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Invisible Grasps: Grip Interference in Anosognosia for Hemiplegia

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Objectives: Previous findings suggest that, in anosognosic patients, their illusory motor experience is based on a "normal" motor intention and planning for the paralyzed limbs. However, these studies involved proximal muscles (shoulder) that can be mediated by the ipsilateral (intact) cortex more than distal muscles (fingers). In the present study, we asked whether, in anosognosic patients, the spared motor intention for the paralyzed limb can go as far as to influence kinematic parameters of distal movements. ***Method:*** Six hemiplegic patients (1 with and 5 without anosognosia) were required to reach and grasp with both hands targets of the same or different size, attached to a plinth. Maximum grip aperture of the right (intact) hand was recorded using an infrared motion capture system. All patients were evaluated with a specific battery for anosognosia and different neurpsychological test. ***Results:*** In the patient affected by anosognosia for hemiplegia, the grip aperture of the healthy hand was influenced by the intended (but not executed) movement of the plegic hand when the patient was trying to reach to grasp targets of different size, $F(2, 14) = 11.87$, $p < .001$. Patients affected by hemiplegia (without anosognosia) didn't show any interference effect between the plegic and healthy hand even when they were asked to reach to grasp targets of different size. ***Conclusions:*** Our results confirm the hypothesis that a spared intention-programming system within the contralateral (damaged) cortex can go as far as to influence distal kinematic parameters of the healthy hand of patients affected by anosognosia for hemiplegia.

Keywords: anosognosia, awareness, motor control, grasping, coupling

Brain-damaged patients affected by hemiplegia (HP) can, sometimes, deny their paralysis and claim they can still move their plegic limbs (anosognisia for HP: AHP; Berti et al., 2005; Fotopoulou et al., 2008). Referring to a forward model of motor control (Blakemore & Frith, 2003), we explained this puzzling pathology proposing that in these AHP patients a damaged comparator, in charge of detecting the mismatch between movement, no movement conditions, is the cause of the denial behavior while the persistence of normal intention to move is the cause of the "erroneous" motor awareness that lead the patients to claim their movement normality. Anatomical findings support this theory. Indeed, in the damaged hemisphere of these patients, a spared supplementary motor area (SMA) has been observed, possibly responsible for their correct motor intention (Berti et al., 2005). In previous experiments, we looked for behavioral effects to confirm this hypothesis, using bimanual movement paradigms. The rationale behind these experiments was that, when we move both arms simultaneously, each one performing a different movement, we can observe an interference effect on the motor performance of each hand (Franz, 2003). This so-called coupling effect is the result of the interaction between conflicting motor programs in noncongruent conditions. Thus, using spatial (i.e., left arm performing circles while right arm is performing lines) and temporal tasks (i.e., left and right arm simultaneously reaching toward different locations), we showed that when AHP patients are asked to move their left plegic limbs, a coupling effect can be observed on the kinematic parameters of the right healthy arm (Garbarini et al., 2012; Pia et al., 2013). These first results confirmed that AHP patients can program a movement with their paralyzed arms, and their illusory awareness of movement is based on their "normal" intention to move.

However, these experimental tasks were both based on proximal movements more than distal movements. Early studies on motor control (Lawrence & Kuypers, 1968) showed that proximal movements (e.g., shoulder movements) can be mediated partially by the ipsilateral cortex while distal movements (e.g., fingers move-

ments) are completely mediated by the contralateral cortex. Indeed, proximal muscles could still be spared in AHP patients who present lesions involving only one hemisphere (e.g., the right hemisphere in the case of a left hemiplegia). An experimental protocol involving distal movements could better focus brain areas involved in this pathology and confirm that coupling effects observed in AHP patients are due to a spared motor intention possibly related to the SMA of the contra-lesional right hemisphere. Thus, in the present study we asked whether, in AHP patients, the spared motor intention for the paralyzed limb can go as far as to influence kinematic parameters of distal movements such as grasping objects. A number of studies pointed out that when we simultaneously grasp different sized objects with each hand (one large and one small object), no interference effect arises between hand apertures, and each hand scales appropriately to its target (Dohle, Ostermann, Hefter, & Freund, 2000). However, a coupling effect between hands' maximum grip aperture (MGA) has been found when healthy participants have to grasp two targets of different sizes but unified in a single object (Jackson, German, & Peacock, 2002). Indeed, participants were asked to grasp with both hands two cylinders attached to a plinth, both with the same size (congruent reaches) or of different sizes (incongruent reaches). In this last condition, it has been demonstrated that bimanually grasping two objects of different sizes attached together generates an interference effect between hands so that each hand tends to have an aperture similar to the aperture of the other hand (Jackson et al., 2002).

