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**Restoring awareness: a review of rehabilitation in anosognosia for hemiplegia**

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## Abstract

Disturbances in body awareness offer important insights into neurocognitive processes involved in the construction of the bodily self. This review will focus on a specific disorder of awareness, namely, anosognosia for hemiplegia (AHP), or the denial of motor deficits contralateral to a brain lesion. Recently some progress has been made towards the management and rehabilitation of AHP, however to date no evidence-based treatment exists. Firstly, recent research on AHP will be reviewed, with the aim of providing an overview of the etiology, clinical presentation and assessment of the syndrome, as well as the major neurological and neuropsychological explanations of the syndrome. This article will then focus on recent advances in the management and rehabilitation of AHP, using a case study example of intervention-based (i.e. video replay) motor awareness recovery (Fotopoulou, Rudd, Holmes & Kopelman, 2009). Finally, a dynamic theoretical model of the multifaceted nature of anosognosia, using a predictive coding framework, will be proposed and future directions for research will also be discussed.

**Keywords:** anosognosia; stroke; motor awareness; perspective; neurorehabilitation.

Conceptualising conscious awareness as a subjective, first-person, phenomenon has often resulted in the marginalisation of its scientific enquiry (Damasio, 1998). Nevertheless, disturbances of self-awareness have fascinated relevant clinical fields such as neurology and psychiatry since the time of Charcot, Freud and Babinski. Nowadays, it is recognised that disturbances in awareness offer an important avenue to investigate the neurocognitive processes involved in the construction of the self (Fotopoulou, 2012). Particularly in regards to the bodily self, the classical work of William James (1890) describes the immediacy of experiences of one's own body, while differentiating between different senses of the self. Within this framework, self-awareness involves both a *sense of ownership*- the feeling that my body belongs to me; and *sense of agency*- the feeling that I am the initiator of an action (Gallagher, 2000). Consequently disorders of self-awareness can involve disturbances of body ownership or agency, or both. This review will focus on a specific disturbance of body agency called anosognosia for hemiplegia (AHP), the apparent unawareness of or, inability to understand paralysis and other sensorimotor deficits following stroke (Cocchini et al., 2009). There is a lack of consensus in the literature on the actual definition of anosognosia (a: without; noso: disease; gnosia: knowledge; see Table 1 for summary of scientific definitions). Babinski (1914) initially used the term anosognosia to describe unawareness of paralysis following stroke, but the term is now used more broadly to include unawareness in many neuropathology's, including traumatic brain injury (Prigatano, 1988), Alzheimer's disease (Reed, Jagust & Coulter, 1993) and schizophrenia (Mohamed, Fleming, Penn & Spaulding, 1999). Anosognosia is often a transient phenomenon, not frequently lasting beyond the acute stage. However, unawareness of illness, especially in early critical stages, may significantly obstruct rehabilitation efforts (Gialanella, Monguzzi, Santoro & Rocchi, 2005; Jehkonen et al., 2006).

This article reviews recent research on AHP, in order to first provide an overview of the clinically variability, assessment methods, associated neuroanatomical and neuropsychological findings and finally the possible causes of the phenomenon. Subsequently, this review will focus on recent rehabilitation efforts. With these aims in mind, a detailed search of the literature was conducted using data base services *PubMed and Web of Knowledge*, searching the keywords: anosognosia, unawareness, stroke, hemiplegia, awareness and rehabilitation. A total of 52 articles were selected, in addition to historically important articles and book chapters. The articles selected were all restricted to the English language, and bibliographies of certain publications were also used.

[INSERT TABLE 1 HERE]

### **Clinical presentation**

AHP presents in different forms and it is important to try to differentiate between the potential varieties of AHP in both classifying patients and when investigating the underlying mechanisms involved (for discussion see Vocat et al., 2010). In the literature, characteristics like the *degree*, *extension*, *partiality*, *specificity* or *unawareness*, as well as the *affectivity* towards the paralysed body part and its *sense of ownership* have been noted to vary (see Table 2 for summary; see also Fotopoulou, 2013). Specifically in terms of the *degree* of AHP, unawareness can vary in severity ranging from a mere indifference to one's disabilities or illness, usually referred to as anosodiaphoria (Babinski, 1914), to blatant denial of limb paralysis and delusional beliefs of ability. Patients may also report illusionary movements- claiming their limb has moved despite demonstration of the opposite. Illusory limb movements are also commonly associated with

