Implicit awareness in anosognosia for hemiplegia: unconscious interference without conscious re-representation

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Some patients with anosognosia for hemiplegia, i.e. apparent unawareness of hemiplegia, have been clinically observed to show ‘tacit’ or ‘implicit’ awareness of their deficits. Here we have experimentally examined whether implicit and explicit responses to the same deficit-related material can dissociate. Fourteen stroke patients with right hemisphere lesions and contralesional paralysis were tested for implicit and explicit responses to brief sentences with deficit-related themes. These responses were elicited using: (i) a verbal inhibition test in which patients had to inhibit completing each sentence with an automatic response (implicit task) and (ii) a rating procedure in which patients rated the self-relevance of the same sentences (explicit task). A group of anosognosic hemiplegic patients was significantly slower than a control group of aware hemiplegic patients in performing the inhibition task with deficit-related sentences than with other emotionally negative themes (relative to neutral themes). This occurred despite their explicit denial of the self-relevance of the former sentences. Individual patient analysis showed that six of the seven anosognosic patients significantly differed from the control group in this dissociation. Using lesion mapping procedures, we found that the lesions of the anosognosic patients differed from those of the ‘aware’ controls mainly by involving the anterior parts of the insula, inferior motor areas, basal ganglia structures, limbic structures and deep white matter. In contrast, the anosognosic patient without implicit awareness had more cortical lesions, mostly in frontal areas, including lateral premotor regions, and also in the parietal and occipital lobes. These results provide strong experimental support for a specific dissociation between implicit and explicit awareness of deficits. More generally, the combination of our behavioural and neural findings suggests that an explicit, affectively personalized sensorimotor awareness requires the re-representation of sensorimotor information in the insular cortex, with possible involvement of limbic areas and basal ganglia circuits. The delusional features of anosognosia for hemiplegia can be explained as a failure of this re-representation.

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Introduction

Some patients with central neurological damage are apparently unable to acknowledge their contralesional motor deficits. This rare neuropsychological symptom is termed anosognosia for hemiplegia (AHP)—a term implying lack of ‘knowledge’ of the deficit (Babinski, 1914). In extreme cases, patients appear to believe that their limbs are completely functional. Some may even claim that they do move on request, while in reality their paralysed limbs remain motionless (Feinberg et al., 2000; Fotopoulou et al., 2008). Other patients may provide excuses (confabulations) to account for the fact that the limbs are not moving (for review, see Fotopoulou, 2010); still others may admit they cannot move their limbs, but they show complete indifference towards their deficit (anosodiaphoria) (Critchley, 1953). AHP can be accompanied by other delusional beliefs. For example, patients may claim that their paralysed limb belongs to someone else (somatoparaphrenia) (Gerstmann, 1942). AHP occurs more frequently following right than left hemisphere brain damage (but see Cocchini et al., 2009). No available treatment exists for AHP, although temporary remission has been reported following vestibular stimulation (Rubens, 1985); and permanent reinstatement of awareness was recently reported in a patient with severe AHP, following self-observation during video replay (Fotopoulou et al., 2009).

AHP has been viewed by some as a secondary consequence of sensory feedback deficits, such as spatial or personal neglect (Cutting, 1978; Levine, 1990). Others have proposed that AHP might result from the combination of sensory deficits and higher-order cognitive deficits such as confusion, confabulation and memory impairments (Levine, 1991; Berti et al., 1996). However, double dissociations have been demonstrated between AHP and each of the aforementioned deficits (Bisiach et al., 1986; Starkstein et al., 1992; Heilman et al., 1998; Berti et al., 2005; Coslett, 2005; see also Heilman and Harciarek, 2010 for review). Moreover, Marcel et al. (2004) found that neither sensory loss, nor intellectual impairment, nor their combination, provides a complete explanation of AHP.

Alternatively, AHP has been explained as specific deficit of motor planning (Heilman et al., 1998; Frith et al., 2000; Berti et al., 2005). A recent study showed that altered awareness of action in AHP reflects an abnormal dominance of representations of intended movements over sensory feedback about the actual effects of movement (Fotopoulou et al., 2008). However, such a finding cannot explain why some patients deny their motor deficits even when not attempting to move, or why other patients may selectively forget instances of detected motor failure and even related injuries. Some authors suggest that the delusional features of AHP are the result of a psychological defence against excessive depression or anxiety (Weinstein and Kahn, 1955, but see Bisiach and Geminiani, 1991; Heilman et al., 1998).

Others have argued that at least some features of AHP cannot be explained by disruption of sensorimotor mechanisms and that neuromotivational factors need to be taken into account (Feinberg et al., 1994; Ramachandran, 1995; Solms, 1995; Frith et al., 2000; Marcel et al., 2004; Vuilleumier, 2004; Turnbull et al., 2005; Fotopoulou, 2010). Thus, AHP can be seen as a multifaceted phenomenon, with each facet perhaps requiring a separate explanation (Marcel et al., 2004; Vuilleumier, 2004; Heilman and Harciarek, 2010). In addition, AHP has been observed to take different forms in different patients (e.g. Marcel et al., 2004; Orfei et al., 2007), suggesting that different types of patients with AHP exist, and this heterogeneity must be taken into account both when classifying patients and when attempting to explain the mechanisms underlying the various clinical manifestations of the phenomenon (for discussions, see Karnath and Baier, 2010; Vocat and Vuilleumier, 2010).

One important but poorly investigated distinction is between the explicit and implicit features of AHP (for discussion, see also Vocat and Vuilleumier, 2010). Several investigators have noted that some patients with AHP show indications of ‘tacit’ or ‘implicit’ awareness of their deficits, i.e. ‘knowledge that is expressed in task performance unintentionally and with little or no phenomenal awareness’ (Schacter, 1990, p. 157). Thus, while patients may explicitly deny their paralysis, they may be unconsciously processing some components of their deficits, including the emotional aspects. For example, a severely anosognosic patient who persistently denied her paralysis and all associated disabilities spontaneously told junior doctors during a ward round: ‘Perhaps it would be really useful to you to come and see me at a time when I’ll be really ill and unable to move’ (Fotopoulou et al., 2009). Another patient with AHP who was explicitly denying her paralysis unceasingly complained about everyday difficulties with an emotional intensity that better fitted her devastating disability than these minor everyday disappointments (Fotopoulou and Conway, 2004). However, beyond the level of single cases or case series (e.g. Ramachandran, 1995; Berti et al., 1998; Nardone et al., 2007), this issue had not been systematically explored in AHP until recently. In contrast, the unconscious processing of cognitive and emotional information has been experimentally investigated and confirmed in other neuropsychological syndromes, including hemispatial neglect (Marshall and Halligan, 1988), blindsight (Weiskrantz et al., 1974), prosopagnosia (Tranel and Damasio, 1985) and amnesia (Johnson et al., 1985).