Capitalizing on this result, in the following experiment, we recruited one AHP patient (patient M. A.) and five HP patients, and we asked all participants to reach and grasp one object (with a large or a small diameter) unimanually, or two connected objects in a congruent and incongruent conditions. Our aim is to verify if this grip amplitude interference can be generated even in absence of movement execution, solely based on normal intentional processes. In congruent conditions, both objects were of the same size (both with a large diameter or both with a small diameter), and in incongruent conditions, each object had a different size (one large and one small objects). Our hypothesis was that the AHP patient, requested to grasp two objects in a incongruent condition, should program a specific grip with her left plegic hand, and this program should influence the MGA of the right healthy hand, replicating the effect found by Jackson and colleagues (2002) in healthy participants, while HP patients should not show any interference between hands when performing the same incongruent bimanual task. This finding would confirm that interference effects in AHP patients are caused by a spared intentional/programming system in the right, damaged hemisphere and also show that this intention to move can go as far as to influence distal kinematic parameters.

Material and Methods

Participants

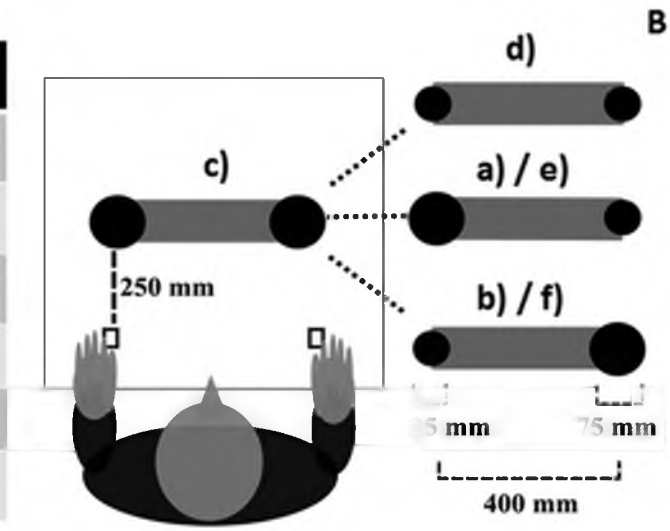
Six neurological patients with focal right brain lesions due to cerebrovascular accident were recruited at the Don Gnocchi Hospital (Milan, Italy). Patients' inclusion criterion was the presence of complete contra-lesional left upper limb plegia, as reported by the responsible neurologist and confirmed by a motor impairment examination carried out according to a clinical protocol (Spinazzola et al., 2008), with the score ranging from 0 (*no paralysis*) to 3 (*complete paralysis*). Following these criterion, six patients with complete left paralysis of the upper limb were admitted to the study: five HP and one AHP patients. Motor awareness was assessed by calculating a deviation score between patients' self-evaluation and the neurologist evaluation of the actual execution of unimanual and bimanual actions (Score 0–2; Spinazzola et al., 2008). Cognitive impairment was evaluated using Mini-Mental State Examination (MMSE; cut-off = 24) to test for general cognitive deficits (Folstein, Folstein, & McHugh, 1975) and Frontal Assessment Battery (FAB; cut-off = 14) to test executive functions (Dubois et al., 2000). Cognitive impairment severity was decided based on the number of tests under cut-off (both MMSE and FAB over cut-off = no impairment; MMSE or FAB under cut-off = medium impairment; both MMSE and FAB under cut-off = severe impairment). Spatial neglect, often present after right lobe strokes, was evaluated using the following tests: clock drawing test (Ishiai, Sugishita, Ichikawa, Gono, & Watabiki, 1993), bisection test (Halligan, Cockburn, & Wilson, 1991), Albert test (Albert, 1973), Diller test (Diller & Weinberg, 1977), and pictures copy and completion (Halligan et al., 1991). Impairment severity was decided based on the number of neglect test under cut-off (0 = neglect absence, 1–2 = mild neglect, 2–4 = severe neglect). AHP patient M. A. (Age: 66, male, Education: 5 years, Time since the stroke onset: 2 weeks) showed lesions over the right frontal lobe, in particular at the level of the premotor cortex (Brodmann area 6) but sparing supplementary motor area, as well as the right insular cortex and at the level of the basal ganglia (see Figure 1A for more details). At the time of the researchers' visit, patient M. A. presented anosognosic symptoms only for his upper left plegic limb, verbally denying this motor deficit. When asked to move his upper plegic arm, M. A. focused his gaze on the arm and after a couple of seconds reported that he performed the movement. When asked about the outcome of the movement, he reported that it was a simple task. Also, doctors reported that in the first week since the stroke onset, M. A. tried to walk outside his bed, falling to the ground and thus showing at least a form of implicit anosognosia for his lower left limb. However, no signs of anosognosia for his lower limb were found at the time of the visit. HP patients (Males: 4, Females: 1; mean age ± standard deviation: 70 ± 3.7; mean education ± standard deviation: 4.5 ± 2.5; time since stroke ± standard deviation: 11.5 ± 4.8 weeks) were all well aware of their hemiplegia and showed no symptoms of anosognosia for their motor deficit. HP patients' lesion sites involved damage at the level of frontoparietal areas and subcortical lesions involving internal capsule and basal nuclei. Exclusion criterions were: (a) previous neurological or psychiatric history; and (b) a complete visual field deficit. All participants gave informed consent, and the study was approved by the Local Ethical Committee. See Figure 1A for a complete overview of the neuropsychological tests administered and lesion sites.

