The Motor Unawareness Assessment (MUNA): a new Tool for the Assessment of Anosognosia for Hemiplegia

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Abstract

Background: Anosognosia for hemiplegia (AHP) is a condition in which patients with paralysis are unaware of their motor deficits. Research into AHP is important for improving its treatment and providing insight into the neurocognitive mechanism of motor awareness. Unfortunately, most studies use assessments with widely recognized limitations.

Aim: To develop a psychometrically validated assessment of AHP.

Method: We developed a 40-item Motor Unawareness Assessment (MUNA) and administered it to 131 right-hemisphere stroke patients. Principal Component Analysis (PCA) was used to identify the underlying factor structure. Receiver Operating Characteristics (ROC) analysis was used to determine diagnostic cut-offs, and Area Under the Curve (AUC) analysis used to assess these cut-offs. Relationships with demographic, clinical and neuropsychological variables were explored.

Results: Five factors were identified: explicit motor awareness, implicit motor awareness, impaired sense of ownership, agency and illusory movement, and emotional reactions. Established cut-offs had excellent sensitivity and specificity. Clinical, neuropsychological and demographic variables did not predict overall MUNA score but were related to specific subcomponents.

Conclusion: The MUNA can differentiate various facets of AHP and provides a detailed profile of (un)awareness. The MUNA can therefore provide robust assessment for research purposes and assist clinicians when developing targeted rehabilitation.

Keywords: anosognosia for hemiplegia; motor awareness; asomatognosia; emotions in body awareness; bodily awareness assessment

Introduction

Anosognosia for hemiplegia (from the Greek; a = without, nose = illness, gnosis = knowledge, AHP) describes a striking neurological condition in which patients, typically affected by right-hemisphere stroke, are seemingly unaware of their resultant motor deficits, which can include complete paralysis of one side of the body (i.e. hemiplegia). The term was introduced by Babinski (1914) and has been the subject of clinical and experimental studies for over a century. Importantly, a lack of awareness is associated with more negative outcomes after stroke (Gialanella & Mattioli, 1992; Hartman-Maeir, Soroker, & Katz, 2001). Thus, being able to identify patients with impaired awareness is critical to ensuing optimal recovery, as well as understanding the condition. Unfortunately, the identification of AHP is not a simple task.

Accumulating research has led to the general conclusion that AHP is a highly heterogeneous, multifactorial, or multidimensional disorder (Orfei, Caltagirone and Spalletta, 2009; Vocat & Vuilleumier, 2010). AHP symptoms may be specific to one, contralesional limb (arm or leg) or involve both of them. Symptoms can fluctuate, with patients giving more or less consistent responses in different moments and situations (e.g. during a formal interview or during rehabilitation). Furthermore, AHP may concern different aspects of the deficit: its nature (e.g. I can move my arm), cause (e.g. pain prevents me from moving) or its consequence for a specific action or for the patient's everyday life (e.g. I can drive a car). Some anosognosic patients state that they are able to move their paralyzed limbs, to walk, or carry out daily life activities without needing help (explicit unawareness). In contrast, other patients admit to their paralysis (explicit awareness), but behave or attempt to act as if they can move normally (behavioural, implicit unawareness, e.g., Cocchini, Beschin, Fotopoulou, Della Sala, 2010; Moro, Pernigo, Zapparoli, Cordioli, & Aglioti, 2011). Sometimes, patients recognize their current motor deficits, but are not able to anticipate their inability to perform specific actions (anticipatory unawareness, Marcel, Tegnér and Nimmo-Smith, 2004; Moro et al., 2011; D'Imperio, Bulgarelli, Bertagnoli, Avesani and Moro, 2017a; Cocchini, Beschin and Della Sala, 2018). Furthermore, adverse emotional reactions have been reported, with patients showing contemptuous attitudes for their motor impairments (e.g., use of negative names to describe their affected limbs, hate for the paralysed limbs, defensive reactions,) or a lack of concern or interest (anosodiaphoria, Babinski, 1914; see for example Turnbull, Evans, Owen, 2005; Gainotti, 2012 for a more detailed consideration of the diverse emotional reactions that can follow AHP).

This heterogeneity has resulted in long-standing problems with the assessment and understanding of AHP (Jenkinson, Preston, Ellis, 2011). For instance, AHP was initially considered a secondary consequence of sensory or attentional disorders (Levine, 1990), but double dissociations were subsequently found between AHP and basic sensory and visuo-attentional deficits (Bisiach, Vallar, Perani, Papagno, Berti, 1986; Marcel et al., 2004; Small & Ellis 1996). More recently AHP has been explained as a specific deficit of motor awareness (Frith, Blakemore & Wolpert, 2000; Berti & Pia, 2006), resulting in assessment procedures that require the execution of actions, "confrontation tasks" (i.e. requesting patients to perform a currently impossible, everyday action with their affected limb, e.g. clapping one's hands together), and corresponding behavioural measures of performance (Ramachandran, 1995; Fotopoulou, Tsakiris, Haggard, Vagapoulou, Rudd, Kopelman, 2008; Della Sala, Cocchini, Beschin, Cameron, 2009; Fotopoulou, Pernigo, Maeda, Rudd, Kopelman, 2010; Moro et al., 2011; Garbarini, Rabuffetti, Piedimonte, Pia, Ferrarin, Frassinetti et al., 2012). Experimental procedures for assessing observed differences in implicit versus explicit awareness (see above), and that capture changes in awareness following attempts to move (i.e. emergent awareness; Berti, Ladavas, Della Corte, 1996; Marcel et al., 2004; Moro, 2013; Moro, Scandola, Bulgarelli, Avesani and Fotopoulou, 2015a; D'Imperio et al., 2017a), have also been developed (see Nurmi Laihosalo & Jenkonen, 2014; for a review).

