CORTEX 92 (2017) 187–203

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

Modulating anosognosia for hemiplegia: The role of dangerous actions in emergent awareness

Daniela D'Imperio [a,b], *Cristina Bulgarelli* [c], *Sara Bertagnoli* [b], *Renato Avesani* [c] and *Valentina Moro* [b,*]

[a] Social Neuroscience Laboratory, Department of Psychology, Sapienza University, Rome, Italy
[b] NPSY.Lab-Vr, Department of Human Sciences, University of Verona, Italy
[c] Department of Rehabilitation, Sacro Cuore-Don Calabria Hospital, Negrar, Verona, Italy

ARTICLE INFO

Article history:
Received 6 December 2016
Reviewed 25 January 2017
Revised 14 March 2017
Accepted 12 April 2017
Action editor Paolo Bartolomeo
Published online 21 April 2017

Keywords:
Anosognosia for hemiplegia
Emergent awareness
Danger in awareness
Error monitoring
Modulation of awareness

ABSTRACT

Anosognosia for hemiplegia is a lack of awareness of motor deficits following a right hemisphere lesion. Residual forms of awareness co-occur with an explicit denial of hemiplegia. The term emergent awareness refers to a condition in which awareness of motor deficits is reported verbally during the actual performance of an action involving the affected body part. In this study, two tasks were used to explore the potential effects of i) attempting actions which are impossible for sufferers of hemiplegia and ii) attempting actions which are potentially dangerous. Sixteen hemiplegic patients (8 anosognosic, and 8 non-anosognosic) were asked to perform both potentially dangerous and neutral actions. Our results confirm an increase in emergent awareness in anosognosic patients during the execution of both of these types of action. Moreover, actions that are potentially dangerous improved the degree of awareness. However, lesions in the fronto-temporal areas appear to be associated with a reduced effect of action execution (emergent awareness) while lesions in the basal ganglia and amygdale and the white matter underlying the insula and fronto-temporal areas are associated with a lesser degree of improvement resulting from attempting to perform dangerous actions.

1. Introduction

The term anosognosia (from the Greek, α = without, νόσος = disease, γνώσις = knowledge) refers to a lack of awareness of sensory, motor or cognitive (i.e., language, memory) deficits. Babinski (1914) described a specific form of unawareness known as Anosognosia for hemiplegia (AHP) that selectively involves an incapacity to admit motor deficits and that mainly occurs as a consequence of right hemisphere lesions (Pia, Neppi-Modona, Ricci, & Berti, 2004; Vocat, Staub, Stroppini, & Vuilleumier, 2010; but see also Cocchini, Beschin, Cameron, Fotopoulou, & Della Sala, 2009; Jehkonen, Laihosalo, & Kettunen, 2006a). Anosognosic patients fail to acknowledge or recognize their paralysis and they claim that they are able to carry out everyday activities which are in reality impossible for them.

Sensory loss, intellectual impairment or a combination of these cannot fully explain the syndrome (Marcel, Tegnér, & Nimmo-Smith, 2004). Furthermore, double dissociations

* *Corresponding author*. Department of Human Sciences, University of Verona, Lungadige Porta Vittoria 17, 37129 Verona, Italy.
E-mail address: valentina.moro@univr.it (V. Moro).
http://dx.doi.org/10.1016/j.cortex.2017.04.009

have been demonstrated between AHP and proprioceptive impairment (Cocchini, Beschin, Fotopoulou, & Della Sala, 2010), spatial or personal neglect (Vocat et al., 2010), confabulation and deficits in frontal lobe functions (Heilman & Harciarek, 2010 for review) and other disorders in body representation, in particular somatoparaphrenia and feelings of disownership relating to affected limbs (Moro, Pernigo et al., 2016; Moro, Zampini, & Aglioti, 2004).

AHP is in fact a heterogeneous, multicomponential syndrome which may be influenced by a combination of partially different causes and which may manifest partially different symptoms (Davies, Davies, & Coltheart, 2005; Marcel et al., 2004; Vocat et al., 2010).

A crucial role in the syndrome was initially attributed to lesions in the parietal lobe (Bisiach, Vallar, Perani, Papagno, & Berti, 1986; Heilman, 1991) and in the wide networks of fronto-temporo-parietal integration (Pia, Neppi-Modona, Ricci, & Berti, 2004). More recently, the premotor cortex (Berti et al., 2005) and the insula (Karnath, Baier, & Nägele, 2005) have been identified as the core systems in AHP, with lesions associated with the symptoms in subcortical structures (the basal ganglia and amygdale) and in white matter tracts (Fotopoulou, Pernigo, Maeda, Rudd, & Kopelman, 2010; Moro, Pernigo et al., 2016; Moro, Pernigo, Zapparoli, Cordioli, & Aglioti, 2011; Vocat et al., 2010).

Damage to different parts of these networks has been linked to various expressions of the syndrome, with specific anosognosic symptoms occurring along with residual forms of awareness. For example, in the case of explicit anosognosia and implicit awareness, patients verbally deny their paralysis but act as if they know about their paralyzed body parts (Cocchini et al., 2010; Fotopoulou et al., 2010; Moro et al., 2011). This may have a significant impact as these implicitly aware patients will not try to stand up or act alone (as they risk hurting themselves) and will ask for help when necessary. In these cases rehabilitation is generally more efficacious (Gialanella, Monguzzi, Santoro, & Rocchi, 2005; Jehkonen, Laihosalo, & Kettunen, 2006b).

Another dissociation has been reported between deficits in awareness which refer to the self and to other people. Although the majority of people suffering from AHP fail to acknowledge paralysis both in themselves and in other people, some patients deny the motor deficits only when answering questions which refer to themselves. This may indicate that in the former situation the motor awareness deficits relate to the actions per se, while in the latter they are specific to the patient's own body actions (Marcel et al., 2004; Moro et al., 2011; Ramachandran & Rogers-Ramachandran, 1996; Ramachandran, 1996).

A form of Emergent Awareness has been previously described (Moro, 2013; Moro, Scandola, Bulgarelli, Avesani, & Fotopoulou, 2015; Moro et al., 2011). In this condition, when the anosognosic patients are asked to actually perform an action using the affected body parts they are able to verbally state that they cannot perform the action due to their motor deficits (Moro et al., 2011). This indicates that the intention to act (and/or actually acting) may modify any explicit, verbal knowledge of the deficits. More generally, this suggests that a modulation in AHP may be induced by ad-hoc experimental manipulation.

We investigated this topic by means of an experiment in order to establish whether there is a relationship between the top-down processes required to carry out specific actions and the effects of the characteristics pertaining to that action, in particular if they are of an emotional as compared to neutral nature. In fact, fluctuations in awareness in AHP are influenced by both sensory-motor and high cognitive functions (Fotopoulou, 2015 for review) and the role of emotional components has been previously reported (Besharati et al., 2014; Nardone, Ward, Fotopoulou, & Turnbull, 2008).

In the present study, anosognosic and hemiplegic non-anosognosic patients (HP) were asked to execute a number of everyday actions, which were impossible for them due to their paralysis. Their judgment regarding their proficiency in carrying out the actions (Della Sala, Cocchini, Beschin, & Cameron, 2009; Moro et al., 2011) was asked at various times: i) in a preliminary interview which focused on the specific actions to be performed (Semantic awareness); ii) before starting to execute the action (Anticipatory awareness); iii) during execution (Emergent awareness) and iv) after the attempt to act (Post-error awareness) (Moro et al., 2011). Moreover, the experiment was devised to determine whether the nature of the action had in itself an impact on awareness. To this end, half of the actions were neutral (i.e., they could be executed in safety, without risk of injury) and the other half were dangerous (i.e., patients could potentially hurt themselves).

We expected that real attempts to carry out actions would increase awareness in the AHP patients, with more realistic judgments being expressed during the execution of the action and/or after failing. Moreover, we expected that the Emergent Awareness effect would be stronger in dangerous as compared to neutral actions. A detailed analysis of the patients' lesions (Bates et al., 2003; Rorden, Karnath, & Bonilha, 2007) was also carried out in order to integrate behavioral and anatomical data associated with AHP, and in particular to investigate any modulations due to emergent awareness and the characteristics of the actions they performed.

2. Materials and methods

2.1. *Participants*

Sixteen patients suffering from left hemiplegia (absence of movement, MRC scale – Medical Research Council, 1986; see Table 1) as a consequence of a right hemisphere stroke were recruited at the Rehabilitation Unit, Sacro Cuore Hospital (Negrar, Verona) over a period of one year. They were divided into two groups based on the presence or otherwise of AHP. This was assessed by means of the Bisiach scale (Bisiach et al., 1986) and the Berti interview which investigates symptoms related to upper and lower limbs separately (Berti, Làdavas, & Della Corte, 1996). For the Bisiach scale, a partially modified version of the scoring was used (Bisiach et al., 1986) in which 0 = the disorder is spontaneously reported or mentioned by the patient following a general question about his/her complaint; 1 = the disorder is reported only after a specific question about the strength of his/her left limbs; 1.5 (not reported in the original version of the scale) = general deficits

Table 1 – Demographic and clinical data of patients with (AHP) and without (HP) anosognosia for hemiplegia. Pt = patient, G = gender, Educ = years of education. Test Int = the number of days between lesion onset and assessment, CT/MRI Int = the number of days between lesion onset and the CT/MRI scan, Exp Int = interval of time between lesion onset and experimental task. Sens = sensory deficits; Motor = motor deficits. [1]MRC Test, [2]Berti's Interview, [3]Bisiach's Scale (The additional score of 1.5 refers to the conditions when general deficits and some motor impairments are reported, but not related to the presence of hemiplegia), DSO = Disturbed sensation of limb ownership[4] (Moro, Pernigo, et al., 2016). UL = Upper Limb, LL = Lower Limb, Na = not available, T = temporal, O = occipital, F = frontal, P = parietal, Th = thalamus. − = deficits present; + = deficits not present. Pathological scores are in bold. For each group Mean or (Median for MRC Test, Berti's Interview and Bisiach's Scale) and St.dev. (Standard deviation) values are reported. ** = Mann–Whitney Tests show significant differences ($p < .01$) between two groups (no other significant results between the two groups).