Apparatus and Procedure

Targets and distances replicated the experimental setup proposed by Jackson and colleagues (2002). See details in Figure 2b. Subjects were seated in front of a table (1350 × 850 mm) with their back leaning comfortably against the rear of the chair. The

A

Patient	Neglect	Cognitive impairment	Apraxia Ide/con	AHP test	Lesion Site
AHP M.A.	+	-	-/+	2	R ft, bn
HP 1	+	-	-/-	0	R th, ic, bn
HP 2	++	-	-/+	0	R ftp, ic
HP 3	-	-	-/-	0	R fp, ic
HP 4	-	-	-/+	0	R fp, ic
HP 5	-	-	-/-	0	R fp, po, bn



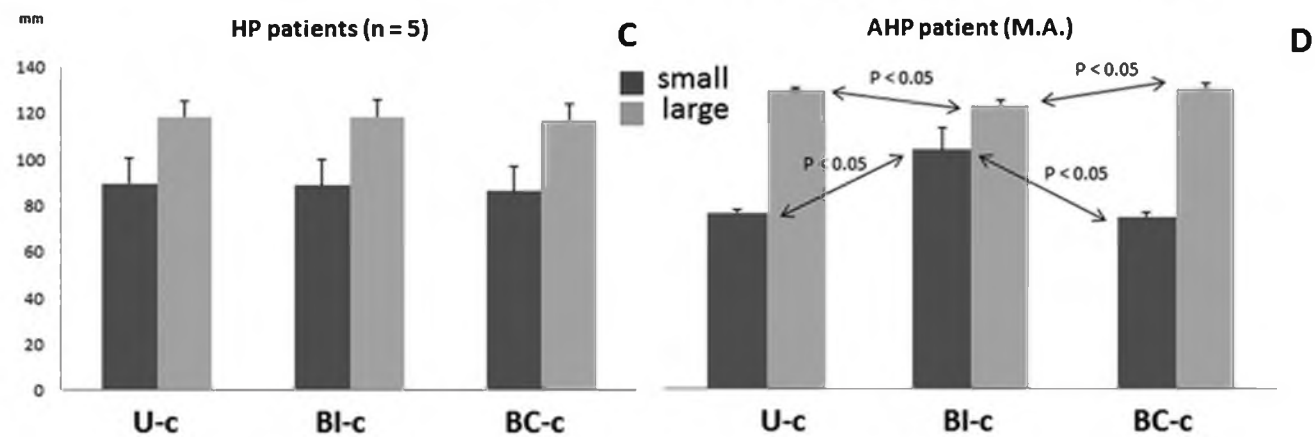


Figure 1. (A) Neurospychological test scores and lesion sites. Left neglect diagnosis based on medical reports and the following tests: clock drawing test, bisection test, Albert test, Diller test, pictures copy and completion (− = absent, + = mild neglect, ++ = severe neglect). Cognitive impairment diagnosis based on medical reports and Mini-Mental State Examination, Frontal Assessment Battery (− = absent,+ = mild impairment, ++ = severe impairment). Idemotor/constructive apraxia diagnosis based on medical reports and gesture production/repetition (for each: − = absent, + = present). Anosognisia for hemiplegia (AHP) test, 0 = no anosognosia, 1 = moderate anosognosia, 2 = severe anosognosia. Lesion sites: R = right, ft = frontotemporal, fp = frontoparietal, ftp = frontotemporoparietal, bn = Basal nuclei, ic = internal capsule, Po = pons. (B) Apparatus and procedures representation. Respectively, (C) HP and (D) AHP patients' results on the *y* axis the MGA in mm, gray bars represent large cylinders and white bars represent small cylinders, error bars represent SEM.

objects to be grasped were placed on the table, to the right and to the left of the subjects' medium sagittal plane. Starting positions for right and left hand were placed on the same line as the participants' shoulders and marked with a white tape square (30 mm) on the surface of the table. The targets consisted of wooden cylindrical dowels: one large (diameter = 75 mm) and one small (diameter = 25 mm). The distance between targets' centers was of 400 mm, and a wooden plinth unified them in one single object (Height = 50 mm; Width = 50 mm; Length = 445 mm). Targets were at a distance of 250 mm from the starting positions (see Figure 1B). MGA performed during the reaching movement was recorded through two retro-reflective markers (diameter = 5 mm) attached to the tip of the index finger and the thumb (radial side of the nail and ulnar side of the