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Behavioural Monitoring Disorders in Unilateral Spatial Neglect: Productive Symptoms and Impaired Awareness of Disease

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Abstract

This doctoral thesis investigates the relationships between disorders of behavioural monitoring (including “productive” behaviours and unawareness of neuropsychological deficits) and unilateral spatial neglect in right-brain-damaged patients.

One main monitoring disorder is recurrent perseveration, namely a “productive” motor symptom frequently found in target cancellation tasks: we demonstrate, in two specific tasks (Experiments 1 and 2), that the disposition of the stimuli and the type of target modulate its severity. Neglect patients showing perseveration in visuo-motor exploratory tests perseverate also in drawing tasks. No correlation between omission and perseveration errors is found, supporting the functional independence of the two deficits. In the context of a two-component hypothesis, perseveration (the first component) is a specific disorder that manifests in a variety of tasks, particularly those requiring serial graphic production; unilateral spatial neglect (the second component) may trigger and facilitate the production of perseveration errors. Moreover results indicate that patients with perseveration are not disproportionately impaired in tasks assessing executive, visuo-spatial short-term memory, and attentional functions, suggesting the specificity of the monitoring disorder associated with spatial neglect. Lesion analysis indicates damage to the right insula as a relevant neural correlate of perseverative behaviour.

Experiment 3 shows that perseverating patients produce a majority of substitution errors during a word reading task, suggesting that also this type of paralexic neglect error can be considered a “productive” manifestation.

The clinical, experimental and neural features of another monitoring deficit and "positive" manifestation referring to the personal space, "somatoparaphrenia", are reviewed: somatoparaphrenia is a symptom usually associated with right-sided hemispheric lesions, most often characterized by a delusion of disownership of contralesional body parts. Possible pathological factors may include a deranged representation of the body concerned with ownership, mainly right-hemisphere-based, and deficits of multisensory integration.

Finally, Experiment 4 investigates anosognosia for unilateral spatial neglect by a quantitative assessment. Results indicate that unawareness for spatial attentional and representational deficits is not a pervasive disorder, and that some tasks can evoke different degrees of awareness. In addition, the scores assigned by neglect patients to their performance in spatial tasks are not modulated by the different conditions of the estimation tasks.

In conclusion, we demonstrate that: 1) "productive", as "defective", manifestations of unilateral spatial neglect are multifarious; 2) these "positive" phenomena are independent of general executive deficits and of the severity of the spatial neglect syndrome; 3) the neural bases of motor productive disorders included the right insula; 4) neglect patients are not globally anosognosic about their spatial defective performances.

Riassunto

"Deficit di monitoraggio del comportamento nella negligenza spaziale unilaterale: sintomi produttivi e consapevolezza di malattia compromessa"

Questa tesi di dottorato esamina la relazione fra i disturbi di monitoraggio del comportamento e la negligenza spaziale unilaterale in pazienti con lesione cerebrale a carico dell'emisfero destro.

Uno dei principali disordini di monitoraggio è la presenza di perseverazioni ricorrenti, un sintomo motorio di tipo "produttivo" frequentemente riscontrato in compiti di cancellazione di stimoli-bersaglio: abbiamo dimostrato che, in due specifici compiti (Esperimenti 1 e 2), la disposizione degli stimoli sul foglio e il tipo di stimolo-bersaglio modulano la gravità di questo disturbo. Pazienti con negligenza spaziale unilaterale e perseverazioni in test di esplorazione visuo-motoria perseverano anche in compiti di disegno. Non sono state riscontrate correlazioni fra gli errori di omissione e di perseverazione, a supporto dell'ipotesi dell'indipendenza funzionale dei due deficit. Nel contesto di un'ipotesi a due componenti, il comportamento di perseverazione (prima componente) è uno specifico disturbo che si manifesta in vari compiti, in particolare in quelli che richiedono produzioni grafiche seriali; la negligenza spaziale unilaterale (seconda componente) può innescare e facilitare la produzione di errori di perseverazione. Inoltre i risultati indicano che pazienti con perseverazioni non sono compromessi in maniera rilevante in compiti che valutano le funzioni esecutive, attentive e di memoria a breve termine visuo-spaziale. Analisi lesionali mostrano il danno dell'insula destra come correlato neurale rilevante dei comportamenti perseveratori.

L’Esperimento 3 mostra che i pazienti perseveranti effettuano un maggior numero di errori di sostituzione durante un compito di lettura di parole, suggerendo che anche questo tipo di errore di lettura possa essere considerato come una manifestazione “produttiva” della negligenza spaziale unilaterale.

Le caratteristiche cliniche, sperimentali e neurali di un altro deficit di monitoraggio e manifestazione “positiva” riferita allo spazio personale, la “somatoparafrenia”, sono state revisionate: la somatoparafrenia è un sintomo tipicamente associato a lesioni a carico dell’emisfero destro, spesso caratterizzata dall’idea delirante di non-appartenenza di parti del corpo controlaterali alla lesione. Possibili fattori patologici alla base del disturbo possono essere una disturbata rappresentazione del corpo relativa al senso di appartenenza, basata soprattutto sull’emisfero destro, e deficit di integrazione multi-sensoriale.

Infine l’Esperimento 4 esamina l’anosognosia per la negligenza spaziale unilaterale tramite una valutazione quantitativa. I risultati indicano che l’inconsapevolezza per i deficit di attenzione e rappresentazione spaziale non è un disordine pervasivo e che diversi compiti possono elicitare vari gradi di consapevolezza. Inoltre i punteggi di valutazione assegnati dai pazienti con negligenza spaziale unilaterale alla propria prestazione risultano stabili e non modulabili dalle diverse condizioni dei test di autovalutazione.

In conclusione, abbiamo dimostrato che: 1) le manifestazioni “produttive”, così come quelle “deficitarie”, della negligenza spaziale unilaterale sono molteplici; 2) questi fenomeni di tipo “positivo” sono indipendenti da deficit del funzionamento esecutivo e dalla gravità della negligenza spaziale; 3) le basi neurali dei disordini motori produttivi comprendono l’insula destra; 4) i pazienti con negligenza spaziale unilaterale non risultano globalmente anosognosici rispetto alle loro prestazioni spaziali deficitarie.

INTRODUCTION

I. Unilateral spatial neglect: definition and characteristics

Unilateral spatial neglect (USN) is a debilitating neuropsychological syndrome characterized by the failure to report, respond to or orient towards contralesional stimuli (Vallar, 1998; Bisiach and Vallar, 2000; Heilman et al., 2003; Husain, 2008). USN, which is a consequence of unilateral brain damage, is more frequent and severe after lesions to the right-hemisphere (Halligan et al., 2003) which impact the left side space; however patients suffering from right USN after left-hemisphere lesions are on record (Beis et al., 2004; Pia et al., 2009a; Bultitude and Rafal, 2010).

Left spatial neglect is considered a multi-componential syndrome: the manifestations of this disorder are heterogeneous and can emerge in dissociate forms, concerning perceptual, pre-motor and/or representational aspects (Vallar, 2001; Bartolomeo, 2007; Vallar and Mancini, 2010). Moreover neglect symptoms may appear in connection with the mid-sagittal plane of the body (egocentric neglect) or the contralesional side of external objects (allocentric neglect) (Halligan and Marshall, 1993). Neglect patients typically appear to be completely unaware about their defective performance; however there is evidence that neglected information is not completely lost and it is possible that patients implicitly elaborate the stimuli of which they deny any perception (Marshall and Halligan, 1988; Berti, 2002). Not only do signs of neglect emerge in a structured neuropsychological evaluation, they also have a significant impact on routine activities such as eating, displacement and social interactions (Azouvi et al., 2003). Spatial neglect has been found to be linked to a minor functional long-term outcome (Paolucci et al., 2001 and 2008; Jehkonen et al., 2006).

A number of mechanisms may contribute to the genesis of USN. Some theories suggest it may be caused by attentional deficits, such as the disengagement of attention from the ipsilesional stimuli (Posner et al., 1987), the rivalry between two hemispheric attentional vectors (Kinsbourne, 1993) or the asymmetric competences of the two hemispheres in orienting attentional resources towards the space (Heilman and Van Den Abell, 1980). On the other hand the representational hypotheses point to a role of defective internal spatial representation (Bisiach, 1993). Quite the opposite of being contradictory, these theories may in fact be complementary; they may provide possible explanations to justify the large series of heterogeneous manifestations of this syndrome, which includes attentional and representational components that are susceptible to being selectively damaged by the cerebral lesion.

Historically USN has been described as a “parietal syndrome” (Brain, 1941), but subsequent studies also emphasize the contribution of other cerebral regions implicated in the genesis of the disorder. Left neglect is frequently associated to right inferior-posterior parietal lesions, especially to the angular gyrus (Heilman et al., 1983; Vallar and Perani, 1986; Mort et al., 2003; Golay et al., 2008; Verdon et al., 2010); additionally several studies suggest the implication of the right superior temporal gyrus (Karnath et al., 2001 and 2005, who identify this cerebral region as the critical site; see also Corbetta et al., 2005; Committeri et al., 2007; Golay et al., 2008) and of the right frontal premotor cortex (Husain et al., 1997; Corbetta et al., 2005; Committeri et al., 2007; Verdon et al., 2010). The damage to the insula (Manes et al., 1999; Karnath et al., 2004; Corbetta et al., 2005; Golay et al., 2008) and to subcortical structures such as thalamus and basal ganglia (Vallar and Perani, 1986; Ferro et al., 1987; Karnath et al., 2004; Ringman et al., 2004; Corbetta et al., 2005) may also produce USN. Considering that USN is an heterogeneous syndrome, some studies focus on the correlates of different forms of neglect, demonstrating that egocentric symptoms are more related to parietal structures (Hillis et al., 2005; Medina et al., 2009) and the allocentric ones to the temporal cortex (Hillis et al., 2005; Medina et al., 2009; Verdon et al., 2010). Moreover the anatomical correlates of perceptive/motor components of USN has been investigated: several evidences indicate an association between perceptive symptoms and posterior (parietal) lesions, on the one hand, and motor impairment and anterior (frontal) lesions, on the other (Bisiach et al., 1990a; Coslett et al., 1990; Tegner and Lavander, 1991; Bottini et al., 1992; Làdavas et al., 1993; Na et al., 1998), but these data are not conclusive (Husain et al., 2000). Some researchers also highlight the importance of white matter lesions in intrahemispheric disconnections (Doricchi and Tomaiuolo, 2003; Bartolomeo et al., 2007): the damage of the superior longitudinal fasciculus, bringing about the interruption of the communication between the frontal and the parietal lobes in the right hemisphere, may contribute to the genesis of neglect. However, a recent study suggests that lesions of gray (versus white) matter structures seem to be a stronger predictor of USN (Karnath et al., 2009).

To sum up, the anatomical correlates of left USN involve a complex cortico-subcortical network in the right hemisphere, including the parietal, temporal and frontal premotor regions, as well as subcortical structures (thalamus and basal ganglia) and white matter fibres connecting frontal and parietal lobes (Halligan et al., 2003; Golay et al., 2008; Verdon et al., 2010).

II. Negative and positive symptoms

During neuropsychological assessments, brain-damaged patients with USN exhibit various forms of pathological behaviour concerning the defective exploration of the contralesional side of the space (examples are provided in Figure 1 below), such as the omission of stimuli in target cancellation tasks, a rightward bias during line bisection tests, abandoning copies of a model prior to completion, reading of the ipsilesional part of a sentence or a word. Neurological patients can reveal signs of USN also in the absence of real visual stimuli, e.g., in the flawed representation of a mental image (Bisiach and Luzzatti, 1978; Beschin et al., 1997; Lepore et al., 2004; Rode et al., 2007).

All these phenomena refer to the *negative* or *defective* manifestations of the hemispatial neglect syndrome, characterized by the absence of a specific reaction that would be expected and required. However left neglect consists also of a set of *positive* or *productive* symptoms (Vallar, 1998; Vallar, 2001), including additional behaviour that is not relevant to the task.

Complementary to the well-known impaired perception and exploration towards the contralesional side of space, neglect patients can exhibit inappropriate manifestations in both their personal and extrapersonal domains. Three forms of this productive behaviour are reported here in detail, as they are the focal point of the experimental studies included in this thesis.

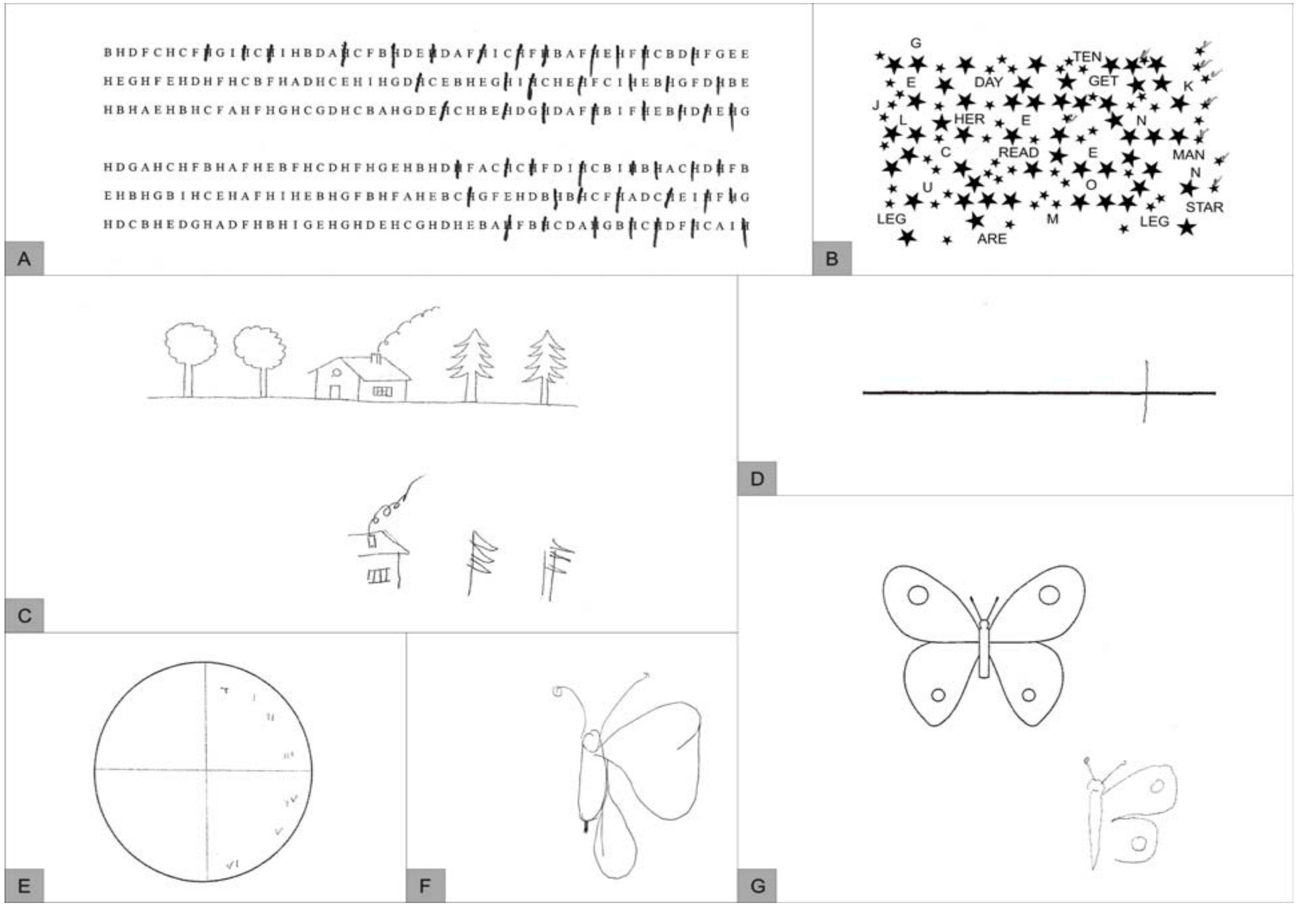

Figure 1: Examples of neglect in tests performed by right-brain damaged patients: left-side omissions in target cancellation tasks, where the task required that all the Hs (A) or little stars (B) be marked; allocentric and egocentric symptoms when reproducing a complex figure (C): the patient completely omitted the two trees on the left and drew only the ipsilesional part of the other three elements; the rightward bias in the bisection of a line (D); signs of representational neglect in drawing a clock (E) and a butterfly (F) from memory; the left-side omissions of a butterfly in a copy drawing test (G).

- Motor perseveration

Perseveration refers to the continuation of a behaviour that persists inappropriately after a termination of or change in task demands, or in the absence of the appropriate stimulus (Sandson and Albert, 1987). Perseverative responses have been recorded in a variety of tasks, especially in target cancellation tests: referring to the performance in this type of test, perseveration have been classified into two categories (Na et al., 1999; Rusconi et al., 2002). On the one hand “simple” perseveration refer to the patients’ behaviours that repeatedly cross out targets (‘‘a tendency to overscore the lines already drawn’’). On the other hand, patients may also draw ‘‘extra’’ targets, and subsequently cross them out, or add gratuitous unrelated elements (e.g., the patient’s signature, an animal, etc.): these types of perseveration are defined ‘‘complex’’.