Pt	Age	G	Educ	Test Int	CT/MRI Int	Exp Int	Lesion	Sens	MRC UL[1]	MRC LL[1]	Berti UL[2]	Berti LL[2]	Bisiach[3]	DSO UL[4]
AHP 1	64	M	18	66	86	99	FP Th	+	0	1	**1**	**1**	**1.5**	+
AHP 2	74	F	5	103	124	123	FP Th	−	0	1	**1**	**2**	**2**	−
AHP 3	47	M	8	34	77	49	TO	−	0	2	0	**1**	Na	−
AHP 4	53	F	8	48	31	52	F	−	1	2	**1**	**1**	**3**	+
AHP 5	63	M	13	13	16	17	TP	−	0	1	**1**	**2**	**3**	+
AHP 6	57	F	10	61	61	62	FTP	−	1	1	**1**	**2**	**2**	−
AHP 7	83	M	5	11	11	20	FP Th	−	0	1	**1**	**1**	**1.5**	−
AHP 8	76	M	5	>30	Na	Na	FTP	−	1	3-	**1**	**2**	**3**	−
Mean (Median)	64.6		9	48	58	60.3			(0)	(1)	(1)**	(2)**	(2.5)**	
St.dev.	12.3		4.6	32.4	41.2	39								
HP 1	64	M	5	70	Na	85	Na	+	2	4	0	0	0	−
HP 2	55	F	13	76	71	77	FTP Th	−	1	3	0	0	0	−
HP 3	54	M	8	52	85	65	F, Th	−	0	0	0	0	0	−
HP 4	72	F	5	91	100	102	FTP	+	0	0	0	0	0	−
HP 5	66	F	17	103	Na	106	Na	−	0	0	0	0	0	−
HP 6	75	M	5	33	30	55	FP	−	2	3-	0	0	0	−
HP 7	70	M	17	45	46	53	Th	+	2	2	0	0	0	−
HP 8	64	M	5	36	30	50	FTP	−	3-	2	0	0	0	−
Mean (Median)	65		9.3	63.2	60.3	74.1			(1.5)	(2)	(0)	(0)	(0)	
St.dev.	7.5		5.4	25.8	29.5	22								

and some motor impairments are reported, but these are not related to the presence of hemiplegia (e.g., a previous unrelated surgical operation or arthrosis); 2 = the disorder is acknowledged only after its demonstration by means of routine techniques during a neurological examination; 3 = no acknowledgment of the disorder can be obtained. The Berti interview investigates awareness relating to the upper and lower limbs separately and there is a 3-point score (Berti et al., 1996): 0 = the patient answers correctly to the first group of questions about the reasons for his/her being in hospital. With regard to the lower limbs, he/she acknowledges the paralysis when specifically questioned about the left leg; 1 = the patient acknowledges being in hospital and/or being affected by a stroke, but denies any impairment to his/her limbs. However the patient admits that his/her left arm does not reach out to touch the examiner's hand and/or that he/she is unable to walk; 2 = the patient claims that he/she has reached out to touch the examiner's hand and/or he/she is able to walk.

Due to the limits of these structured interviews in terms of accurately assessing awareness (for a discussion about the assessment of AHP, see Cocchini & Della Sala, 2010), we confirmed the patients' diagnoses with the help of their clinicians' reports and an accurate analysis of the patients' verbal statements. In fact, it is well known that when patients are engaged in a rehabilitation program, they are often asked about their paralysis and in some way "learn" the responses to direct questions. Because of this, a further in depth but unstructured interview was used to investigate specific aspects of awareness, for example their judgment with regard to their autonomy in everyday activities (e.g., getting dressed, using a knife and fork) and their reactions to what the doctors said about their paralysis (e.g., "The doctor says you have some problems when you try to move your limbs. Do you agree with this?"). For example patient AHP 3 declared that he was not able to move his left arm, but he did not acknowledge his paralysis and gave irrational explanations. In addition, he declared that he was able to carry out daily life activities without any help (e.g., "I do not know why I can move, but I am sure I am able to light a fire"). In spite of the fact that his upper limb was completely paralyzed, he did not agree with the doctors' opinion regarding his motor deficits, declaring that he moved his left arm less than the right one because of pain. With reference to his Lower Limb, he declared that he was able to walk (although with a stick) while in fact he could not. The other patients' responses are reported in the Supplementary materials A.

In this way eight patients were diagnosed as being affected by AHP (scores ≥ 1 on the Bisiach scale and/or at least in one section of the Berti Interview). The other eight patients did not present any signs of anosognosia (all scores = 0) and these constituted the control group (HP, Table 1).

The two groups were matched for age, gender, education and the interval between lesion onset and the dates of the assessment, the CT/MRI examinations and the experimental task (Table 1). The patients did not have a prior history of psychiatric or neurological diseases. They gave their consent to participate in the study which was approved by the local ethics committee (CEP prot. N. 39216) and was carried out in accordance with the guidelines in the Declaration of Helsinki (2013).

2.2. Preliminary neuropsychological examination

Although some patients had scores under cut-off in the assessment of their general cognitive profile (MMSE, Folstein, Folstein, & McHugh, 1975), this was mainly due to visuospatial problems (Table 2). Indeed, all of the patients were well oriented in space and time at the time of the experimental task.

All of the patients (except one in the HP group) failed in tests assessing frontal functions (Frontal Assessment Battery – FAB; Appollonio, Leone, Isella, Piamarta, Consoli, Villa et al., 2005), while short and long verbal memory (Forward digit span and Story recall; Spinnler & Tognoni, 1987) was spared in the majority of the participants.

The AHP group showed more symptoms of extra-personal neglect than the HP group (Line Bisection, Albert Test and Copy Test; Wilson, Cockburn, & Halligan, 1987), while personal neglect (Comb and Razor Test; McIntosh, Brodie, Beschin, & Robertson, 2000) was present in both groups. Finally, only two patients in the HP group were over cut-off on the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983).

2.3. Experimental task

In order to investigate the role of attempting to perform actions in modulating patients' awareness (Emergent awareness) and the effects of actions which were potentially dangerous, an ad-hoc task was devised.

The participants were asked to judge their proficiency in the execution of specific actions (neutral or dangerous) in four different situations: i) during an interview, ii) before the attempt to act, iii) during and iv) after the actual attempt to act.

As this main task was executed in a first-person perspective, another task (*Judgment of Others' actions*) was administered in which the patients had to judge the abilities of another hemiplegic patient with regard to the same actions (for Method and Results, see in Supplementary materials B). This control task allowed us to evaluate any potential dissociation in AHP patients in their judgments relating to themselves and to other people.

2.3.1. Stimuli

20 bimanual or full body actions which were impossible for hemiplegic patients were selected. Another 4 unimanual actions involving the healthy hand were used as a control to check the consistency of the patients' responses and their attention to the task.

The 20 experimental actions were divided into two blocks. The first block consisted of 10 actions that involved the full-body (FB e.g., going downstairs, using a wheelchair). The second block consisted of 10 upper-body actions (UB e.g., cutting nails with scissors, using a ruler to draw a line). The realistic nature of the setting was guaranteed by the choice of everyday activities.

Table 2 – Neuropsychological data. Neuropsychological assessment of general functions, memory, neglect and emotional state in the patients with (AHP) and without (HP) anosognosia for hemiplegia. ST = short term, LT = long term, FW = forward, VE = visual extinction, - = deficit present, + = deficit not present. Imp = Impossible to assess, Na = not available. All scores are corrected for age and/or education. Pathological scores are in bold. Scores at cut-off are in *italic*. For each group Mean and St.dev. = Standard deviation values are reported. * = Significant differences ($p < .05$) between the two groups at *T*-Test.

Pt	General and Frontal		Memory			Neglect					Mood
	MMSE	FAB	Story recall ST	Story recall LT	Digit Fw	Bisection	Albert	Copy	VE	Comb	HADS
AHP 1	**22.2**	**7.2**	7.5	9	8	**0**	**18**	**1**	–	**–.42**	14
AHP 2	**14.7**	**3.3**	**0**	**0**	**2**	**0**	**10**	**0**	–	0	13
AHP 3	**16.62**	**11.7**	6.5	6.5	8	**2**	32	**1**	Imp	**–.36**	10
AHP 4	27	**11.9**	4.8	7.8	9	9	**34**	**2**	+/–	**–.29**	5
AHP 5	**21.27**	**4**	**3.3**	4.4	**4**	**0**	**12**	**0**	–	**–.125**	Na
AHP 6	27	**4.1**	5.5	5.5	**4**	**6**	**24**	**0**	–	**–0.8**	Na
AHP 7	24.4	**8**	6.3	5.3	**2**	**4**	**12**	**0**	–	**–.47**	Na
AHP 8	**18.7**	**3.5**	6.5	6.4	7	**3**	**18**	**0**	–	**–0.4**	13
Mean	21.5	6.7	5	5.6	5.5	3	20*	0.5		–.36	11
St.dev.	4.6	3.6	2.4	2.7	2.8	3.2	9.2	0.7		0.2	3.7
HP 1	24.9	**8**	**0**	4.4	4	**6**	36	3	–	**–0.6**	Na
HP 2	24	**9.3**	9	8.5	7	8	36	**1**	+	0	Na
HP 3	28.74	**10.2**	6.5	7.7	6	9	40	**0**	+	0	8
HP 4	**21**	**1**	**3.1**	2.3	**5**	**0**	**12**	**0**	Imp	**–0.2**	11
HP 5	25.2	18	6.6	7.7	Na	9	36	4	Na	Na	Na
HP6	**19**	**7.9**	6.4	4.7	Na	**1**	**24**	**0**	–	**–.21**	Na
HP 7	25	**11.9**	5.3	6.4	7	7	36	4	Na	**–0.5**	**18**
HP 8	**18.9**	**6.8**	3.8	3.8	9	**0**	**22**	**1**	+	**–.13**	**20**
Mean	23.3	9.1	5.1	5.7	6.3	5	30.2*	1.6		–.23	14.25
St.dev.	3.4	4.8	2.7	2.2	1.7	4	9.8	1.8		0.2	5.7

In order to test the impact of actions which were potentially dangerous, in each block there were 5 neutral (N) and 5 potentially dangerous (D) actions. In the FB block, the actions were dangerous because the patients were at risk of falling or getting hurt (e.g., moving from a wheelchair to a bed). Actions in the UB block were potentially dangerous for everybody regardless of paralysis (e.g., cutting one's own nails with scissors). The actions were selected so that each D action corresponded to a N action in terms of similarity of execution (e.g., moving a full pan from a gas ring – Lifting up a tray with glasses) or purpose (e.g., walking – using a wheelchair) (see Table 3).

2.3.2. *Procedure*

The order of the two blocks (FB and UB) was counterbalanced between the participants with breaks of 20–30 min between the blocks.

The task was executed in four steps. The participants were first asked Yes/No questions to judge whether they could perform the actions which they would be requested to carry out in the experiment ("Can you do this?", for the answer "No" the score was 0). In the case of a positive answer, they were then asked to rate their ability on a 10-point Likert scale ("How well can you do it?" – with scores ranging from 1 = "I cannot do it" to 10 = "I can do it without any problems"). The final score represented a measure of the participants' Semantic awareness.

Next, the patients were put in a real situation, they were given the necessary tools and were then requested to perform each of the actions. Before starting, the same general question ("Can you do it?") was asked. Again, in the case of a positive answer, participants were requested to predict their proficiency on a 10-point Likert scale ("How well can you do it?"). This was considered a measure of Anticipatory awareness.

In the third step, the patients were asked to actually carry out the action and the same two questions were asked during their attempt. This provided a measure of Emergent awareness.

Finally, after failing in the attempt, the questions were asked again. This was a measure of Post-Error awareness.

All of the attempts to act were realized in absolute safety and the patients were stopped before any risk of injury might occur. The FB actions were executed in the gym of the rehabilitation department where patients could carry out their attempts under the supervision of a physiotherapist. The UB actions were executed in a room in the occupational therapy department, at desk or a sink under the supervision of the experimenter. Any potential disturbance or distraction (e.g., the presence of other people or environmental noise) was eliminated.

2.3.3. *Comparison with the judgment of the physiotherapist*

In order to measure the patients' lack of awareness regarding their ability to execute specific actions during the experiment, their judgment (Semantic awareness) was compared to that expressed by their physiotherapist (Pht judgment) with reference to the same action and with the same criteria of response (Yes/No questions and in the case of a positive answer, giving a score from 1 to 10 on a Likert scale).