Despite this large body of research, only a handful of studies have specifically attempted to develop and validate an assessment of AHP (Nimmo-Smith, Marcel and Tegnér, 2005; Della Sala et al., 2009; Cocchini et al., 2018). The assessments available focus on single dimensions of the syndrome (e.g. verbal/explicit or implicit awareness, motor abilities or abilities to execute daily life activities) and do not include other associated aspects such as asomatognosia (i.e. a body ownership disturbance that can include impairment existence, self-recognition and sense of belonging; Jenkinson, Moro and Fotopoulou, 2018), and abnormal emotional reactions. Therefore, these measures fail to differentiate between symptoms that are specific to AHP from those that co-occur and overlap with other cognitive disorders. Contemporary theories have also suggested that AHP is caused by a functional disconnection between networks processing top-down beliefs about oneself and others (i.e. mentalization, see Fotopoulou, 2015), from those processing bottom-up errors regarding the current state of the body (see Pacella, Foulon, Jenkinson, Scandola, Bertanoli Avesani, et al., 2019). However, AHP measures typically do not capture these recent ideas.

The aim of this study was to overcome these limitations, with the development and psychometric validation of a new assessment able to investigate the various different aspects of AHP and other concomitant disorders of body awareness. In particular, based on recent empirical and theoretical advances, we considered as the crucial elements of a comprehensive assessment of AHP the aspects directly associated with motor awareness (i.e. implicit and explicit awareness, awareness for daily life activities, anticipatory awareness) along with symptoms associated with mentalization, body representations and emotional reactions. The battery of questions included in this new assessment were selected based on contemporary findings in AHP and administered to a large sample of right brain damaged patients with or without clinical signs of AHP. Our large sample enabled us to examine the factor structure of our assessment using Principal Component Analysis (PCA), and to identify the cut-off values for each of these components. As a final step, in a series of regression analyses, we examined the potential role of other neuropsychological (e.g. neglect, attention, orientation, memory, executive functions, left/right disorientation, apraxia), demographic (age, education), and clinical variables (motor and sensory deficits, interval from the Lesion, MRC for upper and lower limbs) in predicting AHP.

Materials and methods

Patients

One hundred and thirty-one patients with damage to the right hemisphere were consecutively recruited from four acute stroke wards in the United Kingdom and one neurorehabilitation clinic in Italy (IRCSS Sacro Cuore Hospital, Negrar, Verona, Italy) over a period of five years. Data for 25 of the current anosognosic patients and 17 of the controls have been previously described in small sample group studies (D’Imperio, et al., 2017a - AHP N =8; Besharati , Kopelman, Avesani, Moro, Fotopoulou, 2015; Besharati, Forkel, Kopelman, Solms, Jenkinson, Fotopoulou, 2016 – AHP N =17, HP N = 17).

Patients were eligible if they had (i) a stroke-induced right hemisphere lesion as confirmed by clinical neuroimaging; (ii) contralateral upper limb motor deficits (Medical Research Council (MRC) Scale; Matthews, 1976). Exclusion criteria were: (i) previous history of neurological or psychiatric illness; (ii) medication with severe cognitive or mood side-effects; (iii) severe language (verbal comprehension deficits), general cognitive impairment (severe spatial-temporal disorientation and/or severe attentional disorders), or mood disturbance (severe depression) that precluded completion of the study assessments. These functions were clinically assessed and patients were excluded only when they could not maintain attention for the duration of the assessment (due to attentional disorders or depression) or they did not comprehend the questions (for language disorders) or the situation (due to spatial-temporal disorientation). All patients gave written informed consent and the research was conducted in accordance with the guidelines of the Declaration of Helsinki (2013) and approved by the Local Ethical Committees.

The diagnosis of AHP was ascertained by means of a scoring modified version of the scale by Bisiach and colleagues (Bisiach et al., 1986). In this scale, if the disorder is spontaneously reported by the patient following a general question about their complaints, the score is ‘0’ = no anosognosia; ‘1’ is scored if the disorder is reported only following a specific question about the strength of the patient's limbs; 2’ is scored if the disorder is acknowledged only after demonstration; and ‘3’ is scored if no acknowledgement of the disorder can be obtained. We also considered an intermediate score of ‘1.5’ (see D’Imperio et al., 2017a) when, after a specific question, patients report motor impairments, but without referring them to the presence of paralysis (but for example to a previous unrelated surgical operation or arthrosis). This is considered an intermediate condition, because patients identify motor disorders but fail in acknowledging the correct cause and nature of deficits. We considered patients as anosognosic when the scores were ≥1.5.