In recent years the interest about the tendency of right-brain damaged patients to produce perseverative behaviours, and the relationships of these disorders with the negative symptoms of the neglect syndrome, is increased and these phenomena have been investigated systematically. Some studies have examined retrospectively the prevalence of perseveration in cancellation tasks and its association with contralesional neglect.

In 60 right-brain-damaged patients with left spatial neglect (Na et al., 1999), perseveration was found in more than 30% of the patients, most frequently repetitive cancellation, and, in a few patients, the cancelling of extra lines, drawn by the patients themselves. In a series of 181 right- and left-brain-damaged patients with and without neglect, and patients with probable dementia of the Alzheimer-type (Rusconi et al., 2002), in a circle cancellation task perseveration was found to be associated with contralesional neglect, and with right-brain-damage (86% of the 35 neglect patients had right-sided hemispheric lesions). In a series of 206 subacute stroke patients (Nys et al., 2006), perseveration was again found to be associated with contralesional neglect in the star cancellation task of the behavioural inattention test (Wilson et al., 1987), with no differences in prevalence between left- and right-brain-damaged patients.

In all three studies, perseveration in right-brain-damaged patients took place mainly in the ipsilesional right hand-side of the cancellation sheet, with an ipsi-contralesional gradient (Na et al., 1999; Nys et al., 2006; Rusconi et al., 2002). All these group studies (Na et al., 1999; Nys et al., 2006; Rusconi et al., 2002), while suggesting that perseveration is more frequent in patients with contralesional neglect, also show that the two disorders may occur independently. Patients may show perseveration without omissions, and omissions without perseveration (Na et al., 1999; Rusconi et al., 2002), conjuring up a double dissociation, which suggests the independence of the two phenomena (Vallar, 2000).

The precise relationships between the severity of perseveration and that of contralesional neglect are however matter of controversy (Manly et al., 2002; Rusconi et al., 2002; Bottini and Toraldo, 2003; Toraldo et al., 2005). While some evidence emphasizes the close association between the two manifestations, with perseveration being “driven” by the presence of contralesional neglected stimuli, the allochiria/directional hypokinesia interpretation does not provide a comprehensive explanation of this phenomenon (see Toraldo et al., 2005 for a discussion). An alternative (or integrating) hypothesis suggests that the occurrence of perseveration reflects the combined effect of the ipsilesional attentional bias, on the one hand, and the repetitive visuo-motor activity, on the other hand, with the first component triggering the second, productive, disorder (Rusconi et al., 2002). This debate also is reflected in the different statistical approaches. Neglect has been reported to be more severe in patients with perseveration (Na et al., 1999), but no correlation has been found between omission and perseveration errors (see Rusconi et al., 2002 for a re-analysis of the data of Na et al., 1999). Nys et al. (2006) found no correlation between omission and perseveration scores, as Rusconi et al. (2002) did; however the correlation proved to be significant when USN (i.e., crossed targets) was correlated to a perseveration percentage (see Toraldo et al., 2005, for discussion). Finally, other recent studies failed to find any correlation between omission and perseveration errors (Vallar et al., 2006; Pia et al., 2009b) and also between omissions and perseveration percentages (Pia et al., 2009b).

The link between negative and positive symptoms in brain-damaged patients with left USN has been investigated also by analysing the effect of experimental manipulations or rehabilitation tools normally used to improve the defective manifestation of this pathology, but on the whole the results are unclear. For example, a single session of prism adaptation temporarily improved omission and perseveration in a group of neglect patients (Vallar et al., 2006). However one single case study found that four sessions of prism adaptation reduced omissions but increased perseveration during the star cancellation task in one right-damaged patient with left USN (Nys et al., 2008). A recent case report demonstrated that the monocular patching treatment reduced omission but not perseveration errors in a patient with right-hemisphere damage and left hemi-inattention (Khurshid et al., 2009). However Kim et al. (2009) found that moving the background of the cancellation task to the left to help neglect patients with recurrent perseveration perceive additional areas of the neglected space, reduced both pathological manifestations.

The anatomical correlates of the perseverative disorder suggest that anterior frontal lesions and subcortical damage (Rusconi et al., 2002), particularly of the basal ganglia (caudate nucleus) (Nys et al., 2006; Pia et al., 2009b), are more frequent than posterior lesions (Na et al., 1999; Rusconi et al., 2002).

- <u>Paralexic addition errors in neglect dyslexia</u>

Right-brain-damaged patients may have difficulty in reading tasks, making errors in the contralesional part of the letter strings (Kinsbourne and Warrington, 1962). This disorder, known as neglect dyslexia, is a reading deficit frequently related to the USN syndrome (Làdavas et al., 1997; Arduino et al., 2002; Stennken et al., 2008; Vallar et al., 2010). Neurological patients can exhibit both neglect dyslexia and other manifestations of USN. However these two disorders can also emerge independently (Lee et al., 2009) and there is evidence that these deficits are double-dissociated (Bisiach et al., 1990b). Furthermore, signs of contralesional visual neglect can coexist with an ipsilesional reading disorder, which emphasizes the independence of these deficits (Cubelli et al., 1991).

Left neglect reading responses can be distinguished from other types of peripheral dyslexia errors through the identification of a precise "neglect point" (Ellis et al., 1987). On the basis of this criterion, reading errors are defined as neglect only if *"target and error words are identical to the right of an identifiable neglect point, but share no letters in common to the left of the neglect point"* (page 445). Applying this principle, neglect errors can be classified into three categories (Ellis et al., 1987) as follows:

- *Omissions*: patients omit one or more contralesional letters in the string. For example, when the verbal stimulus “famiglia” (family) is read as “miglia” (mile).
- *Substitutions*: patients substitute one or more contralesional letters in the string. For example, when the verbal stimulus “famiglia” is read as “*c*amiglia” (nonword in Italian).
- *Additions*: patients add one or more letters in the contralesional section of the string. For example, when the verbal stimulus “famiglia” is read as “*s*famiglia” (nonword in Italian).

Reading errors in which no neglect point can be found, i.e., the errors do not occur systematically in one side of the string, are defined as *visual* errors (e.g., when “famiglia” is read as “fa*n*iglia”).

The proportion of neglect errors varies across patients, with substitutions and omissions being the most frequent types of neglect reading errors (see Vallar et al., 2010 for a review). These two error types may be ascribed to a diverse severity of the attentional deficit, with omission errors occurring in patients with a more severe spatial bias whereas substitutions occur when patients encode the position of the misread letters (Ellis et al., 1987). According to this view, patients producing substitution errors might be more sensitive to lexical effects because the substituted letters, even if not explicitly identified, are implicitly processed. However this is not always the case: the literature reports evidence both in support of (Arduino et al., 2002) and against (Riddoch et al., 1990) this hypothesis. Moreover, in contrast with the encoding theory, a study of oculomotor performance by patients with neglect dyslexia highlighted the correspondence between eye movement and reading accuracy, suggesting that the misread contralateral letters are not always registered (Behrmann et al., 2002). Therefore the rationale underlying the production of specific types of reading deficit is still unclear and might reflect different mechanisms.

Errors of addition are the most infrequent neglect reading deficit and have frequently been ascribed to a productive or confabulatory response (Chatterjee, 1995; Vallar et al., 2006), since they are characterised by the irrelevant addition of verbal material not present in the string and extraneous letters.

Regarding the anatomical correlates of neglect dyslexia, most studies suggest the implication of the posterior rather than the anterior cerebral regions (Kinsbourne and Warrington, 1962; Takeda and Sugishita, 1995; Stenneken et al., 2008; Lee et al., 2009; Vallar et al., 2010).

- Somatoparaphrenia

The somatoparaphrenia symtom-compex is a set of bodily productive symptoms often associated with other manifestations of the USN syndrome.

In 1942 Gestmann reported the observation of two patients with right-brain lesions who presented delusional ideas about the ownership of their contralateral limbs. Gerstmann (1942) suggested this term to denote these "*illusions or distortions concerning the perception of and confabulations or delusions referring to the affected limbs or side*", and "*specific psychic elaboration (marked by the formation* *of illusions, confabulations and delusions) with respect to the affected members or side of the body, believed or experienced as absent”*.

Therefore this pathologic disorder refers to all delusional beliefs regarding body parts contralateral to the brain lesion and it is not traced back to confusion, disorientation or to a more general cognitive impairment. The main, but not exclusive, manifestation of this disorder is the delusional belief that a part of the contralesional hemi-body does not belong to the patient, with the frequent attribution of his ownership to another person.

Historically the somatoparaphrenia has been defined as the “positive” form of the anosognosia for hemiplegia. Gerstmann distinguished somatoparaphrenia from *autosomatamnesia* and *autosomatagnosia,* respectively the “amnestic and agnostic unawareness of the impaired parts or half of the body, varying from simple neglect of their presence to the experience of their nonexistence”. Critchley (1953) underlined this link between somatoparaphrenia and anosognosia. Critchley summarized the possible distortions of the *body image* associated with parietal disease in nine categories as follows: 1) unilateral neglect (motor, sensory, visual); 2) lack of concern over the existence of hemiparesis (anosodiaphoria); 3) unawareness of hemiparesis (anosognosia); 4) defective appreciation of the existence of hemiparesis, with rationalization; 5) denial of hemiparesis; 6) denial of hemiparesis with confabulation; 7) loss of awareness of one body-half (which may or may be not paralysed): asomatognosia or hemidepersonalisation; 8) undue heaviness, deadness or lifelessness of one half (hyperschematia); 9) phantom third limb, associated with a hemiparesis. In Critchley’s taxonomy, somatoparaphrenia (i.e., #6) is closely associated with unawareness and active denial of motor deficits.

Importantly, Critchley noted that these phenomena are not "…sharply demarcated. Not infrequently one condition merges into another; or perhaps alternates with another".

Somatoparaphrenia is a specific disorder to be differentiated by the following other deficits of the body representation:

- The personification of paralyzed limbs (Critchley, 1955): contralesional limbs are referred to as invested with a personality or identity (e.g., with nicknames).
- The nosoagnosic overestimation of the unaffected side of the body (Frederiks, 1969).
- The supplementary phantom limb sensations (Riddoch, 1941).
- The alien hand phenomenon: the occurrence of movements of an upper limb those are unintended although clearly directed to some purpose (Della Sala et al., 1991).
- The "main étrangère" phenomenon: the lack of recognition by the patients of their left hand, when asked to touch it with the right hand only without visual control (Brion and Jedynak, 1972).
- The misoplegia (Critchley, 1974): aggressive behaviour in various forms (verbal, motor, or both) exhibited by hemiplegic patients towards the affected side.

III. Anosognosia for unilateral spatial neglect

The term "anosognosia" was introduced in 1914 by Babinski to indicate a lack of awareness of neurological disturbances consequent to a brain lesion. The neurological patients described by Babinski (1914) were unable to recognise their paralysis or never mentioned the motor deficit: this condition was called anosognosia for hemiplegia. As the early clinical observations revealed, the unawareness of motor dysfunctions can appear in more or less severe forms, ranging from complete anosognosia to anosodiaphoria (indifference toward the acquired neurological deficit). Even if the majority of studies focus on the lack of awareness for the motor impairment, literature does include evidence of anosognosia for other neurological problems, as somatosensory and visual-field (Celesia et al., 1997) deficits.

The awareness disorder does not account for the presence of a global cognitive deterioration; it is characterised by selectivity and specificity, with patients being aware of one deficit and unaware of another: this supports the hypothesis that anosognosia is not a monolithic disorder but that separated monitoring components can be disrupted by brain lesions (see Vallar and Ronchi, 2006; Starkstein et al., 2010; Prigatano, 2010, for reviews).

Anosognosia for neurological deficits is usually evaluated through the observation of the patient's behaviour, and a short interview with increasingly specific questions to investigate the extent of his/her awareness of the disease (Cutting et al., 1978, Bisiach et al., 1986, Starkstein et al., 1992, Feinberg et al., 2000). In recent years, another type of assessment has been proposed regarding anosognosia for hemiplegia, with more implicit questions about the patient's ability to perform bimanual/bipedal tasks (Marcel et al., 2004, Nimmo-Smith et al., 2005).

The prevalence of the deficit has been seen to be asymmetric, with anosognosic patients having a higher frequency of right-hemisphere lesions (Starkstein et al., 1992, Adair et al., 1995, Pia et al., 2004), though it should be kept in mind that unawareness following left-hemisphere damage could be underestimated due to linguistic deficits that make a precise assessment of this phenomenon difficult (Adair et al., 1995; Della Sala et al., 2009). In right-brain damaged patients, anosognosia for contralesional neurological deficits, especially for left hemiplegia, is frequently – but not always – associated with USN (Vallar, 1998; Appelros et al., 2007; Spalletta et al., 2007). The neural correlates of anosognosia for hemiplegia are partially overlapped by those of left spatial neglect: recent studies underlined the importance of premotor and insular cortical regions, as well as subcortical structures, in the genesis of the disorder (Starkstein et al., 1992, Karnath et al., 2005, Berti et al., 2005).

The term anosognosia is also used to indicate the impaired awareness of cognitive deficits, such as aphasia (Lebrun, 1987), memory disease (Akai et al., 2009) and constructive apraxia (Rinaldi et al., 2010). Although it is commonly held that USN patients are not aware of their defective perception and exploration of the contralesional hemi-space, only very few studies in the scientific literature have systematically examined this characteristic of the neglect syndrome.

Berti, Làdavas and Della Corte (1996) examined anosognosia for USN in reading and drawing tasks, testing 34 right-brain-damaged patients with complete left hemiplegia. Left USN was assessed by cancellation, drawing and reading tests; the latter two tasks also evaluated awareness of the deficit. Patients were interviewed after the reading and drawing tests: they were requested to state if the sentence read was meaningless and if the drawing was well executed. The examiner scored the patients' answers as anosognosic if there was a negation and/or a confabulation about the defective performance. Results showed that not all USN patients were unaware of their "neglect" performance; some were able to elaborate the feedback of the outcome of the test. Another important point highlighted by this study was the independence of the different forms of anosognosia, with unawareness of USN and motor deficits being dissociated.

The Catherine Bergero Scale (CBS, Azouvi et al., 1996; 2003) is a useful tool to assess the presence of anosognosia for USN; it provides both a functional evaluation of USN in routine activities and, at the same time, a measure of awareness about everyday difficulties. The patients' ability in ten real-life situations (e.g., dressing, eating, personal hygiene) is scored using a 4-point scale: the final result is compared with a self-evaluation made by the patients on the same activities, revealing any unawareness of the spatial attention deficit. Significant correlations were found between anosognosia and conventional test scores and between anosognosia for USN and for neurological deficits (Azouvi et al., 1996).

Finally, in 2000 Jehkonen and colleagues investigated this phenomenon by asking right-brain-damaged patients directly if they had difficulty observing a part of space, supplying "left", "right", "none" or "both sides" responses. The efficacy of this type of verbal evaluation was limited in that it only used a generic question about global spatial perception to investigate the disorder, admitting only a yes/no response. Fourteen out of twenty-one neglect patients exhibited unawareness of the deficit, while seven neglect patients appeared non-anosognosic. The study clarified the view that anosognosia for different deficits can occur in dissociated forms, confirming the double-dissociation between anosognosia for neglect and for hemiplegia. Moreover the general unawareness of the impairment was independent of anosognosia for spatial neglect, suggesting that awareness is not a general category including monitoring competences for specific deficits.

IV. Productive manifestations and unawareness: defective control of performance

Productive behaviour in personal and extra-personal space, as well as the lack of awareness of the impaired performance, can be accounted for by defective monitoring manifestations.

Patients with perseveration in target cancellation tasks are not able to inhibit this “positive” activity, expressing a series of phenomena ranging from continuous and/or repetitive marks to the addition of irrelevant materials (Sandson and Albert, 1986; Vallar et al., 2006). In tasks which require cancellation of the presented targets, perseverating patients are not able to suppress the inappropriate motor responses even when visual feedback on their performance is available. This is especially evident in patients with left neglect, where the frequency of perseverative phenomena is higher than in other neurological conditions (Rusconi et al., 2002). Lack of inhibition can also emerge in reading tasks by productive verbal responses. The addition of letters on the left-hand side of the target cannot be explained by either the incomplete perception of the word or an implicit encoding of the left letters which completes the stimulus, because the final result would be longer than the original stimulus; therefore this productive error seems to suggest the presence of a defective inhibitory mechanism (Chatterjee, 1995).

Monitoring processes can also fail in the detection and discrimination of own/other body parts: somatoparaphrenic patients firmly denied that certain parts in their contralesional hemi-body were theirs (Gerstmann, 1942), frequently attributing ownership to another person. Even if the examiner explains this delusion with logical arguments and clinical demonstrations, these patients are unable to modify their perception.

A defective control of performance emerge also in patients with anosognosia for USN: even when given direct feedback on the errors in their performance in structured or functional assessments (Azouvi et al., 1996; Berti et al., 1996), they frequently argue that the result of the task is flawless. By analogy with a model of movement control (Desmurget and Grafton, 2000), the not processed discrepancy between the intentional cognitive performance and the real outcome reflects a disorder in the monitoring system.

This thesis focuses on these pathological monitoring processes, and specifically those which result in defective inhibitors and the failure of performance control. The productive manifestations and their co-occurrence are analyzed in the first section; unawareness in the neglect syndrome and the possible modulations of this characteristic are extensively examined in the second section.