2.3.4. *Modulation of AHP*

Finally, in order to investigate potential general fluctuations in AHP due to the manipulations performed in the experiment, a general measure of awareness (General awareness) was recorded at the beginning and at the end of each of the two blocks (4 measurements in total).

This scale was developed from a previously validated assessment (Marcel et al.'s modified interview; Marcel et al., 2004; Moro et al., 2011) with the participants being asked one standard question on general awareness ("Do you feel anything unusual on your body?", scores 0 = completely aware, 5 = slightly aware and 10 = completely unaware), two questions on the general sensory-motor abilities of their upper and lower body parts (e.g., "Do you feel anything unusual on your left arm?", scores 0 = completely aware, 5 = slightly aware and 10 = completely unaware) and 7 questions regarding their proficiency in bimanual or bipedal everyday actions different from those used in the experimental task (e.g., "Can you clap your hands?" requiring a Yes/No answer and in the case of a positive response allocating a score on a 10-point Likert scale). In this way the total score ranged from 0 to 100.

The same procedure was repeated for the second block (see the timeline in Fig. 1).

2.3.5. *Statistical analyses*

According to the Likert scale, the range of scores was from 0 to 10, with 0 when the action was judged impossible and 10 when the patient or the physiotherapist (Pht) declared that the

Table 3 – Experimental actions. The 24 actions are shown. Left column, the 4 control actions; Central column: the 10 Full-body actions; Right column: the 10 Upper-body actions. The 20 experimental actions are divided into two blocks of dangerous (D) and neutral (N) actions. D actions are linked to a corresponding N action (e.g., Walking – Using the wheelchair).

Control actions		Full-body (FB)	Upper-body (UB)
Looking to the side	*D*	Walking	Putting a nail in a wooden block
Blowing one's nose		Moving from the wheelchair to the bed	Lighting a candle
Drinking from a glass		Going down the stairs	Cutting one's nails with scissors
Tilting the body		Lifting a heavy box	Washing a big knife in a sink
		Standing up from sitting	Moving a large full pan from the gas ring
	N	Using the wheelchair	Using a ruler to draw a line
		Turning over in the bed	Sharpening a pencil
		Going into an elevator to use it	Opening a big tube of cream
		Scratching both knees	Washing a big spoon in a sink
		Maintaining a sitting position	Lifting a tray with glasses

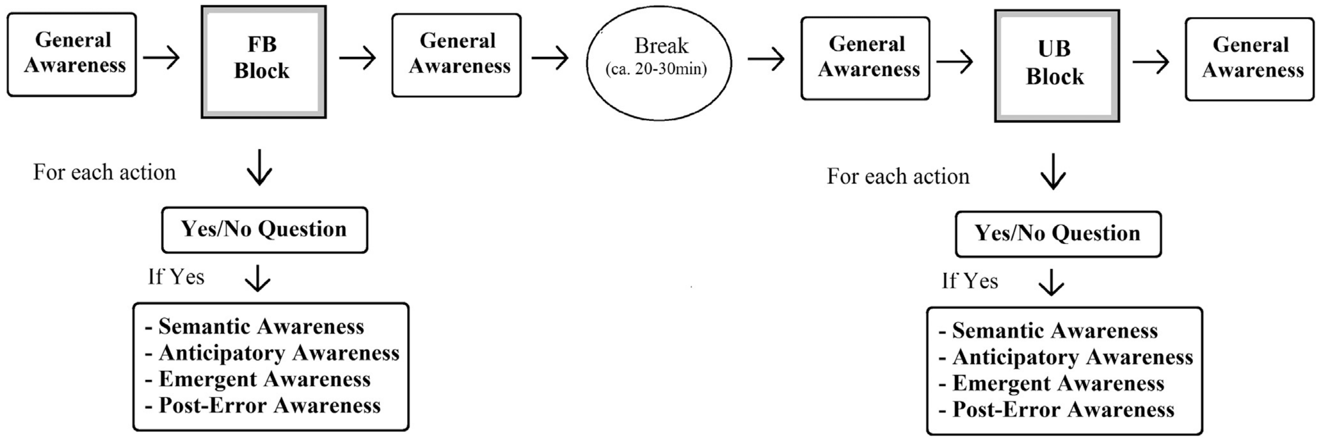


Fig. 1 – Experimental task. The general timeline of the First person-perspective task. The two blocks were counterbalanced between subjects. The measure of General awareness was recorded before and after each block. For each action, the questions about proficiency assessed semantic, anticipatory, emergent and post-error awareness.

action was possible without any difficulties. Given the ordinal nature of the data, these were analyzed by means of a cumulative logit model (Agresti, 2002) in R (R Development Core Team, 2015 with a cumulative link mixed model – clmm function of the ordinal package, Christensen, 2015). The cumulative logit model makes it possible to compare several factors in an ANOVA-like way using the ANalysis Of DEviance Test (ANODE, McCullagh & Nelder, 1989). For all analyses, the random intercept of the model was the subject due to the fact that the sample was small (Bates, Kliegl, Vasishth, & Baayen, 2015).

In order to evaluate the patients' degree of awareness, the judgment of the Pht was compared to those expressed by the patients in the first step of the task (Semantic awareness) by means of a 2 (Evaluator: Pht *vs* Patient) × 2 (Group: AHP *vs* HP) ANODE Test.

The modulation of awareness induced by the experimental task was computed in a 2 (Group: AHP *vs* HP) × 4 (Time: Semantic, Anticipatory, Emergent, Post-Error) × 2 (Action: Dangerous *vs* Neutral) × 2 (Block: FB *vs* UB) ANODE Test.

Finally, to investigate any potential generalization of the effects of the experiment on actions other than those executed, the participants' scores in the General Awareness Assessment were analyzed across time in a 2 (Group: AHP *vs* HP) × 2 (Interval: Before *vs* After block) × 2 (Block: FB *vs* UL) ANODE Test.

All the post-hoc analyses were computed by means of the Least-Square Means (lsmeans) Test (Lenth, 2016), a specific analysis for ordinal data, with Bonferroni corrections for multiple comparisons (Bonferroni, 1936).

2.4. *Lesion mapping*

Although the number of patients in the two groups was relatively small, we carried out an explorative analysis of their lesions. To compare the two groups, we analyzed the patients' lesions by means of a voxel-based lesion symptom mapping (VLSM) technique. The patients' structural MRI scans were mapped with the MRIcron software (http://www.cabiatl.com/mricro/mricron/index.html) (Rorden & Brett, 2000) by drawing on the standard T1-weighted MRI template (ICBM152) of the Montreal Neurological Institute (MNI) coordinate system, approximately oriented to match the Talairach space (Talairach & Tournoux, 1988). For the procedure, the template was oriented on the mid-sagittal and mid-coronal axes to match each original MRI scan orientation as closely as possible. Successively, an experienced clinician (SB) blind traced each lesion manually onto the rotated template, while another expert clinician (VM) checked all the drawings in a double-blind procedure. For each patient the outcome was a map of the damaged areas with each voxel labeled as 0 (intact) or 1 (lesioned). Finally, all the lesion maps were rotated back to the canonical orientation in order to align them to the standard sterotaxic MNI space (in 2 mm × 2 mm × 2 mm voxel) and they were filtered with a custom mask based on the ICBM152 template to exclude the voxels of lesions outside the white and gray matter brain tissues.

An analysis of the volume of the lesions was computed with Non-Parametric Mapping (NPM) software (Rorden et al., 2007). In order to investigate the neural correlates of AHP, we compared the lesion maps of the two groups by means of a subtraction technique and a voxel based lesion comparison based on the Libermeister binomial test (False discovery rate – FDR corrected, Benjamini & Hochberg, 1995).

The outcome of the subtraction and the significant lesion maps of the voxel-based lesion techniques were superimposed onto T1 templates to calculate the number of lesioned voxels in various cerebral areas and the center of the mass in each damaged area. This was then overlapped onto the Automatic Anatomical Labeling (AAL) template (Tzourio-Mazoyer et al., 2002) to provide information on the gray matter and onto the Tractography based Atlas of human brain connections Projection Network (Natbrainlab, Neuroanatomy and Tractography Laboratory) (Catani & Thiebaut de Schotten, 2012; de Schotten et al., 2011) for the white matter.

In addition, in order to analyze the neural correlates of reduced emergent awareness (as indicated by a lack of modulation in the comparison between the responses in Semantic, Anticipatory, Emergent and Post-Error), we carried out a VLSM analysis with *t*-test statistics on the whole sample of patients (with the exception of two HP, in total 14 patients). In the analysis, we used the differences in responses at various times during the task as continuous predictors (Bates et al., 2003; Moro et al., 2011; Rorden et al., 2007). The same analysis was carried out to explore the neural correlates relating to the reduced effects of potentially dangerous actions, taking into consideration the differences in patients' scores referring to dangerous as compared to neutral actions in the measures relating to Anticipatory and Emergent awareness.

All of these statistics were implemented for each voxel in the brain (Rorden et al., 2007) and the outcomes indicate the voxels which were damaged in those patients with a statistically worse performance (at p-value $< .05$ and corrected for multiple comparison by using a FDR correction). It is to be noted that, while the behavioral results in our tasks provide information about improvements in awareness due to experimental manipulation, the analyses of lesions furnish data regarding the patterns of lesions associated with the lack of any such improvement.

3. Results

In the trials involving unimanual actions, all of the participants (AHP and HP) declared that they were able to perform the actions and demonstrated a good level of attention to the task giving consistent responses.

3.1. *Behavioral data*

The results of the comparison between the judgments given by Patients and Phts indicate a main effect of Evaluator ($LR\chi^2_{(1)} = 43.62$, $p < .01$) and the Evaluator*Group interaction ($LR\chi^2_{(1)} = 64.73$, $p < .01$). Post-hoc analyses show that only in the AHP group was there a difference between the judgment of the Pht and the patient ($p < .01$) (Fig. 2). In addition, the Phts judged the performance of the HP group as being better than that of the AHP group, probably due to the fact that the former had a slightly better motor performance. Crucially, while the AHP patients overestimated their motor ability ($p < .01$, Fig. 2), the HP group tended to underestimate their abilities, although without there being any really significant differences in comparison to the judgments of the Phts. Finally, the difference in judgment between the two groups of patients was significant ($p < .01$).

An analysis of the modulation in awareness induced by the task showed that the main factors of Group ($LR\chi^2_{(1)} = 9.01$, $p < .01$), Time ($LR\chi^2_{(3)} = 31.29$, $p < .01$) and Action ($LR\chi^2_{(1)} = 19.24$, $p < .001$) and the Group*Time ($LR\chi^2_{(3)} = 10.08$, $p = .02$), Group*Block ($LR\chi^2_{(2)} = 13.77$, $p < .01$) and Action*Block ($LR\chi^2_{(2)} = 49.62$, $p < .01$) interactions were significant.

Post-hoc tests of the Group*Time interaction indicate that in the AHP group awareness improved in Emergent Awareness versus Semantic ($p < .01$) and Anticipatory Awareness ($p = .05$), and in Post-Error Awareness versus Semantic ($p < .01$) and Anticipatory Awareness ($p < .001$). In contrast, there were no statistical differences in the results of the HP group (Fig. 3a).

In the Group*Block interaction, only the AHP group showed a significant difference between FB and UB ($p < .01$), with greater awareness in actions involving the full body with respect to those involving the upper body (Fig. 3b).