In order to take into account the potential variability of AHP symptoms in time and in relation to the context of the questioning we also used a second, established measure of AHP, namely a structured interview (Berti, et al., 1996), including general questions regarding the consequences of stroke (e.g., 'How is your left arm? Can you move it?') and confrontation questions (e.g., 'Please, touch my hand with your left hand. Have you done it?'). In this interview full acknowledgement of paralysis is scored as '0', while denial of the paralysis despite acknowledging not having reached for the examiner's hand is scored as '1'; and a score of '2' is given when patients denied both motor impairments and the failure in reaching for the examiner's hand. We considered patients as anosognosic when they scored 1 or 2, as in previous studies (e.g., Berti et al.,1996). Patients were considered as anosognosic when failed in at least one of the two tests.

Using these assessments, 64 patients were classified as anosognosic (AHP group) and 67 as not anosognosic (HP group). However, 2 of the HP patients were excluded as, although not anosognosic, they presented with clear symptoms of somatoparaphrenia, which made them ineligible as controls. Another 29 patients (16 AHP and 13 HP) were excluded from the analyses, as more than 15 % of their responses to the Motor Unawareness Assessment (see below) were missing, because of technical issues and time constraints. These 29 patients were missing an average of 32.3 (standard deviation = 11.4) questions (63.4% of the whole task). The clinical and demographical data of the remaining sample of 100 patients (48 AHP and 52 HP) are reported in Table 1, with significant differences between groups in age, gender, left upper and lower limb strength, and (as expected) anosognosia.

Table 1 here

Neuropsychological examination

A battery of neuropsychological tests (in the parallel Italian and English versions) covering general cognitive profile, memory, personal and extrapersonal neglect, apraxia and executive function was administered to the participants (AHP = n. 48; HP = n. 52). Full details of tests used are provided in Supplementary Materials (SM1). The results of this assessment are reported in Table 2, with significant differences found between groups in tests of general cognitive function, long-term memory, personal and extrapersonal neglect, and left-right orientation. Figure 1 shows the comparison between the two groups in the frequency of deficits across cognitive domains.

Figure 1 and Table 2 here

The Motor UNawareness Assessement (MUNA)

Using existing studies as a guide, 40 items were generated to assess awareness of both the upper and lower contralesional limbs (Table 3). The first three questions (Q1-3) investigated general awareness regarding the patient's medical history and reason(s) for hospitalization (Bisiach et al., 1986; Berti et al, 1996); then, 9 items (Q4-12) directly focused on motor deficits, in particular motor abilities (Q4-5; Starkstein, Fedoroff, Price, Leiguarda, Robinson, 1992; Berti et al., 1996; Marcel et al., 2004) and their consequences for the capacity to perform daily life activities (Q6-7; Berti et al., 1996; Ramachandran & Rogers-Ramachandran, 1996; Nimmo-Smith et al., 2005). Two questions referred to mentalisation, asking the patient to consider a third-person perspective on the illness. These questions reported what the doctors said about the patient's conditions ("Doctors tell me you can no longer move your left arm") and then asked for a patient's judgment (Q-8-9; Feinberg, Roane, Ali, 2000). Finally, two "confrontation tasks" were administered, asking the patients to actively raise their left arm and declare if they had been able to do the action (Q10; Cutting et al.., 1978; Starkstein et al., 1992; Berti et al, 1996), or passively raise the left hand with the right hand and say if they felt weakness in their left arm (Q12, Feinberg et al., 2000). The same question was also asked after a passive movement performed by the examiner, who lifted the patient's left arm (approximately 10cm) and then gently dropped it on the right side of the patient's body midline (Q11, Feinberg et al., 2000).

Three other items (Q13-15) investigated implicit awareness following the procedure by Cocchini and colleagues (Cocchini et al., 2010). Patients were invited to carry out three daily life activities: i) taking a tray with glasses on it without dropping the glasses (Q13); ii) taking a book from the examiner's hands and opening it on a set page (Q14); iii) wearing a glove for the left hand (Q15). These tasks are usually better performed using both hands but could also be performed using only one hand by approaching the task in different way ("aware strategy" Cocchini et al., 2010).

Explicit awareness for deficits in daily life activities (Marcel et al., 2004; Nimmo-Smith et al., 2005; Orfei et al., 2009) was investigated by means of three other questions: a general question (Q16); an item regarding the ability to perform specific activities (getting dressed, getting about and eating, Q17); and a question about the need of help from relatives and friends (Q18).

The patients' capacity to anticipate their future clinical condition and make a prediction about recovery (i.e. "anticipatory awareness", Orfei et al., 2009; Marcel et al., 2004; Moro, 2013; D'Imperio et al., 2017a) was investigated in three questions (Q19-21) concerning the prediction of how the motor skills of the upper and lower limbs were expected to be the in following week; in particular, if they predict they would be able to move their limbs (Q19-20) and to walk (Q21).

A series of questions followed, which investigated symptoms often associated with AHP, including asomatognosia or "disturbed sensation of limb ownership" (DSO, Baier and Karnath, 2008; Jenkinson et al., 2018, Q22-24), illusory movements (Feinberg et al., 2000, Zampini, Moro and Aglioti, 2004, Q25-28), objectivation/personification (Q29-33, Cutting et al., 1978) and feeling of alien hand (Q34, Cutting et al, 1978). Finally, the last 6 questions were focused on the patients' emotional reactions towards their upper paralyzed limb (Q35-40 Cutting et al., 1978; Marcel et al., 2004).