reported false memories (e.g. “I just walked to the bathroom myself, I’m just too tired to show you now”). In terms of *partiality*, some patients deny their motor deficits in every aspect tested, while others may verbally accept their deficit, but fail to acknowledge their functional consequences (e.g. they try to stand and walk), or vice versa. Differences in partiality are also suggested by studies (Cocchini et al., 2009; Fotopoulou et al., 2010; Moro et al., 2011) that show that some, but not all, patients show either explicit, or, implicit awareness of their deficits (‘Tacit’ or ‘implicit’ awareness is defined as ‘knowledge that is expressed in task performances unintentionally and with little or no phenomenal awareness’; Schacter, 1990, p. 157). Other studies also find that some patients with AHP show greater motor awareness in third-person perspective as opposed to first-person perspective tasks (Fotopoulou et al., 2011; Marcel et al., 2004). Moreover, the specificity of unawareness can vary, in that some patients only deny their hemiplegia, while accepting other stroke-induced deficits, while other patients deny all stroke-related deficits. Some patients may also show a morbid dislike or hatred for their paralysed limb (i.e. misoplegia; Critchley, 1955, 1974) as opposed to the opposite emotional response, anosodiaphoria (Babinski, 1914). Finally, only a subset of AHP patients may also present with disruptions in their own sense of body ownership, asomatognosia (the inability to recognise one’s own body), or somatoparaphrenia (bodily ownership delusions; Gerstmann, 1942). This clinical variability suggests that AHP is a multifaceted and heterogeneous phenomenon, but this position remains debated in the literature.

[INSERT TABLE 2 HERE]

## **Assessment**

A number of assessment measures have been designed to assess AHP. The disparity between the tests however has resulted in vague diagnostic criteria and prevented a single 'gold standard' assessment from being developed (see Orfei et al. 2007; Jenkinson et al. 2011, for review).

Cutting (1978) was one of the first to introduce a formal assessment measure of anosognosia and related phenomena. His detailed questionnaire proved to be a useful supplement to clinical observations. Clinical assessments further improved by introducing the use of a frequently used 4-point scale, used by the clinician to quantify the severity of the patient's unawareness and ultimately classified as mild, moderate or severe (Bisiach, Vallar, Perani, Papagno & Berti, 1986). The scale serves to differentiate between patients who are unaware of their paralysis, but recognise their deficit when asked and are unable to perform a specific movement, from patients who hold an active delusional component of anosognosia, producing false beliefs of having moved their hemiplegic limb. A more sensitive measure was later developed to assess the relationship between verbal anosognosia and related confabulations (Feinberg, Roane & Ali, 2000). This interview consisting of 10 questions, not only determines the severity of unawareness, but identifies the presence of illusionary movements. A shortcoming of both, the Bisiach scale and the Feinberg and colleagues interview, is their reliance on explicit and verbal means of assessment. The Berti et al. (1996) interview provides a measure of both implicit and explicit awareness, and differentiates between unawareness for lower and upper limb paralysis, using both verbal and behavioural responses. The interview also estimates awareness of current motor ability in activities of daily living (e.g. clapping hands and walking).

Many other assessment methods have more recently been developed (see Cocchini et al., 2010; Della Sala et al., 2009; Marcel, Tegner & Nimmo-Smith, 2004; Prigatano, 2005; Starkstein et al., 2006) to assess and classify AHP more reliably. These methods assess the clinical variability of

AHP in greater detail and hold the potential for better diagnostic accuracy and homogeneity in the field. Yet despite this progress, it is clear that further psychometric testing and validation is needed to help define the diagnostic and assessment criteria for AHP (Orfei, 2007; Jenkinson et al., 2011). An important aim of clinical research in AHP is not just to identify the presence or absence of unawareness of motor paralysis (see next section), but rather to understand the multidimensional nature of the phenomenon (Vocat et al., 2010). In order to help refine already existing assessment methods and develop new tools, innovative and dedicated research on the clinical variability of AHP is needed, as well as a disciplinary move away from binary distinctions and towards multifactorial criteria.

