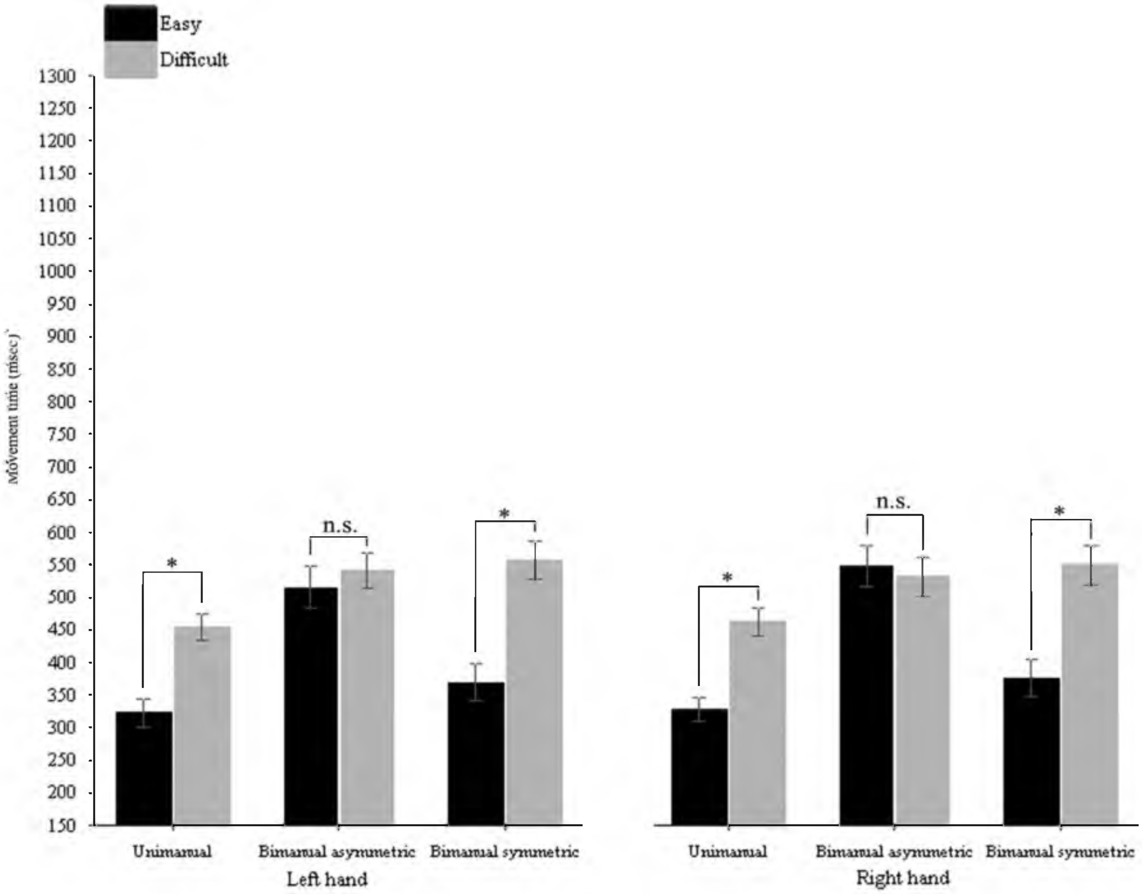

Fig. 3 – Mean MTs and SE (ms) of the C group. * = significant ($p < .05$); n.s. = non significant ($p > .05$).