nail, respectively), whose 3-D spatial coordinates were captured with an optoelectronic SMART system (BITIS, Milan, Italy) and then analyzed using a custom Matlab program (The Mathworks). We asked participants to reach and grasp the targets (the wooden cylinders) and to slightly lift them, using the right hand to grasp the cylinder on the right part of the plinth and the left hand to grasp the cylinder on the left part of the plinth. In all conditions, we always used two cylinders connected by a plinth, and we modulated the size of one or both cylinders, asking participants to grasp the cylinder on the right or to use both hands to grasp both cylinders. We had the following six conditions (see Figure 1B for a schematic representation of all conditions):

Figure 2. Anosognisia for hemiplegia patient (M. A.) reconstructed lesions. Lesion reconstructed from CT scans. Darker gray area represents damaged brain areas.

A Unimanual condition (U-c) where participants were asked to grasp, only with their right hand, a small cylinder. In this condition a large cylinder was shown on the opposite side of the plinth (a).

A U-c where participants were asked to grasp, only with their right hand, a large cylinder. In this condition, a small cylinder was shown on the opposite side of the plinth (b).

A bimanual congruent condition (BC-c) where participants were asked to grasp with both hands two large (connected) cylinders (c).

A BC-c where participants were asked to grasp with both hands two small (connected) cylinders (d).

A bimanual incongruent condition (BI-c) where participants were asked to grasp a small cylinder with the right hand and a large cylinder with the left hand (e).

A BI-c where participants were asked to grasp a small cylinder with the right hand and a large cylinder with the left hand (f).

In U-c (a and b), even if the request was to grasp only one target, we still put in front of participants two cylinders on a plinth. One cylinder in front of the right hand of the participant was either large (a) or small (b), and the cylinder on the left side (not to be grasped) was of the opposite size. This method was chosen to control attentional effects due to opposite size objects in the visual field. It is to be noted that the only difference between these conditions and Bc-c conditions (e and f) was in the task request: that is, in the BI-c to use both hands to reach and grasp two cylinders and in the U-c to reach and grasp with the right hand only the right cylinder.