Table 3

Administration and Scoring Procedure

The task was administered in a quiet room, with the patient sitting upright in bed or in a wheelchair in front of a table, and his/her hands resting on the armrests of the wheelchair or by his/her side. The items were read out and repeated when the patient did not understand or was not sure about the request. Furthermore, clarifications about questions were given when necessary. The order of the items was fixed, and a pause was set after Q15. Other breaks were allowed whenever necessary and emotional support was offered when the patient showed emotional reactions. Different examiners administered the task (VM; SBes; VG; SBer; SP; CB) who were preliminary trained about the procedure of administration. Patients responded verbally and their responses were faithfully recorded by the examiner who transcribed everything the patient said. Responses (with the exception of the first two open questions not considered in the scoring) were successively transformed into scores as follows: the score 2 indicated the absence of awareness in patients' responses or the presence of disturbed bodily feelings (Q22-34) and emotional reactions (Q35-40); the score 1 was attributed when some degree of doubt or uncertainty in response were present; 0 indicated the absence of symptoms.

For the items Q13-Q15 (implicit awareness), the objects were put on the table in front of the patient who was asked to execute actions (lifting a tray, opening a book, wearing a glove). In this case, we used a score of 2 when the participant behaved as if she/he could use two hands with a failure in action; 1 meant that the patient carried out the action using one hand (or started trying with two hands but immediately corrected) but showing some hesitation; 0 was given when the participant promptly executed the action with one hand (e.g., taking the tray in the center or placing the book on the table) or using an "aware" strategy (e.g. using the mouth to help put on the glove). No verbal response was asked for these three items. The administration of the scale took 10 to 20 minutes and the responses were immediately transcribed by the examiner. Scoring was done based on the transcription of patients' reports by two examiners (VG and SBert). In case of disagreement, the patients' responses were discussed with a third examiner (VM) until a common decision was taken. Patients reactions to the questions and clinical observations emerged during MUNA administration are reported in SM2.

Statistical analyses

Identification of different facets of AHP

A Principal Component Analyses (PCA, Pearson, 1901) with *oblimin* rotation was executed, taking into consideration all items, except the first two general questions, which were included to provide a lead-in and context to subsequent questions.

Prior to the main analysis, three preliminary checks were executed to establish the suitability of conducting a PCA (see SM3). In addition, the correlation between the MUNA scores and the scores on the Bisiach test was used as Concurrent Validity. We used the Bisiach test for this purpose as it is one of the most widely used assessments of AHP and provides a good initial measure of unawareness for clinical purposes.

The number of components to be extracted was estimated by means of a Parallel Analysis (Horn, 1965), which is considered one of the most robust methods for this type of analysis (Velicer & Jackson, 1990). Then, the PCA with *oblimin* rotation was applied to obtain the different components. The items were considered to be part of a component only if: i) their loadings were greater than .5 or less than -.5; ii) their communalities were greater than .4 (the proportion of variance in common with the other items, Costello & Osborne, 2005); iii) and the Complexity Index was between 1 and 2 (the average number of components needed to account for the item; a value ranging between 1 and 2 means that the variable loads only on to one component; Hofmann, 1978)

Calculation of the MUNA total score and component scores (with cut-offs).

For each component resulting from the PCA, the Cronbach's alpha and a cut-off score of the component were computed. In order to compute the score for each component, the values of the questions loading on that component were summed (no items reversed coded). The MUNA total score was obtained by summing all items between Q3 and Q40.

Receiver Operating Characteristics (ROC) analysis was applied to the overall MUNA total score, and to each component score, in order to find the cut-offs useful to distinguish the presence or absence of the deficit expressed by each component. The cut-off for each score (total score and each component score) was computed as the tradeoff between specificity (i.e. the proportion of actual non-anosognosic patients correctly identified) and sensitivity (the proportion of actual anosognosic patients correctly identified). The quality of the cut-off was assessed by means of the Area Under the Curve (AUC), whose scores can be interpreted as "excellent" when AUC = .90-1; "good" AUC = .80-.90; "fair" AUC = .70-.80; "poor" AUC = .60-.70 and "fail" when AUC = .50-.60 (Fawcett, 2006)

MUNA and other clinical variables

Finally, to explore if MUNA scores are modulated by various clinical, demographic and neuropsychological variables, for each component score a series of one-way regression analyses (Holm-Bonferroni corrected) were computed. The variables entered as predictors in these regressions were: the sensory impairment score, MRC upper and lower limbs score, age, interval from lesion, education, extrapersonal neglect (i.e. the percentage of extrapersonal neglect tests on which the patient showed a deficit), personal neglect (i.e.

comb/razor test score), and a general Cognitive Severity index (indexed by the sum of deficits in: 1) orientation and vigilance; 2) general cognitive ability [MMSE]; 3) memory; 4) executive function [FAB], 5) apraxia, and 6) left-right disorientation; with presence of deficit = 1 and absence of deficit = 0 for all these functions).

All statistical analyses were conducted using the R statistical software (R Core Team, 2019), the package *psych* (Reyelle, 2018) for PCA and parallel analysis, and the package *ROCR* (Sing, Sander, Beerenwinkel and Lengauer, 2005) for the ROC analysis.