### **Incidences and Duration**

AHP occurs more frequently following right perisylvian lesions, and less often in left perisylvian lesions (Nathanson et al., 1952; Heilman et al., 1998; Cocchini et al., 2009). A wide range of frequencies have been reported on the prevalence of anosognosia for hemiplegia. These variations can mostly be attributed to difference in diagnostic criteria, time and type of assessment (see also above) and variations in patient recruitment and selection (Orfei, Caltagirone & Spalletta, 2009). Initial studies reported a frequency of 33 to 58% of AHP in stroke patients (Cutting, 1978; Bisiach et al., 1986), more recently however a meta-analysis of studies reported a frequency ranging from 20 to 44% depending on the time of assessment (Pia, Neppi-Modona, Ricci & Berti, 2004). Orfei and colleague's (2007) review further identified a prevalence of 7 to 77%. However, Karnath, Baier and Nagele (2005) used a more sensitive measure of AHP, only classifying patients as anosognosic after scoring a minimum of 2 on the Bisiach scale (i.e., the disorder acknowledged only after demonstration of paralysis, Bisiach et al., 1986). Consequently, a much lower rate of AHP was reported: 10-18% in acute and subacute

patients. In the first longitudinal study on AHP, the evolution of unawareness overtime was documented in 58 right-hemisphere patients assessed at three different time intervals: 3 days (hyperacute), 1 week (subacute) and 6 months (chronic). They reported a frequency of 38% in the hyperacute stage, dropping to 18% after 1 week and only 5% remaining aware in the chronic stage.

Cocchini and Della Sala (2010) however, suggest that both low incidence of anosognosia in the chronic phase and following left-hemisphere damage may be a result of poor diagnostic tools used. Patients for example, may have actually “learned” the “correct” response after repeated awareness questions, rather than having a genuine remission of their unawareness. The “true” incidence of anosognosia in left-hemisphere brain damaged patients may also be obstructed by dependency on language abilities in awareness assessments. This has resulted in a recently developed tool, the Visual-Analogue Test for Anosognosia for motor impairment (VATA-m), which is designed to assess anosognosia with aphasic patients (Della Sala, Cocchini, Bechin & Cameron, 2009). Using this tool, this group has indeed noted that anosognosia in aphasic patients may be commonly underreported due to verbal assessment constraints.

### **Etiology of Anosognosia**

The precise neurological and psychological causes of AHP have been difficult to establish. It has however been mostly accepted (Marcel et al., 2004; Orfei et al., 2007; Vocat et al., 2010; Fotopoulou et al., 2013) that a combination of a number of factors, rather than a single deficit, is likely to account for the range of clinical presentations and variability in anosognosia (Vuilleumier, 2000, 2004; Vocat et al., 2010). Yet the precise neurological and psychological



causes and their critical combination remain unclear. Below we review the major neuroanatomical and neuropsychological explanations of AHP to date.

### *Neuroanatomical accounts*

Recent improvements in structural neuroimaging methods, software and analysis have resulted in several new studies that attempt to identify the precise brain regions that are associated with AHP. However this has led to the identification of multiple lesions sites, and sometimes opposing findings. This can be accounted for by the often fluctuating and wide variability found in unaware patients, but also by the scan quality (e.g. use of computed tomography, CT, vs. magnetic resonance imaging MRI), lesion mapping methods and analysis, and the diagnostic criteria and tests used (Jenkinson et al., 2011).

Taking into account reported findings from both CT and MRI scans, Pia et al. (2004) conducted a meta-analysis using 85 AHP cases. The lesion sites identified included the frontal, parietal, temporal, and occipital cortical regions, and at a subcortical level the thalamus, basal ganglia, corpus callosum, internal capsule, corona radiata, insula, lateral ventricular, and amygdalae. Their results further suggested that, at a cortical level, frontoparietal damage was the most frequent lesion site, and basal ganglia and thalamus lesions being most likely to account for unawareness following damage to a single subcortical area. A combination of both cortical and subcortical structures were therefore found to play a significant role in causing unawareness.