PRODUCTIVE SYMPTOMS

EXPERIMENT 1

Perseveration in target cancellation and drawing tests: the role of executive deficits

[With kind permission from Elsevier: Ronchi, R., Posteraro, L., Fortis, P., Bricolo, E., and Vallar, G. (2009). "Perseveration in left spatial neglect: Drawing and cancellation tasks". *Cortex*, *45*(3), 300-312. http://www.cortexjournal.net/]

- Aim of the study

Perseveration in USN is mainly found in patients with anterior (frontal) and subcortical lesions (Rusconi et al., 2002). Based on this evidence, we ran an experiment to verify if perseveration can be associated with a "dysexecutive" syndrome (Luria, 1966; Stuss and Benson, 1986).

A previous study (Nys et al., 2006) fails to find a relationship between perseveration and letter fluency test. The objective of the present experiment is to verify and extend this result, administering a more comprehensive battery of "frontal"/"dysexecutive" tests, in order to assess the role of executive deficits in right brain-damaged patients with USN and perseveration. The presence of a visuo-spatial short-term memory deficit, a possible component deficit of the USN syndrome (Husain et al., 2001; Malhotra et al., 2004 and 2005), is also evaluated.

We also aim at quantitatively assessing the presence of this pathological phenomenon in both cancellation and drawing tasks, where clinical evidence suggests that perseveration may occur (Gainotti and Tiacci, 1971). Since defective errors (i.e., omissions) can affect cancellation performance on these tests differently, suggesting that they can be partially independent (Kinsella et al., 1993), it can also be expected that this dissociation will be present in productive errors.

Finally, we assess the differences in eliciting perseveration of the various cancellation tasks.

- <u>Materials and methods</u>

Participants

Twenty-one right-hemisphere-damaged patients participated in this study. The aetiology of the focal lesion was vascular in 20 participants (16 ischemic, four haemorrhagic) and neoplastic in one patient; the site of lesions was assessed by CT or MRI scan. The sample included five females and 16 males with a mean age of 64.29 years (S.D. ± 12.43, range: 34-85), and a mean education of 9.71 years (S.D. ±5.75; range: 0-18). The main duration of disease in the 20 stroke patients was 3.3 months (S.D. ±6.27, range: 0.4-28.8). All patients were right-handed, and had no history or neurological evidence of previous neurological diseases, psychiatric disorders, or dementia. Contralesional motor, somatosensory, and visual half-field deficits, including extinction to tactile and visual stimuli, were assessed by a standard neurological exam (Bisiach et al., 1983). Anosognosia, personal neglect, and somatoparaphrenia were also evaluated (Bisiach et al., 1986; Vallar et al., 2003). The patients' demographic and neurological data are summarized in Table I. For tests with no available norms, control data were provided by 21 neurologically unimpaired right-handed patients, matched for age (M= 63.86, S. D. ±12.63), sex (five females, 16 males), and years of education (M= 10, S.D. ± 5.5).

Table I. Demographic and neurological data of the 21 right-brain-damaged patients participating in the study.

Patient	Sex/Age	Education (years)	Length of illness (months)	Aetiology/ Lesion site	Neurological deficit M	SS	V	Associated deficit AN	PN	SP
P1	M/63	13	1.2	I/Th	+	+	-	-	-	-
P2	F/72	5	1.9	I/PO ic	+	+	-	-	-	-
P3	F/79	5	1.0	I/sub	+	-	+	-	-	-
P4	M/51	13	0.4	I/sub	+	-	-	-	-	-
P5	M/60	8	1.7	H/ Th ic	+	e	-	-	-	-
P6	F/68	5	1.5	H/Bg ic	+	-	-	-	-	-
P7	M/81	13	=	N/FP(rolandic)	+	-	-	-	-	-
P8	M/53	8	28.8	I/FTP	+	-	-	-	-	-
P9	M/59	5	1.4	I-H /FTP	+	+	+	-	-	-
P10	M/60	5	0.9	I/FT In Bg	+	+	+	+V	-	-
P11	M/68	4	0.6	I/TP	+	+	+	+V	-	-
P12	M/34	9	1.2	H/TP Bg	+	+	+	+V	-	-
P13	M/75	18	6.3	I/FTPO In Bg	+	+	+	+M	-	-
P14	M/50	13	7.8	H/FTP(sylvian)	+	+	+	-	-	-
P15	M/76	17	1.3	I/FTP In Bg	+	+	+	+SS-V	-	-
P16	F/68	2	1.4	I/FTP In	+	+	+	+M-SS	-	-
P17	M/76	0	2.3	I/TP Bg	+	e	e	+M	-	-
P18	M/57	18	2.4	I/FT Bg	+	-	-	-	-	-
P19	M/85	18	2.2	I/TPO Crb	+	-	+	-	-	-
P20	F/53	8	1.3	I/FTPO In Bg	+	+	+	+SS-V	-	-
P21	M/62	17	0.9	I/TP In Bg	+	+	+	+SS-V	-	-

I/H/N: ischemic / hemorrhagic/neoplastic lesion. F: frontal; P: parietal; T: temporal; O: occipital; In: insula; ic: internal capsule; Th: thalamus; Bg: basal ganglia; sub: subcortical; Crb: cerebellum; M/SS/V: left motor/somatosensory/visual half-field deficit. e: contralesional extinction. AN: anosognosia; PN: personal neglect; SP: somatoparaphrenia. +/- presence/absence of impairment.

Neuropsychological assessment

The assessment for USN included the following tests.

- *Line bisection*. The patients' task was to mark with a pencil the mid-point of six horizontal black lines (two 10 cm, two 15 cm, and two 25 cm in length, all 2 mm in width), presented in a random fixed order. Each line was printed on an A4 sheet, with the centre of each line being aligned with the mid-sagittal plane of the subject's body. Participants used their right hand, which is unaffected by motor deficits in right brain-damaged patients. The score was the deviation of the participants' mark from the objective midpoint, measured to the nearest mm; a positive score denoted a rightward displacement, a negative score a leftward displacement. The mean bisection error of the present control group was +0.74 mm (S. D. ±1.98, range -2.3 +5.67).
- *Letter cancellation* (Diller and Weinberg, 1977). The patients' task was to cross out all of 104 H letters (53 in the left-hand side, and 51 in the right hand-side of the sheet), printed on an A3 sheet, together with other letter distracters. In neurologically unimpaired participants the maximum difference between omission errors on two sides of the sheet was two (Vallar et al., 1994).
- *Star cancellation* (Wilson et al., 1987). The patients' task was to cross out all of the 56 black small stars (30 in the left-hand side, 26 in the right-hand side) printed on an A4 sheet, together with distracters (larger stars, letters, and English words). In the present control group the mean number of omissions was 0.43 (S. D. ±0.6, range 0-2), with one target being the maximum difference between the number of omission errors in the two sides of the sheet.

- *Line cancellation* (Albert, 1973). The patients' task was to cross out all of the 40 black lines printed on an A4 sheet with no distracters. There were two conditions: a) lines were distributed at random in the sheet (20 in the left-hand side, and 20 in the right-hand side); b) lines were distributed in four quadrants 13.8 cm wide and 9.5 cm high, with 10 lines per quadrant; the four quadrants were separated by a white cross-shaped area 2 cm wide. Each of the two conditions was presented twice, with an ABBA order. In the present control group, the mean number of omissions was 0.06 (S. D. ±0.24, range 0-1), with the maximum difference between the number of omission errors in two sides of the sheet being one target.
- *Drawing*. Patients were required a) to copy two figures [a daisy and a complex figure with two trees in the left-hand side, two pine trees in the right-hand side, and a house in the centre of an A4 sheet (see Gainotti et al., 1972)], and b) to draw from memory the hours of a clock in a circular quadrant (diameter 12 cm), printed on an A4 sheet.

The assessment for executive, "frontal", functions included the following tests:

- *Phonemic Verbal Fluency* (Novelli et al., 1986). This task required patients to produce, within 60 seconds for each letter, as many words as they could, beginning with a given letter ("F", "P", "L").
- *Semantic Verbal Fluency* (Novelli et al., 1986). This task required patients to produce, within 60 seconds for each category, as many words as they could, belonging to a given category ("cars", "animals", "fruits").
- *Stroop Colour-Word Interference test* (Caffarra et al., 2002). This test included three sets of stimuli, and three tasks: 1) words printed in black ink (the patient's

task was to read each colour name), 2) coloured circles (the patient's task was to name the colour of each target), 3) colour words printed in incongruous coloured ink (the patient's task was to name the colour ink of each colour name, without reading the words). The stimuli were arranged in a vertical column. Two scores were computed: a) the "time interference", based on the time spent on the three tasks [T= T3- (T1+T2)/2]; b) the "error interference", based on the errors made on the three tasks [E= E3- (E1+E2)/2].

- *Weigl's sorting test* (Spinnler and Tognoni, 1987). This test included 12 wooden stimuli, differing in five dimensions (form, colour, size, thickness, and "suit" printed on the top: a club, heart, or diamond). The patients' task was to sort in groups, according to one of the criteria, the stimuli, presented on a table in a random arrangement. When patients sorted the stimuli correctly, according to one criterion, the examiner invited them to sort the stimuli according to a different criterion, until all criteria were discovered. If patients were unable to find out a criterion, the examiner moved to a "passive modality", with the patients' task being to detect the criterion by which the examiner grouped the items.

Adjusted and "equivalent" scores (Capitani and Laiacona, 1997) are available for all tests. The equivalent scores, which provide scores comparable across different tasks, range from "0" (defective performance) to "4" (very good performance, see psychometric details in Capitani and Laiacona, 1997).

The assessment for visuo-spatial short-term memory included the following tests.

- *Corsi's Block tapping test* (Orsini et al., 1987). Nine white cubes were arranged over a board. The examiner tapped sequences of increasing length in a fixed order, with the patients' task being to tap the same sequence, immediately after presentation. The test continued until the patient failed at a given length (less than three out of five sequences were correctly recalled). The spatial span score was the length of the longest sequence correctly recalled. Adjusted and equivalent scores were available.

- *Corsi's Vertical test* (see Figure 2). This was a modified version of the standard Corsi's Block tapping test. Nine white cubes were arranged over a vertical board 60 cm high and 14 cm wide; the distance between each cube was 1.5 cm. The procedure was identical to that used for the standard Block tapping test of Orsini et. al. (1987). In the present control group the mean span was 3.38 (SD ±1.07, range 2-6).

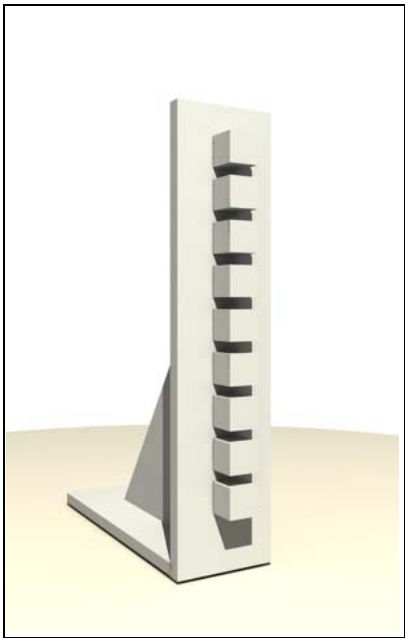

Figure 2: The vertical version of the Corsi test

Procedure

Cancellation tasks

In all three cancellation tasks, patients were required to cancel out all targets in the display, whose centre was aligned with the mid-sagittal plane of the patients' body. Specifically, patients were required to cross out each target making a single mark on it. In the present study, investigating the relationships between USN and perseveration errors, patients were classified as showing evidence of spatial neglect if their score on at least one out of the three cancellation tasks indicated a rightward bias, with reference to available norms (Vallar et al., 1994), or the performance of neurologically unimpaired control participants (line and star cancellation tasks). The patients' performance in line bisection was not used as classification criterion, since in the published studies investigating the relationships between spatial neglect and perseveration, cancellation tasks were used (Na et al., 1999; Nys et al., 2006; Rusconi et al., 2002; Bottini and Toraldo, 2003; Toraldo et al., 2005; Manly et al., 2002; Mark et al., 2004; Vallar et al., 2006). However, since patients may show left neglect in cancellation, but not in bisection tasks, and vice versa (Halligan and Marshall, 1992; Marshall and Halligan, 1995), it was assessed whether or not patients showing left neglect solely in line bisection exhibited perseveration in cancellation tasks. Furthermore, the relationships between the line bisection error and the omission and perseveration errors in cancellation tasks were investigated by correlation analyses.

In the cancellation tasks, the following omission and perseveration error scores were computed:

- *Omission errors*. In patients classified as showing left neglect, an omission percent error score [(number of omissions / number of targets) X 100] was computed for each cancellation task. The total omission error score in the neglect group was the mean of the scores in all three cancellation tasks.

- *Perseveration errors*. The method devised by Vallar et al. (2006) was used to compute a perseveration score: 1-crossing a target with more than one distinct mark; 2-drawing a new target; 3-drawing a new target, and subsequently crossing it out; 4-complex drawings (e.g., the patient's signature).
- *Perseveration index*. This index was based on repeated marks (i.e., perseveration errors scored "1" in the perseveration score described above): [(number of cancellation single marks + number of added marks / number cancelled targets]. In patients without perseveration, the index was 1, namely the number of marks was equal to the number of cancelled targets. In patients showing perseveration, the index was greater than 1. To provide an example, in a patient crossing out 20/40 targets, one target three times (i.e., two additional crossings out, after the first, correct, cancellation) the index was: 20 (crossed targets) + 2 / 20 = 1.1). Patients who made one or more repeated marks, in at least one out of the three cancellation tasks, were classified as showing perseveration (see a similar classification procedure in Nys et al., 2006). Na's (1999) perseveration percentage (number of targets with perseverative marks/total number of targets cancelled x 100) did not appear to capture one relevant aspect of the severity of perseveration. Since the numerator of Na's (1999) perseveration percentage is the "number of targets with perseverative marks", Na's percentage does not distinguish, for instance, a target marked twice vs. a target marked five times. Nevertheless, in order to compare the present data with published findings more closely, also Na's (1999) perseveration percentage was computed.

On the basis of their performances in the cancellation tasks, patients were divided into two groups, showing (N+), and not showing (N-) USN. Subsequently, the N+ and N- groups were subdivided into patients showing (P+), and not showing (P-), perseveration.

<u>Drawing tasks</u>

- *Omission errors*. The following scores were used. a) Daisy (range 0-2): 0 (flawless copy); 0.5 (partial omission of the left-hand-side of the daisy); 1.0 (complete omission of the left-hand-side of the daisy); 1.5 (complete omission of the left-hand-side of the daisy, and partial omission of the right-hand-side of the daisy); 2.0 (no drawing, or no recognizable element). b) Five-element complex drawing (range 0-5): 0 (flawless copy); 0.5 (for each partial omission of one component, e.g., the left-hand-side of a tree); 1.0 (for each omission of one component); the horizontal ground line was not considered for scoring. c) Clock drawing by memory (range 0-12): 0 (flawless drawing); 1 (for each omission or left-to-right translocation of an hour from the left-hand-side quarters of the quadrant; the “12” and “6” hours were scored as translocated when displaced in the right-hand-side quadrants). The total neglect (omission and translocation) score was the sum of the scores in the three drawing tasks.
- *Perseveration errors*. For the purpose of scoring, each drawing was considered comprising the following components: daisy (corolla, stalk, leaves), complex drawing (from left to right: two trees, the house, and two pine trees), clock drawing (the 12 hours). For each component, the following scores were given: 0 (no perseveration); 1 (repetition of single marks); 2 (repetition of the complete component, both by copying it or tracing its contours); 3 (for the adding of each

new component). The total perseveration score was the sum of the scores in the three drawing tasks.

Statistical analyses

The data were analysed by nonparametric statistics (Siegel and Castellan, 1988). The patients' performances were compared with the control data by t tests (Crawford and Garthwaite, 2002; Crawford and Howell, 1998) .

- <u>Results</u>

Spatial neglect in cancellation and bisection tasks

Seven patients (P1-P7) were classified as N-, and 14 (P8-P21) as N+, on the basis of their performance in the cancellation tasks. The letter and star cancellation tasks revealed left spatial neglect in 12 out of 14 patients (86%), the line cancellation task in six patients (43%). A preliminary analysis showed that the percent omission error scores in the two conditions of the line cancellation task did not differ from each other. The patients' scores were 14.46% in the line-distributed-at-random, and 14.29% in the line-distributed-in-four-quadrants conditions (Wilcoxon signed ranks test: $T = 7$; $z = 0.73$; p = n.s.).

Two patients showed neglect in the letter task only, and two in the star task only. No patient exhibited neglect in the line cancellation task only. A Friedman two-way analysis of variance by ranks with three dependent variables (star, line, and letter percent omission scores) revealed a significant difference between tasks ($\chi^2 = 16.62$; d.

f. = 2; $p = 0.00025$). Multiple comparisons showed that the percent omission scores in the star (35.08%), and in the letter (35.58%) tasks differed from the line task (14.38%) ($p < 0.01$), with no other comparison being significant.

In the line bisection task, a Kruskal-Wallis one way analysis of variance by ranks showed a difference among control participants (M= +0.74 mm, S. D.= ±1.98, range -2.3 – +5.67), N- (M= +0.86 mm, S. D.= ± 2.84, range -2.7 - +5.5), and N+ (M= +13.14 mm, S. D.= ± 17.96, range -2.6 - +69.33) patients (KW= 12.28, d. f. = 2, $p = 0.0022$). Multiple comparisons revealed differences between the control group and the N+ patients ($p < 0.01$), and between N+ and N- patients ($p < 0.05$).