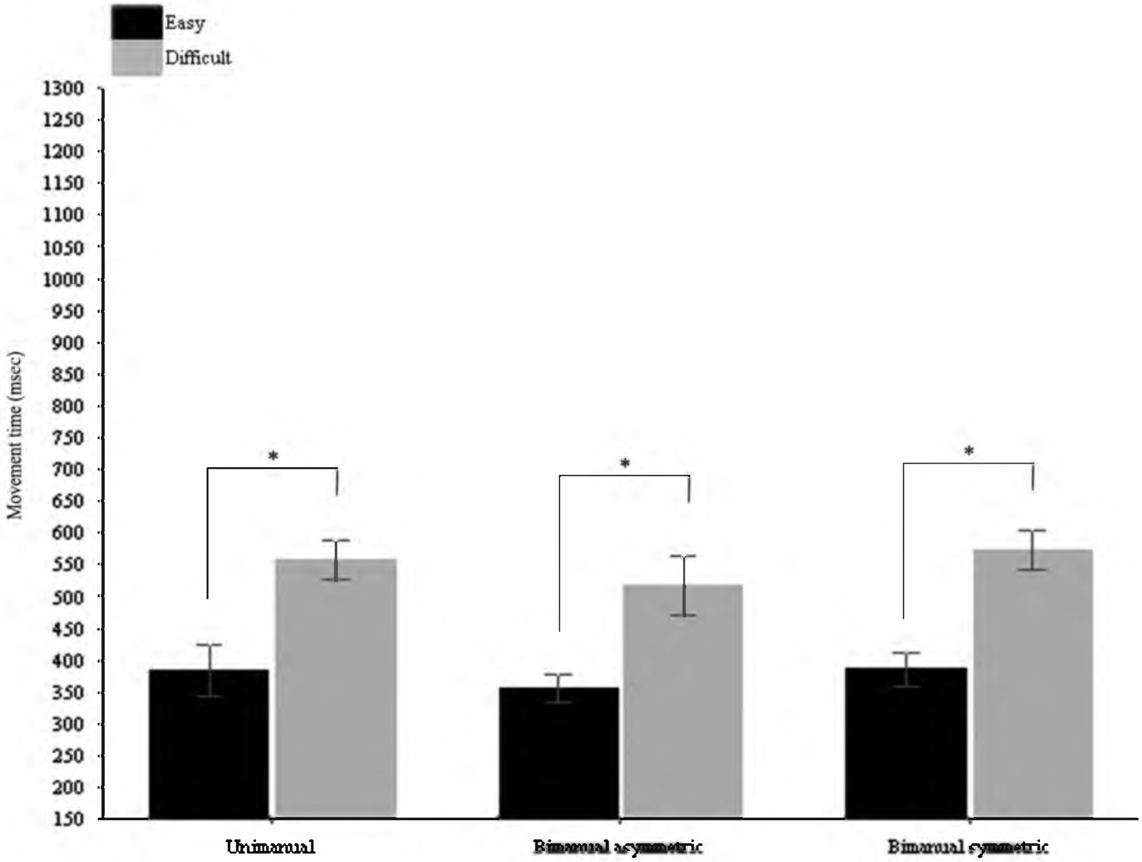

Fig. 4 – Mean MTs and SE (ms) of the HP group. * = significant ($p < .05$).