The study of damaged areas related to motor planning and the role of the insula in AHP has recently become a center of much interest and debate in the literature. In a lesion analysis study

Karnath, Baier, and Nagele (2005) analyzed both CT and MRI scans of 27 patients: 14 with both hemiplegia (HP) and AHP patients, and 13 with only HP (control group). Both control and experimental groups were matched for age, lesion size and acuity, degree of hemiparesis, severity of neglect, sensory loss and visual fields deficits. The lesions were mapped using MRIcon software on slices of a T1-weighted template MRI scan. The right posterior insula was identified as the only structure with greater damage in AHP patients. This runs in parallel to Craig's (2009, 2010) model of self-awareness, in which he identifies the anterior insular cortex as the centre for all subjective feelings and self-awareness.

In contrast, a lesion mapping study using both CT and MRI scans conducted by Berti et al. (2005) compared three patient groups: 17 patients with AHP, unilateral neglect and left hemiplegia (experimental group); 12 patients with unilateral neglect and left hemiplegia, and no AHP (control group); and 1 patient with left hemiplegia, AHP, and no unilateral neglect (case-study of 'pure anosognosia'). They studied the anatomical distribution of lesions by superimposing the lesion plots of the two groups and conducting an anatomical chi-square distribution of the comparison. Their analysis concluded that anosognosia is characterized by damage to the dorsal premotor cortex (BA 6 and 44 specifically), the somatosensory cortex, the primary motor cortex (BA 4), the insula, area 46 (frontal agranular cortex) cortex and in some cases in the dorsolateral prefrontal cortex. When compared to the case-study of 'pure anosognosia', the same areas were identified with the exception of the dorsolateral prefrontal cortex, and the addition of the insula. Areas related to motor monitoring were therefore identified as critical for the presence of anosognosia.

The results of Vocat & Vuilleumier's (2010) longitudinal study describe in detail above, also used CT and MRI scans to conduct an anatomical lesion analysis using a voxel based statistical mapping method (voxel-based lesion symptom mapping, VLSM). In the hyperacute phase (3 days) insula damage and adjacent subcortical lesions were identified, similar to those reported by Karnath et al. (2005). While the persistence of AHP was associated with lesions in the premotor area, cingulate gyrus, parietotemporal junction and medial temporal structures, which support Berti et al. (2005) findings supporting the crucial role of the premotor cortex.

Fotopoulou, Pernigo, Maeda, Rudd & Kopelman (2010a) also conducted a lesion analysis using patient's CT and MRI scans, but uniquely correlated experimental data with lesion data. They used these results to identify and group patients into those with "implicit" awareness and "explicit" awareness, and compared them to a group of hemiplegic controls patients with hemispatial neglect, but no AHP. They aimed to identify the brain areas involved with different types of AHP (see section on clinical presentation), specifically the neural correlates related to implicit and explicit awareness. The authors found that frontal, parietal and occipital areas of the cortex were more frequently damaged in patients that had both implicit and explicit awareness. Interestingly, the insular cortex was more frequently damaged in patients with intact implicit awareness, but without explicit awareness. These results offer support to the neural dissociation between implicit and explicit awareness, therefore suggesting that clinical variability found in AHP may be associated with different lesion sites. Similarly, Moro, Pernigo, Zapparoli, Cordioli and Aglioti (2011) conducted a lesion mapping study in order to identify different neural structures involved in different types of anosognosia (i.e. implicit and explicit awareness). Twelve patients with severe hemiplegia and AHP were compared to a control group of 12

hemiplegic patients with no AHP. Lesions from CT and MRI scans were analyzed using Voxel Lesion Symptom mapping (VLSM) comparing damaged areas in anosognosic and non-anosognosic patients. They further identified the lesional correlates of patients with deficits in implicit and explicit awareness. Similar to Fotopoulou et al. (2010a) impaired implicit awareness was associated with damage to subcortical areas including the basal ganglia, and impaired explicit awareness was more frequently related to cortical regions, including the frontal, temporal and parietal structures.