In order to ascertain whether the patients, classified as not showing USN on the basis of cancellation tasks, exhibited neglect on the bisection task, the bisection score of each of the seven N- patients was compared against the score of the control group. Only the bisection error (+5.5 mm) of patient #5 differed from the score of the control group ($t = 2.349$, $p = 0.015$).

The correlation between the bisection and the total omission error scores of N+ patients was not significant (Kendall rank-order coefficient: T = 0.33; $z = 1.59$; p = n.s.).

Perseveration in cancellation tasks

All seven N- patients (including patient #5, who made a rightward error in line bisection) made no perseveration errors in the cancellation tasks. N+ patients were further subdivided into six patients not showing (N+P-: P8-P13), and eight patients showing (N+P+: P14-P21) perseveration.

The severity of neglect in the N+P- and N+P+ patients was compared by a Mann-Whitney test, which revealed no significant difference between the total omission error scores of the two groups ($z = 1.16$, p = n.s.). A perusal of the scores showed, if anything, a trend towards a more severe neglect in N+P- (M= 44.47%, range 3.53 – 87.69%) than in N+P+ (M= 16.25%, range 4.17 – 64.38%) patients.

Figure 3 shows in the N+P+ group the perseveration index (A) and Na's (1999) perseveration percentage (B) in the three cancellation tasks. Table II shows the omission and perseveration scores, indexes, and percentages, as well as the bisection scores of each patient. A perusal of the patients' scores shows a higher degree of perseveration in the star cancellation task. A Friedman two-way analysis of variance by ranks with three dependent variables (star, line, and letter cancellation) revealed a significant difference among tasks ($\chi^2 = 6.74$; d. f. = 2; $p = 0.034$). Multiple comparisons showed that the perseveration index in the star task differed from those in the other two cancellation tasks ($p < 0.05$). As for Na's (1999) perseveration percentage, a Friedman two-way analysis of variance by ranks with three dependent variables (star, line, and letter cancellation) revealed no significant difference among tasks ($\chi^2 = 4.52$; d. f. = 2; p = n.s.). As noted in the methods section, the present perseveration index is a more sensitive measure to capture perseveration behaviour. The scores of patients #19 (star: index 1.10, percentage 7%) and of patient #20 (letter: index 1.11, percentage 9%) reveal a greater index score. The two patients made more than one perseveration per target. This pathological behaviour is captured by the index, but not by the percentage score.

Table II. Performance of the 21 right-brain-damaged patients in the tasks assessing USN (bisection, cancellation) and perseveration (cancellation).

PATIENT GROUP			CANCELLATION TASKS											
			Omission Score			Perseveration score			Perseveration Index			Na et al.'s (1999) Perseveration percentage		
		Line Bisection	Star	Letter	Line	Star	Letter	Line	Star	Letter	Line	Star	Letter	Line
P1	N-	+3	--	--	--	--	--	--	--	--	--	--	--	--
P2	N-	-1	--	--	--	--	--	--	--	--	--	--	--	--
P3	N-	-2.7	--	--	--	--	--	--	--	--	--	--	--	--
P4	N-	-0.8	--	--	--	--	--	--	--	--	--	--	--	--
P5	N-	+5.5	--	--	--	--	--	--	--	--	--	--	--	--
P6	N-	-0.3	--	--	--	--	--	--	--	--	--	--	--	--
P7	N-	+2.3	--	--	--	--	--	--	--	--	--	--	--	--
P8	N+P-	-1.5	0%	10.58%	0%	--	--	--	--	--	--	--	--	--
P9	N+P-	+69.3	85.71%	94.23%	83.13%	--	--	--	--	--	--	--	--	--
P10	N+P-	+8	19.64%	0%	0%	--	--	--	--	--	--	--	--	--
P11	N+P-	+16.2	46.43%	68.27%	0%	--	--	--	--	--	--	--	--	--
P12	N+P-	+9.3	67.86%	86.54%	11.25%	--	--	--	--	--	--	--	--	--
P13	N+P-	+11.7	89.29%	85.58%	51.88%	--	--	--	--	--	--	--	--	--
P14	N+P+	n.a.	26.79%	12.50%	1.25%	1	2	0	1.02	1.02	1	2%	2%	0%
P15	N+P+	-2.6	7.14%	23.08%	0%	2	0	0	1.04	1	1	4%	0%	0%
P16	N+P+	+2.8	5.36%	10.58%	0%	2	0	0	1.04	1	1	4%	0%	0%
P17	N+P+	+10.5	12.50%	0%	0%	1	0	6[§]	1.02	1	1.05	2%	0%	5%
P18	N+P+	+10.3	0%	18.27%	0%	12	0	0	1.21	1	1	21%	0%	0%
P19	N+P+	+19.3	26.79%	13.46%	3.75%	4	0	7	1.10	1	1.09	7%	0%	9%
P20	N+P+	+7.7	76.79%	66.35%	50%	1	4	0	1.08	1.11	1	8%	9%	0%
P21	N+P+	+9.8	26.79%	8.65%	0%	3	0	0	1.07	1	1	7%	0%	0%

n.a.: not assessed; [§]P17 made 2 simple and 1 complex perseveration errors, scored 4

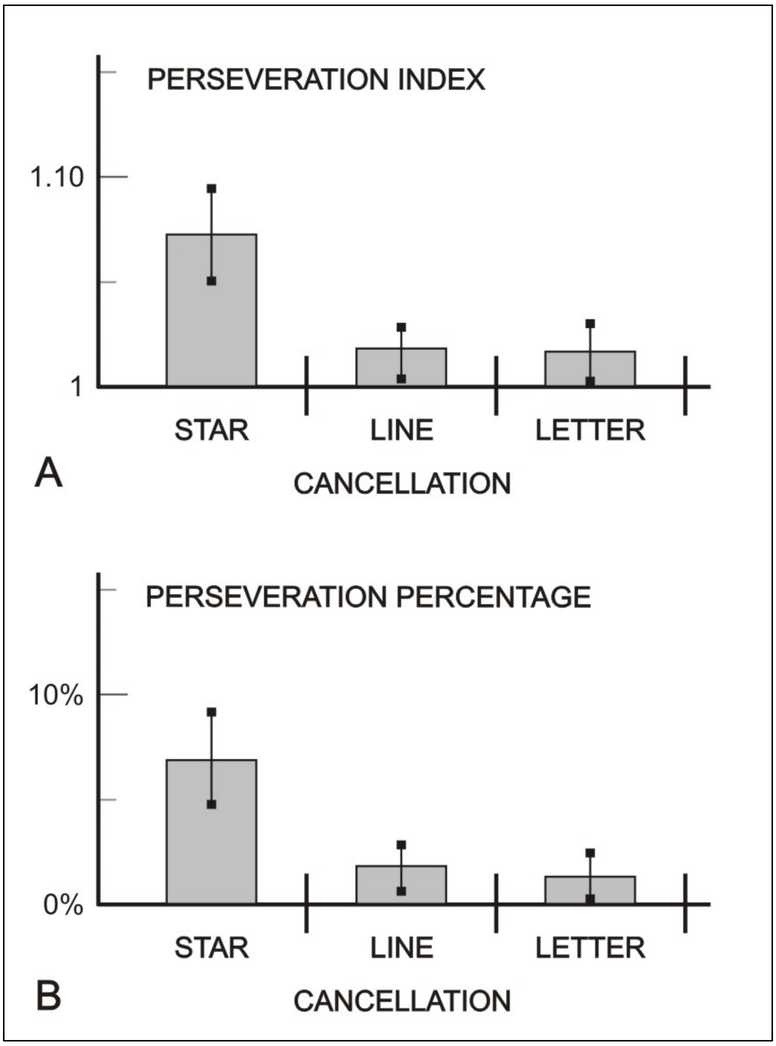

Figure 3. (A) Perseveration index (s.e) in eight N+P+ patients, by task; (B) Perseveration percentage (s.e.) (Na et al., 1999) in eight N+P+ patients, by task.

In the star cancellation task all eight patients showed perseveration, while in both the letter and the line tasks only two out of the eight N+P+ patients (25%) showed perseveration (χ^2 with Yates' correction for continuity = 6.67; d. f. = 1; p = 0.0098). In the line cancellation tasks, patient #17 made two simple and one complex perseveration errors in the line-distributed-in-four-quadrants condition, patient #19 seven simple perseveration errors in the line-distributed-at-random condition.

In the star cancellation task, where all patients made perseveration errors, a Wilcoxon signed ranks test showed that the perseveration score was higher in the ipsilesional right-hand side (M= 2.38), compared with the contralesional left-hand side (M= 0.88) (T = 2; z = 2.03; p = 0.043). The correlation between the omission (M= 22.77%) and the perseveration (M= 3.25) scores was not significant (Kendall rank-order coefficient: T = -0.37; z= -1.27; p = n.s.). Also the correlations between the perseveration index (1.07) and the omission score (Kendall rank-order coefficient: T = -0.04; z = -0.14; p = n.s.), and between the perseveration percentage (7%) and the omission score (Kendall rank-order coefficient: T = 0.04; z = 0.14; p = n.s.) were not significant.

No significant correlations were found in the N+P+ group between the bisection score (M= +8.26 mm) and the perseveration score (Kendall rank-order coefficient: T = 0.25; z = 0.79; p = n.s.), the perseveration index (Kendall rank-order coefficient: T = 0.29; z = 0.92; p = n.s.), and the perseveration percentage (Kendall rank-order coefficient: T = 0.15; z = 0.47; p = n.s.).

Executive and spatial short-term memory functions

Table III shows the mean correct (adjusted, where norms were available) scores of the N-, N+P-, and N+P+ groups in the executive and short-term memory tasks. Kruskal-Wallis one-way analyses of variance by ranks revealed no significant difference among the N-, N+P- and N+P+ groups for Phonemic verbal fluency (KW = 0.45; d. f.= 2; p = n.s.), Stroop colour-word Interference test (time interference: KW = 0.18; d. f.= 2; p = n.s.; error interference: KW = 2.59, d. f. = 2; p = n.s.), and Weigl’s sorting test (KW = 5.50; d. f.= 2; p = 0.064). This trend towards significance reflects a difference between the performances of N- and N+P+ patients (p= 0.0599). In the Semantic verbal fluency task a significant difference was found (KW = 8.54; d.f. = 2; $p = 0.014$); multiple comparisons revealed a difference between the N+P+ group and the other two groups ($p < 0.05$).

Table III. Performance of the 21 right-brain-damaged patients in tasks assessing executive and visuo-spatial short-term memory function. All scores are "adjusted scores", but the raw scores of the vertical Corsi's Block tapping test; the number in brackets indicates the patients with pathological "equivalent scores".

PATIENTS' GROUP	Phonemic Fluency	Semantic Fluency	Colour-Word Stroop Interference		Weigl's Sorting Test	Corsi's Test	
			Time	Error		Standard	Vertical
N- (n=7)	25.14 (1)	35.00 (0)	22.96 (1)	-0.18 (0)	11.07 (0)	4.86 (0)	2.86
N+P- (n=6)	23.21 (2)	35.00 (0)	25.50 (2)	0.13 (0)	9.71 (0)	2.42 (3)	2.00
N+P+ (n=8)	21.75 (3)	28.75 (1)	24.45§ (2)	2.32§ (1)	7.84 (1)	3.97 (1)	2.00

§ The Stroop task was not given to P17 (N+P+), who was illiterate.

In the Corsi's Block tapping test a Kruskal-Wallis one-way analysis of variance by ranks showed a significant difference among the N-, N+P- and N+P+ groups (KW = 10.84; d. f.= 2; $p = 0.0044$); multiple comparisons revealed a difference between the N- and the N+P- groups ($p < 0.01$), with no other comparison being significant.

In the Corsi's Block tapping vertical test, where no norms were available, a Kruskal-Wallis one-way analysis of variance by ranks was performed, in order to compare the scores of control participants, N-, and N+ patients. A significant difference was found (KW= 13.66; d. f. = 2, $p = 0.0011$). Multiple comparisons revealed significant differences between controls and N+ patients ($p < 0.01$). A further Kruskal-Wallis one-way analysis of variance by ranks in N-, N+P-, and N+P+ patients showed no significant differences among groups (KW= 3.06, d. f. = 2, p = n.s.).

In the N+P+ patients no significant correlations were found between the star perseveration index and Phonemic fluency (Kendall rank-order coefficient: T = 0.37; z = 1.28; p = n.s.), Semantic fluency (Kendall rank-order coefficient: T = -0.15; z = -0.53; p = n.s.), Stroop colour-word Interference test (Kendall rank-order coefficient; time interference: T = -0.29; z = -0.92; p = n.s.; error interference: T = -0.45; z = -1.42; p = n.s.), and Weigl's sorting test (Kendall rank-order coefficient: T = -0.34; z = -1.18; p = n.s.). Also the correlations between the patients' performances in the executive tasks and the star perseveration percentage [Kendall rank-order coefficient: Phonemic fluency: T = 0.49; z = 1.70; p = n.s.; Semantic fluency: T = -0.04; z = -0.14; p = n.s.; Stroop colour-word Interference test (time interference: T = -0.15; z = -0.47; p = n.s.; error interference: T = -0.31; z = -0.97; p = n.s.), and Weigl's sorting test: T = -0.31; z = -1.07; p = n.s.] were not significant.

The correlations of the star perseveration index with visuo-spatial short-term memory performance were not significant (Kendall rank-order coefficient; Corsi's Block tapping test: T = 0.29; z = 0.99; p = n.s.; Corsi's Block tapping vertical test: T = -0.05; z = -0.16; p = n.s.). Also the correlations between the star perseveration percentage and the patients' performance in the two tests assessing visuo-spatial short-term memory (Kendall rank-order coefficient; Corsi's Block tapping test: T = 0.25; z = 0.87; p = n.s.; Corsi's Block tapping vertical test: T = 0.05; z = 0.17; p = n.s.) were not significant.

Finally, Table III shows also the number of N+P+ patients who had a disproportionate low "equivalent score" in the tasks assessing executive and spatial short-term memory function. It is apparent that only a few patients had a defective score, with the percentage of impaired patients ranging from one out of eight (12.5%) in most tasks to a maximum of three out of eight (37.5%) in the Phonemic fluency task.

Neglect and perseveration in drawing

Figure 4 shows the total neglect scores in the drawing tasks. It is apparent that N- patients made less neglect errors that N+P- and N+P+ patients. A Mann-Whitney test revealed a significant difference ($z = -2.94$, $p = 0.002$) between the N- group and the N+ group, that pooled together patients showing (P+) and not showing (P-) perseveration. No difference in the neglect scores was found between the N+P- and the N+P+ patients ($z = 0.06$, p = n.s.).

Figure 5 shows the total perseveration scores of the N-, N+P-, and N+P+ groups, with N+P+ patients making more perseveration errors. A Kruskal-Wallis one-way analysis of variance showed a difference among groups (KW = 15.45, d. f. = 2; $P = 0.0004$); multiple comparisons revealed a difference between the N+P+ group and the other two groups ($p < 0.05$). A Wilcoxon signed ranks test with two dependent variables (perseveration scores in the left-hand and right-hand sides of the drawings) revealed a significant difference in the N+P+ group ($T = 2.5$; $z = 2.17$; $p = 0.03$), with the patients' perseveration scores being M= 5.63 (range 0-11.5) in the left-hand side and M= 11.5 (range 7.5-19) in the right-hand-side of the sheet.

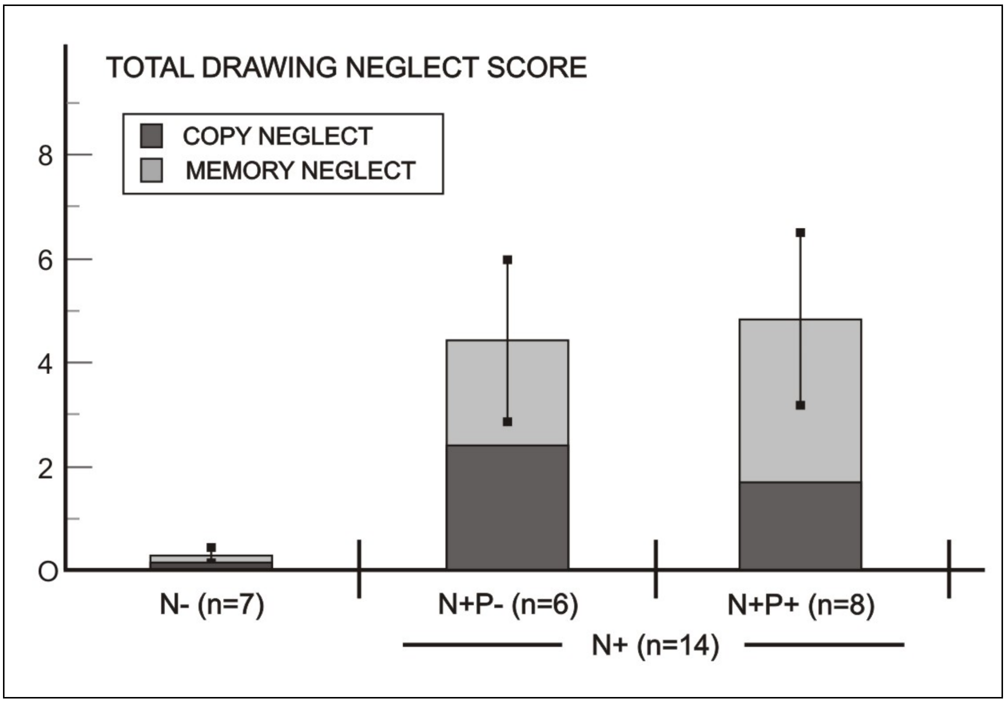

Figure 4. Total drawing neglect score (s.e.) by patients' groups (N-, N+P-, and N+P+), and by task (copy, memory).