In a recent group study, Cocchini and colleagues (2010) showed that patients’ behaviour did not always reflect their explicit estimations of their own abilities in a self-report questionnaire. Specifically, two patients approached a series of bi-manual tasks that if they could use both hands but did not show unawareness in a self-report measure, while another eight patients showed the opposite result. The authors interpreted their findings as a double dissociation between explicit and implicit awareness for motor deficits. However, this study used two different and unrelated tests to...
measure the two forms of unawareness. This raises the possibility that the two tasks were distinct in some components or items, posing differing challenges for reasons other than variability in response explicitness.

To conclude reliably that implicit and explicit awareness dissociate within a single patient or across groups, implicit versus explicit modes of responding need to be assessed using identical, or well-controlled and balanced, material presented in the same modality. In addition, the material should be compared with other material of similar emotional value, to control for the potential role of negative emotions associated with one’s deficits. Finally, independent confirmation of ‘unawareness’ by tests used in previous studies would provide additional validity to the measures used to establish unawareness for hemiplegia. To our knowledge, such comparisons have not yet been undertaken in the study of AHP.

Taking all of this into consideration, the current study aimed to compare directly the explicit and implicit processing of the same, emotionally ‘controlled’, experimental material. To this end, we employed a verbal inhibition test (based on a standardized verbal equivalent of the Stroop procedure) and examined whether patients with AHP were slower in performing the inhibition task when the material of the test included deficit-related information than when it included other negative or neutral themes. Typically, selective slowing of responses in emotional Stroop-like tests is thought to reflect ‘unconscious’ response competition between the processing of emotional self-threatening information and the requirement to complete the task (e.g. Pratto and John, 1991; Wentura et al., 2000). In our study, such selective slowing would suggest that although patients with AHP show poor explicit awareness of their hemiplegia, they may be implicitly aware of it and hence behave accordingly when confronted with paralysis-related material. Importantly, our task allows the direct comparison of explicit and implicit processing of the same verbal experimental material by each patient, and controls for the role of negative emotions.

Furthermore, using lesion mapping procedures, we aimed to investigate the neural correlates of unawareness. As in previous studies of lesion localization in AHP (Ellis and Small, 1997; Berti et al., 2005; Karnath et al., 2005; Baier and Karnath, 2008; see also Pia et al., 2004 for an extensive meta-analysis), we performed lesion comparisons between hemiplegic patients with and without AHP in order to distinguish between the neural correlates of AHP and the parietotemporal network commonly associated with spatial neglect and other common symptoms of right hemisphere damage. Importantly, previous lesion localization studies have not taken into account the behavioural dissociation between implicit and explicit awareness, and thus our study aimed to specify previous findings based on such investigations.

Materials and methods

Subjects

Fourteen adult neurological patients were consecutively recruited from an acute rehabilitation stroke unit. Berti et al. (1996) have suggested that given the clinical heterogeneity of AHP, studying cases with denial of complete contralateral hemiplegia can generate more reliable findings than investigating patients with mild or moderate hemiparesis. Accordingly, inclusion criteria were: (i) complete left upper limb hemiplegia (completely paralysed left arm as reported by the responsible neurologist and confirmed by direct motor impairment examination); (ii) unilateral right hemisphere lesions (as detected by CT or MRI neuroimaging investigations); and (iii) <7 years of education or an estimated premorbid Full Scale Intelligence Quotient based on the Wechsler Test of Adult Reading (Wechsler, 2001) <70; (iii) medication with severe cognitive, mood or side-effects; and (iv) severe language impairment (i.e. insufficient communicative ability).

Patients were classified as having AHP on the basis of an open interview that explored their awareness of motor deficits (Berti et al. 1996). This included (i) a first set of general questions: e.g. ‘Why are you in the hospital?’; (ii) specific questions about motor ability: e.g. ‘How is your left arm? Can you move it?’; and (iii) confrontation questions: e.g. ‘Please, touch my hand with your left hand. Have you done it?’ The total score indicating awareness of upper limb motor impairment ranged from 0 to 2. A score of 0 was given if patients acknowledged their motor impairments; a score of 1 was given if patients did not acknowledge their motor impairments but recognized not having reached for the examiner’s hand; and a score of 2 was given if patients denied both motor impairments and the failure in reaching for the examiner’s hand. Patients were considered to be anosognosic when they did not acknowledge the contralateral hemiplegia after repeated and specific questioning by the examiner (scores 1 and 2). The scale developed by Feinberg et al. (2000) was used as a second measure of unawareness. This consists of 10 questions, including general open questions, e.g. ‘Do you have weakness anywhere?’ or ‘Is your arm causing you any problems?’ and confrontation questions, e.g. when left arm is lifted and dropped in right hemispace: ‘It seems there is some weakness. Do you agree?’ A score of 0 was given if the patient showed awareness of deficit, 0.5 for partial awareness and 1.0 for complete unawareness or denial.

The study included seven patients with right hemisphere damage with complete left arm hemiplegia and AHP (the AHP group) and seven patients with right hemisphere damage with complete left arm hemiplegia but without AHP (the HP group). Only one patient (AHP5) showed somatoparaphrenia (she believed her left arm was her husband’s). There were no indications of disturbed sense of limb ownership (Bair and Karnath, 2008) in any of the other patients. All patients showed complete or very severe left leg hemiplegia at the time of the assessment. Another five patients met the above inclusion and exclusion criteria but were not recruited due to time restrictions. All patients underwent neurological and neuropsychological assessment. All participants gave written informed consent according to the Declaration of Helsinki and the study was approved by the local trust’s ethical committee.

Neuropsychological assessment

In addition to the anosognosia tests mentioned above, all patients were assessed using standardized tests. Premorbid intelligence was assessed using the Wechsler Test of Adult Reading (Wechsler, 2001). Current intelligence was assessed using five Wechsler Adult Intelligence Scale-III (Wechsler, 1998) subtests: (i) vocabulary; (ii) similarities; (iii) digit span; (iv) arithmetic; and (v) matrix reasoning. Visual fields were tested with the customary ‘confrontation’ technique (Bisiach et al., 1986). Unilateral visuospatial neglect was assessed using the conventional subtests of the Behavioural Inattention Test,
including line crossing, letter cancellation, star cancellation, figure and shape copying, line-bisection and representational drawing. The 'one item test' (Bisiach et al., 1986) and 'comb/razor test' (McIntosh et al., 2000) were used for the assessment of personal neglect. Three subtests of the Rivermead Assessment of Somatosensory Performance (Winward et al., 2002) were used for the measurement of sensory functions 'surface touch', 'tactile extinction' and 'proprioception'. Reasoning abilities were assessed using the Cognitive Estimates Test (Shallice and Evans, 1978) and the Proverbs subtest of the Delis–Kaplan Executive Function System (Delis et al., 2001). Inhibition of automatic responses was assessed with the Hayling Test (Burgess and Shallice, 1997; see below for detailed description). The Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) was used to assess depression and anxiety (scores 0–7 = normal range; 8–10 = borderline; >10 = severe levels of anxiety or depression). The Rosenberg Self-Esteem Scale (Rosenberg, 1965) was used to measure self-esteem (range 0–30; 15–25 = normal range; <15 = low self-esteem). Patients' demographic characteristics and their performance on the aforementioned neuropsychological tests are summarized in Table 1.