### *Neuropsychological explanations*

Early accounts of AHP regarded the phenomenon to be a secondary consequence of sensory deficits, specifically neglect (visual and tactile), which often co-occurs with AHP in right-hemisphere damage (Cutting, 1978; Levine, 1991). It was also suggested that a combination of sensory deficits and other higher-order functions (e.g. memory and confabulation) result in AHP (Berti et al., 1996; Levine, 1991). However, a series of studies have since shown double dissociations between AHP and primary or high-order sensory deficits and a number of other higher-order cognitive deficits (Bisiach et al., 1986; see Heilman & Harciarek, 2010 for review), showing that these deficits may not be necessary for its occurrence. It is nevertheless probable that the aforementioned factors can lead to greater severity of unawareness or predispose patients to AHP when other contributing factors are also present (Marcel et al., 2004; Fotopoulou, 2013).

More recent accounts have emphasized issues of motor planning and monitoring, rather than sensory deficits. Established computational models of the motor system proposed that motor awareness is dependent on the comparison between predicted and actual sensory information

(Miall & Wolpert, 1996). Various studies have attempted to explain anosognosia using such models of motor control and awareness. It has been thus influentially proposed that AHP results from a specific deficit of forward motor monitoring (Berti et al., 2005; Frith et al., 2000). Here it is argued that there is an inconsistency in the predicted movement- based on intentions; and actual movement- based on sensory feedback. Fotopoulou et al. (2008) investigated these proposals experimentally using realistic prosthetic hands to generate visual feedback of movements in AHP patients, while manipulating whether they had the intention to move themselves (self-intention) or someone else would move their arms (other intention). Their results showed that in AHP the illusory perception of movement in a non-moving hand occurred significantly more often in self- versus other-intention trials, thus reflecting an abnormal dominance of motor intentions about the predicted effects of the movement over visual sensory information about the actual effects of the movement. In addition, a recent study by Garbarini and colleagues (2012) provides a behavioral demonstration of intact motor intentions in AHP. Garbarini and colleagues compared the performance on a classical bimanual interference, or coupling task, with three right-hemisphere brain damaged stroke patients, with 10 healthy, age matched controls. During this task the participants are asked to draw lines with their right hand (intact hand for AHP patients) and to draw circles with their left hand (paralyzed hand for AHP patients) while blindfolded. The lines drawn by the intact hand in AHP patients became more oval, offering evidence that there was an intention to move the paralyzed hand.

It is however important to consider that pure motor accounts for AHP do not explain the full range of clinical variability (e.g. delusions and affectivity; Fotopoulou, 2012). Many authors have also proposed that AHP should not only be explained by a disruption of sensorimotor

mechanisms, but neuromotivational factors must also be considered (Solms, 1996; Vuilleumier, 2004; Feinberg, 2007; Fotopoulou, 2010b). There has been a long tradition of regarding anosognosia as a psychological defense, most importantly dating back to the work of Weinstein and Kahn (1955). This motivational account of anosognosia has been mostly set aside for its lack of emphasis on the associated brain regions involved and the lack of experimental data.

However, there has been a recent shift to reinvestigate the role of emotional and motivational factors associated with AHP (Feinberg, 2007; Orfei et al., 2007; Nadrone et al., 2007; Vocat et al., 2010, Fotopoulou et al., 2010). With the emergence of an ‘affective neuroscience’ (see Panksepp, 1998)- emphasising the brain systems involved in basic human emotions in mammals- it is more widely recognised that ‘non-emotional’ processes, such as memory and attention, and emotional processes often overlap and can commonly involve the same neural mechanisms. Some authors (Turnbull & Solms, 2007; Fotopoulou, 2010b) have therefore suggested that traditional motivational accounts of AHP could be modified to include a combination of factors, both neurocognitive and neuroemotional.

As the role of the right-hemisphere, particularly in the anterior insular cortex, for processing affective information (Damasio, 2000; Craig, 2009) and social cognition (Frith & Frith, 1999) is now increasingly recognised, there is scope for empirical investigations on the social-emotional underpinnings of AHP following right-hemisphere lesions. Although it has been suggested by some authors that the right hemisphere is specialised for negative emotions (e.g. Davidson, 2001), and the subsequent loss of negative affect in AHP, it has been demonstrated by numerous studies that a range of emotions, both positive and negative, can be experienced by these patients (Ramachandran, 1996; Kaplan-Solms & Solms, 2000; Turnbull et al., 2005). Descriptive case