Finally, in the Action*Block interaction, the post-hoc analyses indicated significant differences between dangerous and neutral actions for both the FB and UB blocks (both $p < .01$) with a greater awareness for dangerous as compared to neutral actions in both groups (Fig. 3c).

The results regarding the modulation of General Awareness show main effects for Group ($LR\chi^2_{(1)} = 7.91$, $p < .01$) and Interval ($LR\chi^2_{(1)} = 5.49$, $p = .02$), without significant interactions. With the aim of conducting a limited exploration, we computed a post-hoc analyses between Group and Interval. Only in the AHP group was there a difference ($p = .04$) in awareness between the Before and After blocks (regardless of the order of the blocks). However, this difference did not persist when the Bonferroni correction was carried out ($p = .07$) (Fig. 3d).

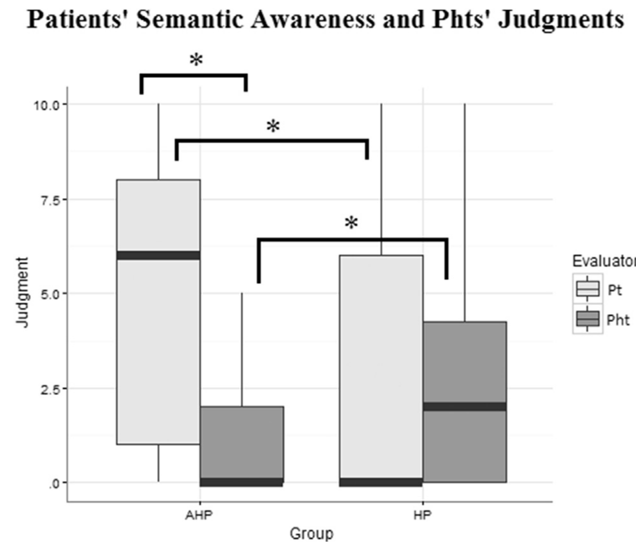


Fig. 2 – Semantic awareness of proficiency in experimental actions and Phts' Judgments. The judgments of Pt (Patients) and PhT (Physiotherapists) are reported for the two groups (AHP and HP). The range on the y-axis is between 0 and 10 as recorded during the task. The box represents the first and the third quartile of data, and the darker line inside is the median. The bottom and the top whiskers are respectively 1.5*Interquartile range lower and 1.5*Interquartile range higher. * = Significant results ($p < .01$).

3.2. *Voxel lesion symptoms mapping*

3.2.1. *Comparison between groups*

There were no significant differences in the extent of the lesions affecting the AHP and HP groups (AHP mean = 241.49 cc, SD = ±122.88 cc; HP mean = 123.00 cc, SD = ±123.31 cc; $t_{(12)} = 1.78$, $p = .09$) (see Fig. 4). A statistical comparison between the two groups (Fig. 4D) showed that the cortical areas which were mainly compromised in the AHP group were the right supramarginal gyrus, the inferior parietal cortex, the superior temporal pole, the insula, the rolandic operculum and the prefrontal gyrus. In addition, the basal ganglia (in particular the

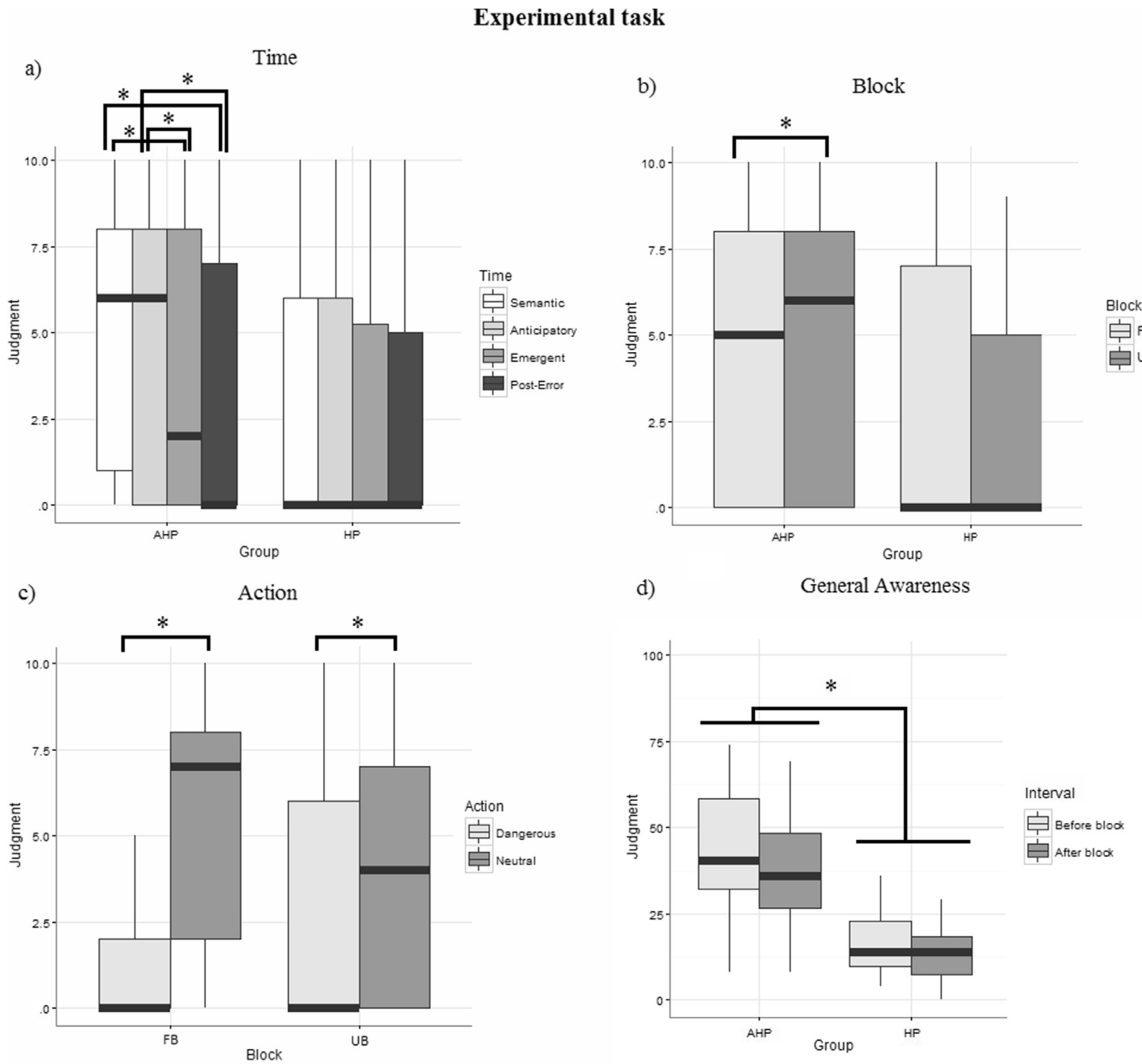


Fig. 3 – Results of the experimental task. The judgments of patients ranging between 0 and 10 as recorded during the task are reported. Lower judgments refer to higher awareness and vice versa higher judgments refer to lower awareness. The box represents the first and the third quartile of data, and the darker line inside is the median. The bottom and the top whiskers are respectively 1.5*Interquartile range lower and 1.5*Interquartile range higher. a) Judgments of the two Groups are reported according to Time, b) Judgments of the two Groups are reported according to Block, c) Judgments of the Blocks are reported according to type of Actions (not separated for Group), d) Total scores at General Awareness Interview. * = Significant results ($p < .01$).

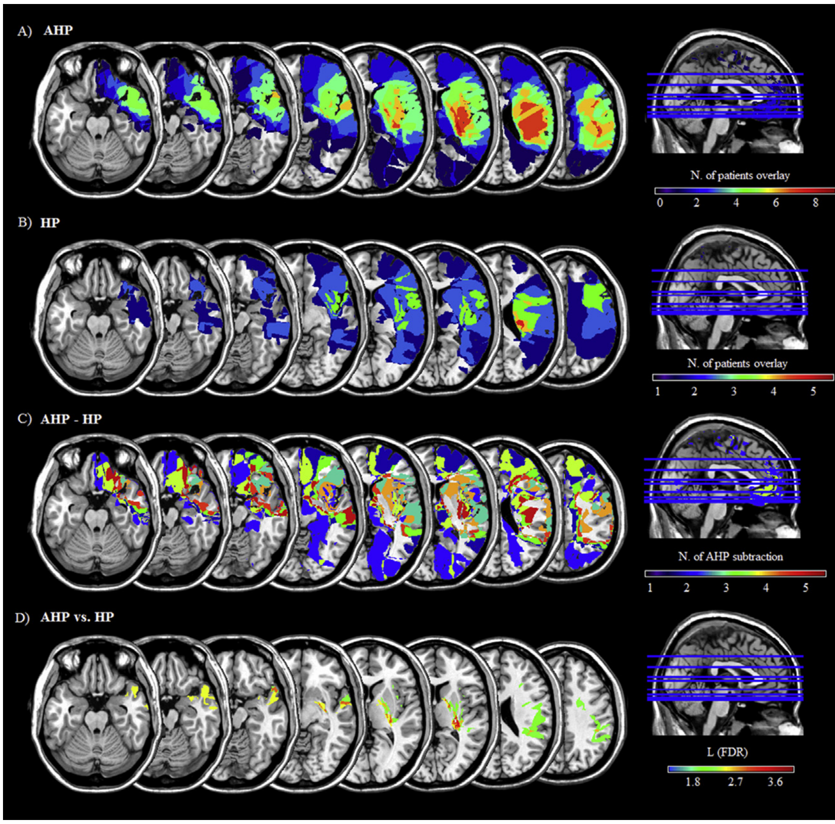
putamen and the amygdale) proved to be damaged in the AHP group. The lesions extended into the white matter, involving in particular the long segment and anterior segments of the right arcuate and the cortical spinal tracts.

3.2.2. *Lesions associated with a lack of emergent awareness*

In order to identify the networks specifically involved when there was no modulation in awareness, we calculated an index of Emergent awareness [(Anticipatory awareness/ Emergent awareness)/Anticipatory awareness]*100. This was computed on the total of the Likert-scale scores for each participant in order to detect any fluctuation between the different kinds of awareness (the ratio between Anticipatory and Emergent awareness) which had been modulated with respect to the initial level of awareness.

Lesion mapping results indicate which damaged area was related to a lower index value, i.e., with a lesser degree of Emergent awareness. This index was used as an independent predictor in a VLSM involving all of the participants (*t*-test statistics).