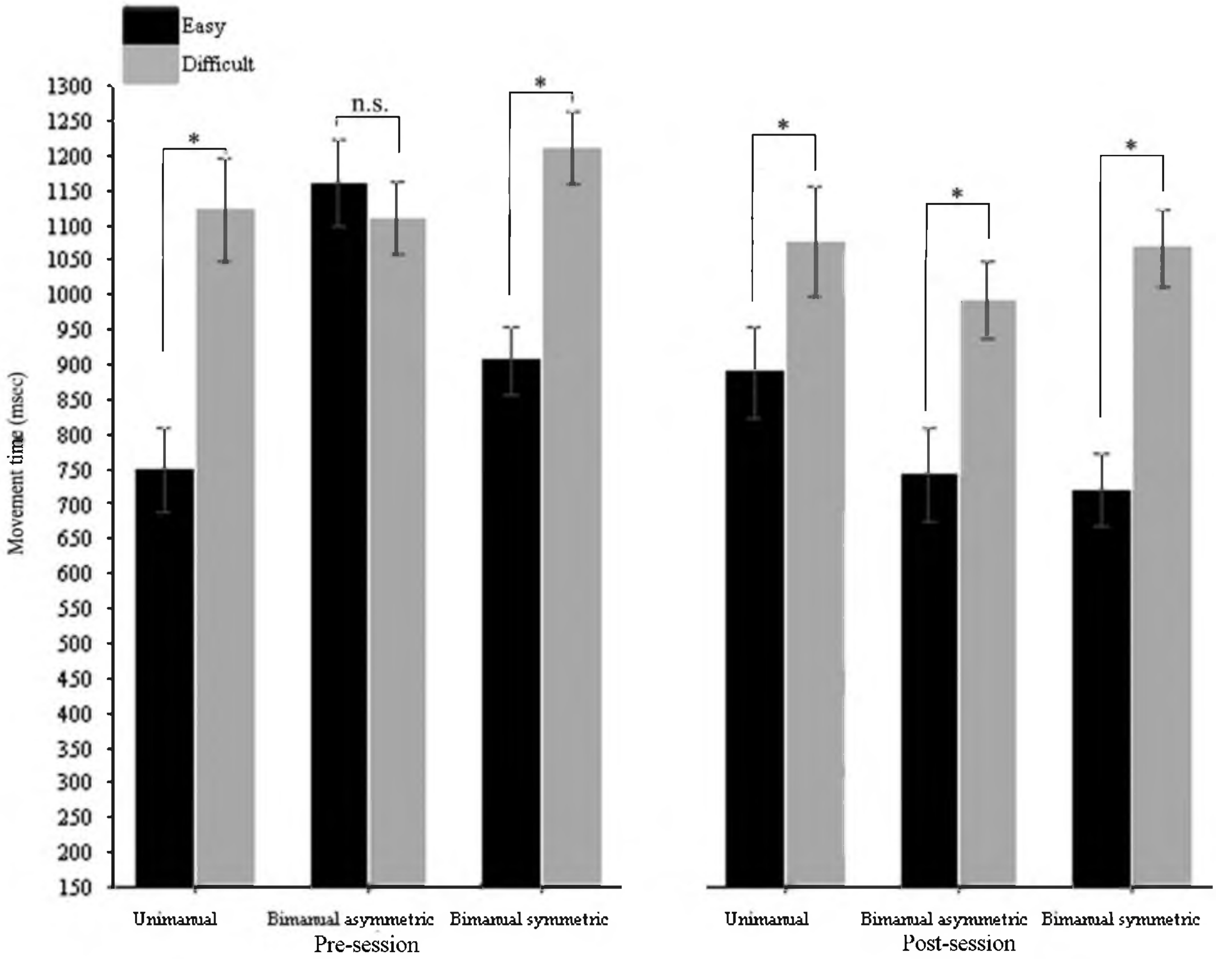

Fig. 5 – Mean MTs and SE (ms) of the AHP patient in the pre and post-session. * = significant ($p < .05$); n.s. = non significant ($p > .05$).

conditions: the movements of the two hands initiated and terminated each trial simultaneously mainly because the hand that had to go to the easy target slowed. These data indicate that the temporal components of the motor programs of one hand affect the motor parameter of the movements executed by the other hand.

Crucially, we found that, in the AHP patient, the temporal patterns in fulfilling requests for both unimanual and bimanual movements were the same as in non-plegic subjects. Indeed, the right hand MTs increased with task difficulty in unimanual and bimanual symmetric conditions, which confirms that in the healthy part of the body Fitt's law was working properly. Moreover, in bimanual asymmetric conditions, the MTs of the two hands started and finished simultaneously. Again, as in healthy subjects, this was due to the slowing of the right hand going to the easy target (Fitt's law violation). It should be remembered that the AHP patient could perform only right hand movements to the easy (near) target location. Therefore, the same hand going to the same target (right easy target) varied its MT according to the intention/programming operation triggered by the task demands. This shows that, in the bimanual asymmetric condition, the AHP patient normally intended/programmed movements of the left plegic hand. Note that extrapersonal neglect did not affect the representation of motor programs. This result is consistent with the data showing that AHP and neglect are two distinct phenomena (Berti et al., 2005).

It is demonstrated here, for the first time, that although motor awareness is dramatically altered in AHP patients, the temporal rules of central motor programming are still working, thereby further supporting the idea that the mechanisms that govern normal motor performance are preserved in these patients. Hence, the delusional belief of moving a paralyzed arm is not a mere verbal confabulation, but, rather, emerges from the activity of motor control areas that impose normal temporal constraints on the non-paralyzed arm. On the contrary, HP patients not only can generate internal representations of voluntary movements but can also register the mismatch between the predicted and actual motor states. This leads to normal motor awareness. Consequently, HP patients, being normally aware of their motor impairment, no longer try to move their plegic limbs (and, therefore, do not show any temporal constraints).

Our interpretation is supported by anatomical data (see Fig. 1). First, all the patients had lesions involving internal capsule (IC), whose damage is correlated to the severity of the motor deficit (Vocat et al., 2010). Cortical areas related to the subjective feelings of conscious intention to move (Desmurget et al., 2009) in medial premotor cortex (i.e., Supplementary Motor Area and pre Supplementary Motor Area) were intact in all patients, confirming that both AHP and HP patients can potentially intend and program movements with the plegic limb. The crucial difference between AHP and HP patients was that the neural structures known to be related to the comparator system lying in the lateral premotor cortex (lPMC) (Berti et al., 2005; Garbarini et al., 2012; Vocat et al., 2010) were massively damaged only in the AHP patient (and partially in only one HP patient). We must emphasize that larger patient samples are required to strengthen these anatomical correlations.

Our findings are also in line with previous data on the nature of coupling effects. Franz and Ramachandran (1998) demonstrated the presence of coupling effects in the absence of actual movements, that is in patients with phantom limb sensation and proposed that coupling effects arise from central signals (e.g., sensory predictions) rather than on actual feedback (see also Drewing et al., 2004; Spencer et al., 2005). A number of subsequent works have confirmed the strict relation between coupling effects and sensory prediction, even in the absence of movements and/or feedback (e.g., patients with peripheral sensory loss; Drewing et al., 2004) or visual feedback (e.g., vision precluded; Spencer et al., 2005). Note that a crucial difference between amputees and AHP patients is that in the latter the brain damage affecting the comparator system prevents to realize that the subjective experience of moving the paralyzed limb is non-veridical; whereas, although some amputees can intentionally manipulate their phantom, all are aware that actual movements do not occur. In any case, the fact that temporal coupling occurs in both actual bimanual movements and when an active limb movement is combined with an illusory limb movement strongly supports the view that internal mechanisms might be sufficient to produce these effects.

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