studies and experimental investigations have persistently shown that AHP patients experience a variety of both positive and negative emotions, but the exact incidence, range and variety of emotional change (e.g. misoplegia, catastrophic reactions, anosodiaphoria) experience by anosognosics needs to be fully explored ~~but the incidences and diversity of emotional changes (i.e. emotion regulation) remains to be more fully explored~~ (Turnbull et al., 2005). Even in the earliest reports of anosognosia, Babinski (1914) identified the relationship between unawareness and lack of emotional concern (anosodiaphoria). In Kaplan-Solms and Solms' (2000) case series, some patients presented with explicit dislike or hatred for their paraplegic arm (misoplegia), while others presented with a fluctuation of emotion including so-called 'catastrophic reactions' (sudden, intense episodes of tearfulness and emotional breakdown) that was followed by transient awareness of their deficit (also see Turnbull et al., 2002). Taken together this raises an important question regarding the potential influence of emotion on unawareness of deficit. There is a need for future studies to further explore the possible relationship between emotion, both positive and negative, and unawareness of deficit. Given that patients' emotions have a significant role in any rehabilitation effort, the findings should provide valuable insight into effective rehabilitation strategies of these patients.

### **Awareness recovery**

AHP is often a transient phenomenon with spontaneous recovery occurring within days, weeks or months from onset. However, even when motor unawareness is present only in the early critical stages, it can significantly obstruct rehabilitation (Gialanella et al., 2005; Jehkonen et al., 2006). For example, anosognosia is said to be associated with longer hospital admissions (Maeshima et al., 1997) and poor functional recovery (Gialanella et al., 2005). Additionally,

systematic reviews of the literature suggest that approximately 30% of AHP patients remain unaware beyond the acute stage (Orfei et al., 2007; Pia et al., 2004). Recently some progress has been made in the management and rehabilitation of AHP (Prigatano & Morrene-Stupinsky, 2010; Jenkinson Preston & Ellis 2011), but there is still no accepted treatment for AHP.

### *Rehabilitation 'guidelines' and social emotional factors*

In an extensive review on rehabilitation efforts in AHP, Prigatano & Morrene-Stupinsky (2010) offer some clinical guidelines for the management of AHP patients. They make the recommendation that it is important to first clearly determine: the severity and types of AHP and the associated neurological and neuropsychological deficits. Subsequently, it is important that good rapport with the patients and their family is established, and finally a detailed and individualized rehabilitation plan is developed, including encouraging the patient through the therapy (also see Jenkinson et al., 2011).

Furthermore Fotopoulou (2008) suggests a few practical guidelines for those involved in the rehabilitation of confabulating patients, which can be similarly used and adapted for AHP patients. These recommendations specifically encourage clinicians and family members: (1) to respond to the patients statements at face value with natural interest and curiosity, (2) to discreetly suggest and add correct background information to their stories, when possible, (3) to pace the conversation with the patient and to try stay within the conversational topic, (4) to explore memories, beliefs and current facts, by taking into account both the patient's emotions and emotions of others and their need for a shared reality. Fotopoulou (2008) further proposes that conversations using a "third-person" perspective with the patient may be an alternative



method used for enhancing both therapeutic rapport and patients' awareness of brain-related injury. For example, in the case-study presented, the patient appeared to confabulate less when the examiner conducted the assessment using a "third-person" voice (e.g. "I knew a man who suffered from a brain injury" or "do you think this man can lead a satisfactory life?").

Other studies have similarly concluded that patients with AHP are more likely to acknowledge their deficit when asked in the third- as opposed to first- person questions (Marcel, Tegner and Nimmo-Smith, 2004). More recent case investigations also suggest that such patients' may initially come to understand their illness through third person encounters. For example, patient ED could only understand and later internalize that she had a stroke by use of a third-person observation: "The doctors tell me I have had a stroke, they must be right. I am not so sure, but the doctors are the experts, so I must have had a stroke" (Besharati, Kopelman, Avesani, Moro & Fotopoulou, Submitted). As discussions in the "third-person" may be a powerful tool used in rehabilitation interventions, Fotopoulou (2008, 2010b) also suggests that the social context of the anosognosia/confabulation, and the patients' social environment, are equally as important.