Independent sample t-tests revealed that the groups did not differ in age, education or time since onset at assessment. As expected, the awareness scores of the two groups differed significantly in both interviews used. The two groups did not differ in their general premorbid or current intelligence scores and there were no significant differences in their reasoning and inhibition abilities as measured by three executive tasks. However, both groups performed worse than would be expected on the basis of their premorbid IQ on the Wechsler Adult Intelligence Scale-III Matrix reasoning subtest and on the Cognitive Estimates Test, suggesting difficulties in both visual and verbal abstract thought and problem-solving. Both groups showed basic left visual and sensory deficits. In addition, both groups showed left visuospatial, sensory and personal neglect. Interestingly, the latter appeared significantly more severe in the AHP group. The scores of both groups were considered to be within normal limits for a patient population in a general hospital on the Hospital Anxiety and Depression Scale, but patients with AHP showed lower scores (not statistically significant) for depression and anxiety compared with patients with hemiplegia.

Finally, both groups scored within the normal limits of the general population in the self-esteem measure and there were no differences between them.

Experimental investigations

Design and analysis

We used an inhibition task to study implicit processing of deficit-related material and a rating task to study explicit processing of the same material. The experiment manipulated the effect of group (the AHP group versus the HP group) and the effects of emotional content ('negative', 'neutral' and 'deficit-related' sentences) on explicit ratings of self-relevance and separately on implicit measures of response latency (reaction times) and the number of suppression errors on a modified inhibition (Stroop-like) task. As in several studies using the Stroop procedure with emotional material (e.g. Charash and McKay, 2002; Kampman et al., 2002), we computed composite measures of interest by subtracting each participant's mean ratings, mean response latencies and mean number of errors for 'neutral' sentences from their mean ratings and mean response latencies, and mean number of errors for 'negative' and 'deficit-related' sentences, respectively. This design allowed for 2 (AHP group versus HP group) × 2 ('negative' minus 'neutral' versus 'deficit-related' minus 'neutral' sentences) comparisons.

In order to explore which and how many of the patients with AHP differed significantly from controls in their explicit ratings and implicit responses to deficit-related sentences, we used the Revised Standardized Difference Test (RSDT; Crawford et al., 1998; revised in Crawford and Garthwaite, 2005). This is a specialized statistical test developed for comparing the difference between a patient's performances on two tasks with the distribution of differences in controls.

It was developed specifically for use in neuropsychological studies with small control samples and can address the question of whether there is evidence of dissociation between two different tasks in an individual patient.

This study employed a modified version of the Hayling Test (Burgess and Shallice, 1997), a standardized test of 'automatic response suppression'. The original test has two sections, both consisting of 15 sentences that are missing the last word. The critical Section 2 requires the subject to complete the sentence with a word that is completely 'unconnected' to the sentence in every way. In other words, this section requires the subject to inhibit an automatic verbal response and to generate a different response that must be completely unrelated to the theme of the sentence. It yields two measures of the ability of the participant to suppress a response (an error score and the time taken to respond). Thus, in summary, this test provides a measure of response suppression, which has been shown to be impaired in some patients with frontal lobe lesions (Burgess and Shallice, 1997).

The Emotional Hayling Task

Section 2 of the original Hayling Test was modified to manipulate the emotional theme of the sentences. The Emotional Hayling Task used in the present investigation consisted of 30 sentences that were missing the last word. They varied in theme as follows: (i) 10 sentences related to cars and motoring issues (emotionally neutral sentences hereafter referred to as 'neutral'); (ii) 10 sentences related to violence and physical assault (emotionally negative sentences hereafter referred to as 'negative'); and (iii) 10 sentences related to stroke and motor deficit (emotionally negative sentences specifically related to patients' deficits hereafter referred to as 'deficit-related'). Other than this emotional theme manipulation, the three sets of sentences were matched for syntactic structure, word count and semantic content as closely as possible.

Example 1: (i) neutral sentence: 'A tow truck is often used to pull broken-down cars off the...'; (ii) negative sentence: 'An ambulance is often used to take assaulted people to the...'; and (iii) deficit-related sentence: 'A hoist is often used to lift paralysed patients off the...'.

Example 2: (i) neutral sentence: 'Some cars can be repaired following motor accidents but others might be left with some permanent mechanical...'; (ii) negative sentence: 'Some people recover completely following physical attacks but others might be left with some permanent emotional...'; and (iii) deficit-related sentence: 'Some people recover completely following brain damage but others might be left with some permanent motor...'.

A pilot study with 23 adults (11 males and 12 females, graduate students with mean age 22.5 years and SD 3.6 years, range 20–33 years) was conducted to validate the Emotional Hayling Task in relation to the original standardized Hayling Test. All subjects completed the original and modified Hayling Test on separate sessions, in counterbalanced order. There were no gender differences in the performance of either test. Furthermore, the reaction times and errors in both males and females were never greater than 2SD from the mean of each subject for each category of content ('neutral', 'negative' or 'deficit-related'). Performance on the original Hayling Test (response inhibition speed and errors) was positively correlated with performance on the Emotional Hayling Task ($r = 0.78$, $P < 0.01$ and $r = 0.81$, $P < 0.01$).
Table 1 Groups’ demographic characteristics and neuropsychological profile