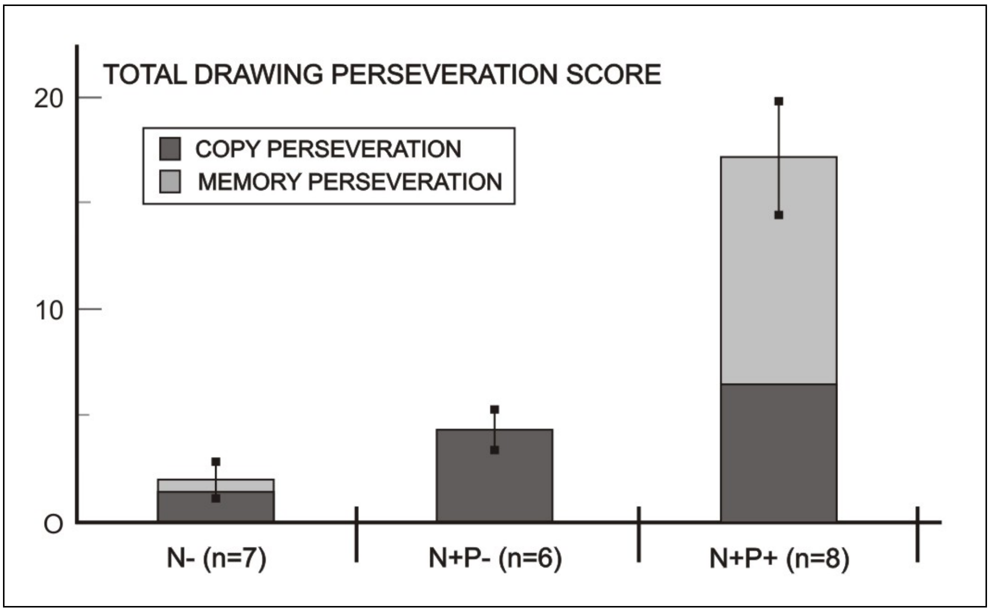

Figure 5. Total drawing perseveration score (s.e.) by patients' groups (N-, N+P-, and N+P+), and by task (copy, memory).

Two further Kruskal-Wallis one-way analyses of variance were performed on the copy and memory scores. For the copy perseveration scores, a difference among groups was found (KW = 6.16, d. f. = 2; P = 0.046); multiple comparisons indicated a trend towards a difference between the N- and the N+P+ (p = 0.06). For the memory perseveration scores, a difference among groups was found (KW = 16.61, d. f. = 2; P = 0.0002); multiple comparisons revealed differences between the N+P+ patients and the other two groups ($p < 0.01$). A perusal of the individual data of the eight N+P+ patients showed that five patients exhibited more perseveration errors in the memory tasks, two more perseveration in the copy tasks, and one an equal number of perseveration errors. Two patients (#14 and #20) made no perseveration errors during copy, but scored nine and 11, respectively, in the memory condition. No patient had a flawless performance in the memory condition. Particularly, patient #17 scored 19 in the copy condition, and five in the memory condition. Conversely, patient #21 scored seven in the copy condition, and 24 in the memory condition (see Table IV). The difference was significant (χ^2 with Yates' correction for continuity = 15.18; d. f. = 1; p = 0.0001).

The correlation between the total neglect (M= 4.81) and perseveration drawing (M= 17.13) scores in the N+P+ patients was not significant (Kendall rank-order coefficient: T = 0.11; z = 0.38; p = n.s.). The correlations of the total perseveration drawing score with both the perseveration index (Kendall rank-order coefficient: T = -0.11; z = -0.39; p = n.s.), and the perseveration percentage (Kendall rank-order coefficient: T = -0.08; z = -0.27; p = n.s.) in the star cancellation task were not significant.

Table IV. Neglect and perseveration error scores of the 21 right-brain-damaged patients in drawing tasks (copying a daisy and a complex figure, drawing a clock from memory). Groups are based on the patients' performances on the cancellation tasks (see Table II).

PATIENT	GROUP	NEGLECT SCORE			PERSEVERATION SCORE		
		Daisy	Complex Figure	Clock	Daisy	Complex Figure	Clock
P1	N-	0	0	0	0	0	0
P2	N-	0	0	0	0	0	0
P3	N-	0	0.5	0	0	2	3
P4	N-	0	0	0	2	2	1
P5	N-	0	0.5	0	0	2	0
P6	N-	0	0	0	0	2	0
P7	N-	0	0	1	0	0	0
P8	N+P-	0	0.5	0	6	2	0
P9	N+P-	1	4.5	0	3	1	0
P10	N+P-	0	1	0	2	1	0
P11	N+P-	0	1.5	1	2	4	0
P12	N+P-	1	2.5	3	0	3	0
P13	N+P-	0	2.5	8	2	0	0
P14	N+P+	0	0	0	0	0	9
P15	N+P+	0	0.5	0	3	4	12
P16	N+P+	0	1.5	6	0	4	14
P17	N+P+	0	0.5	10	1	18	5
P18	N+P+	0	0	1	7	0	7
P19	N+P+	1	3	1	1	7	3
P20	N+P+	1	4	7	0	0	11
P21	N+P+	0	2	0	4	3	24

In the N+P+ patients no significant correlations were found between the total perseveration drawing score and Phonemic verbal fluency (Kendall rank-order coefficient: $T = 0.25$; $z = 0.88$; p = n.s.), Semantic verbal fluency (Kendall rank-order coefficient: $T = 0.34$; $z = 1.18$; p = n.s.), Stroop colour-word Interference test (Kendall rank-order coefficient: time interference: $T = -0.29$; $z = -0.92$; p = n.s.; error interference: $T = 0.45$; $z = 1.42$; p = n.s.), and Weigl's sorting test (Kendall rank-order coefficient: $T = 0.07$; $z = 0.26$; p = n.s.). Also the correlation between the total perseveration drawing score and the performance in Corsi's Block tapping test was not significant (Kendall rank-order coefficient: T = 0.16; z = 0.56; p = n.s.). Conversely, the correlation between the total perseveration drawing score and the performance in Corsi's Block tapping vertical test was marginally significant (Kendall rank-order coefficient: T = -0.56; z = -1.94; p = 0.052).

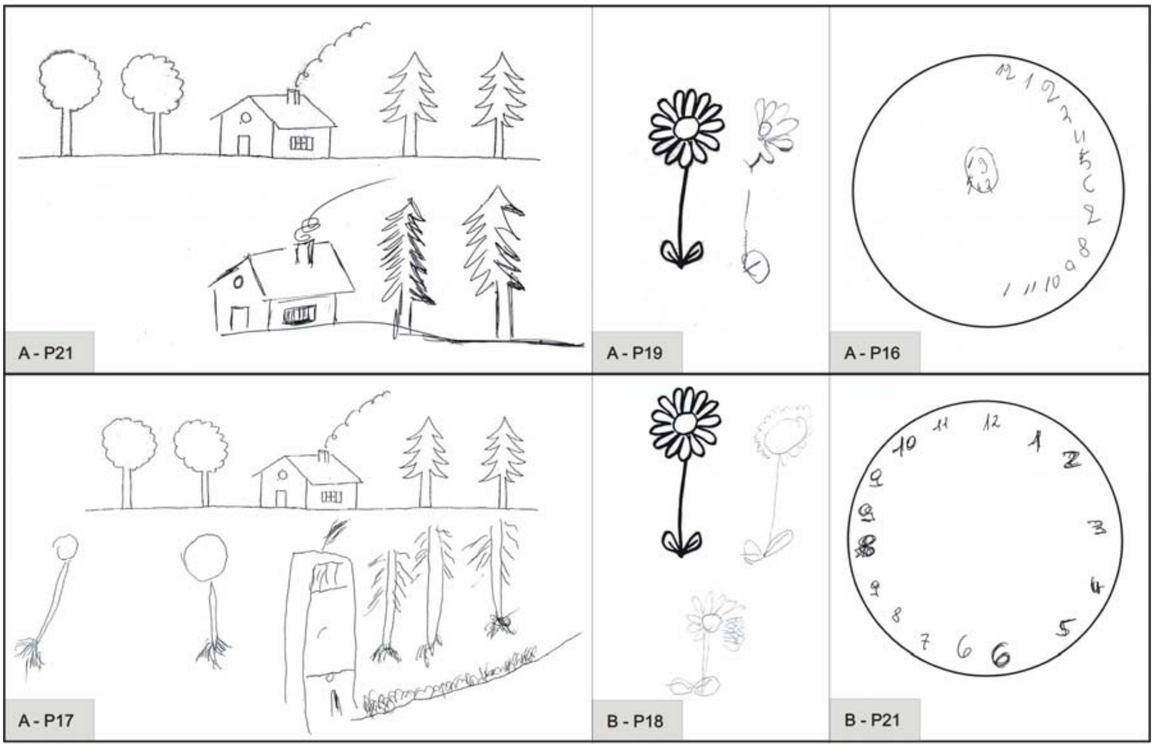

Figure 6

(A) *Examples of drawings with omission and perseveration errors in N+P+ patients.* Complex figure (P21: omission of two left-sided trees, perseveration on the house (chimney, and window), and on the right-hand sides of the two right-sided pine trees. P17: omissions in the right-hand side of the house, which is also distorted ipsilesionally; addition of one pine tree, of grass and roots). Daisy (P19: left-hand-side omission of petals, right-sided perseveration in the lower petals). Clock drawing from memory (P16: rightward translocation of hours; perseveration of several hours: 1, 9, 3, 4, and 5).

(B) *Examples of drawings with perseveration without omission errors in N+P+ patients.* Daisy (P18: addition of right-sided lower petals and of a second daisy on the right-hand top side). Clock drawing from memory (P21; addition of the 6, 8, and 9 hours, and repeated tracing of hours).

Figure 6 shows examples of perseveration errors in drawing. It is apparent that patients may show neglect-related errors and perseveration (figure 6-A). In the individual drawing, omission and perseveration errors may occur in dissociated form, with patients showing only perseveration (figure 6-B).

- Conclusion

Right brain-damaged patients with left USN, who show perseveration in cancellation tasks, also exhibit this behaviour when drawing from memory and when copying. The memory condition seems to elicit more perseveration errors in N+P+ patients, with N+P- patients making no errors in drawing from memory. However, the patterns of perseveration in the individual patients suggest a double dissociation between the copy and the memory conditions, with some patients showing more perseveration in copying, and others in drawing from memory. It should be noted, however, that while two N+P+ patients show perseveration exclusively in the memory condition (P14, and P20, see table IV), none exhibit perseveration in the copying tasks only.

The perseveration errors made by right-brain-damaged patients cannot be accounted for in terms of impaired executive functions. In a number of tasks with available norms, based on the performance of neurologically unimpaired participants (phonemic and semantic fluency, a Stroop colour-word interference task, Weigl's sorting test), the only difference that emerges among the groups is in the Semantic fluency task, where N+P+ patients differ from N- and N+P- patients. However only one out of the eight N+P+ patients (12.5%) have a defective score (0) in this task, while one patient score the maximum of 4, and one score 2.

Nor can perseveration in cancellation and drawing tasks be accounted for by associated impairment of visuo-spatial short-term memory; no difference is found between N+P- and N+P+ patients in either the standard Corsi's block tapping task, or in a vertical version devised to overcome the lateral bias of patients with left spatial neglect (Malhotra et al., 2005).

No significant correlations emerge between omission and perseveration in the present study, in which the perseveration score, the present perseveration index, and Na's (1999) perseveration percentage have been used.

Finally, we employ three target cancellation tasks to assess perseveration. Neglect patients tend to make more perseveration errors in the star cancellation task than in the letter and the line cancellation tasks; furthermore, this task elicits perseveration errors in all of the eight patients susceptible to making this error, whereas only two out of the eight show perseveration in the letter and in the line cancellation tasks. This finding may be at odds with the comparable sensitivity to spatial neglect of the star and the letter cancellation tasks. The letter cancellation task is as effective as the star task for the purpose of detecting neglect, but elicits much less perseveration. These findings suggest that partly different mechanisms may underlie omission (i.e., neglect) versus perseveration errors.

EXPERIMENT 2

Perseveration and disorganised visual search

- <u>Aim of the study</u>

The previous experiment demonstrated that neglect patients exhibit more recurrent perseveration in the star cancellation task than in the letter cancellation task, whereas the omission score is comparable in the two tasks. Distracters are used in both tests, to render them homogeneous with respect to the target/non-target discrimination. However there are other differences present in the tests: the type of target (non-verbal versus verbal), the size of the area presented for the test (A4 sheets and A3 sheets) and the distribution of the stimuli on the sheet (random versus rows). This latter characteristic is considered to have potentially a key role in eliciting perseveration.

Cancellation tasks recruit different cognitive processes, e.g., memorization of the correct target to cancel and the discrimination between targets, pre-marked targets and distracters. In addition certain tests (i.e., the star cancellation task where stimuli are printed randomly) may require more attentional resources because patients have to organize an efficient visual exploration strategy, monitor their search and avoid repeating areas that they have already examined. These resources could be limited in neglect patients: in fact there is evidence to suggest that a disorganized target search is typical of stroke patients with right-brain lesions (Donnelly et al., 1999) and some studies have stressed the association between defective visual search strategies and neglect syndrome (Chedru et al., 1973; Weintraub and Mesulam, 1988). Patients showing perseveration could have an additional obstacle to their visual-search performance where the task requires attention to a plurality of components contemporaneously: even if this is not sufficient in itself to explain the presence of perseveration, it is possible that a defective visual search organization could exacerbate their tendency to re-mark targets. A study by Mark and collaborators (2004) provides support for this hypothesis, demonstrating that perseverative behaviour is associated to different degrees of disorganisation in visual search.

We therefore set perseverating patients cancellation tasks involving verbal and non-verbal stimuli in both ordered and scattered formats to further verify if random distribution of stimuli is in fact a critical element in eliciting perseveration. This test is set also with the additional aim of verifying whether omission errors are influenced by scattered target distribution. Finally we verify whether perseverating patients present reduced attentional resources, assessing the presence of a divided attention deficit in this group of neglect patients.

- <u>Materials and methods</u>

Participants

Twenty-six patients (11 males, 15 females; mean age: 65 years, SD: ± 14.3, range: 34-87); mean education: 11.3 years, SD: ± 5.1, range: 5-18) with right hemisphere lesions were included in this study. The aetiology of the focal lesion was vascular in 25 participants (19 ischemic, six haemorrhagic) and neoplastic in one patient; the lesion site was assessed by CT or MRI scan. All patients were right-handed, and had no history or neurological evidence of previous neurological impairments or psychiatric disorders.

Table V. Demographic and neurological data of the 26 right-brain damaged patients.

	Sex	Age	Education (years)	Aetiology/ Lesion site	Neurological deficit M	SS	V	Associated deficit Anoso	Np	SP
P1	F	66	5	N / F-T	+	e	e	-	-	-
P2	M	65	5	I / bg-ic	+	e	e	-	-	-
P3	M	87	17	I / P-T-O-crb	-	-	+	-	-	-
P4	F	82	13	I / Sylvian region	+	+	e	-	-	-
P5	F	72	5	I / T-P-bg-ic	+	-	-	-	-	-
P6	F	83	13	I / Sylvian region	+	+	+	+SS	-	-
P7	M	77	17	I-H / Sylvian region	+	+	+	+SS-V	-	-
P8	M	63	17	I-H/ F-P-bg	+	+	e	-	+	-
P9	F	77	8	I / bg-th	-	-	-	-	-	-
P10	F	78	5	I-H / Sylvian region	+	+	+	-	+	-
P11	F	81	5	H / T-P-O	na	na	na	na	na	na
P12	F	37	8	H / F-bg	+	+	+	-	-	-
P13	M	61	17	H / F-s-cort	-	e	e	-	-	-
P14	M	70	17	I / T-P-O	+	-	+	-	-	-
P15	F	56	8	H / cc	-	e	-	-	-	-
P16	F	53	17	I / F-T-P-bg	+	+	e	+SS	-	-
P17	M	65	17	I / Sylvian region	+	+	+	+SS	-	-
P18	F	75	8	I / F-T-bg	+	e	-	+M	-	-
P19	M	71	18	I / Sylvian region	+	+	+	+SS	-	-
P20	M	54	17	I / bg-ic	+	+	+	+SS-V	+	-
P21	F	38	13	I / F-T-O-In-ic	+	+	+	+SS-V	-	-
P22	F	34	12	I-H / Sylvian region	+	+	+	+SS-V	-	-
P23	F	57	8	H / F-P-In-bg	+	+	e	+SS	-	-
P24	M	61	5	I / Sylvian region	-	-	+	-	-	-
P25	M	54	13	I / F-T-In	-	-	-	-	-	-
P26	F	73	5	H / F-s-cort	+	+	+	+SS-V	+	-

I: ischemic lesion; H: haemorrhagic lesion; N: neoplastic lesion; F: frontal; P: parietal; T: temporal; O: occipital; In: insula; ic: internal capsule; th: thalamus; bg: basal ganglia; s-cort: sub-cortical; crb: cerebellum; cc: corpus callosum.
M: left motor deficit; SS: left somatosensory deficit; V: visual half-field deficit; e: extinction; ANOSO: anosognosia; Np: personal neglect; SP: somatoparaphrenia; +: presence of deficit; -: absence of deficit; na: not assessed.