Although this lesional analysis has an explorative significance, in our patients a lack of Emergent awareness is not



AHP v. HP L(FDR)

E) GREY MATTER

Area	N Voxel	N% Voxel	x	y	z
Precentral Gyrus	2367	8.75	45	-13	47
Rolandic Operculum	980	9.13	51	8	-1
Insula	472	3.34	30	11	-18
Amygdala	165	8.40	32	-6	-11
Inferior Parietal	1805	16.77	37	-50	38
SupraMarginal Gyrus	3866	24.51	43	-37	23
Angular Gyrus	1528	10.92	47	-45	23
Putamen	560	6.58	29	-19	5
Pallidum	396	18.10	20	-3	8
Heschl	62	3.20	37	-22	8
Superior Temporal	1219	4.83	61	2	-10
Superior Temporal P	1658	15.56	54	21	-18
Middle Temporal Po	524	5.53	53	8	-31

F) WHITE MATTER

Area	N Voxel	N% Voxel	x	y	z
Anterior Commissure	542	10.23	31	-5	-11
Arcuate Anterior Segment	3400	40.61	40	-36	21
Long Segment	95	29.30	37	-36	21
Arcuate Posterior Segment	669	8.02	31	-33	10
Cortico Ponto Cerebellarum	298	5.88	28	-27	7
Cortico Spinal	3173	14.38	27	-21	6
Internal Capsule	1019	5.83	29	-27	5
Optic Radiations	405	11.10	30	-24	6
Uncinate	1263	16.78	28	-3	-11

Fig. 4 – Lesion mapping between groups. Mapped lesions displayed in axial view and in a central sagittal slice for: Overlay images of A) AHP patients (center of mass = *x* 30, *y* −10, *z* 20), with bar of index of number of total patients overlaid and B) HP patients (center of mass = *x* 34, *y* −10, *z* 24), with bar of index of number of total patients overlaid. Comparison between the two groups: C) subtraction of the HP groups from the AHP group (center of mass = *x* 29, *y* −9, *z* 19), with bar of index indicating the number of AHP patients who survive to subtraction; and D) results from comparison between two groups at the Liebermeister (*L*) binomial analysis (center of mass = *x* 39, *y* −16, *z* 17), with bar of *L* value (FDR corrected) of significant areas (*p*-value < .05). Statistical results from *L* comparison for E) grey and F) white matter, with number, percentage (%) of voxels for each area and MNI coordinates (only areas with impaired percentage of voxel bigger than 5%). All lesions are in the right hemisphere. The same axial sections are shown in A–D.

associated with specific lesions but is correlated to damage involving a wide fronto-temporo-parietal network, in particular the insula, the ventral inferior frontal area and the temporal lobe. In addition, the basal ganglia, amygdale and white matter around these are damaged (see Fig. 5).

3.2.3. *Lesions associated with reduced effects resulting from attempts to perform actions of a dangerous nature*

To ascertain which damaged areas were involved when the participant's level of awareness did not increase as a result of attempting a potentially dangerous action, the index was computed as: [(Neutral/Dangerous)/Neutral]*100. Again, we considered the fluctuations between different kinds of actions (the ratio between Neutral and Dangerous actions), modulated with respect to the initial level of awareness in Neutral actions.

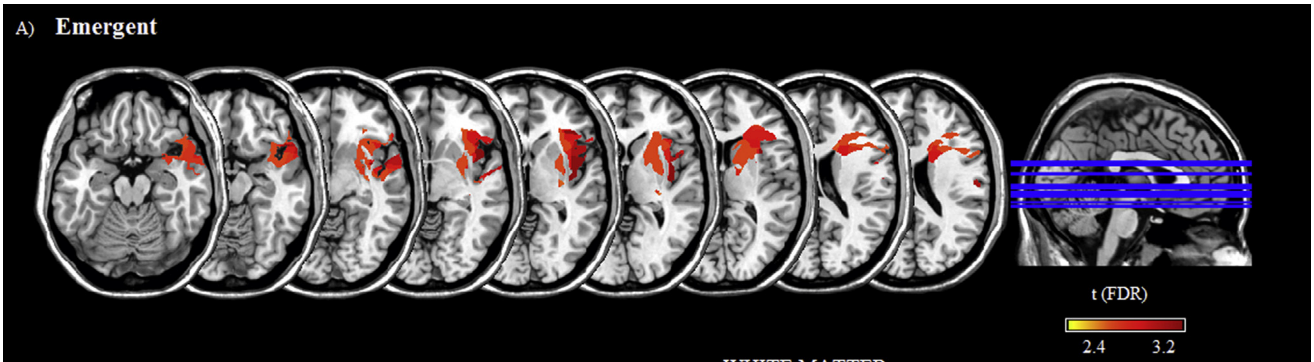
The index was first calculated on the sum of each patient's scores for Anticipatory awareness and then on the sum of the scores for Emergent awareness. We computed two different VLSM (*t*-test statistics) in order to identify the damaged area (lower index) relating to a reduced influence of Dangerous actions on, respectively, Anticipatory and Emergent awareness.

The results regarding the reduced influence of Dangerous actions on Anticipatory awareness indicate that this lack of effect is associated with cortical and subcortical lesions in frontal areas, the insula, the rolandic operculum and the basal ganglia (Fig. 6A–C).

The reduced influence of Dangerous actions on Emergent awareness is associated with damage to the insula, the basal ganglia and amygdale, and the white matter around these structures (Fig. 6D–F).

4. Discussion

Nowadays, it is widely accepted that AHP is a multifaceted syndrome (Fotopoulou, 2015; Orfei et al., 2007; Vuilleumier, 2004) and that residual forms of awareness may be spared in anosognosic patients (Cocchini et al., 2010; Moro et al., 2011).



GREY MATTER

B)

Area	N Voxel	N% Voxel	x	y	z
Inferior Frontal Operculum	1218	10.90	52	22	-1
Inferior Frontal Triangularis	2440	14.24	43	29	-1
Orbital Inferior Frontal gyrus	1314	9.56	51	20	-5
Insula	5889	41.68	40	10	-12
Amygdala	140	7.12	31	-7	-10
Caudate	1640	20.65	22	23	10
Putamen	3493	41.06	26	17	11
Pallidum	457	20.87	28	-5	-5
Superior Temporal	931	3.68	45	0	-8
Superior Temporal Pole	2661	24.98	46	18	-14
Middle Temporal Pole	594	6.27	56	8	-18

WHITE MATTER

C)

Area	N Voxel	N% Voxel	x	y	z
Cortico Spinal	695	3.15	13	-1	6
Inferior Occipital Frontal Fasciculus	1474	11.73	36	4	-9
Internal Capsule	2099	12.01	23	22	10
Uncinate	965	12.82	35	2	-8

Fig. 5 – Lesion mapping with behavioral data for Emergent awareness. A) Lesions associated with a lack of Emergent awareness are displayed in axial view and in a central sagittal slice. *t* value (FDR corrected) of significant areas ($p > .01$) are reported (center of mass = *x* 36, y 14, *z* 6). Table of significant lesions with number and percentage of voxels for each area for B) grey and C) white matter (only areas with impaired percentage of voxel bigger than 3%).

Very recent studies also suggest that modulation of the symptoms is possible by means of specific manipulation, for example changing the patient's perspective of self-observation (Besharati, Kopelman, Avesani, Moro, & Fotopoulou, 2015; Fotopoulou, Holmes, & Kopelman, 2009), activating the intention to act (Moro, Pernigo, et al., 2015; Moro, Scandola, et al., 2015) or inducing specific emotions (Besharati et al., 2014).

The purpose of this study was to investigate the possibility of activating residual forms of awareness by asking the patients to execute everyday actions in specific conditions.

In particular, we focused on: i) the potentially positive influence of attempts to act on patients' awareness of their deficits (Emergent awareness) and ii) the potential impact on anosognosia of attempting to perform actions with dangerous characteristics (Actions of a dangerous nature). Our results support and expand previous data (Moro et al., 2011) indicating that AHP patients may show signs of a form of emergent awareness. In fact, the patients' degree of awareness increases during the actual attempt to act, in comparison to Anticipatory awareness which is present before execution. In addition, the attempt to perform potentially dangerous actions positively influences these effects, independently of the various different phases of the action (semantic, anticipatory, emergent or post-error awareness) and comprising an improvement in awareness in both the AHP and control groups. Finally, an amelioration (although not statistically significant) in the degree of General Awareness (which does not relate directly to the specific actions which were used in the experiment) was recorded after the execution of the experimental tasks. This may be important in terms of devising rehabilitation strategies.

4.1. *The assessment of anosognosia for hemiplegia*

The categorization of our patients as anosognosic or non-anosognosic was initially done based on their scores on the Bisiach scale and in the Berti interview – two well-known and widely used instruments in AHP diagnosis. To overcame some limitations related to the scoring procedures of these instruments, we also considered an intermediate score for the Bisiach scale and the qualitative analysis of patients' statements regarding their paralysis.

We can assume that the two groups of patients really differed in terms of awareness and in effect their performance did differ in the experimental task. Moreover, we administered a further ad-hoc questionnaire in which specific items regarding self-reported proficiency in bimanual and bipedal actions (other than those used in the experimental task) were used as a measure of General Awareness (Marcel et al.'s modified interview, Marcel et al., 2004; Moro et al., 2011). As the scores in this interview ranged from 0 to 100, it offered us the possibility to detect any fluctuation in awareness occurring before and after executing the experimental task.

An analysis of the lesions confirmed the data from previous literature on the topic, in which a wide right fronto-

A) **Dangerous in Anticipatory Awareness**

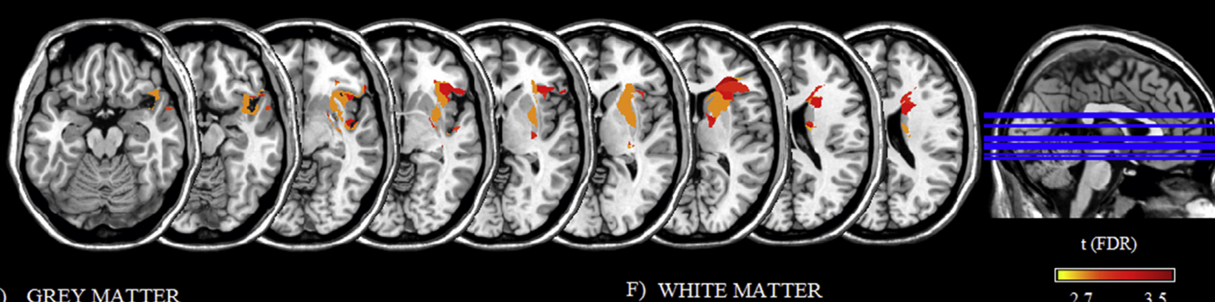
B) GREY MATTER

Area	N Voxel	N% Voxel	x	y	z
Orbital Inferior Frontal gyrus	1278	9.30	51	20	-5
Rolandic Operculum	3153	29.38	51	7	-1
Insula	7230	51.17	40	10	-12
Supramarginal gyrus	1269	8.05	41	-30	25
Caudate	1209	15.22	13	8	8
Putamen	3552	41.74	29	-16	10
Pallidum	154	7.04	19	0	7
Heschl gyrus	658	33.98	45	-12	5
Superior Temporal	773	3.06	45	0	-8
Superior Temporal Pole	1009	9.47	46	18	-14

C) WHITE MATTER

Area	N Voxel	N% Voxel	x	y	z
Arcuate Anterior Segment	3985	47.60	43	-3	15
Long Segment	138	35.29	35	-29	22
Cortico Spinal	1297	5.88	27	-11	10
Inferior Occipital Frontal Fasciculus	1064	8.47	36	4	-9
Internal Capsule	1604	9.18	26	4	21
Uncinate	328	4.36	35	2	-8

D) **Dangerous in Emergent Awanreness**



E) GREY MATTER

Area	N Voxel	N% Voxel	x	y	z
Inferior Frontal Triangularis	1544	9.01	38	38	5
Orbital Inferior Frontal gyrus	1225	8.91	42	19	-14
Insula	2735	19.36	41	14	-13
Amygdala	71	3.61	30	-8	-11
Caudate	1773	22.33	14	13	16
Putamen	3146	36.97	26	17	11
Pallidum	297	13.57	28	-8	-5
Superior Temporal Pole	542	5.09	45	18	-14