<table>
<thead>
<tr>
<th></th>
<th>AHP (n = 7)</th>
<th>HP controls (n = 7)</th>
<th>t</th>
<th>df</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>64.00</td>
<td>56.86</td>
<td>0.97</td>
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<td>Education (years)</td>
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<td>Days from onset</td>
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<td>21.29</td>
<td>0.32</td>
<td>8.13</td>
<td>0.76</td>
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<td>105.50</td>
<td>0.37</td>
<td>5.05</td>
<td>0.73</td>
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<tr>
<td>Berti awareness left upper limb</td>
<td>1.43</td>
<td>0.00</td>
<td>7.07</td>
<td>6</td>
<td>0.01</td>
</tr>
<tr>
<td>Berti awareness left lower limb</td>
<td>1.86</td>
<td>0.14</td>
<td>7.07</td>
<td>6</td>
<td>0.01</td>
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<td>AHP questionnaire</td>
<td>5.64</td>
<td>0.93</td>
<td>0.37</td>
<td>5.05</td>
<td>0.73</td>
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<td>WAIS—III vocabulary</td>
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<td>9.00</td>
<td>0.41</td>
<td>10</td>
<td>0.69</td>
</tr>
<tr>
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<td>9.17</td>
<td>0.54</td>
<td>10</td>
<td>0.60</td>
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<td>0.60</td>
<td>7</td>
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<tr>
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<td>9.00</td>
<td>1.28</td>
<td>7</td>
<td>0.24</td>
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<tr>
<td>Visual fields right</td>
<td>9.29</td>
<td>9.86</td>
<td>2.45</td>
<td>12</td>
<td>0.03</td>
</tr>
<tr>
<td>Visual fields left</td>
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<td>5.71*</td>
<td>1.80</td>
<td>12</td>
<td>0.10</td>
</tr>
<tr>
<td>Visual fields both</td>
<td>1.14*</td>
<td>2.43*</td>
<td>1.25</td>
<td>12</td>
<td>0.24</td>
</tr>
<tr>
<td>RASP surface touch left—max 30</td>
<td>6.57*</td>
<td>6.23*</td>
<td>0.13</td>
<td>12</td>
<td>0.90</td>
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<td>3.86</td>
<td>0.63</td>
<td>12</td>
<td>0.54</td>
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<td>RASP sensory extinction—max 12</td>
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<td>7.5</td>
<td>1.11</td>
<td>7</td>
<td>0.30</td>
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<tr>
<td>RASP proprioception—max 30 movement detection left</td>
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<td>4.43</td>
<td>0.00</td>
<td>12</td>
<td>1.00</td>
</tr>
<tr>
<td>RASP proprioception—max 30 direction detection left</td>
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<td>2.31</td>
<td>0.31</td>
<td>9.28</td>
<td>0.76</td>
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<tr>
<td>Combr/razor test right</td>
<td>27.9</td>
<td>23.14</td>
<td>0.77</td>
<td>6.49</td>
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<td>16.00</td>
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<td>0.17*</td>
<td>2.11</td>
<td>7.6</td>
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<td>BIT total score</td>
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<td>84.00*</td>
<td>0.18</td>
<td>11</td>
<td>0.86</td>
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<td>Line crossing right</td>
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<td>16.17</td>
<td>1.44</td>
<td>5</td>
<td>0.21</td>
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<tr>
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<td>13.50*</td>
<td>1.82</td>
<td>10</td>
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<td>1.22</td>
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<td>10.00*</td>
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<td>11</td>
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<td>22.33</td>
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<td>Copy</td>
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<td>2.71*</td>
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<td>Representational drawing</td>
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<td>0.23</td>
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<td>Line bisection centre</td>
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<tr>
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<td>4.29</td>
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</tr>
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<td>Hayling Test errors</td>
<td>3.86</td>
<td>3.00</td>
<td>0.76</td>
<td>10.07</td>
<td>0.46</td>
</tr>
<tr>
<td>Proverbs</td>
<td>7.80</td>
<td>12.00</td>
<td>1.64</td>
<td>8</td>
<td>0.14</td>
</tr>
<tr>
<td>Cognitive estimates</td>
<td>9.29*</td>
<td>8.33*</td>
<td>0.73</td>
<td>11</td>
<td>0.48</td>
</tr>
<tr>
<td>HADS depression</td>
<td>4.57</td>
<td>7.43</td>
<td>1.11</td>
<td>12</td>
<td>0.29</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>8.00</td>
<td>7.86</td>
<td>0.05</td>
<td>12</td>
<td>0.96</td>
</tr>
<tr>
<td>Self-esteem</td>
<td>21.57</td>
<td>20.71</td>
<td>0.32</td>
<td>12</td>
<td>0.76</td>
</tr>
</tbody>
</table>

AHP questionnaire = Feinberg et al. (2000) Awareness Questionnaire; Berti awareness = Berti et al. (1996) Awareness Interview; BIT total score = sum of scores of the conventional sub-tests of the Behavioural Inattention Test; Combr/razor test = tests of personal neglect. Bias on the latter is calculated according to McIntosh et al. (2000); HADS = Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983); Proverb test = Delis Kaplan—Executive Functions System—Proverbs Subtest (Delis et al. 2001); RASP = The Rivermead Assessment of Somatosensory Performance (Winward et al., 2000); Self-esteem = Rosenberg Self-Esteem Scale (1965); Visual fields = the customary ‘confrontation’ technique (Bisiach et al., 1986); WAIS—III = Wechsler Adult Intelligence Scale—3rd Edition (Wechsler, 1998); WTAR = Wechsler Test of Adult Reading (Wechsler, 2001).

a Scores below tests’ cut-off point, or more than 1 SD below the average mean.

*Significant differences between the groups, P<0.05.

**Trends towards significance, P<0.10.
Implicit awareness in anosognosia for hemiplegia

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P<0.001, respectively), indicating that the Emotional Hayling Task is a valid test of verbal inhibition.

Procedure and scoring

The original Hayling Test and the Emotional Hayling Task were administered in separate sessions scheduled at least 2 days apart. The original Hayling Test was administered in the first session in all patients to increase their familiarity with the test’s procedure and demands. In the second session, the instructions from the original Hayling Test (Part 2) were again read out to participants. They were informed that a new series of sentences would be read to them. Sentences were read out clearly in a neutral manner and at a steady pace. Participants were informed that they would be timed. Two practice examples were given to each participant, as in the original test. The sentences of the Emotional Hayling Task were read out to participants in a random order, and timing began as soon as the last word of the incomplete sentence was read. Patients’ answers were scored for reaction time in milliseconds using a handheld Samsung stopwatch.

The original Hayling Test’s scoring guidelines and instructions were followed as closely as possible. As in the original test, reaction times and the following errors were noted: (i) connected completions and (ii) somewhat connected completions. For example, the answer ‘hospital’ to the sentence ‘An ambulance is often used to take assaulted people to the...’ was considered a ‘connected completion’ error. The answer ‘floor’ to the sentence ‘A hoist is often used to lift paralysed patients off the...’ was considered a ‘somewhat connected completion’ error. Finally, the answer ‘classroom’ to the sentence ‘A tow truck is often used to pull broken-down cars off the...’ was considered a correct (unconnected) response. Unlike the original Hayling Test, reaction times were not rounded up to seconds but were recorded in milliseconds. In addition, reaction times that were above or below 3 SD of the participant’s mean reaction time per sentence type were excluded from the analysis as outliers (Kampman et al., 2002). This occurred only twice and not in the same patient.

In a final, third session, scheduled at least 2 days after the Emotional Hayling Task session, the 30 incomplete sentences of the Emotional Hayling Task were read out to participants in a random order, and they were asked to rate how much the theme of each completed sentence was relevant to them in their current situation on a scale from 1 to 10 (anchored at ‘1 = not relevant to my current situation at all’ and ‘10 = extremely relevant to my current situation’). Their responses were not timed.