Results

The preliminary checks indicated that the data were suitable for a PCA analysis (see SM3). Concurrent Validity of the questionnaire was confirmed by the correlation of the MUNA's total score with the Bisiach's score (Pearsons' $\rho = .69$)

Identification of different facets of AHP

The principal component analysis showed good indexes of fit, with the Root Mean Square of the residuals = .07 (empirical $\chi^2 = 686.486$, $p < .001$), and the fit based upon off diagonal values = .936 (it is expected to tend towards 1). Parallel analysis suggested extrapolating 5 components from the PCA. Based on the contents of the items loading on each of these components, we named them as follows: Explicit motor awareness; Implicit motor awareness; Impaired Sense of Ownership; Impaired sense of Agency; and Emotional reactions. *Explicit motor awareness* refers to the items where a verbal judgment of one's motor abilities was requested. As expected (Cocchini et al., 2010; Fotopoulou et al., 2010; Moro et al., 2011), disorders in *Implicit motor awareness* (i.e. the patient plans and executes bimanual actions as if he/she in some way knows that the contralesional arm is paralyzed) are shown by the items where patients' are asked to use "aware strategies" in order to execute the actions. *Impaired Sense of Ownership* refers to the sense, feeling or judgement that my body belongs to me and is ever present. *Agency and Illusory movement* describes the sense to be the actor of one's own movements. Finally, *Emotional reactions* refers to emotional states directly associated with the presence of a paralysis.

In Table 4 the loadings of all the items for each component, with the communalities (h^2; Costello & Osborne, 2005) and the Complexity Index (Hofmann, 1978), are reported. Crucially, the five components do not correlate with each other (Table 4, lower part)

Table 4 here

After the PCA, five questions were removed from the calculation of the single components' scores, because these showed too low communalities and too high Complexity Indexes (Q22, Q29, Q31, Q35 & Q38). Therefore, these questions were used to compute the MUNA total score, but not the 5 components' scores.

Calculation of the MUNA total and component scores and their cut-offs

The cut-offs for the MUNA total score (cut-off ≥ 27) and the scores of the 5 components (explicit awareness ≥ 11; implicit awareness ≥ .75; Sense of ownership ≥ 3; Sense of agency ≥ 2; emotional reactions ≥ 6; Robust score ≥ 13) are reported in SM4 (Table SM 4.1) based on the ROC analyses and considering sensitivity and specificity (the values of sensitivity and specificity for each score are reported in Table SM 4.2). The AUCs indicate that the scores able to discriminate between anosognosic and non-anosognosic patients are those referring to Explicit Awareness (AUC = .96), the MUNA total (AUC = .92) and Implicit Awareness scores (AUC = .78). The other scores (Impaired Sense of Ownership, Impaired Sense of agency, Emotional reactions) are not specific for anosognosia and fail in distinguishing the two groups (AUC values < .54).

The components that are specific to AHP are Explicit and Implicit awareness. Among the AHP group, 30 showed deficits in both explicit and implicit awareness, 14 only in explicit and 4 only in implicit awareness. Among the HP group, 1 showed deficits in both explicit and implicit awareness, 3 only in explicit and 11 only in implicit awareness. In order to calculate a global score for AHP, a score was computed by summing the scores of the Explicit and Implicit Awareness (Robust MUNA score, Cronbach's α=.94; AUC = .98). This cut-off represents a more specific and robust index of AHP.

As a further, exploratory analysis, we compared the frequencies of disorders in the single component between the two groups. Based on the cut-offs, the percentages of patients suffering from impaired Sense of Ownership (AHP = 41.67%; HP = 38.46%), Sense of Agency (AHP = 45.83%; HP = 51.92%) and Emotional reactions (AHP = 41.67%; HP = 55.77%) are similar in the two groups and no statistical differences emerge from the comparison (χ^2) between groups.

Anosognosia and other clinical variables

The complete results of the linear regressions are reported in the Supplementary Materials (Table SM 5). In summary, the MUNA total score was not predicted by any of the clinical and demographical variables considered. However, the Robust MUNA and Explicit motor

Awareness scores were predicted by Extrapersonal neglect ($p = .004$ and $p = .007$ respectively). Implicit motor awareness was predicted by Personal Neglect ($p = .03$), and impaired Sense of Ownership by Sensory Impairment ($p = .014$). Finally, Emotional Reactions were predicted by Sensory Impairment ($p = .001$, greater scores, more emotional reactions), Years of Education ($p = .034$, higher education, fewer emotional reactions) and Interval from Lesion ($p = .032$, longer interval, more emotional reactions).