F) WHITE MATTER

Area	N Voxel	N% Voxel	x	y	z
Cortico Spinal	740	3.35	15	2	10
Inferior Occipital Frontal Fasciculus	1153	9.17	36	-25	-5
Internal Capsule	1963	11.24	26	29	15
Uncinate	346	4.60	25	-2	-7

Fig. 6 – Lesion mapping with behavioral data for actions of a dangerous nature. Two different VSLM separate analyses of lack of Dangerous effect in Anticipatory and Emergent actions showed similar results: A) Lesions of lack of Dangerous effect in Anticipatory awareness (center of mass = *x* 37, *y* 0, *z* 11). Table of significant lesions with number and percentage of voxels for each area for B) grey and C) white matter. D) Lesions of lack of Dangerous effect in Emergent awareness (center of mass = *x* 30, *y* 16, *z* 5). Table of significant lesions with number and percentage of voxels for each area for E) grey and F) white matter. The statistical lesions are shown in axial view and in the middle sagittal slice, t-value (FDR corrected) are reported only for significant areas ($p > .01$) and only areas with impaired percentage of voxel bigger than 3%.

temporo-parietal network is usually associated with AHP(Pia et al., 2004). In this network a main role is attributed to the ventral frontal areas (Berti et al., 2005; Fotopoulou et al., 2010; Kortte et al., 2015), the insula (Fotopoulou et al., 2010; Karnath et al., 2005; Moro, Pernigo et al., 2016; Vocat et al., 2010), but also of subcortical structures such as the basal ganglia and amygdale (Fotopoulou et al., 2010; Moro et al., 2011; Vocat et al., 2010) and the white matter around them (Moro, Pernigo et al., 2016).

We also found lesions in the supramarginal gyrus and inferior parietal cortex. This indicates that in this AHP group the damage was spread in a more posterior and cortical direction with respect to previous studies (Berti et al., 2005; Fotopoulou et al., 2010; Karnath et al., 2005; Moro, Pernigo et al., 2016; Moro et al., 2011).

The cortical parietal damage also explains the presence of visual spatial neglect which was recorded in all of the patients in the AHP group (Bartolomeo, de Schotten, & Chica, 2012; Moro, Pernigo et al., 2016 in Supplementary materials).

A hypothesis regarding a more general disorder in the ability to monitor motor actions has been proposed (Saj, Vocat, & Vuilleumier, 2014). As a comparison between the judgments of the AHP group with reference to themselves as compared to others (shown in SM) did not show significant differences, we cannot totally exclude this interpretation. Nevertheless, observing the performance of each individual patient provided confirmation of the results of a previous study concerning the existence of a dissociation (Moro et al., 2011). In fact, although four out of seven patients in this study (one of them did not perform the other-referred task) showed symptoms of AHP both in the self- and other referred conditions, two patients displayed a significantly greater degree of anosognosia in the self-referred condition and one in other-referred condition.

Finally, the FB actions were judged to be more difficult than the actions involving only the upper limbs (UB). Our results may be at least in part explained by the fact that the motor deficit in lower limbs was evident in our patients who were all in a wheelchair. This seems to be in apparent contrast with the results of the Berti scale, in which AHP patients seem to be more anosognosic with reference to their lower than their upper limbs. In reality, the performance rating on that scale for upper and lower limbs are not comparable since for the lower limb there is no confrontation task while there is for the upper limb (i.e., after being questioned about their ability to walk, the patients were not asked to actually try as they were for the upper limb). In addition, the patients were given daily training in FB actions during the rehabilitation sessions, while most of the bimanual actions were not performed by the patients during their stay in hospital. Thus, we cannot exclude the possibility that some learning mechanisms relating to their difficulty in performing those actions might contribute to an implicit update in their autobiographical memory (the Personal Data Base, Morris & Mograbi, 2013). However, these everyday experiences in rehabilitation training were not enough to make AHP patients aware of their paralysis, as they were anosognosic with regard to both upper and full body actions. As a difference between full-body and upper body actions was only manifested by the AHP group (and not the HP group), we exclude the possibility that this depended on a general difference in the degree of difficulty relating to the FB actions as compared to the UB actions.

Hence it is important not to consider AHP as an all-or-nothing phenomenon. It is a multifaceted, complex syndrome that needs to be assessed in a variety of contexts, at different times and with several different methods (Nurmi & Jehkonen, 2014 for review). When it is properly investigated, the issue of fluctuations in symptoms may be addressed in order to help patients to increase awareness (Besharati et al., 2015; Moro, Pernigo, et al., 2015; Moro, Scandola, et al., 2015).

4.2. *Emergent awareness*

Emergent Awareness in AHP has been described (Moro et al., 2011; Moro, Scandola, et al., 2015) as the explicit awareness that emerges during an attempt to act. It may be detected when AHP patients become more aware of their own deficits when they are asked to actually perform actions or to explain the reasons why they fail.

The concept originates from the hierarchical model of awareness devised by Crosson and colleagues (Crosson et al., 1989; Moro et al., 2011; Orfei et al., 2007). This describes three levels of awareness: (1) intellectual awareness, i.e., the generic ability to recognize a deficit (e.g., "I suffered a stroke"); (2) emergent awareness, in which a patient becomes declaratively aware of his/her deficits only when asked to perform an action with the affected body part (i.e., by means of a "confrontation": e.g., "I thought I was able to do this action, but now I'm realizing it is impossible for me") and (3) anticipatory awareness, i.e., the ability to anticipate the effects of a deficit, i.e., admitting the inability to perform an action before it becomes evident in a real situation (e.g., stating beforehand: "I cannot jump because of my paralysis"). This model posits a hierarchical relation between the three levels so that anticipatory awareness is thought of as the highest level (and thus the first to be affected in cases of AHP) which is followed by emergent and then intellectual awareness. However, in cases of AHP it is possible that individual patients may show varying degrees of deficit in these three forms of awareness (Marcel et al., 2004; Moro et al., 2011).

The first study which tested this theory in AHP demonstrated empirically that when patients were asked to perform movements with their affected body parts, emergent awareness was manifested in a group of patients who were more generally unaware of their deficits (Moro et al., 2011). This finding suggests that intellectual and perhaps even anticipatory awareness may increase as a result of failed attempts to perform an action.

The efficacy of this approach has also been confirmed in a study of rehabilitation where a specific error-based program was administered to four AHP patients (Moro, Scandola, et al., 2015). Unfortunately, the number of patients involved in both of these previous studies was small and only bimanual actions were employed. Thus, further data were required in order to confirm and expand this initial evidence.

In line with the data resulting from these two studies, the AHP patients in the present study judged their ability to perform actions as being worse when they were actually placed in a real condition to act in comparison to the judgment that they gave during a preliminary out-of-context interview (Semantic Awareness) or before being placed in a situation where they were required to act (Anticipatory Awareness). This improvement in awareness was also present after the execution of the action, when patients compared their previous judgment with their failure to perform (Post-Error awareness).

The Forward Dynamic model helps to explain our results. According to this model, motor awareness is based on the congruence between action planning and the prediction of the sensory consequences of the same action. When a given movement does not occur as intended and planned, a mismatch between predicted and actual sensory feedback is detected by a brain comparator that brings about conscious awareness of an error (Blakemore, Frith, & Wolpert, 2001; Fotopoulou et al., 2008). In AHP, the symptoms derive from a defective functioning of the comparator which for some reason is incapable of detecting this mismatch (Bottini et al., 2010; Fotopoulou et al., 2008). In this framework, we consider that the intention to act combined with the request to evaluate performance may have an important role in the patient's capacity to monitor any discordance between the original intention and the sensory feedback thus contributing toward an improvement in Emergent awareness (Moro et al., 2011). The process induces the use of cognitive and metacognitive strategies and executive processes (necessary for the intention, and the monitoring and evaluation of performance) which are not spontaneously activated in AHP patients. This can be a very important resource for recovery.

4.3. *The effect of potentially dangerous actions*

It is well known that the characteristics of a stimulus and the emotions these characteristics arouse have an impact. For example, there is previous evidence that the emotional nature of the stimuli used may implicitly influence and often enhance a patient's performance in some various neuropsychological conditions, such as neglect, visual extinction and prosopagnosia (Moro et al., 2012; Vuilleumier & Schwartz, 2001; Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004; Vuilleumier et al., 2002; de Gelder, Frissen, Barton, & Hadjikhani, 2003). The presence of dangerous objects also interferes with movements by evoking a specific aversive affordance (Anelli, Borghi, & Nicoletti, 2012; Anelli, Nicoletti, Bolzani, & Borghi, 2013) which probably has the main purpose of preparing the motor networks to act in order to protect the self (Azevedo et al., 2005; Bradley, Codispoti, Cuthbert, & Lang, 2001). Dangerous stimuli may also be efficacious as they improve the impaired motor control of involuntary movements, as shown in a patient suffering from anarchic hand and magnetic apraxia, where involuntary grasping and groping significantly reduced in the presence of dangerous objects (e.g., a piece of broken glass) but not in the presence of neutral objects (e.g., a glass) (Moro, Pernigo, et al., 2015).

This modulation of the emotions is thought to be based on the direct modulatory effects of subcortical structures (in particular the amygdale) that promote the processing of emotionally salient events (Amaral & Price, 1984; Sah, Faber, Lopez de Armentia, & Power, 2003; Vuilleumier et al., 2004).

The role of emotional and motivational components in AHP has been investigated a number of times (Bisiach & Geminiani, 1991; Ramachandran, 1996; Vuilleumier, 2004) and the difficulty which AHP patients have in accepting and tolerating an aversive emotional status has been interpreted as a problem concerning the emotional-regulation system of negative feelings relating to the self (Kaplan-Solms, 2000; Turnbull, Evans, & Owen, 2005; Turnbull, Jones, & Reed-Screen, 2002).

According to the “defense” theory (e.g., Weinstein & Kahn, 1950, 1955), the misattribution of negative emotions may be related to a refusal to explicitly acknowledge a person's own deficits. However, when spared, a certain degree of implicit knowledge of deficits could induce a process of repression (Anderson & Green, 2001). This latter hypothesis has been confirmed in recent studies showing that AHP patients can evoke implicit negative emotional reactions when given information regarding their hemiplegia and this then interferes with their performance in attentional (Nardone et al., 2008) or verbal-inhibition tasks (Fotopoulou et al., 2010).

Our results confirm these data and expand them by providing evidence of the positive effect of potentially dangerous actions resulting in a greater degree of explicit awareness of hemiplegia. Interestingly, the effect of potentially dangerous actions was seen in both groups in the present study, suggesting that the processes underlying protective activation or alerting may be spared in AHP patients. Emotional negative stimuli have been found to have an activating role in a recent study (Besharati et al., 2014) that investigated the influence of emotions on explicit awareness. In this outstanding paradigm, negative or positive self-referential emotions were induced by giving, respectively, disapproving or approving social feedback to the participants about their performance. Although the AHP patients were capable of experiencing both negative and positive feelings, only the former induced a temporary improvement in explicit self-awareness (Besharati et al., 2014). Nevertheless, as potentially dangerous actions alter judgments of proficiency in both the AHP and HP groups, we cannot exclude the possibility that some action avoidance processes come into effect (Turnbull, Fotopoulou, & Solms, 2014). In fact, potentially dangerous actions are avoided, if possible, by everyone and the patients' responses may simply reflect an escape reaction manifested in their claim that they are not able to perform the action. In this case, rather than an increase in awareness, the emotional response to dangerous actions would simply match the patients' real incapacity to act, meaning that the response is only apparently an index of awareness. Unfortunately, this hypothesis was not investigated in the present study.