The global cognitive efficiency was assessed using the Mini Mental State Examination (Folstein et al., 1975) to exclude the presence of dementia. Contralesional motor, somato-sensory and visual-field defects were evaluated by the standard neurological examination; anosognosia for neurological deficits was also assessed (Bisiach et al., 1986). Information on neurological and associated deficits was not available for the patient #11. The patients' demographic and neurological data are reported in Table V.

Thirty-four right-handed neurologically unimpaired participants, matched for age (mean: 66.7 years, SD: ± 4.9), sex (12 males, 22 females) and years of education (mean: 10.9 years, SD: ± 4.9), were also tested as a control group (C).

Materials

The following neuropsychological tests were set to determine the presence of USN:

- *Line bisection*. Participants were asked to mark the mid-point of six horizontal black lines (all were 2 mm in width; lengthwise, two measured 10 cm, two 15 cm, and two 25 cm). The score was the mean deviation of the participants' marks from the objective midpoint (in mm). A positive score denoted a rightward bias, a negative score a leftward bias. The mean bisection error of the control group was -0.91 mm (SD 2.4, range -6.5 / +5.2).
- *Letter cancellation*. The participants were given a A3 sheet with 104 letter Hs (53 in the left-hand side and 51 in the right-hand-side) mixed with other letters, and were instructed to mark requested all the Hs once. The test was set in two conditions: 1) in the standard version of the test (Diller and Weinberg, 1977), the targets were arranged in six rows; 2) in the modified version the letters were scattered randomly over the sheet (see the Figure 7-A). In neurologically

unimpaired participants the maximum difference between omission errors on two sides of the sheet (omissions on the right – omissions on the left) was two for the standard version of the task (Vallar et al., 1994) and three for the scattered compared to the performance of the control group.

- *Star cancellation*. The participants were given a A4 sheet with 60 small black stars (30 in the left-hand side and 30 in the right-hand-side) mixed with distracters (big stars, letters, and Italian words), and were instructed to mark requested all the stars once. The test was set in two conditions: 1) the standard version of the test, with the targets scattered on the sheet (modified versions of Wilson et al., 1987); 2) the modified version of the task in which the stimuli were neatly arranged in six rows (see the Figure 7-B). In the present control group the maximum difference between the number of omission errors in two sides of the sheet (omissions on the right – omissions on the left) was one target, both for the standard and the modified version of the test.

The presence of a divided attention deficit was assessed by the following test:

- *Dual Task* (Baddeley et al., 1997). A digit span and a motor tracking task were set separately first, then together, for two minutes. A percent score was computed by comparing performance efficiency on the single tasks (digit and tracking) to the condition in which the participants performed both. The mean percentage score of the control group was 90%.

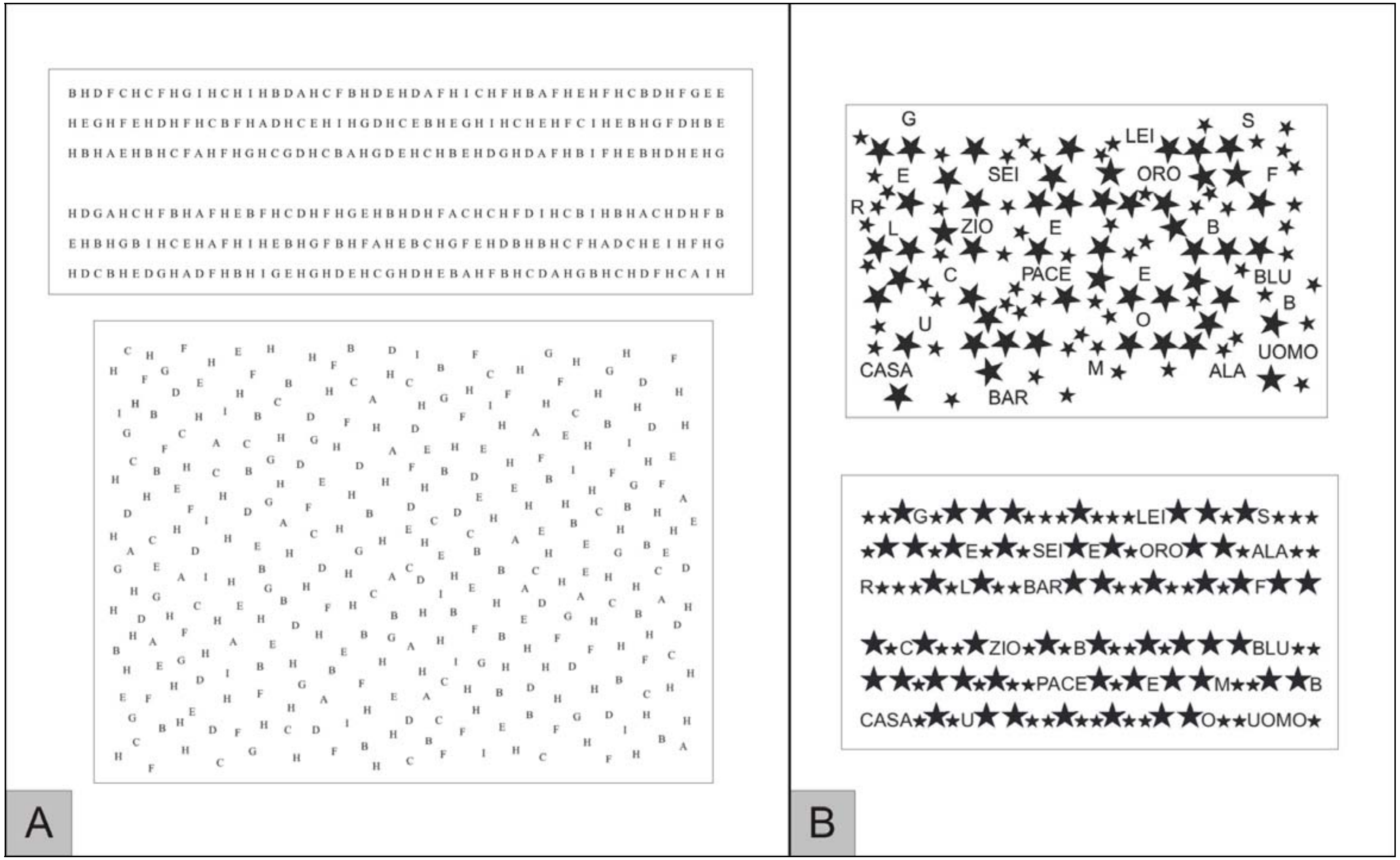

Figure 7. The standard (top) and the modified (bottom) versions of the letter (A) and star (B) cancellation tests.

Procedure

Patients were classified as affected by left spatial neglect syndrome (N+) if their performance in one of the cancellation tests (considering both versions of star and letter tasks) and/or in the line bisection task revealed a pathological rightward bias, with reference to the available norms or to the control group's performance. As in the previous experiment, an omission percentage score [(number of omissions/number of targets)*100] was computed for patients classified as affected by left neglect in each cancellation task.

In the cancellation tasks the participants were required to mark all targets once only: the number of recurrent (Na et al., 1999; Vallar et al., 2006) perseverations, i.e., the number of all additional marks, was recorded. Considering the major sensibility of the perseveration index compared to the Na's perseveration percentage in the detection of perseveration (see the previous experiment for details), only the perseveration index was computed in the second experiment [(number of cancellation single marks + number of added cancellation marks)/number of cancelled targets]. Based on the control group's performance, patients who made at least one repeated cancellation mark, in at least one of the four cancellation tests, were classified as showing perseveration. Therefore patients who did not show perseverative motor behaviour (P-) were assigned a perseveration index of "1" whereas patients (P+) who made one or more perseverations were assigned a perseveration index greater than "1" (according to the number of additional marks made).

Lesion localisation

Patients' lesions were drawn on a standard MRI template using MRIcro software (Rorden & Brett, 2000).

Statistical analyses

Parametric analyses were performed on the omission scores on the target cancellation tasks and on the attentional scores in the Dual Task where data met the assumptions of the ANOVA. Because percentage scores in these tasks were not normally distributed, percent responses were converted into the arcsin of the square root of the raw values. Perseveration performances were compared using non-parametric tests (Siegel and Castellan, 1988). The relationships between omission and perseveration errors in cancellation tasks were explored with Pearson's correlation analyses.

- <u>Results</u>

Omissions

Twenty out of 26 right-brain-damaged participants were classified as neglect patients (N+), with six patients not being affected by neglect (N-). Three out of 20 (15%) N+ patients showed neglect in the cancellation tasks only and three (15%) in the line bisection test only: the other 14 patients (70%) exhibited left neglect in both tasks.

Figure 8 shows the mean omission percentages obtained by the N+ group on the four cancellation tasks. A repeated measure ANOVA on the omission percentages with 'Test' (two levels: Star and Letter) and 'Disposition' (two levels: Arranged and

Scattered) as ‘within subjects’ factors was performed. The main factor ‘Disposition’ was significant (F = 11.6, d.f. = 1, p = 0.003), revealing a greater number of omissions when targets were scattered (mean omission score: 30.46%) than when arranged (mean omission score: 24.98%; p < 0.01) on the sheet, independently of the type of target. An examination of the individual results in each test revealed that 13 out of 20 N+ (65%) had a pathological performance in the star-scattered cancellation test whereas only nine patients (45%) omitted in the star-arranged version of it. In the letter cancellation test, the performance of 11 (55%) out of 20 neglect patients was pathological in the arranged version of this task and 16 (80%) out of 20 N+ participants were defective in the scattered versions.

In the omission percentage analysis the main factor ‘Test’, although not significant (F = 3.36, d.f. = 1, p = 0.08), revealed that more targets were globally omitted in the letter cancellation tasks.

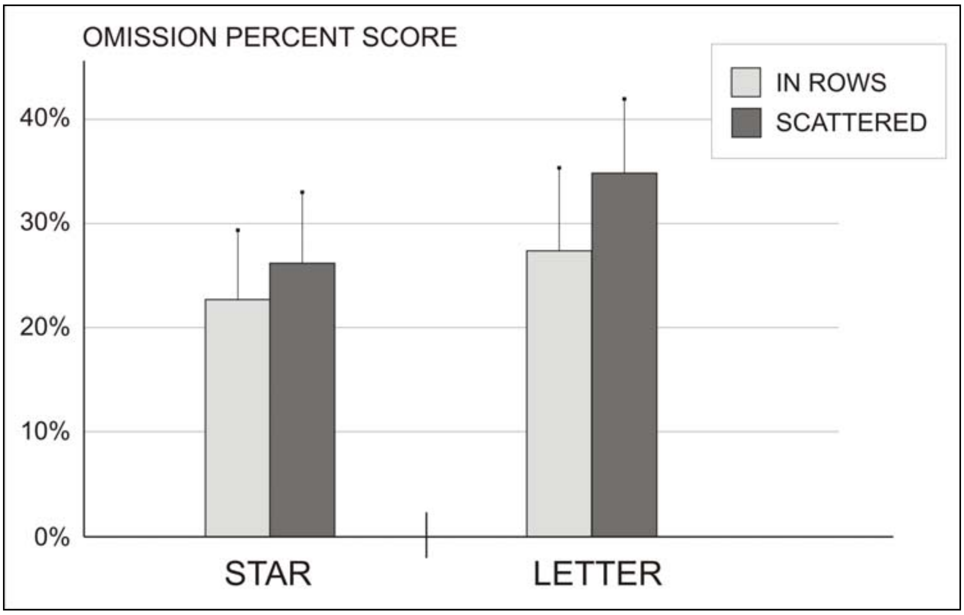

Figure 8. The omission percentage score (s.e.) of the 20 neglect patients in the two versions of the star and letter cancellation tasks.

Perseveration

Eleven patients showed perseveration in target cancellation tasks (P+), while 15 were not perseverating (P-). Ten out of the 11 P+ participants were classified as neglect patients (N+P+).

The amount of perseveration made by the P+ patients is reported in Table VI. All perseverating patients made one or more perseveration errors in the scattered version of the star cancellation task, whereas only three (27.3%) perseverated when the stars were arranged in rows. Similarly a greater number of patients (six out of 11 participants, 54.5%) showed perseveration on the disorganized version of the letter cancellation test compared to the test in which the letters were arranged in rows (only one out of 11 participants, 9.1%).

Table VI. Perseveration indexes of the 11 P+ patients in the four cancellation tasks.

		CANCELLATION TASKS			
		Star		Letter	
	GROUP	scattered	in rows	scattered	in rows
CF	N-P+	1.04	1	1	1
FA	N+P+	1.08	1.05	1.02	1
MJ	N+P+	1.15	1	1	1
PR	N+P+	1.10	1	1	1
SG	N+P+	1.52	1	1.33	1.12
PG	N+P+	1.08	1	1.02	1
TC	N+P+	1.10	1	1.01	1
PC	N+P+	1.04	1.03	1	1
BS	N+P+	1.04	1	1.05	1
TM	N+P+	1.05	1	1	1
RE	N+P+	1.37	1.17	1.03	1

A Wilcoxon signed ranks test with two dependent variables (perseveration indexes in scattered stars versus stars in rows tests) revealed a significant difference in the P+ group (T = 0; z = 2.3; p = 0.003), with greater perseveration produced in the scattered version of the test; the same result emerged from a comparison of the two versions of the letter cancellation task (T = 0; z = 2.2; p = 0.028). Further analyses were performed to verify if the type of the stimulus contributes to the perseverative motor responses. The Wilcoxon signed ranks test showed that no significant differences were found when the in-rows-version of the tests (stars and letters) were compared (T = 3; z = 0.3; p = n.s.), but the perseveration indexes estimated in the scattered versions of the star and letter cancellation tasks differed (T = 1; z = 2.8; p = 0.004), with the stars eliciting more recurrent perseveration than the letters (see Figure 9).

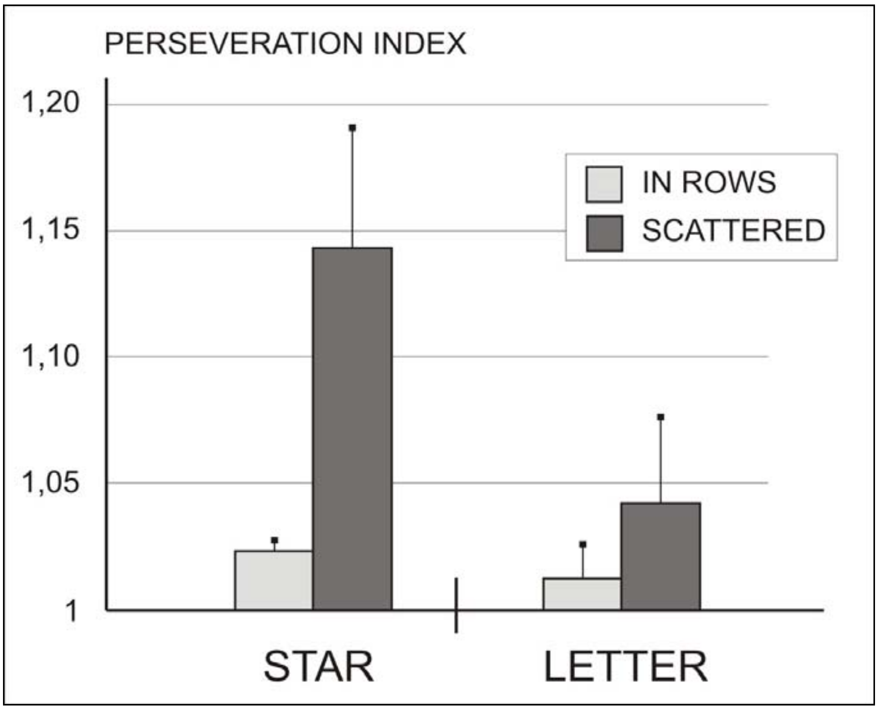

Figure 9. The perseveration index (s.e.) of the 11 perseverating patients (11P+) in the two versions of the star and the letter cancellation tasks.

The same non-parametric analyses were performed on the perseverating neglect subgroup's data (N+P+). The results were comparable, showing that the scattered versions of the star ($T = 0$; $z = 2.8$; $p = 0.005$) and the letter ($T = 0$; $z = 2.2$; $p = 0.028$) cancellation tasks elicited more perseverative marks than the corresponding arranged versions; moreover the comparison between the arranged ($T = 3$; $z = 0.7$; p = n.s.) and scattered ($T = 1$; $z = 2.7$; $p = 0.007$) version of the two tests confirmed the previous findings.

The correlation of the perseveration index with the percentage omission score of the scattered star cancellation task (the test which elicited the most productive behaviour) was not significant in either the P+ group (Pearson coefficient: $r = -0.20$; p = n.s.) or the N+P+ subgroup (Pearson coefficient: $r = -0.29$; p = n.s.).