To summarize, both the AHP and HP groups completed an implicit awareness test consisting of a verbal inhibition task, which included sentences of varying emotional content (‘neutral’, ‘negative’ and ‘deficit-related’). Subsequently, both groups were also asked to make explicit ratings of the self-relevance of the same sentences (explicit awareness task). It was expected that while the patients with AHP would rate the ‘deficit-related’ sentences as less self-relevant than controls, they would be significantly slower than controls in completing the inhibition task (due to unconscious interference) with these sentences than with other emotionally ‘negative’ sentences (both relative to ‘neutral’ sentences).

Lesion analysis methods

Patient lesions were mapped on slices of the T1-weighted MRI scan template (ICBM152) from the Montreal Neurological Institute. This template is approximately oriented to match Talairach space (Talairach and Tournoux, 1988). All lesion plots were drawn on the standard Montreal Neurological Institute space (2×2×2 mm) by one of us (S.P.), who was blind as to which patient group each scan was from. By using the MRICro software (http://www.cabiatl.com/mricro/mricro/index.html; Rorden and Brett, 2000), the template was first rotated to match the orientation of the patient’s MRI or CT scan. The scan images of the patient’s brain were then normalized and aligned (by digital image editing software) to superimpose onto the rotated template slices. The patient’s lesions were outlined on the rotated template, resulting in a map in which each voxel was labelled either 0 (intact) or 1 (lesion). Afterwards, the 3D volumes obtained were rotated back to match the stereotaxic space of the Montreal Neurological Institute T1-weighted template by using the interpolation of the nearest-neighbour voxels. The derived volumes representing the lesions of each patient were superimposed onto the ‘automated anatomical labelling’ template (http://www.cyceron.fr/web/aal_anatomical_automatic_labeling.html; Tzourio-Mazoyer et al., 2002) to determine the lesion voxels of the different cerebral structures as calculated by the MRICro software (Rorden et al., 2007). The lesion involvement of white matter structures and connections was achieved by means of the lesion plots’ overlap with the ‘white matter parcellation map’ template (Mori et al., 2008).

Results

Explicit awareness

The groups’ explicit ratings of self-relevance to ‘deficit-related’, ‘neutral’ and ‘negative’ sentences are shown in Table 2. As expected, the patients with AHP rated the ‘deficit-related’ sentences as less self-relevant than did the patients with hemiplegia. This difference was not observed for the ‘neutral’ and ‘negative’ sentences. To verify the statistical significance of these differences, we conducted a 2 (AHP group versus HP group) × 2 (‘negative’ minus ‘neutral’ versus ‘deficit-related’ minus ‘neutral’ sentences) repeated measures ANOVA. This revealed that the self-relevance of sentences was rated as significantly different depending on their content, F(1,12) = 204.5, P < 0.001, and that there was an interaction between patient group and the content of the sentences, F(1,12) = 98.8, P < 0.001. Post hoc Bonferroni corrected t-tests (α=0.025) revealed that the two groups differed significantly in the difference ‘deficit-related’ minus ‘neutral’ sentence ratings, t(12) = 3.7, P < 0.025. This difference was not significant for the composite measure of ‘negative’ sentences (‘negative’ minus ‘neutral’ sentence ratings), t(12) = 0.4, P = 0.7. These results confirm that the patients with AHP rated the ‘deficit-related’ sentences as significantly less self-relevant than the patients with hemiplegia, relative to both groups’ ratings of ‘neutral’ sentences.

It is also noteworthy that all patients with AHP rated ‘deficit-related’ sentences as less self-relevant than any of the hemiplegic controls, and their individual scores were significantly different from the mean of the hemiplegic control group, as determined by Crawford’s test (Crawford and Howell, 1998; Crawford and Garthwaite, 2002), t’s = 4.8–7.7, P’s < 0.002. These results confirm that the anosognosic patients, selected on the basis of two established tests of motor awareness (Berti et al., 1996; Feinberg et al., 2000), showed denial of their deficits in our experimental task both individually and as a group. This confirmed the validity of our novel explicit awareness task.
Implicit awareness

Reaction times

The groups’ average reaction times in each content category for correct and error responses, as well as for correct responses only, are presented in Table 2. A 2 (AHP group versus HP group) × 2 (‘negative’ minus ‘neutral’ versus ‘deficit-related’ minus ‘neutral’ sentences) repeated measures ANOVA revealed that reaction times were not overall significantly different depending on the sentence content, F(1,12) = 2.7, P = 0.12, but there was a significant interaction between group and content of sentences, F(1,12) = 8.2, P < 0.05. Post hoc Bonferroni corrected t-tests (α = 0.025) revealed that the two groups differed significantly in the difference (‘deficit-related’ minus ‘neutral’ sentences) reaction times, t(12) = 3.2, P < 0.025, but not in the difference (‘negative’ minus ‘neutral’ sentences) reaction times, t(12) = 0.4, P = 0.66.

In a second analysis, we explored the reaction times of the two groups for only correct responses. In this analysis two subjects, AHP4 and HP5, who had <10 correct responses (22/30 and 24/30 errors, respectively) were excluded as outliers (see also Kampman et al., 2002). A 2 (AHP group versus HP group) × 2 (‘negative’ minus ‘neutral’ versus ‘deficit-related’ minus ‘neutral’ sentences) repeated measures ANOVA revealed that reaction times were not overall significantly different depending on the sentence content, F(1,10) = 1.7, P = 0.22, but there was a significant interaction between group and content of sentences, F(1,10) = 6.34, P < 0.05. Post hoc, Bonferroni corrected t-tests (α = 0.025) revealed that the two groups differed significantly in the difference (‘deficit-related’ minus ‘neutral’ sentences) reaction times, t(10) = 2.6, P < 0.025, but not in the difference (‘negative’ minus ‘neutral’ sentences) reaction times, t(10) = 1.7, P = 0.1.