Another interesting result is that actions with dangerous attributes have an effect on all kinds of awareness, not only when the action is in progress (Emergent awareness) but also before the action starts (Semantic and Anticipatory awareness). It is thus possible that, in addition to the subcortical emotional processes linked to action planning, more top-down, semantic factors (i.e., knowledge of the danger involved in a action) influence the effect.

In a similar way, neuro-anatomical studies have shown that the representation of actions involving dangerous stimuli is associated with a cortical activation in a general network (Baumgartner, Willi, & Jäncke, 2007; Hajcak et al., 2007; Oliveri et al., 2004) that integrates emotional information with behavioral and cognitive motor responses (Pessoa & Adolphs, 2010). Both subcortical areas, such as the basal ganglia (Butler et al., 2007; Phelps et al., 2001), amygdale and putamen (Romano, Gandola, Bottini, & Maravita, 2014), and cortical regions probably contribute in a fronto-insula/limbic inhibitory regulation (Phelps et al., 2001; Sierra & Berrios, 1998). Our analyses of the lesions are mainly explorative, due to the small number of patients, but they support this hypothesis. In fact, the lack of an ameliorative effect resulting from a request to perform a potentially dangerous action (in particular with reference to the responses relating to Emergent awareness) is significantly linked to damage to the basal ganglia and amygdale (Hormigo, Vega-Flores, & Castro-Alamancos, 2016) and in the white matter underlying the insula and fronto-temporal areas.

In the present study, the awareness of the AHP patients increased to a greater degree with FB as compared to UB actions. This is particularly interesting since FB actions (e.g., standing up or walking) are in fact potentially dangerous only for patients suffering from paralysis while UB actions may be dangerous for everybody (e.g., putting a nail in a wooden block or lighting a candle). This might represent an index of some residual forms of implicit awareness (see also Fotopoulou et al., 2010; Nardone et al., 2008).

An implicit bodily response to potentially dangerous stimuli has been found in a recent study (Romano et al., 2014) where the anticipatory reaction of skin conductance to threatening stimuli was recorded in hemiplegic and somatoparaphrenic patients, subjects with hemiplegia and anosognosia for hemianesthesia and hemiplegic patients without deficits in body representations. Crucially, the authors found a reduced conductance response in the somatoparaphrenic patients, specifically relating to the contralesional arm which they considered did not belong to their body. In contrast, anosognosic patients showed implicit responses which were analogous to those of patients who only suffered from paralysis.

4.4. *Limitations and conclusions*

This study has some limitations. As with most studies on AHP, the number of patients is small. This is mainly due to the rarity of the syndrome and the difficulty of finding patients with a sufficient degree of attention, which was necessary to complete the task. Unfortunately we could not examine in depth the level of anxiety and depression in the patients and the data from the HADS were not available for all of them. Nevertheless, clinicians did not identify specific problems relating to mood or anxiety in the patients recruited for the study.

Taking everything into consideration, our results confirm the existence of various different forms of awareness and the possibility of activating residual emergent awareness in order to restore an explicit recognition of the patient's motor deficits. Attempting actions and a subsequent analysis of the motor errors which have occurred (with adequate emotional support) might be crucial in the recovery from anosognosia (Moro, Pernigo, et al., 2015; Moro, Scandola, et al., 2015), especially in contexts which do not offer effective training programs (Kortte & Hillis, 2011; see; Jenkinson, Preston, & Ellis, 2011; Prigatano & Morrone-Strupinsky, 2010; but see; Besharati et al., 2015). Our experiment provides new evidence regarding the influence of the emotional and motivational components of actions on AHP (as in Besharati et al., 2014) and is thus potentially useful in rehabilitation.

Acknowledgments

We thank Valeria Gobbetto for her help in collecting data and Flaminia Giarola for her help in recruiting the patients. VM is funded by University of Verona, Italy (Bando di Ateneo per la Ricerca di Base 2015). DD is funded by Sapienza University of Rome, Italy.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.cortex.2017.04.009.

REFERENCES

Agresti, A. (2002). Logit models for multinomial responses. *Categorical Data Analysis* (2nd ed., pp. 267–313).

Amaral, D. G., & Price, J. L. (1984). Amygdalo-cortical projections in the monkey (*Macaca fascicularis*). *Journal of Comparative Neurology, 230*(4), 465–496.

Anderson, M. C., & Green, C. (2001). Suppressing unwanted memories by executive control. *Nature, 410*(6826), 366–369.

Anelli, F., Borghi, A. M., & Nicoletti, R. (2012). Grasping the pain: Motor resonance with dangerous affordances. *Consciousness and Cognition, 21*(4), 1627–1639.

Anelli, F., Nicoletti, R., Bolzani, R., & Borghi, A. M. (2013). *Keep away from danger: Dangerous objects in dynamic and static situations*.

Appollonio, I., Leone, M., Isella, V., Piamarta, F., Consoli, T., Villa, M. L., et al. (2005). The Frontal Assessment Battery (FAB): Normative values in an Italian population sample. *Neurological Sciences, 26*(2), 108–116.

Azevedo, T. M., Volchan, E., Imbiriba, L. A., Rodrigues, E. C., Oliveira, J. M., Oliveira, L. F., … Vargas, C. D. (2005). A freezing-like posture to pictures of mutilation. *Psychophysiology, 42*(3), 255–260.

Babinski, J. (1914). Contribution e l'etude des troubles mentaux dans hemiplegie organique cerebrale (anosognosia) [contribution to the study of mental disorders in hemiplegia (anosognosia)]. *Revue Neurologique, 27*, 845–848.

Bartolomeo, P., De Schotten, M. T., & Chica, A. B. (2012). Brain networks of visuospatial attention and their disruption in visual neglect. *Frontiers in Human Neuroscience, 6*(110), 1–10.

Bates, D., Kliegl, R., Vasishth, S., & Baayen, H. (2015). *Parsimonious mixed models*. arXiv preprint arXiv:1506.04967.

Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., et al. (2003). Voxel-based lesion–symptom mapping. *Nature Neuroscience, 6*(5), 448–450.

Baumgartner, T., Willi, M., & Jäncke, L. (2007). Modulation of corticospinal activity by strong emotions evoked by pictures and classical music: A transcranial magnetic stimulation study. *NeuroReport, 18*(3), 261–265.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society B, 57*, 289–300.

Berti, A., Bottini, G., Gandola, M., Pia, L., Smania, N., Stracciari, A., … Paulesu, E. (2005). Shared cortical anatomy for motor awareness and motor control. *Science, 309*(5733), 488–491.

Berti, A., Làdavas, E., & Della Corte, M. (1996). Anosognosia for hemiplegia, neglect dyslexia, and drawing neglect: Clinical

findings and theoretical considerations. *Journal of the International Neuropsychological Society, 2*(05), 426–440.
Besharati, S., Forkel, S. J., Kopelman, M., Solms, M., Jenkinson, P. M., & Fotopoulou, A. (2014). The affective modulation of motor awareness in anosognosia for hemiplegia: Behavioural and lesion evidence. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 61*, 127–140.
Besharati, S., Kopelman, M., Avesani, R., Moro, V., & Fotopoulou, A. (2015). Another perspective on anosognosia: Self-observation in video replay improves motor awareness. *Neuropsychological Rehabilitation, 25*(3), 319–352.
Bisiach, E., & Geminiani, G. (1991). Anosognosia related to hemiplegia and hemianopia. In *Awareness of deficit after brain injury* (pp. 17–39).
Bisiach, E., Vallar, G., Perani, D., Papagno, C., & Berti, A. (1986). Unawareness of disease following lesions of the right hemisphere: Anosognosia for hemiplegia and anosognosia for hemianopia. *Neuropsychologia, 24*(4), 471–482.
Blakemore, S. J., Frith, C. D., & Wolpert, D. M. (2001). The cerebellum is involved in predicting the sensory consequences of action. *NeuroReport, 12*(9), 1879–1884.
Bonferroni, C. E. (1936). *Teoria statistica delle classi e calcolo delle probabilita*. Libreria internazionale Seeber.
Bottini, G., Paulesu, E., Gandola, M., Pia, L., Invernizzi, P., & Berti, A. (2010). Anosognosia for hemiplegia and models of motor control: Insights from lesional data. *The Study of Anosognosia*, 363–379.
Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: Defensive and appetitive reactions in picture processing. *Emotion, 1*(3), 276.
Butler, T., Pan, H., Tuescher, O., Engelien, A., Goldstein, M., Epstein, J., … Chang, L. (2007). Human fear-related motor neurocircuitry. *Neuroscience, 150*(1), 1–7.
Catani, M., & de Schotten, M. T. (2012). *Atlas of human brain connections*. Oxford University Press.
Christensen, R. H. B., & Christensen, M. R. H. B. (2015). *Package 'ordinal'*.
Cocchini, G., Beschin, N., Cameron, A., Fotopoulou, A., & Della Sala, S. (2009). Anosognosia for motor impairment following left brain damage. *Neuropsychology, 23*, 223–230.
Cocchini, G., Beschin, N., Fotopoulou, A., & Della Sala, S. (2010). Explicit and implicit anosognosia or upper limb motor impairment. *Neuropsychologia, 48*, 1489–1494.
Cocchini, G., & Della Sala, S. (2010). Assessing anosognosia for hemiplegia for motor and language impairment. In G. P. Prigatano (Ed.), *The study of anosognosia*. New York: Oxford University Press.
Crosson, B., Barco, P. P., Velozo, C. A., Bolesta, M. M., Cooper, P. V., Werts, D., et al. (1989). Awareness and compensation in postacute head injury rehabilitation. *The Journal of Head Trauma Rehabilitation, 4*(3), 46–54.
Davies, M., Davies, A. A., & Coltheart, M. (2005). Anosognosia and the two-factor theory of delusions. *Mind & Language, 20*(2), 209–236.
Della Sala, S., Cocchini, G., Beschin, N., & Cameron, A. (2009). Vata-m: Visual-analogue test assessing anosognosia for motor impairment. *The Clinical Neuropsychologist, 23*(3), 406–427.
Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189–198.
Fotopoulou, A. (2015). The virtual bodily self: Mentalisation of the body as revealed in anosognosia for hemiplegia. *Consciousness and Cognition, 33*, 500–510.
Fotopoulou, A., Pernigo, S., Maeda, R., Rudd, A., & Kopelman, M. A. (2010). Implicit awareness in anosognosia for hemiplegia: Unconscious interference without conscious representation. *Brain: a Journal of Neurology, 133*(12), 3564–3577.
Fotopoulou, A., Rudd, A., Holmes, P., & Kopelman, M. (2009). Self-observation reinstates motor awareness in anosognosia for hemiplegia. *Neuropsychologia, 47*(5), 1256–1260.
Fotopoulou, A., Tsakiris, M., Haggard, P., Vagopoulou, A., Rudd, A., & Kopelman, M. (2008). The role of motor intention in motor awareness: An experimental study on anosognosia for hemiplegia. *Brain: a Journal of Neurology, 131*(12), 3432–3442.
de Gelder, B., Frissen, I., Barton, J., & Hadjikhani, N. (2003). A modulatory role for facial expressions in prosopagnosia. *Proceedings of the National Academy of Sciences, 100*(22), 13105–13110.
Gialanella, B., Monguzzi, V., Santoro, R., & Rocchi, S. (2005). Functional recovery after hemiplegia in patients with neglect: The rehabilitation role of anosognosia. *Stroke; a Journal of Cerebral Circulation, 36*, 2687–2690.
Hajcak, G., Molnar, C., George, M. S., Bolger, K., Koola, J., & Nahas, Z. (2007). Emotion facilitates action: A transcranial magnetic stimulation study of motor cortex excitability during picture viewing. *Psychophysiology, 44*(1), 91–97.
Heilman, K. M. (1991). Anosognosia: Possible neuropsychological mechanisms. In *Awareness of Deficit After Brain Injury: Clinical and Theoretical Issues* (pp. 53–62).
Heilman, K. M., & Harciarek, M. (2010). Anosognosia and anosodiaphoria of weakness. *The Study of Anosognosia*, 89–112.
Hormigo, S., Vega-Flores, G., & Castro-Alamancos, M. A. (2016). Basal ganglia output controls active avoidance behavior. *Journal of Neuroscience, 36*(40), 10274–10284.
Jehkonen, M., Laihosalo, M., & Kettunen, J. E. (2006a). Impact of neglect on functional outcome after stroke–a review of methodological issues and recent research findings. *Restorative Neurology and Neuroscience, 24*(4–6), 209–215.
Jehkonen, M., Laihosalo, M., & Kettunen, J. (2006b). Anosognosia after stroke: Assessment, occurrence, subtypes and impact on functional outcome reviewed. *Acta Neurologica Scandinavica, 114*, 293–306.
Jenkinson, P. M., Preston, C., & Ellis, S. J. (2011). Unawareness after stroke: A review and practical guide to understanding, assessing, and managing anosognosia for hemiplegia. *Journal of Clinical and Experimental Neuropsychology, 33*(10), 1079–1093.
Kaplan-Solms, K. (2000). *Clinical studies in neuro-psychoanalysis: Introduction to a depth neuropsychology*. Karnac Books.
Karnath, H. O., Baier, B., & Nägele, T. (2005). Awareness of the functioning of one's own limbs mediated by the insular cortex? *The Journal of Neuroscience, 25*(31), 7134–7138.
Kortte, K. B., & Hillis, A. E. (2011). Recent trends in rehabilitation interventions for visual neglect and anosognosia for hemiplegia following right hemisphere stroke. *Future Neurology, 6*(1), 33–43.
Kortte, K. B., McWhorter, J. W., Pawlak, M. A., Slentz, J., Sur, S., & Hillis, A. E. (2015). Anosognosia for hemiplegia: The contributory role of right inferior frontal gyrus. *Neuropsychology, 29*(3), 421.
Lenth, R. V. (2016). Least-squares means: the R Package lsmeans. *Journal of Statistical Software, 69*, 1–33.
Marcel, A. J., Tegnér, R., & Nimmo-Smith, I. (2004). Anosognosia for plegia: Specificity, extension, partiality and disunity of bodily unawareness. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 40*(1), 19–40.
McCullagh, P., & Nelder, J. A. (1989). In *Generalized linear models* (Vol. 37). CRC Press.
McIntosh, R. D., Brodie, E. E., Beschin, N., & Robertson, I. H. (2000). Improving the clinical diagnosis of personal neglect: A reformulated comb and razor test. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 36*(2), 289–292.
Medical Research Council. (1986). *Aids to the examination of the peripheral nervous system*. London: Bailliere Tindall.