Divided Attention

Thirteen of the 15 P- patients and nine of the 11 P+ patients took the Dual Task. Two non-perseverating and two perseverating patients were not able to perform it.

A one-way ANOVA with 'Group' (three levels: C, P- and P+) as 'between subjects' factor was performed on the Dual Task percent scores. The analysis was significant ($F = 3.6$, d.f. = 2, $p = 0.034$): Tukey post hoc tests revealed a significant difference between control participants (90%) and perseverating patients (81.8%, $p < 0.05$), with no other comparisons being significant. It is interesting to note that the performance of the P-patients (84.6%) was between the mean scores obtained by the controls and the perseverating patients, showing that a trend, albeit not significant, is present in the three groups.

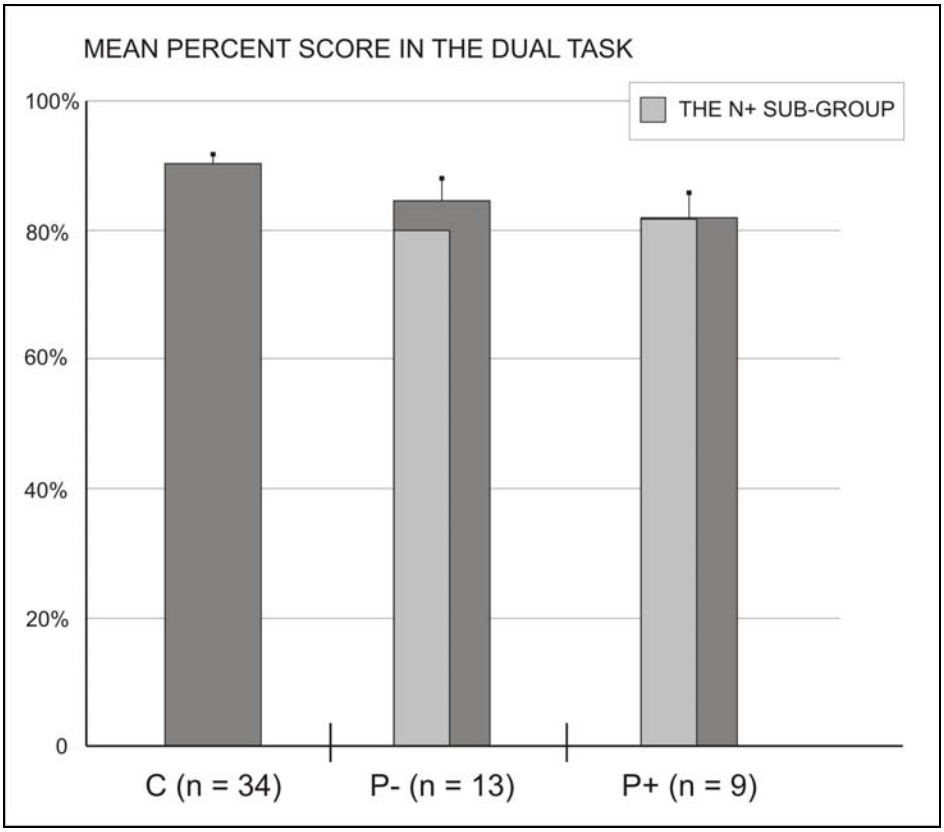

Figure 10. The percentage score (s.e.) of perseverating, not perseverating and control participants in the Dual Task.

A further ANOVA was performed comparing the results obtained by C, N+P- (n = 8) and N+P+ (n = 8) participants on the Dual Task. The analysis indicated that no significant differences were present (F = 2.8, d.f. = 2, p = n.s.). The performance on the task assessing divided attention did not differ between control participants (90%), neglect patients without perseveration (79.9%) and neglect patients with perseveration (81.7%). Figure 10 displays the mean percentage scores of the groups in the Dual Task.

Anatomical correlates

Only patients with spatial neglect were mapped in order to correctly evaluate the cerebral regions damaged in patients with and without perseverative symptoms. Lesion images were available for mapping for nine out of 10 N+P+ and nine out of 10 N+P- patients. The remaining N+P+ patient was reported as having a cortico-subcortical anterior lesion involving the frontal cortex; the N+P- patients for whom structural images were not available had frontal lesions extending to the basal ganglia.

The lesion maps for each N+P+ patient and their overlaps are shown in Figure 11; in this group the overlap of the patients' lesion sites was coded with increasing frequencies from violet (n = 1) to red (n = 9). It can be seen that the presence of perseverative behaviour in our patients was related to lesions in the right insula and, marginally, the right putamen.

The lesion maps for each N+P- patient and their overlaps are shown in Figure 12. The overlap of the patients' lesion sites was coded, as previously, from violet (n = 1) to red (n = 9) to indicate increasing frequency. Firstly, it is important to note that the maximum overlap was not present in this group, as the sites of the lesions were more spread out than in the perseverating group. As can be observed from the illustration, the lesions of the non-perseverating neglect patients were more posterior, provoking temporo-parietal cortico-subcortical damage.

Lastly, the lesions were subtracted: Figure 13 shows that in our patients the right insula is the specific region for perseverative behaviour in the neglect syndrome.

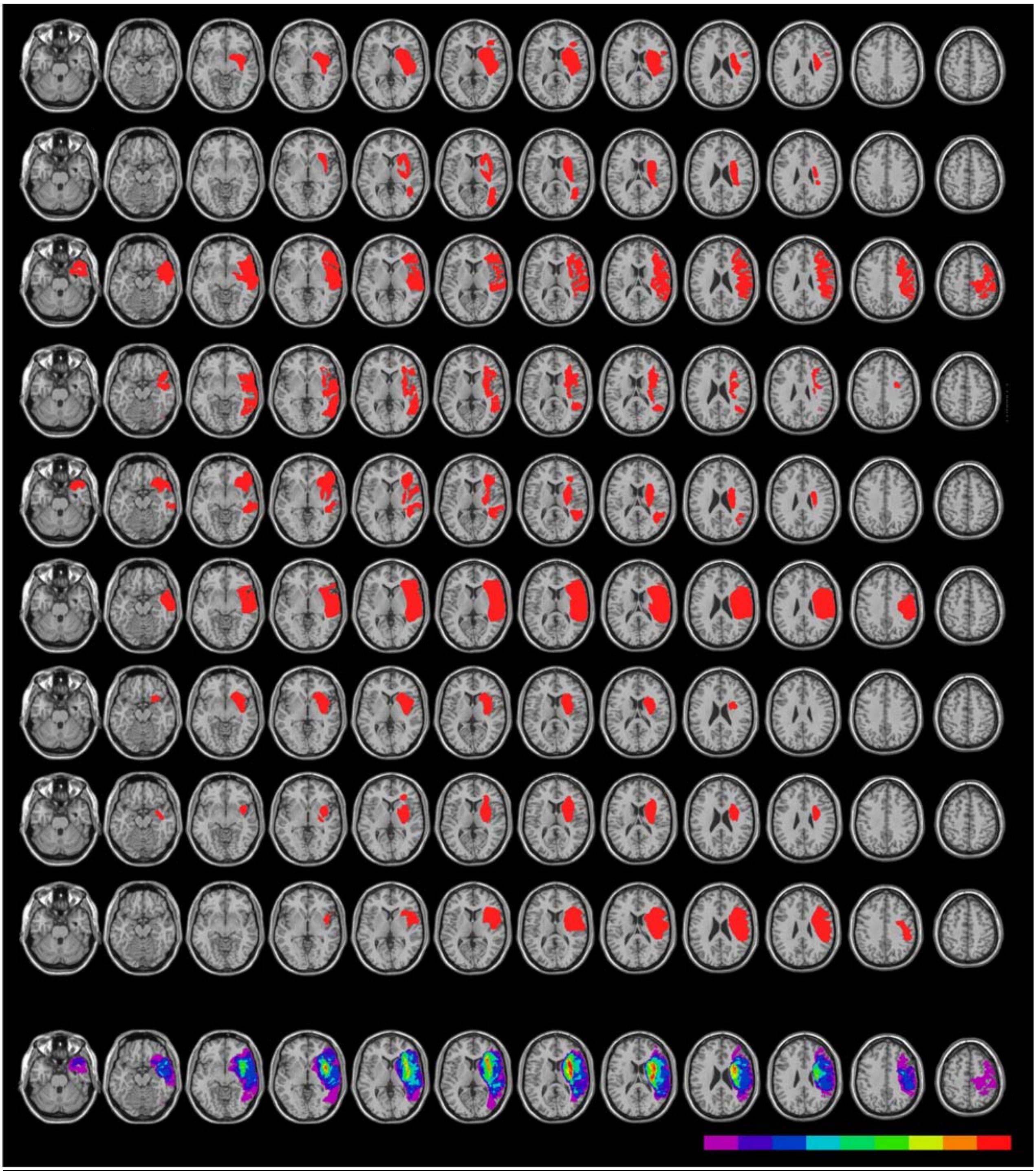

Figure 11. Lesion maps of nine N+P+ patients and their lesion overlap. Each individual lesion has been superimposed onto a standard brain format conforming to stereotactic space.

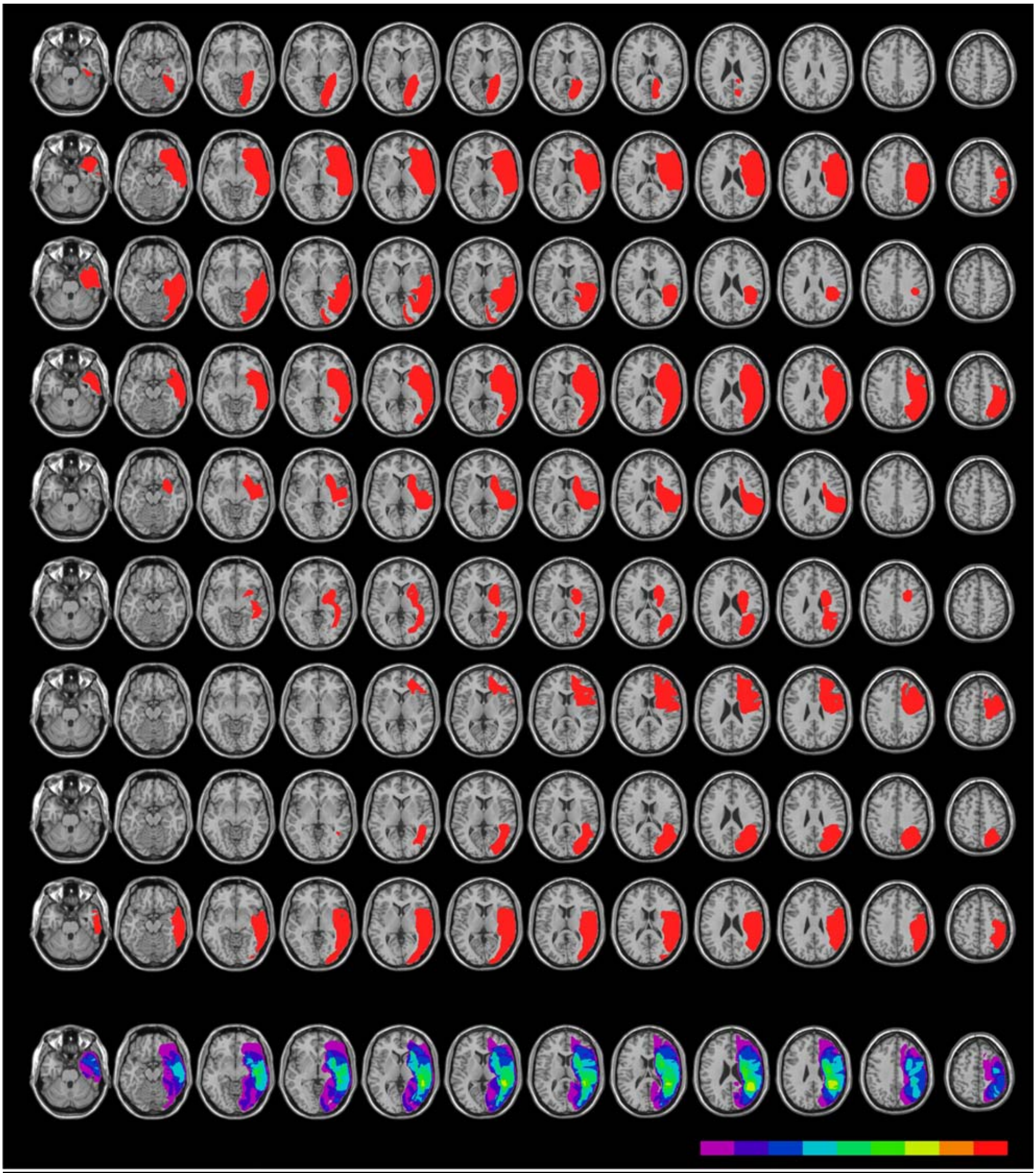

Figure 12. Lesion maps of nine N+P- patients and their lesion overlap. Each individual lesion has been superimposed onto a standard brain format conforming to stereotactic space.

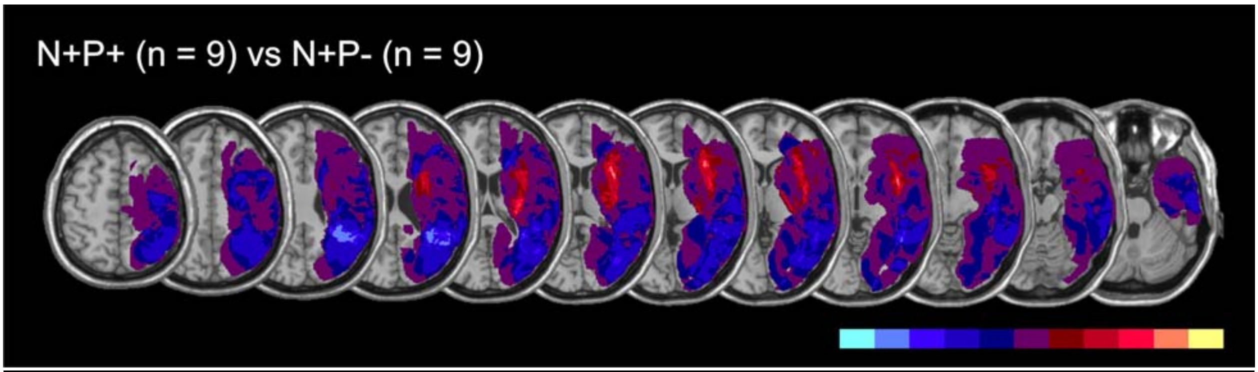

Figure 13. Lesion subtraction of patients showing neglect and perseveration comparing to patients showing neglect without perseveration. Each individual lesion has been superimposed onto a standard brain format conforming to stereotactic space.

- Conclusion

The results of this experiment confirm that scattered targets can influence both negative and positive manifestations (Vallar, 2001) of USN.

The main aim of this second experiment is to analyse the potential impact of disorganized stimuli on recurrent perseveration. Our data show that perseveration is frequent when stimuli are disposed randomly over the sheet. This finding, which is in line with those of Mark and collaborators' (2004), suggests that the re-marking of targets can be exacerbated by the difficulty encountered by the neglect patient in planning an efficient research strategy when stimuli are scattered. However the random arrangement of the stimuli is not the only factor contributing to this impairment, as the typology of target also appears to be an important element. In fact the perseveration index is greater in the star cancellation task than in the letter task, but only in the scattered condition.

Moreover a previous study (Mark et al., 2004) postulated that the number of targets omitted may be influenced by a disorganized visual search, failed to reveal any significant correlations between these components. However they only evaluated ten patients with neglect: in our study we increase the sample size from ten to twenty cases, and show that this tendency reaches significance with more omission errors being committed when the stimuli are distributed randomly. As in Mark et al.’s study, our experiment fails to reveal significant correlations between omission and perseveration errors, which supports the hypothesis that the two pathological phenomena are independent.

The Dual Task score analysis reveals a trend towards defective resources of divided attention in perseverating patients. The results obtained by these patients on two tasks performed simultaneously are inferior to those of the control group; however their performance is comparable to that of brain-damaged patients without perseverative symptoms.

With regard to brain correlates associated with productive behaviour in target cancellation tasks, the role of the right insula seems to be relevant.

EXPERIMENT 3

Omissions, substitutions and additions: neglect dyslexia in a word reading task

- Aim of the study

Some studies investigated the presence, the frequency and the type of reading neglect errors in patients with neglect dyslexia, examining their association with the other defective manifestations of spatial neglect syndrome. The scientific literature demonstrates that neglect dyslexia and certain “negative” symptoms of hemi-inattention can appear independently (see Vallar et al., 2010 for a review). However no studies have investigated the relationship between different productive symptoms in neglect patients, as for example the potential co-occurrence of various forms of perseverative behaviour in target cancellation tests on the one hand and productive responses in reading tasks on the other. Addition errors in neglect dyslexia are considered as productive manifestations of the USN syndrome (Vallar et al., 2006), whereas omissions are classified as typical “negative” reading errors. The status of substitution errors is less well defined: in fact patients producing substitutions actively elaborate the target, changing letters on the left side of the string.

A third experiment is run i) to investigate the incidence of various forms of reading errors in patients with left neglect who showed perseverative symptoms in target cancellation tests and ii) to verify whether the presence of neglect dyslexia is associated to a more severe USN in conventional tests, as the data in the literature are not clear on this point (Behrmann et al., 2002; Lee et al., 2009).