Table 2  Groups’ performance on the Emotional Hayling Task

<table>
<thead>
<tr>
<th>Emotional Hayling Task scores</th>
<th>AHP (n = 7)</th>
<th>HP (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explicit (ratings)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘Negative’</td>
<td>1.9 (0.4)</td>
<td>1.8 (0.7)</td>
</tr>
<tr>
<td>‘Neutral’</td>
<td>3.1 (1.7)</td>
<td>3.5 (2.3)</td>
</tr>
<tr>
<td>‘Deficit-related’*</td>
<td>3 (0.8)</td>
<td>7.9 (0.6)</td>
</tr>
<tr>
<td>Implicit (reaction times)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>correct responses only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘Negative’</td>
<td>8.4 (7.4)</td>
<td>8.2 (5.5)</td>
</tr>
<tr>
<td>‘Neutral’</td>
<td>7.6 (8.4)</td>
<td>6.4 (2.8)</td>
</tr>
<tr>
<td>‘Deficit-related’*</td>
<td>17.7 (16.5)</td>
<td>5.7 (2.9)</td>
</tr>
<tr>
<td>Implicit (reaction times)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>correct responses only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘Negative’</td>
<td>5.9 (4.4)</td>
<td>7.2 (3.6)</td>
</tr>
<tr>
<td>‘Neutral’</td>
<td>6.7 (7.4)</td>
<td>4.5 (1.8)</td>
</tr>
<tr>
<td>‘Deficit-related’*</td>
<td>16.8 (17.2)</td>
<td>3.7 (2.2)</td>
</tr>
<tr>
<td>Implicit (errors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘Negative’</td>
<td>4.7 (2.6)</td>
<td>5 (2.4)</td>
</tr>
<tr>
<td>‘Neutral’</td>
<td>4.4 (2.6)</td>
<td>5.1 (2.3)</td>
</tr>
<tr>
<td>‘Deficit-related’*</td>
<td>4 (2.7)</td>
<td>6.4 (2.6)</td>
</tr>
</tbody>
</table>

* Significant difference between the groups.

Individual patient analysis

We used the specialized RSDT (see the ‘Design and analysis’ subsection) to explore how many of the patients with AHP differed significantly from the control sample in their explicit ratings and implicit responses to deficit-related sentences. We applied this method to the differences between ‘deficit-related’ and ‘neutral’ sentences in explicit ratings versus implicit reaction times, as these were the differential measures that were found to be significantly different between the two groups (see above). As above, we analysed the reaction times for correct responses only and in a separate analysis for correct and incorrect responses.

The RSDT indicated a significant dissociation in all patients with AHP except Patient AHP7, when considering either correct responses and errors (t_e = 1, P = 0.17) or only correct responses (t_e = 1.3, P = 0.12). These results are presented in Table 3. Given this difference, we also looked at the differences between Patient AHP7 and the rest of the AHP group in all of the neuropsychological and psychometric tests administered. Patient AHP7 scored within the range of the rest of the AHP group on all of the neuropsychological tests, including the original Hayling Test. However, he did show a marked difference in self-reported depression, scoring 15 while the rest of the patients scored between 1 and 6 [mean 2.84; SD 2.86]. He also showed the highest score on anxiety (13; AHP group mean 7.16; SD 4.25; range 2–12) and the lowest score on self-esteem (15; AHP...
group mean 22.67; SD 5.08; range 19–29). When assessed with the Crawford test (Crawford and Garthwaite, 2002), only the difference in depression scores was significant \([t = 3.94; P_{(\text{two-tailed})} < 0.05]\).

### Lesion analysis

All the lesions resulted from a single ischaemic or haemorrhagic stroke and were confined to the right hemisphere, mainly in the territory of the right middle cerebral artery. In the AHP group, Patients AHP1, AHP5 and AHP7 suffered from large hemispheric brain lesions affecting most of the right middle cerebral artery territory, involving cortical and subcortical areas. Patients AHP2, AHP3 and AHP4 had subcortical damage affecting mainly the basal ganglia, insula and surrounding white matter. Patient AHP6 showed a hemispheric lesion, mostly subcortical but extending to the medial parts of the frontal and occipital cortex. Figure 1A illustrates the lesions overlapping in three or more patients with AHP. In the control group, Patients HP2, HP3 and HP4 had lesions that were mostly subcortical, extending from the thalamus and the basal ganglia to the insula and the surrounding white matter. Patients HP1 and HP6 had frontotemporo-parietal hemispheric lesions, Patient HP7 had a frontotemporal lesion and Patient HP5’s lesion involved mainly dorsomedial cortical areas and the deep white matter. Figure 1B illustrates the lesions overlapping in three or more patients with hemiplegia.

No significant difference was observed in the total volumes of the lesions in the AHP group (mean 132 cm³, SD = 110) and HP group [mean 93 cm³, SD = 98; \(t(14) = 0.69, P = 0.68\)]. Subtracting HP group lesion plots from the AHP group lesion plots gave a cluster that remained present in at least five patients with AHP. This cluster involved mainly the anterior part of the insula and extended through the anterior corona radiata and the external capsule to the caudate and putamen nuclei (Fig. 1C and D).

By using the non-parametric mapping software available with MRicro, we compared the frequency of lesion voxels in the two groups by computing a binomial test based on the Lieberman measure (false discovery rates corrected), because this binomial test appears to be more sensitive than chi-squared or Fisher’s Exact test (Phipps, 2003). The significant areas emerging from the binomial test were in line with the subtraction results, revealing a superior cluster extending from the rolandic operculum and anterior insula to the caudate and putamen nuclei, and an inferior cluster involving the amygdala and the superior temporal pole. White matter tissue included the anterior corona radiata, the external capsule, the retro-lenticular part of the internal capsule, and the uncinate fasciculus (Fig. 1E and F).

In order to explore a possible causal correlation between the lesions of Patient AHP7 and his lack of implicit awareness, we compared his lesions with those of the others in the AHP group (Fig. 2). The lesions of Patient AHP7 overlapped with several of the common lesion areas of the other patients with AHP, but showed more lesion voxels in posterior (posterior and medial regions of the occipital lobe) anterior (medial regions of the frontal lobe) and dorsolateral cortical regions (pre-central and post-central areas). He also showed fewer lesion voxels in limbic regions (e.g. the amygdala), the basal ganglia and the external capsule.

### Discussion

The present study used an inhibition task to study implicit processing of deficit-related material and a rating task to study explicit processing of the same material in left hemiplegic patients with and without AHP. The main behavioural finding was that patients with AHP were significantly slower than control patients in performing the inhibition task with deficit-related sentences than with other emotionally negative sentences, relative to neutral sentences in both cases. The main finding of the lesion analysis was that the lesions of the patients with AHP differed from those of the hemiplegic controls by involving mainly the anterior parts of
the insula, inferior motor areas, basal ganglia structures, limbic structures and deep white matter. The one patient with AHP who did not show dissociation between implicit and explicit awareness of deficit showed more lesions in cortical frontal areas, including lateral motor and premotor regions, and also in the parietal and occipital lobes.