We recorded eight trials for each condition for a total of 48 trials for participants. Conditions were counterbalanced within subject, in the following fashion: A B C D E F F E D C B A. Each block was composed by four trials, and 2 min of rest between blocks was allowed to all patients.

Before each block, the experimenter indicated both cylinders to the participants, asking them if they could see them both and also to indicate them with their right index finger. After each block where the left hand was involved (namely the BC-c and BI-c blocks), patient M. A. was also asked to report if he correctly performed the movement with his left hand. HP patients were asked about this information only after the first BC-c and BI-c blocks (as they were fully aware of their left plegia).

Analysis and Results

All data were checked for normality, and no difference from normality was found (Shapiro-Wilk test, $p > .05$). We first performed two 3×2 repeated-measures analyses of variance (ANOVAs) with two main factors: condition (U-c, BC-c, BI-c), and size of the right-sided cylinder (large or small). When an interaction was present, we analyzed it with Newmann-Keuls post hoc. To directly compare the AHP patient results with HP patients' results, we performed specific Bayesian one-tailed t tests designed to compare the performance of a single participant to controls (Crawford & Garthwaite, 2007). In all analysis, the dependent variable was the right intact hand MGA (mm).

HP Patients

No HP patient referred to have moved his left plegic hand. Results showed only a significant main effect of size, $F(1, 4) = 27.22$, $p < .01$, explained by an increase of the HP patients' MGA from small ($M = 88.0$ mm) to large cylinders ($M = 117.9$ mm; Figure 1C).

AHP Patient (M. A.)

Patient M. A. claimed, after each bimanual condition block, to have correctly performed the grasping movement with his left hand. Results showed a significant main effect of size, $F(1, 7) = 176.64$, $p < .00001$, explained by an increase of the MGA from small ($M = 72.7$ mm) to large cylinders ($M = 109.2$ mm), and a significant interaction Size $\times$ Condition, $F(2, 14) = 11.87$, $p < .001$. Planned comparisons showed no significant differences in grasping small/large cylinders in U-c ($M = 65.49/110.83$ mm) versus BC-c ($M = 63.8/111.5$ mm). Crucially, post hoc analysis showed a significant difference in grasping small/large cylinders in BI-c ($M = 84.9/105.4$ mm) versus both U-c and BC-c, $p < .05$ (Figure 1D).

Comparisons Between AHP Versus HP Patients

Results showed that the difference in MGA while grasping large cylinders in the BI-c versus BC-c and in BI-c versus U-c was significantly higher in the AHP patient M. A. than in the HP group (respectively: standardized difference between case and controls [Z-DCC] $= -3.205$, $p < .05$ and Z-DCC $= -2.652$, $p < .05$). Furthermore, the difference in grasping small cylinders in the BI-c versus BC-c and in BI-c versus U-c was also significantly higher in the AHP patient M. A. than in the HP group (respectively: Z-DCC $= 4.055$, $p < .01$ and Z-DCC $= 4.043$, $p < .01$).

Finally, the difference in MGA while grasping small versus large cylinders in the BI-c between AHP patient M. A. and HP patients tended toward significance (Z-DCC = −1.888, p = .06).

Discussion

In previous studies, we found that AHP patients can still show kinematic effects when asked to perform bimanual actions (Garbarini et al., 2012; Pia et al., 2013), and we hypothesized that these effects were caused by a spared motor intention related to their plegic arm. However, these spatial and temporal bimanual tasks both involved mainly proximal muscles, with less involvement of distal ones. Different studies drew a distinction between proximal and distal motor control. Classic lesion studies on monkeys showed that both hemispheres can control ipsilateral and contralateral proximal musculature (e.g., used for reaching movements) due to the ventromedial pathway while distal muscles (e.g., used for finger grips) are controlled by the contralateral hemisphere via the lateral pyramidal tract (Brinkman & Kuypers, 1973). Because proximal muscles are governed by both hemispheres, it could be possible that these muscles could be spared in AHP patients who presented lesions involving only one hemisphere (contralateral to the plegic hand). Also, different evidence in the scientific literature points out that proximal and distal muscles belong to cortically separated motor systems. For instance, single unit recordings in monkeys showed that neurons related to proximal muscles and distal muscles are distributed differently in the premotor cortex (Kurata & Tanji, 1986), and more recently, functional studies in humans showed that proximal and distal movements have a different representation on brain regions with proximal movements related to a greater activation of premotor and prefrontal cortices and distal movements related to a greater activity of the supplementary motor area (Yeo, Chang, & Jang, 2013). Furthermore, studies on motor skills acquisition in children are in line with these anatomical and functional studies, showing that proximal development is not a prerequisite for distal development and that these two motor systems can grow separately without heavily depending on each other (Loria, 1980). Taken together, these results suggest the existence of two completely different motor control systems dedicated respectively to the proximal and distal musculature.