The social-emotional factors in recovery from stroke are only just beginning to be recognised and studied (Eslinger, Parkinson & Shamay, 2002). The affective elements involved in AHP have been highlighted by the field of neuropsychanalysis that combines principles from both neuroscience and psychoanalysis (see Solms & Turnbull, 2002). Kaplan-Solms and Solms' (2000) psychoanalytic observations of AHP patients described above provides a in-depth account of how to use neuropsychanalysis to produce psychoanalytic observations in understanding and therapeutically treating AHP patients. Prigatano and Morrone-Strupinsky (2010) similarly

recommend the use of psychotherapy with patients who use denial as a defensive coping mechanism.

### *Awareness interventions*

No evidence-based treatment exists for AHP (Jenkinson et al., 2011; Korte & Hillis, 2011). There has been a long tradition in using vestibular stimulation to initiate a remission of AHP, but unfortunately the results are only temporary (Cappa et al., 1987; Ramachandran, 1995). Beschin, Cocchini, Allen and Della Sala (2012) tested the effect of three types of treatment (optokinetic stimulation, prism adaptation and transcutaneous electrical nerve stimulation) on both neglect and anosognosia in 5 patients with severe AHP and neglect. A transient improvement of awareness was found in one patient using the combination of methods, and a temporary improvement of neglect found in two other patients using the same methods. However, these recent efforts only resulted in a temporary remission of AHP, similarly to vestibular stimulation.

A recent single case study investigation reported the first clinical intervention to successfully lead to an immediate and lasting ~~permanent~~ remission of AHP for the first time in the literature (Fotopoulou, Rudd, Holmes, & Kopelman, 2009). Fotopoulou and colleagues used video replay as an experimental rehabilitation intervention method. Self observation in video replay offers a unique visual perspective by showing the patient both a 3<sup>rd</sup> person (from the outside) and ‘offline’ (watching oneself at a later time than the actual attempt to execute a movement) perspective. Video replay was used to provide visual feedback to a patient with severe AHP. Here we present a brief vignette of the published case study to illustrate the main elements of this approach.

## Case example

LM was a 76-year-old right handed women with 15 years of education. She had no significant previous medical or psychiatric history, and was hospitalised following a right middle cerebral artery (MCA) stroke. She presented with severe left-sided hemiplegia (0/5 power on Medical Research Council scale), mild dysarthria, facial weakness, proprioception deficits and hemispatial and personal neglect. Neuropsychological testing further reported mild executive impairment and anxiety, but no indications of depression. LM had severe AHP, as supported by her scores on both the Berti interview (Berti et al., 1996) and Feinberg Questionnaire (Feinberg et al., 2010). She further claimed that she could perform a number of bimanual and bipedal tasks (e.g. walking and clapping hands), and spontaneously reported false memories of such actions, including walking around the ward and washing and dressing herself without assistance. (Fotopoulou, Rudd, Holms & Kopelman, 2009).

Patients with AHP typically remain anosognosic when their paralysed arm is brought to their ipsilateral (i.e. on the same side of their body) visual field. In contrast, a 90s video clip of LM answering awareness questions was played back to her, therefore providing video-based feedback to the patient. As a result the authors noted an immediate and spontaneous increase in motor awareness pre- and post- video intervention. Directly after the video replay the patient commented on how she had not been very realistic about her hemiplegia, and how watching the video made her change her mind about her motor weakness. LM's awareness recovery was additionally maintained at a one-month (four weeks) follow-up. There was no change in the patient's neuropsychological test scores (e.g. executive tasks, memory), except for her ratings on the Hospital Depression and Anxiety Scale, scoring above the mean for depression. One important interpretation from the authors is that AHP patients may have more intact awareness when observing themselves from a 3<sup>rd</sup> rather than a 1<sup>st</sup> person perspective (Marcel, et al., 2004). A second interpretation is that there are functional and neural differences in 1<sup>st</sup> and 3<sup>rd</sup> person perspectives on our body, and this allows us to differentiate our body from other peoples. Interestingly, since video-viewing also provides the patient with an "offline" perceptive (i.e. they

are not trying to move their arm while watching the video), the impact of motor intentions is not relevant to motor monitoring during video observation. Video-viewing may have therefore facilitated the updating of LM's motor awareness (i.e. 3<sup>rd</sup> person and off-line self observation, using video replay, facilitated 1<sup>st</sup> person body awareness). These results however need to be replicated and the precise mechanisms of this effect, as well as other therapeutic factors that should potentially accompany the intervention (e.g. emotional support), need to be specified.