The selective slowing of responses to emotional stimuli in Stroop-like tests is considered to reflect 'unconscious' response competition between the processing of emotional self-threatening information and the requirement to complete the task (Pratto and John, 1991; Wentura et al., 2000). We propose that our findings in the patients with AHP reflect a similar 'unconscious' response.
competition between the processing of deficit-related information and the requirement to complete the inhibition task. In contrast, patients with AHP did not differ from controls in their overall ability to perform the inhibition task as assessed by the original, standardized test of verbal inhibition (the Hayling Test). Secondly, the observed effect of inhibition in the patients with AHP was based on a ‘differential’ slowing of response times for deficit-related versus neutral words, rather than an absolute measure of response speed (see also Nardone et al., 2007). Thus, it is unlikely that this effect relates to the general inhibitory abilities of the patients with AHP. In addition, the patients with AHP showed more lesions than the hemiplegic patients in right limbic and insular cortex areas (see also below) and a corresponding reduction in the experience and communication of negative emotions (see Heilman and Harciarek, 2010 for review). Nevertheless, it is unlikely that our main experimental effects were driven by these emotional processing difficulties, or any general ‘defence’ function against negative emotions (see below), as patients with AHP did not show a tendency to process other emotionally negative themes differently than hemiplegic controls. Finally, it is unlikely that this effect related to dissociations between modalities, as both the implicit and explicit tasks included listening to, comprehending and verbally responding to the same sentences.

The above considerations suggest that our study provides strong experimental support for implicit awareness of deficit in some anosognosic patients. Implicit awareness has previously been hypothesized based on clinical observations (e.g. Weinstein and Kahn, 1955; Ramachandran, 1995) and case studies (Nardone et al., 2007). The three tables provide a quantitative estimate of the region plots lesioned (i) in Patient AHP7 but not in the other patients with AHP; (ii) in patients with AHP excluding Patient AHP7; and (iii) finally the common lesions of the six patients with AHP and Patient AHP7. For each region, the number (n) and the percentage (n%) of lesioned voxels are shown. MNI = Montreal Neurological Institute.

**Figure 2** Regional lesion plot of Patient AHP7 (in blue, centre of mass: x = 41; y = –22; z = 23). The red and yellow colours represent the lesion voxels of the other six patients with AHP. The number of overlapping lesions is illustrated by different colours coded for increasing frequencies, from dark red (lesion in one patient with AHP) to light yellow (lesion voxels overlap in six patients with AHP).
et al., 2007). The present experimental confirmation of this dissociation is important because the combination of our behavioural and neuroimaging results may thus shed some light on the deficits leading to explicit unawareness in AHP and the potentially intact mechanisms responsible for implicit awareness.

Recent studies have postulated that explicit unawareness in AHP is caused by a deficit in monitoring the discrepancy between intended and actual movement (Frith et al., 2000; Berti et al., 2005; Pia and Berti, 2006). This deficit can lead to the construction of non-veridical motor awareness based entirely on representations of intended movement (Berti et al., 2007; Fotopoulou et al., 2008; Desmurget and Sirigu, 2009). This hypothesis has been supported by neuroimaging evidence (Berti et al., 2005); areas involved in motor preparation and planning (e.g. the supplementary motor area) were found to be spared in patients with AHP. In contrast, lateral premotor regions, which are typically involved in monitoring discrepancies between intention and action, were selectively affected in these patients.

Our neuroimaging results in the present study are consistent with the above proposals, in that motor areas around the rolandic operculum were more frequently damaged in patients with AHP than patients with hemiplegia. Moreover, as in the study of Berti et al. (2005) the supplementary motor area was spared in all the patients with AHP. These results confirm the hypothesis that motor planning is intact in patients with AHP (Frith et al., 2000; Berti et al., 2005) and may lead some patients to form illusory awareness of movements (Fotopoulou et al., 2008; for review see Jenkinson and Fotopoulou, 2010).

However, the dorsal premotor area (e.g. Brodmann area 6) was not damaged more frequently in patients with AHP than patients with hemiplegia in the present study. In Berti and colleagues’ (2005) study, this was the brain region most frequently associated with AHP. In the present study, it was affected in only the patient who showed explicit but not implicit awareness. Only three other patients with AHP had damage to this area and this damage was minimal. This finding suggests that an intact or partly damaged lateral premotor cortex may facilitate implicit awareness of deficit. Future studies will need to explore this finding further and consider the potential role of other brain areas (e.g. parietal areas) in residual sensorimotor monitoring and implicit awareness. Such findings would suggest that implicit awareness is generated within intact sensorimotor mechanisms. Whatever the outcome of such studies, however, our current experimental investigations suggest that such implicit awareness is not sufficient to counter patients’ more general, explicit belief that they can move.

More broadly, the observed dissociation between implicit and explicit awareness is consistent with the observation that AHP sometimes has delusional features that cannot be explained solely on the basis of sensorimotor deficits (Ramachandran, 1995; Solms, 1999; Frith et al., 2000; Vuilleumier, 2004; Fotopoulou, 2010). The latter can perhaps explain the ‘illusion’ of moving (Fotopoulou et al., 2008), but patients with AHP do not simply claim that they have illusions of moving. They instead ignore the wealth of evidence that they are paralysed (e.g. their disabilities, occasional accidents, others’ feedback) and adhere to the ‘delusional’ belief that they have functional limbs. The explanation of the latter belief requires the postulation of another dysfunction that prevents sensorimotor and other failures from being re-represented at a higher level of cognitive self-representation.

Indeed, a number of authors have noted that the delusional, explicit aspects of AHP can best be explained as an inability to attribute motor errors and other failures to oneself and update one’s self-representation accordingly (Ramachandran, 1995; Marcel et al., 2004; Vuilleumier, 2004). Consistent with the present study, these hypotheses are supported by clinical observations of implicit awareness in patients with AHP. For example, Marcel and colleagues (2004) observed that patients with AHP were more accurate in describing their deficits from a third-person than a first-person perspective. Similarly, when Fotopoulou et al. (2009) improved explicit awareness in a patient with AHP (patient LM) by showing her a third-person and ‘off-line’ perspective of her body in a video replay, she also confirmed that at some level she had been aware of her disability all along. Ramachandran (1995) also reported a patient with AHP who was retrospectively able to accurately comment on how long she had been paralysed during temporary lifting of the AHP following vestibular stimulation. Despite this temporary insight, after the stimulation effect wore off, the patient reverted to denying her paralysis and the admission of it during stimulation. Together with the present experimental findings, these observations suggest that in at least some patients with AHP, information about their deficit has been (implicitly) laid down continuously in their memory. Nevertheless, patients lack the ability to integrate these implicit memories into an explicit and stable self-awareness.

Interestingly, negative emotions may be among the information that these patients fail to self-attribute and explicitly experience. For example, the aforementioned improvement of awareness in Patient LM was not associated with improvement in cognitive or sensorimotor functions, but with a quantified increase in depressive symptoms (Fotopoulou et al., 2009). Similar observations of a sudden influx of depressive symptoms (‘catastrophic reactions’; Goldstein, 1939) during episodes of transient awareness have been noted in patients who are otherwise unaware of or indifferent towards their deficits (Kaplan-Solms and Solms, 2000; Turnbull et al., 2002, 2005). In addition, it has been noted that some patients with AHP, who appear emotionally unresponsive towards their deficits, tend nevertheless to experience disproportionately intense negative emotions about minor unpleasant situations and other people (Kaplan-Solms and Solms, 2000; Fotopoulou and Conway, 2004).