Thus, in the present study, we asked whether motor intention for a paralyzed limb can nonetheless be implemented in distal muscles for the execution of fine grasping movements. To investigate this possibility, six HP patients, one with and five without AHP, were asked to perform bimanual reach-to-grasp movements (involving fine distal finger movements). As a target, we used a wooden plinth, upon which we attached two cylinders. This particular setup was used because it has been showed that coupling effects in bimanual reach-to-grasp tasks arise only if the two objects to be grasped are parsed in one single object (Jackson et al., 2002).

According to previous studies (Garbarini et al., 2012; Pia et al., 2013), in bimanual conditions, HP patients without AHP, being fully aware of their motor deficit, only programmed unimanual movements. Indeed, these patients' results only showed a difference in right hand MGA in relation to the size of the targets (larger for large cylinders and smaller for small cylinders).

Crucially, in AHP patient M. A., the right hand MGA was significantly modulated by the illusory grasping that he was convinced to perform with his left (paralyzed) hand. Indeed, in the bimanual incongruent condition (BI-c), the MGA either decreased or increased in respect to both unimanual (U-c) and bimanual congruent conditions (BC-c) depending on the size of the cylinders (small/large) illusory grasped with the patient's paralyzed hand (i.e., a coupling effect was observed). It is worth noting that this effect cannot be explained by an attentional effect due to the simultaneous presentation of two objects, because the same setup, involving two objects, characterized the unimanual condition (U-c), where no coupling effect was observed. Also, the coupling effect shown in the incongruent condition (BI-c) cannot be explained by a general request to move both arms because in the congruent condition (BC-c), where the AHP patient was asked to grasp two targets of the same size, no coupling effects were observed. It is worth noting that no healthy participants were recruited, and future studies on the same topic should aim to recruit both HP patients as well as non-HP patients to have a more complete vision on distal movements in patients affected by anosognosia.

These results demonstrate, for the first time, that an effective motor intentionality for the paralyzed hand can be implemented in distal muscles for the planning of fine grasping movements. They also confirm previous studies on bimanual coupling effects in AHP patients involving proximally mediated bimanual tasks (Garbarini et al., 2012; Pia et al., 2013), disambiguating those findings that could be generated by a spared activity of the ipsilateral (intact) cortex (Lawrence & Kuypers, 1968). In the present study, we focused on distally performed movements, so that all effects we found should be mediated by a spared intention-programming system (Haggard, 2005) within the contralateral (damaged) cortex. In line with other studies, patient M. A.'s lesions confirmed that AHP is characterized by a spared SMA, an area involved in motor programming (Berti et al., 2005; Pia, Neppi-Modona, Ricci, & Berti, 2004) but also fundamental for the generation of bimanual movements (Garbarini & Pia, 2013). Our neuropsychological testing also confirmed that AHP is independent from spatial neglect and cognitive impairment as shown in classical studies on this pathology (Berti, Lådavas, & Corte, 1996). AHP is being described as a disturbance of motor control mechanisms in spite of a spared motor programming system, and bimanual movements represent a crucial methodology to test this hypothesis (Garbarini & Pia, 2013). In this model of motor programming, however, differences between motor system components have not been taken into account. The present results raise the possibility that a spared intentionality can have different effects on proximal or distal motor components, and future studies on AHP should address this possibility utilizing bimanual experiments involving both proximal and distal tasks in the same paradigm.

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