Discussion

The main outcome of this study is a psychometrically developed and validated assessment tool, which has excellent sensitivity and specificity, and captures several known components of AHP. To the best of our knowledge, our assessment is the first to focus on both motor and body awareness, disentangling multiple domains of awareness (implicit and explicit motor awareness deficits, sense of ownership, agency and illusory movement, and emotional reactions) and giving specific cut-off scores for each of these components. Although other measures are available, only two of these are validated in terms of measuring explicit motor awareness (Nimmo-Smith et al., 2005; Della Sala et al., 2009), and none consider the various different components of AHP. Furthermore, AHP was examined in relation to clinical variables and neuropsychological deficits usually associated with the syndrome. Although the AHP and HP groups were statistically different for some clinical and neuropsychological variables, these differences had limited impact on the MUNA's scores. Our task also has good concurrent validity against another widely used measure of AHP (the Bisiach et al., 1986 interview), which, despite its popularity, has several known limitations. Furthermore, although the Bisiach interview may be useful for a very brief first screening, it fails to detect

AHP in a proportion of patients. One advantage of the MUNA scale is the possibility to take into account both implicit and explicit awareness disorders. Administering the whole scale to our patients, 15 patients who fall in the HP group in the Bisiach/Berti test resulted to be AHP (11 for implicit awareness score, 3 for explicit awareness and 1 for both implicit and explicit awareness scores). This indicates a better sensitivity of the MUNA (in particular using both the subscales) compared to the Bisiach test alone. Therefore, we recommend the use of the Robust scales, by using the Explicit and the Implicit scores separately. Furthermore, MUNA offers the possibility of a complete evaluation of awareness, that is necessary for a specific diagnosis and devising of rehabilitation programs.

Five independent components emerged from the Principal Component Analysis: Explicit awareness, Implicit awareness, Sense of Ownership, Agency and Illusory movement, and Emotional reactions. We found that only the first two components (explicit and implicit motor awareness) are specific for the diagnosis of AHP, as the other symptoms are present in both anosognosic and non-anosognosic patients, without statistically significant differences. Thus, the “core” of motor awareness seems to be explicit and implicit awareness, while the other components, although participating in the clinical manifestations of AHP, are independent from it. Thus, for the diagnosis of AHP specifically, the Robust Score (Explicit and Implicit awareness questions only, Q1-Q15) is suggested as a short alternative to the whole battery of questions when there are time constrictions or limitations due to patient fatigue.

However, the use of the whole battery is suggested in clinical practice, in particular when a rehabilitation program is planned. In fact, only consideration of all awareness components allows the clinician to define the patient’s detailed clinical picture and, in this way, to consider the presence of other concurrent symptoms in the treatment. Indeed, the absence of statistical differences in non-motor components does not exclude that the single patient also suffers from disorders in the sense of ownership, agency or emotional reactions that can be precisely quantified thanks to the use of each component cut-off.

Another important general point is that the five components are partially predicted by different cognitive deficits. We found that the two forms of anosognosia correlate with different manifestations of neglect (i.e. explicit awareness with extrapersonal neglect and implicit awareness with personal neglect). This seems to confirm that implicit anosognosia is more related to body representation and internal monitoring (Moro et al., 2011), while explicit anosognosia involves conscious error detection and a failure in the integration of motor and emotional signals useful to update self-referred beliefs (Fotopoulou, 2014; Pacella et al., 2019). The relationship found between Sensory Impairment and Sense of Ownership underlines the importance of somatosensory afferences and proprioception for the sense of bodily self, as also shown by the Rubber Hand Illusion paradigm (Tsakiris & Haggard 2005; Martinaud, Besharati, Jenkinson, Fotopoulou, 2017). Finally, the result that more severe clinical variables impact Emotional Reactions is not surprising, as well as the mitigating effect of Years of Education that probably allows the patients to rationalize their condition and react to it.

Explicit motor awareness

Explicit (un)awareness is the most recognizable, prototypical feature of AHP, and the component of motor awareness most frequently investigated and assessed. Our results for this component are very similar to those from the Bisiach's (1986) and Berti's (1996) tests.

However, in our assessment, 7.69% (4 out of 52) of patients that are not diagnosed by the Bisiach/Berti's tests show deficits of explicit awareness. Conversely, a portion of patients (4 out of 48) that are unaware at the Bisiach/Berti's test, respond correctly in the MUNA questions regarding explicit awareness. A possible explanation for this discrepancy is that Bisiach's test asks questions that are exclusively focused on the patient's motor impairment, referring to the present moment (here and now), while the MUNA's questions of explicit awareness also investigate awareness of the functional effects of motor deficits in the activities of daily life. As discussed below, these questions are very sensitive to assessing AHP. In addition, the first two questions of the battery (very similar to the first questions of the Bisiach'/Berti's tests) were excluded in the calculation of the MUNA score. This practice follows the recommendation by Levine and colleagues (Levine, Calvanio and Rinn, 1991), who suggests that these questions are not informative regarding the actual state of awareness, since patients tend to learn the "correct" or expected responses over time, while remaining anosognosic.

It is interesting to note that in the MUNA the questions associated with daily life activities are those that best capture deficits in explicit awareness (i.e. load more on the component). Thus, the ability to evaluate the wider implications of one's motor deficit, such as its impact on daily life, may be crucial in the diagnosis of AHP. This is also suggested by those tests that are based on the patient's estimation of his/her current ability on bilateral or unilateral tasks, and that show how AHP patients tend to overestimate self-abilities (Marcel et al., 2004; Della Sala et al., 2009).