Thus, it seems that in several patients with AHP, certain dysfunctions prevent awareness of motor failures and the corresponding negative emotions to be integrated with explicit awareness of the self. Some authors have argued that this lack of explicit awareness is caused by psychogenic ‘defence’ mechanisms directed against anxiety and depression (Weinstein and Kahn, 1995). However, the relative neuroanatomical and behavioural specificity of anosognosic behaviours suggests that such purely psychological mechanisms are insufficient to explain AHP (for a recent critical review, see Heilman and Harciarek, 2010). Importantly, the fact that such ‘denial’ behaviours occur following specific brain lesions can allow us to put forward more parsimonious, empirically informed accounts of brain mechanisms that when damaged can
lead to such delusional behaviours and attitudes (see Fotopoulou, 2010 for discussion of this approach, heuristically labelled ‘affective neuropsychology’). Based on our current and previous findings, as well as on results of other groups (Berti et al., 2005; Karnath et al., 2005), we propose that the likely candidate lesions for such impairment in explicit cognitive and emotional awareness include the anterior insular cortex and adjoining frontal areas, with possible involvement of limbic areas and cortico-striato-thalamic pathways. We will briefly discuss these possibilities in relation to the present findings.

Consistent with previous studies (Berti et al., 2005; Karnath et al., 2005; Baier and Karnath, 2008), we found that the anterior parts of the right insula were differentially damaged in patients with AHP. A plethora of recent neuroimaging studies have suggested that anterior parts of the insula seem to be responsible for the re-representation of multisensory, motor and interoceptive information that is first processed in other cortical and subcortical areas and converge in the mid-posterior insula (Critchley et al., 2004; for reviews see Craig, 2009; Tsakiris, 2010). Some authors have proposed on this basis that the anterior parts of the right insular cortex are central areas in the neural circuit that subserves a stable, embodied and emotionally embedded meta-representation of oneself in the present moment (Damasio, 1994; Craig, 2009). This representation inherently creates a subjective, first-person perspective that differentiates between inner and outer spheres and supports all cognitive and emotional operations that require the distinction between self and other (e.g. attribution of agency). It is thus possible that in patients with AHP, damage to the right anterior insula and adjoining frontal areas contributes to impairment in the re-representation of information processed in other sensorimotor and emotional regions. This could render this information more likely to be ignored or attributed to other people and causes (Kaplan-Solms and Solms, 2000; Fotopoulou and Conway, 2004; Marcel et al., 2004) and less likely to be explicitly self-attributed.

It should be noted that in the present study, anterior and middle but not posterior parts of the right insula were differentially damaged in patients with AHP. Karnath and colleagues (Karnath et al., 2005; Baier and Karnath, 2008) proposed that the right posterior insula is uniquely associated with AHP. Berti et al. (2005) found that both anterior and posterior parts of the right insula were among the areas specifically associated with AHP. These discrepancies can potentially be explained by distinct patient recruitment criteria, which are important to note, particularly given the observed clinical heterogeneity of AHP. In the studies of Karnath et al. (2005) there was a high incidence of body ownership disturbances. This association has not been reported in other studies (e.g. Berti et al., 2005). In our study there was only one patient with indications of somatoparaphrenia (Patient AHP5). Interestingly, in this patient, unlike the rest of the patients with AHP, both the anterior and posterior parts of the insula were affected. Taken together, these findings suggest that the right anterior insula may be responsible for an integrated sense of bodily awareness that includes motor agency (see also Farrer and Frith, 2002; Craig, 2009; Tsakiris et al., 2010), while the posterior insula may be a critical part of the network responsible for more basic interoceptive representation and body ownership (Craig, 2002; Olausson, et al., 2005; Tsakiris et al., 2007). Finally, our results, as well as those of previous neuroimaging studies on AHP (Berti et al., 2005; Karnath et al., 2005; Baier and Karnath, 2008), do not directly address the potential role of the left insula in body and emotional awareness (see Craig, 2009 for discussion). Nevertheless, it is noteworthy that some neuroimaging studies of motor and emotional awareness have found bilateral activation of insular cortex (e.g. Farrer and Frith, 2002). Interestingly, a recent study of a patient with epilepsy following herpes simplex encephalitis who developed Cotard’s syndrome (a severe form of unawareness typically including the delusional belief that one is dead, or dying, as well as various other self-deprecatory delusions, suicidal ideation, feelings of guilt and denial of body parts) reported bilateral lesions to the insular cortex (McKay and Cipolotti, 2007). Future lesion studies could thus explore the specific roles of the right and left insular cortex in motor and emotional awareness and importantly their combined functional role.

Our results also suggest an association between AHP and subcortical lesions, including basal ganglia and amygdala damage. Vuilleumier (2004) has argued that damage to subcortical circuits (e.g. basal ganglia) that are involved both in motivation and in detection of ‘errors’ might lead to an inability to revise beliefs based on novel perceptual experience and uncertain bodily states. It is also of interest that the lesions of the one patient (Patient AHP7) who showed increased depression but not implicit awareness of deficit did not include damage to subcortical areas such as the amygdala or the hippocampus and showed a lesser degree of damage to basal ganglia structures. In previous studies, bilateral medial prefrontal cortex and related limbic and striato-pallido-thalamic lesions have been associated with lower levels of depression than damage to dorsal prefrontal areas or more posterior lesions (for review see Koenigs and Grafman, 2009). Interestingly, patients with such lesions in the anterior limbic areas have been found to report low levels of ‘cognitive/affective’ symptoms (such as guilt, self-dislike and sadness) but normal levels of ‘somatic’ symptoms (such as fatigue and changes in sleeping or appetite) (Koenigs et al., 2008).

Given our small sample and the inherent limitations of lesion analysis, our findings regarding the various dissociations observed and their neural correlates are preliminary. Nevertheless, in combination with previous studies, they provide tentative new insights into the psychological and neural mechanisms of the multifaceted AHP syndrome. In short, our findings suggest that: (i) some patients with AHP may show implicit awareness into their deficits, while others do not; (ii) some patients with AHP may show body ownership disturbances, while others do not; and (iii) both of these dissociations may be linked with differences in lesion sites (in motor versus interoceptive awareness areas, respectively). These observations and our previous findings of illusory awareness of movement in AHP (Fotopoulou et al., 2008) are consistent with the suggestion that AHP is a multicomponent and heterogeneous syndrome, encompassing various deficits and different clinical populations (e.g. Marcel et al., 2004; Vuilleumier, 2004; Orfei et al., 2007). Importantly, in the present study we observed that most of our patients with AHP suffered from a specific delusion of first-person awareness linked with damage to the anterior insular...
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