Video replay has also been shown to help improve insight of psychotic patients (Davidoff, 1998). In a more recent study, David, Ster and Zavarei (2012) measured the effect of "self" and "other" video replay on insight of psychosis with a group of 40 schizophrenic patients. Twenty-one patients watched the "self" video and 19 patients watched the "other" video (an actor presenting with the same psychotic symptoms). Both videos resulted in an improvement of insight. Although there was a lack of a clear difference in the effect of the self and other video replay, patient's insight did improve following video replay.

Although video replay draws on a visual 3<sup>rd</sup> person perspective, there is a need to investigate mentalising abilities of AHP patients, in regards to verbal 3<sup>rd</sup> person perspective taking. In a single case-study investigation of a patient with right-hemisphere damage to the frontal and temporal lobes, errors in inhibiting 1<sup>st</sup> person perspective and in judgments relating to the 3<sup>rd</sup> person visual and emotional perspective was reported (Samson, 2005). The right temporal-parietal Junction (TPJ) has also been associated with false belief tasks (Sax & Kanwisher, 2003) and visual-spatial perspective-taking tasks (Aichorn, Perner, Kronbichler, Staffen & Ladurner, 2005), while 1<sup>st</sup> person, egocentric, perspective taking has been associated with the right inferior

parietal cortex (Vogeley & Fink, 2003). Together these findings suggest the crucial role of the right-hemisphere in the capacity to attribute mental states of others. However, to our knowledge there are still no studies that have directly investigated AHP and its associated social cognitive deficits.

### *Proposed model*

Although many theories have been proposed (see Cocchini et al., 2010; Garbarini et al., 2012; Orfei et al., 2009; Vuilleumier, 2004), no single model has been able to account for the multifaceted and heterogeneous nature of AHP. Fotopoulou (2012, 2013) has recently provided an alternative model to explain the multifaceted nature of anosognosia using a Bayesian ‘predictive coding’ framework (Friston, 2010). This framework allows for a single and neurobiologically plausible formulation that incorporates both bottom-up and top-down mechanisms of perception and belief formation. In this context, AHP can be linked to a general antagonism between ‘prior beliefs’ (predictive internal models of the world based on previous learning) and ‘prediction error’ (discrepancies between expected and actual inputs based on interoceptive and exteroceptive signals). In terms of awareness recovery, the model could be used to explain spontaneous recovery (see Vocat et al., 2010) or the invention-based recovery described above (i.e. video replay, Fotopoulou et al., 2009). These changes in unawareness in time can therefore be attributed to a progressive updating of prior beliefs based on accumulating or alternating signals about prediction errors (Fotopoulou, 2012).

### **Conclusion**

Overall, it has been increasingly recognised that AHP is a multifaceted phenomenon, which involves a complex interplay between neurological, emotional and behavioural components (Vocat et al., 2010; Moro, et al., 2011; Fotopoulou et al., 2013). This paper has aimed to explain these complexities by discussing the clinical presentation variability, assessment, prevalence and duration of AHP. The neuroanatomical and neuropsychological causes reviewed, further highlight the multiple factors at play. Rehabilitation strategies in AHP must therefore similarly respond by using a multi-contextual approach (Korte & Hills, 2011), drawing on established guidelines and strategies for motor awareness recovery, while incorporating psychotherapeutic interventions psychotherapy when possible. Yet, despite the heterogeneous nature of anosognosia, the case-study example illustrated how the use of a simple video-based intervention, providing 3<sup>rd</sup> person-offline feedback, led to the lasting remission of AHP for the first time in the literature. However, future studies are needed to replicate this finding, investigate the related emotional factors, and explore the generalisation of self-observation. ~~It is important to keep in mind that this review has been limited to only two databases, which may have resulted in other important sources being overlooked.~~ In addition, the proposed model itself is currently speculative in nature, and requires proper modeling and empirical testing. However, it allows for a new and more dynamic neuropsychological understanding of the mechanisms involved in motor and body unawareness and highlights the possible mechanisms that may allow recovery of motor awareness in the acute stages following stroke.

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