Moro, V. (2013). The interaction between implicit and explicit awareness in anosognosia: Emergent awareness. *Cognitive Neuroscience, 4*(3–4), 199–200.

Moro, V., Pernigo, S., Avesani, R., Bulgarelli, C., Urgesi, C., Candidi, M., et al. (2012). Visual body recognition in a prosopagnosic patient. *Neuropsychologia, 50*(1), 104–117.

Moro, V., Pernigo, S., Scandola, M., Mainente, M., Avesani, R., & Aglioti, S. M. (2015). Contextual bottom-up and implicit top-down modulation of anarchic hand syndrome: A single-case report and a review of the literature. *Neuropsychologia, 78*, 122–129.

Moro, V., Pernigo, S., Tsakiris, M., Avesani, R., Edelstyn, N. M., Jenkinson, P. M., et al. (2016). Motor versus body awareness: Voxel-based lesion analysis in anosognosia for hemiplegia and somatoparaphrenia following right hemisphere stroke. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 83*, 62–77.

Moro, V., Pernigo, S., Zapparoli, P., Cordioli, Z., & Aglioti, S. M. (2011). Phenomenology and neural correlates of implicit and emergent motor awareness in patients with anosognosia for hemiplegia. *Behavioural Brain Research, 225*(1), 259–269.

Moro, V., Scandola, M., Bulgarelli, C., Avesani, R., & Fotopoulou, A. (2015). Error-based training and emergent awareness in anosognosia for hemiplegia. *Neuropsychological Rehabilitation, 25*(4), 593–616.

Moro, V., Zampini, M., & Aglioti, S. M. (2004). Changes in spatial position of hands modify tactile extinction but not disownership of contralesional hand in two right brain-damaged patients. *Neurocase, 10*(6), 437–443.

Morris, R. G., & Mograbi, D. C. (2013). Anosognosia, autobiographical memory and self knowledge in Alzheimer's disease. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 49*(6), 1553–1565.

Nardone, I. B., Ward, R., Fotopoulou, A., & Turnbull, O. H. (2008). Attention and emotion in anosognosia: Evidence of implicit awareness and repression? *Neurocase, 13*(5–6), 438–445.

Nurmi, M. E., & Jehkonen, M. (2014). Assessing anosognosias after stroke: A review of the methods used and developed over the past 35 years. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 61*, 43–63.

Oliveri, M., Finocchiaro, C., Shapiro, K., Gangitano, M., Caramazza, A., & Pascual-Leone, A. (2004). All talk and no action: A transcranial magnetic stimulation study of motor cortex activation during action word production. *Journal of Cognitive Neuroscience, 16*(3), 374–381.

Orfei, M. D., Robinson, R. G., Prigatano, G. P., Starkstein, S., Rüsch, N., Bria, P., … Spalletta, G. (2007). Anosognosia for hemiplegia after stroke is a multifaceted phenomenon: A systematic review of the literature. *Brain: a Journal of Neurology, 130*(12), 3075–3090.

Pessoa, L., & Adolphs, R. (2010). Emotion processing and the amygdala: From a 'low road' to 'many roads' of evaluating biological significance. *Nature Reviews Neuroscience, 11*(11), 773–783.

Phelps, E. A., O'Connor, K. J., Gatenby, J. C., Gore, J. C., Grillon, C., & Davis, M. (2001). Activation of the left amygdala to a cognitive representation of fear. *Nature Neuroscience, 4*(4), 437–441.

Pia, L., Neppi-Modona, M., Ricci, R., & Berti, A. (2004). The anatomy of anosognosia for hemiplegia: A meta-analysis. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 40*(2), 367–377.

Prigatano, G. P., & Morrone-Strupinsky, J. (2010). Advancing the profession of clinical neuropsychology with appropriate outcome studies and demonstrated clinical skills. *Clinical Neuropsychology, 24*(3), 468–480.

Ramachandran, V. S. (1996). The evolutionary biology of self-deception, laughter, dreaming and depression: Some clues from anosognosia. *Medical Hypotheses, 47*(5), 347–362.

Ramachandran, V. S., & Rogers-Ramachandran, D. (1996). Denial of disabilities in anosognosia. *Nature, 582*, 301.

Romano, D., Gandola, M., Bottini, G., & Maravita, A. (2014). Arousal responses to noxious stimuli in somatoparaphrenia and anosognosia: Clues to body awareness. *Brain: a Journal of Neurology, 137*(Pt 4), 1213–1223.

Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioural Neurology, 12*(4), 191–200.

Rorden, C., Karnath, H. O., & Bonilha, L. (2007). Improving lesion-symptom mapping. *Journal of cognitive neuroscience, 19*(7), 1081–1088.

Sah, P., Faber, E. L., De Armentia, M. L., & Power, J. (2003). The amygdaloid complex: Anatomy and physiology. *Physiological Reviews, 83*(3), 803–834.

Saj, A., Vocat, R., & Vuilleumier, P. (2014). Action-monitoring impairment in anosognosia for hemiplegia. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 61*, 93–106.

de Schotten, M. T., Bizzi, A., Dell'Acqua, F., Allin, M., Walshe, M., Murray, R., … Catani, M. (2011). Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with MR diffusion tractography. *NeuroImage, 54*(1), 49–59.

Sierra, M., & Berrios, G. E. (1998). Depersonalization: Neurobiological perspectives. *Biological Psychiatry, 44*(9), 898–908.

Spinnler, H., & Tognoni, G. (1987). Italian group on the neuropsychological study of ageing: Italian standardization and classification of neuropsychological tests. *The Italian Journal of Neuropsychological Sciences, 6*(Suppl. 8), 1–120.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain. 3-Dimensional proportional system: An approach to cerebral imaging*.

Turnbull, O. H., Evans, C. E., & Owen, V. (2005). Negative emotions and anosognosia. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 41*(1), 67–75.

Turnbull, O. H., Fotopoulou, A. K., & Solms, M. (2014). Anosognosia as motivated unawareness: The 'defence' hypothesis revisited. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 61*, 18–29.

Turnbull, O. H., Jones, K., & Reed-Screen, J. (2002). Implicit awareness of deficit in anosognosia? An emotion-based account of denial of deficit. *Neuropsychoanalysis, 4*(1), 69–87.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., … Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage, 15*(1), 273–289.

Vocat, R., Staub, F., Stroppini, T., & Vuilleumier, P. (2010). Anosognosia for hemiplegia: A clinical-anatomical prospective study. *Brain: a Journal of Neurology, 133*(12), 3578–3597.

Vuilleumier, P. (2004). Anosognosia: The neurology of beliefs and uncertainties. *Cortex; a Journal Devoted To the Study of the Nervous System and Behavior, 40*(1), 9–17.

Vuilleumier, P., Armony, J. L., Clarke, K., Husain, M., Driver, J., & Dolan, R. J. (2002). Neural response to emotional faces with and without awareness: Event-related fMRI in a parietal patient with visual extinction and spatial neglect. *Neuropsychologia, 40*(12), 2156–2166.

Vuilleumier, P., Richardson, M. P., Armony, J. L., Driver, J., & Dolan, R. J. (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. *Nature Neuroscience, 7*(11), 1271–1278.

Vuilleumier, P., & Schwartz, S. (2001). Emotional facial expressions capture attention. *Neurology, 56*(2), 153–158.

Weinstein, E. A., & Kahn, R. L. (1950). The syndrome of anosognosia. *AMA Archives of Neurology & Psychiatry, 64*(6), 772–791.

Weinstein, E. A., & Kahn, R. L. (1955). *Denial of illness: Symbolic and physiological aspects*.

Wilson, B., Cockburn, J., & Halligan, P. W. (1987). *Behavioural inattention test*. Titchfield, Hampshire, UK: Thames Valley Test Company.

World Medical Association. (2013). World Medical Association declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA, 310*(20), 2191.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*(6), 361–370.