Another aspect that loads on the explicit component of AHP is mentalization. This result confirms previous experimental and neuroanatomical data indicating the difficulty of

AHP patients in assuming the third person mental (but not necessarily visuospatial) perspective (Besharati et al., 2015) and the correlations of these deficits with disconnection in the limbic system (Pacella et al., 2019) and lesions involving structures that are part of the mentalizing network (Koster-Hale & Saxe, 2013), such as the supramarginal gyrus and the superior temporal gyrus (Besharati et al., 2016). The patients' difficulties with anticipating their difficulties to perform actions in the near future might represent another manifestation of their difficulty to disengage from their current point-of-view and project themselves to another time and space.

Finally, Q10- Q11 and Q12 load on explicit awareness as well. These represent emergent awareness, a condition in which a patient becomes declaratively aware of his/her deficits only when pushed to perform an action with the affected body part (Crosson, Poeschel, Barco, Velozo, Bolesta, Cooper et al., 1989; Moro, 2013). This form of residual awareness may be assessed by means of confrontation tasks (Berti et al., 1996; Moro et al., 2011) and tasks where a judgment about self-proficiency is asked pre- and post- the execution of an action (Marcel et al., 2004). The questions used in this battery (Q10, Q11 and Q12), confirm that around a quarter of AHP patients, (14/48, 28.17 %) present with spared emergent awareness. This may be useful for devising specific rehabilitation training able to increase awareness by analysing action errors (Moro et al., 2015a; D'Imperio et al., 2017a).

We can thus consider that the items regarding the Explicit component of the MUNA cover various facets of the declarative, verbal manifestations of the syndrome. Although each of these loads in the same component of explicit motor awareness, any single AHP patient can show a specific combination of these facets, where the presence and degree of each specific symptom varies. This feature of the MUNA is a further improvement on existing assessments, since it allows the experimenter or clinician to analyse the various facets of explicit awareness by means of a quantitative score and its comparison with normative data.

Implicit motor awareness

The second component that was found to be specific in identifying AHP is Implicit awareness, namely the non-verbal knowledge regarding motor deficits that emerges during execution of behavioural tasks, or implicitly in patients' conversations. The distinctiveness of this component relative to explicit awareness is confirmed by the lack of correlation between these two components. In addition, the index of cognitive severity correlates with implicit but not explicit unawareness, indicating that the more compromised the cognitive functions, the more frequent the lack of implicit awareness.

Our finding of two distinct forms of awareness is consistent with previous studies that have shown a dissociation between deficits in explicit and implicit awareness (Blakeslee & Ramachandran, 1998; Nardone, Ward, Fotopoulou and Turnbull, 2007; Cocchini et al., 2010; Fotopoulou et al., 2010; Moro et al., 2011). In our sample, 4 AHP and 11 HP had deficits in Implicit but not explicit awareness. Thus, a dissociation between the two components is present in both the groups. This confirms how awareness is not an all-or-nothing phenomenon, and anosognosia is an insidious syndrome, not always easy to diagnose especially in those patients who are apparently aware but who can then carry out high risk behaviours in daily life. The MUNA offers the possibility to assess both of these critical components of awareness.

The other components: sense of ownership, agency and illusory movement, emotional reactions.

None of the other components that emerged from the PCA of the MUNA were specific to AHP. This indicates that these symptoms may co-occur with, but are not specific to, AHP. However, these components still deserve specific discussion, since they provide insights into ongoing debates regarding the various facets of self-consciousness, and the interconnectedness of bodily disturbances that can occur after right-hemisphere stroke.

For a long time, disorders in the sense of ownership have been associated with AHP or even considered as a milder form of AHP (Critchley, 1953). However, dissociations between the two clinical conditions have been documented (Invernizzi , Gandola, Romano, Zapparoli, Bottini, Paulesu, 2013; Romano and Maravita, 2019) and at least partially different neural correlates have been found (Gandola, Invernizzi, Sedda, Ferrè, Sterzi Sberna et al., 2012; Romano, Gandola, Bottini and Maravita, 2014; Moro, Pernigo, Tsakiris, Avesani, Eldestyn, Jenkinson, Fotopoulou, 2016). The dissociation has been recently confirmed by a meta-analysis of the literature on the subject (Romano & Maravita, 2019). Our data may be considered as complementary to these, showing that disorders in the sense of body ownership are present in 41.67% of AHP patients. Crucially, a similar percentage of non-anosognosic patients (38.46%) show the same symptoms, suggesting that these disorders may be underestimated in clinical contexts (Cutting, 1978; Martinaud et al., 2017).

It is noteworthy that in our sample, the only clinical variable that impacts on this component was sensory deficits. This indeed suggests that the inability to perceive one's own limb may represent a crucial aspect of the lack of ownership, by inducing a reduction of the sense of familiarity toward the limb (Gandola et al., 2012). This hypothesis is also confirmed by a few studies where somatoparaphrenia is modulated by multisensory stimulation approaches (Bolognini, Ronchi, Casati, Fortis and Vallar, 2014; D'Imperio , Tomelleri, Moretto, Moro, 2017b) and supports the hypothesis that attributes a crucial role in the processing and integration of congruent multisensory signals from one own's body to the sense of ownership (Romano and Maravita, 2019; Romano et al., 2014; Martinaud et al., 2017).

A further factor identified by our analysis of the MUNA was *agency and illusory movement*. Agency is defined as the feeling that one can move and control his/her body and is the agent of his/her body movements (Tsakiris, Longo and Haggard, 2010; Baier & Karnath, 2008). In other words, the sense of agency makes the individual aware of the movement of one's body part as constituting an action of one's own as opposed to the action of someone else or a mere event (Bayne & Pacherie, 2007). Usually, AHP patients do not report disorders in the sense of agency, which are instead typical of anarchic hand syndrome, where patients complaint of having a hand acting on their own will (Della Sala, S. Marchetti, C. Spinnler, H., 1991; Moro, Pernigo, Scandola, Mainente, Avesani, Aglioti, 2015b for a review). Indeed, we record both the presence of abnormal agency (i.e. the feeling that the limb is moving by itself; Q25-Q26), and illusory limb movements (Feinberg et al., 2000), where there is no clear agency component, but the patient has a subjective feeling that the paralysed arm or leg has moved when in reality they know that it remained motionless (Q27-Q28). In our sample, these symptoms do not overlap with AHP and are not specific to AHP patients, as 51.92% of non-anosognosic patients are over cut-off in our interview for this component.

We did not find any correlations between disorders in sense of agency/illusory movement and other clinical variables although the impact of sensory deficits is close to significance (p = .06). It is thus possible that illusory limb movements reflect a dominance of motor outflow over sensory feedback during multisensory processing (Fotopoulou, 2008; 2010) and are independent from awareness of motor deficits (Antoniello and Gottesman, 2019).

Finally, we did not find any difference between the two groups in the final MUNA component of *emotional reactions* associated with the paralysis. Misoplegia and negative feeling towards one own's body have been reported since the first descriptions of anosognosia (Critchley et al., 1953) and the existence of psychogenic "defence" mechanisms that prevent patients from explicitly acknowledging their paralysis have been advanced (Weinstein and Kahn, 1955). However, an experimental study (Besharati, Forkel, Kopelman, Solms, Jenkinson, Fotopoulou, 2014) has specifically investigated the patients' responses to induction of negative and positive emotions, finding that AHP patients are able to process such emotion at some level. In fact, the induction of negative emotion resulted in a significant improvement of motor awareness in anosognosic patients compared to controls, while the positive emotion induction did not. Thus, motivation and emotions also seem to play a role in AHP.

Limitations and Recommendations

Finally, we consider some limitations of our study and recommendations for future research. Firstly, we recruited only right brain damaged patients. This prevented the possibility to investigate the presence of AHP in left brain damaged patients, and to contribute to the debate regarding the hemispheric lateralization of the syndrome. This question has been examined by other researchers (e.g. Della Sala et al., 2009; Cocchini et al., 2018), and assessments designed specifically for the identification of AHP in patients with language deficits. With this in mind, our battery includes a small number of behavioural tasks; however, the largely verbal responses required for the MUNA make it difficult to use with patients suffering from linguistic deficits. Secondly, we did not assess test-retest and inter-rater reliability in the current study, and future research is needed to establish this psychometric property of the MUNA. Finally, there is ongoing debate regarding the neuroanatomical basis of different constituents and disorders of the bodily self. Recent large-scale neuropsychological studies have attempted to address some of these issues by analysing the lesions of patients with AHP and DSO (e.g. Gandola et al., 2012 Invernizzi et al., 2013; Romano et al., 2014; Moro et al., 2016). However, a fruitful avenue for future research will be to analyse the neuroanatomical correlates of the five different components resulting from the MUNA. We predict that the different components should be correlated with at least partially specific neural networks.

In conclusion, we present a new instrument for the diagnosis of AHP, able to investigate the various different facets of the syndrome and to draw a precise profile of each patient’s degree of awareness. Our newly developed tool has good psychometric properties and can be flexibly applied in both research and clinical contexts. This will allow researchers to gain new insights into the components of the bodily self, and clinicians to make specific diagnoses and identify targeted rehabilitation programs.

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In accordance with Taylor & Francis policy and our ethical obligation as researchers, we are reporting that we do not have a financial and/or business interests in a company that may be affected by the research reported in the enclosed paper.

Figure Captions

Figure 1. Cognitive profile of the two groups. The percentage of patients who show deficits in the various different cognitive domains are reported (when more than one test was administered to assess the same cognitive domain, the test with higher frequency of patients under cut-off – i.e. greatest level of impairment - was selected). The cognitive profile of the two groups is qualitatively similar although the percentage of AHP who fail in tests assessing extrapersonal neglect and orientation are higher than in HP group. Orientation = $\chi^2_{(1)} = 5.34$, $p = .02$, Cramer's $V = .23$; General Functions = $\chi^2_{(1)} = 2.57$, $p = .11$, Cramer's $V = .16$; Delayed Memory = $\chi^2_{(1)} = 3.05$, $p = .08$, Cramer's $V = .17$; Comb test = $\chi^2_{(1)} = 1.09$, $p = .30$, Cramer's $V = .10$; Line bisection = $\chi^2_{(1)} = 17.10$, $p < .001$, Cramer's $V = .41$; Representational Drawing = $\chi^2_{(1)} < .001$, $p = 1$, Cramer's $V < .001$; Limb Apraxia = $\chi^2_{(1)} = .02$, $p = .90$, Cramer's $V = .01$; * = $p < .05$; *** = $p < .001$.