- <u>Materials and methods</u>

Participants

Thirty-nine right-handed patients (24 males, 15 females; mean age: 65.4 years, SD: ± 13.6, range: 30-87; mean education: 11 years, SD: ± 5.4, range: 2-18) with right hemisphere lesions were included in this study. The demographic information of the group is shown in Table VII below.

Table VII. Demographic data of the 39 right-brain damaged patients with left spatial neglect.

	Sex	Age	Education (years)		Sex	Age	Education (years)
P1	M	53	8	P21	M	76	17
P2	M	59	5	P22	F	68	2
P3	M	60	5	P23	M	57	18
P4	M	68	4	P24	M	85	18
P5	M	34	9	P25	F	53	8
P6	M	75	18	P26	M	62	17
P7	F	71	13	P27	F	83	13
P8	F	79	4	P28	F	71	5
P9	F	66	5	P29	F	76	8
P10	F	37	8	P30	F	82	13
P11	M	70	17	P31	M	87	17
P12	M	65	17	P32	M	65	5
P13	M	54	18	P33	F	78	5
P14	M	61	5	P34	M	61	17
P15	M	54	13	P35	M	71	18
P16	M	30	13	P36	F	57	8
P17	M	64	18	P37	F	73	5
P18	M	60	13	P38	F	83	4
P19	M	83	13	P39	F	70	13
P20	M	50	13				

The patients were pre-selected on the basis of the presence of left spatial neglect (see materials and procedure below). The aetiology of the focal lesion was vascular in 37 participants (27 ischemic, 10 haemorrhagic) and neoplastic in two patients; the lesion site was assessed by CT or MRI scan. None of the participants had a history or neurological evidence of previous neurological impairments, psychiatric disorders or dementia. Contralesional motor, somato-sensory and visual-field defects were evaluated with the standard neurological examination; anosognosia for neurological deficits was also assessed (Bisiach et al., 1986). Where norms were not available, a group of forty right-handed neurologically unimpaired participants, matched for age (mean: 65.7 years, SD: ±12.9), sex (24 males, 16 females) and years of education (mean: 10.8 years, SD: 5), was tested for control purposes (C).

Materials

The following tests were used to assess the presence of USN:

- *Line bisection* (see Experiment 1).
- *Letter cancellation* (Diller and Weinberg, 1977) (see Experiment 1).
- *Star cancellation* (Wilson et al., 1987) (see Experiment 1).
- *Drawing:* the participants were asked to copy a complex figure with five elements (see Gainotti et al., 1972; see Experiment 1 for details) and draw the hours of a clock in a circular quadrant from memory.

These tasks were presented using the same procedure as the first experiment. For controls, the mean bisection error was -0.89 mm (SD 2, range -6.5 / +2.7) and the maximum difference between omission errors on the two sides of the sheet (omissions on the right – omissions on the left) was two for the star cancellation task. In neurologically unimpaired participants (Vallar et al., 1994) the maximum difference between omission errors on the two sides of the sheet (omissions on the right – omissions on the left) was two for the letter cancellation task.

The reading tests consisted in:

- *Word reading test* (W: 0-35). Each participant was shown a number of real words, from 4 to 12 letters in length, printed individually in black uppercase letters (Arial, pt.18) in a horizontal position in the centre of an A4 sheet. The stimuli were selected from a list of words used in Vallar et al. (1996). Control participants made no errors in this test.
- *Experimental word reading test* (EW: 0-35). The stimuli included in this task were real words from which it was possible to create new words by adding a single letter to the left side of the stimulus. For example, “cultura” (culture) becomes “scultura” (sculpture) by the addition of the letter “s” on the left extremity of the word. The alternative strings would be expected to have a completely different meaning but a similarly high frequency (Vocabolario Elettronico della Lingua Italiana, 1989). The words included in this task had an average written frequency of 7.480. As in the previous task, each word was printed horizontally in the centre of an A4 sheet in black uppercase letters (Arial, pt.18) and presented individually to participants. In this form of the test, the length of each stimulus varied from 4 to 9 letters. Control participants made no errors in this test.

Procedure

All neurological patients were classified as neglect (N+), based on their performance in the target cancellation tests and/or in the line bisection task with reference to the available norms or comparison with the control group's performance. For each target cancellation test an omission percentage score [(number of omissions/number of targets)*100] was computed.

In the cancellations tests participants were asked to cross all targets with a single mark: the examiner noted the presence and the number of recurrent perseverations. Once again the control participants did not make any extraneous cancellation marks in the target cancellation tests, so those neurological patients who showed at least one recurrent perseveration in these tasks were classified as perseverating. The patients were then assigned to two subgroups: patients showing (N+P+) or not showing (N+P-) recurrent perseveration. The perseveration index [(number of cancellation single marks + number of added cancellation marks)/number of cancelled targets] was computed for each test.

For the drawing task, the neglect and perseveration scores used in the first experiment were assigned.

In the reading tests, the participants were requested to read the letter strings, with no time limit. They were allowed to move their head and eyes. The examiner took note of the first verbal response but did not give any feedback. Errors were classified as neglect if it was possible to identify a *neglect point*, namely if target and response were identical to the right of this point but completely different to the left of it (see Ellis et al., 1987 for more details). Therefore all types of neglect (omissions, substitutions and additions) were recorded for both lists (W and EW). A misreading resulting in a combination of two types of error was classified according to the following definitions:

1) omission + substitution: the error was considered as substitution (e.g., the target “criminale” was read “fanale”, with the correct reading of the string “nale”, the omission of the first three letters “cri” and the substitution of the other two letters “mi” with “fa”); 2) substitution + addition: the error was considered as an addition (e.g., the target “arto” was read “porto”, with the correct reading of the string “rto”, the substitution of the letter “a” with “o” and the addition of the letter “p” at the left extreme of the word). Misreadings that were not classifiable as neglect errors were record as visual errors.

Each reading test (W and EW) was divided into two sub-lists of 17 and 18 words at random, the order being W1-EW1-EW2-W2.

Taking the control participants’ performance as the norm (no neglect errors on W and EW), patients were classified as affected by neglect dyslexia (ND+) if they produced at least one neglect error in the base list (W), while those who did not were considered as not dyslexic (ND-).

Statistical analyses

Parametric analyses were performed on the line bisection scores and on the omission percentages of the target cancellation tasks, where data met the assumptions of the ANOVA. Because the neglect scores in cancellation tests were not normally distributed, percent responses were converted into the arcsin of the square root of the raw values. To compare the perseveration performances and the frequency of reading errors produced by perseverating and non-perseverating neglect patients, Poisson frequencies analyses (Agresti, 2002) and non-parametric tests (Siegel and Castellan, 1988) were performed.

The relationships between cancellation and reading scores were explored with Pearson's correlation analyses.

- <u>Results</u>

Neglect severity

Based on their performance in the W list, a first classification was performed: 20 out of 39 patients (51.3%) presented signs of neglect dyslexia (ND+) while the remaining nineteen (48.7%) did not (ND-).

The neglect severity in ND+ and ND- groups was compared. Independent group T-Tests revealed that, compared to the ND- patients, ND+ patients showed a more severe neglect in the line bisection task (mean deviation ND+ = +22.5, mean deviation ND- = +5.2; $t = 3.05$, $p = 0.004$), in the star cancellation test (mean omission score ND+ = 60%, mean omission score ND- = 15%; $t = 5$, $p < 0.001$) and in the letter cancellation test (mean omission score ND+ = 57%, mean omission score ND- = 24%; $t = 3.3$, $p = 0.002$).

An additional classification was made for the ND+ group,: nine out of 20 (45%) dyslexic neglect patients did not show perseveration (9 P-ND+), while 11 out of 20 (55%) dyslexic neglect patients exhibited perseveration (11 P+ND+). The neurological data of these two sub-groups are reported in Table VIII.

Unpaired T-Tests revealed that P-ND+ and P+ND+ groups had similar results in line bisection (mean deviation P-ND+ = +30.6, mean deviation P+ND+ = +15.8; $t = 1.48$, p = n.s.), star cancellation (mean omission score P-ND+ = 73%, mean omission score

P+ND+ = 47%; t = 1.9, p = n.s.) and letter cancellation (mean omission score P-ND+ = 71%, mean omission score P+ND+ = 46%; t = 1.61, p = n.s.) tasks, demonstrating that severity was comparable in the two groups. However a perusal of the neglect scores revealed a trend towards a more severe neglect in P- than in P+ dyslexic patients.

Table VIII. Neurological data of the 20 right-brain damaged patients with neglect dyslexia.

	Group	Aetiology/ Lesion site	Neurological deficit M	SS	V	Associated deficit Anoso	Np	SP
P1	N+P-	I-H / FTP	+	+	+	-	-	-
P2	N+P-	H / TP Bg	+	+	+	+V	-	-
P3	N+P-	I / FTPO In Bg	+	+	+	+M	-	-
P4	N+P-	I / FTP-Bg	+	+	+	+M	-	-
P5	N+P-	H / F-bg	+	+	+	-	-	-
P6	N+P-	I / bg-ic	+	+	+	+SS-V	+	-
P7	N+P-	N / F-T	-	+	+	+SS-V	-	-
P8	N+P-	H / F-T	+	+	+	-	-	-
P9	N+P-	H / P-O	+	+	+	+M-SS-V	+	-
P10	N+P+	I / FTP In Bg	+	+	+	+SS-V	-	-
P11	N+P+	I / TPO Crb	+	-	+	-	-	-
P12	N+P+	I / FTPO In Bg	+	+	+	+SS-V	-	-
P13	N+P+	I / Sylvian region	+	+	+	+SS	-	-
P14	N+P+	I / T-P-bg-ic	+	-	-	-	-	-
P15	N+P+	I / F-P s-cort	+	+	e	+SS	-	-
P16	N+P+	I / bg-ic	+	e	e	-	-	-
P17	N+P+	I-H / Sylvian region	+	+	+	-	+	-
P18	N+P+	I / Sylvian region	+	+	+	+SS	-	-
P19	N+P+	H / F s-cort	+	+	+	+SS-V	+	-
P20	N+P+	H / T-P	+	+	+	+M-SS-V	+	-

I: ischemic lesion; H: haemorrhagic lesion; N: neoplastic lesion
F: frontal; P: parietal; T: temporal; O: occipital; In: insula; ic: internal capsule; bg: basal ganglia; s-cort: sub-cortical; crb: cerebellum.
M: left motor deficit; SS: left somatosensory deficit; V: visual half-field deficit; e: extinction; ANOSO: anosognosia; Np: personal neglect; SP: somatoparaphrenia; +: presence of deficit; -: absence of deficit.

Perseveration

One patient in the P+ND+ group did not perform the star cancellation test; the other 10 made perseverative marks in this task. Only three of 11 (27.3%) patients exhibited recurrent perseveration in the letter cancellation task, while the other eight did not. In line with the previous experiments, a Wilcoxon signed ranks test with two dependent variables (perseveration indexes in the star and letter tests) revealed a significant difference ($T = 4$; $z = 2.4$; $p = 0.017$), confirming that neglect patients with neglect dyslexia produce more perseveration marks in the star cancellation task.

Reading errors

Figure 14 shows the amount of the errors produced in the W list by ND+ patients. A Poisson frequencies analysis with ‘Error’ (three levels: Omission, Substitution and Addition) as ‘within subjects’ factor and ‘Group’ (two levels: P-ND+ and P+ND+) as ‘between subjects’ factor was performed.

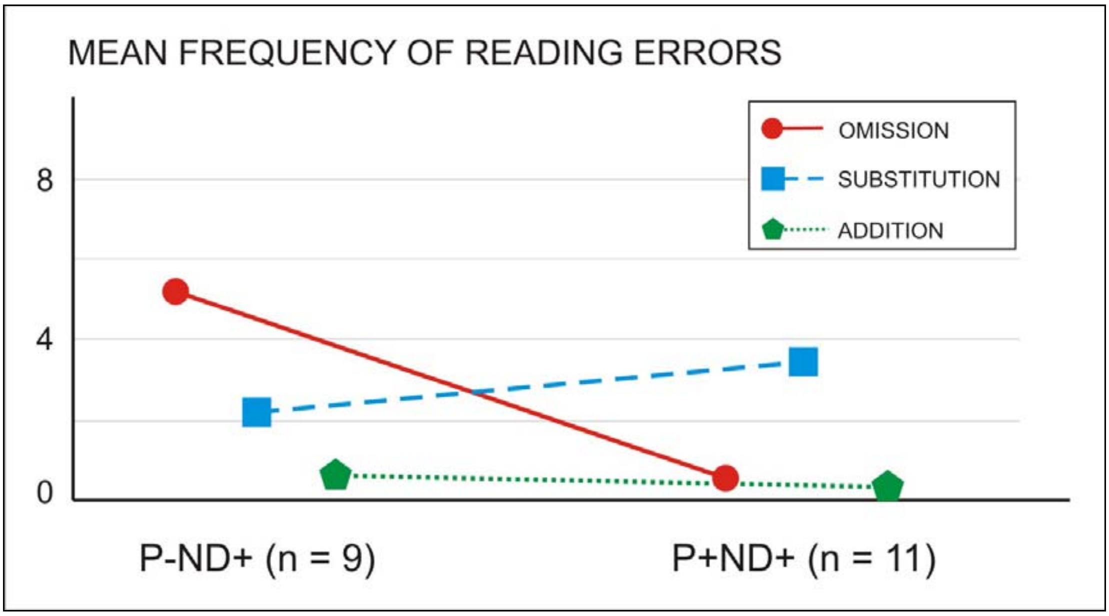

Figure 14. The mean frequencies of the omission, substitution and addition errors produced by P- and P+ dyslexic neglect patients in the W list.

The main factor Error was significant (χ^2 = 32.96; d.f. = 2; $p < 0.001$): multiple comparisons revealed that, independently of the group considered, patients produced less addition errors than substitution ($p < 0.001$) and omission ($p < 0.05$) errors. The interaction 'Error by Group' was also significant (χ^2 = 10.38; d.f. = 2; $p = 0.006$): multiple comparisons showed that in the perseverating group the number of substitutions was significantly greater than the number of omission ($p < 0.01$) and addition errors ($p < 0.001$). No significant differences between the three types of error were found in non perseverating dyslexic patients.

In order to verify whether the experimental condition modulated the production of reading errors, the comparison between errors produced in the W and in the EW lists was performed separately for each group. Figure 15 shows the performance of ND+ patients in the base (W) and experimental (EW) reading lists.

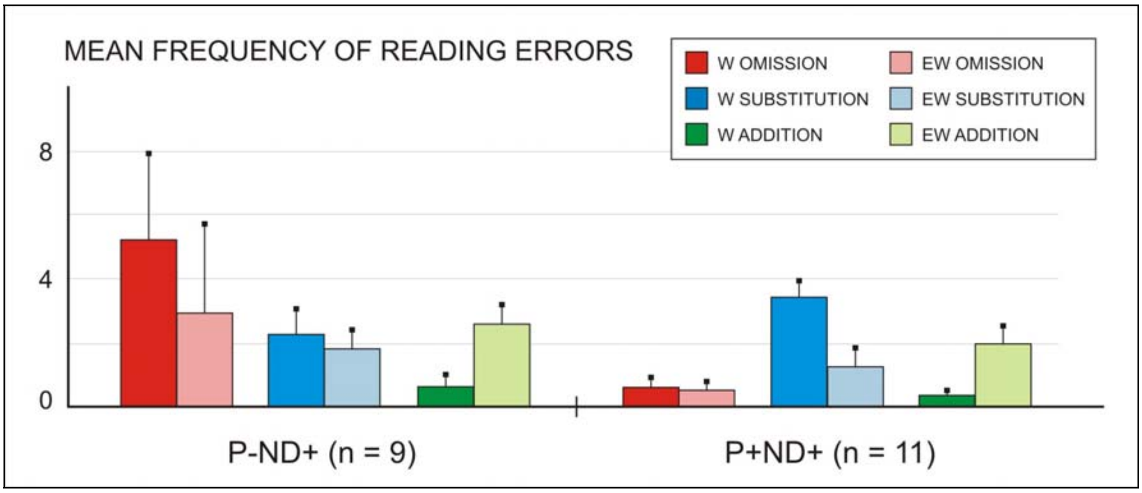

Figure 15. The mean frequencies (s.e.) of the omission, substitution and addition errors produced by P- and P+ neglect patients in the W compared to the EW reading lists.

For P-ND+ participants the Poisson frequencies analysis with ‘Error’ (three levels: Omission, Substitution and Addition) and ‘List’ (two levels: W and EW) as ‘within subjects’ factors revealed significance in the ‘Error by List’ interaction ($\chi^2 = 50.14$; d.f. = 2; $p < 0.001$): multiple comparisons indicated that the number of additions were greater in the EW reading task compared to the W task ($p < 0.01$), with no other comparison being significant.

For P+ND+ participants the Poisson frequencies analysis with ‘Error’ (three levels: Omission, Substitution and Addition) and ‘List’ (two levels: W and EW) as ‘within subjects’ factors revealed significance in the main factor ‘Error’ ($\chi^2 = 27.78$; d.f. = 2; $p < 0.001$): independently of the list considered, perseverating patients made more errors of substitution than omission ($p < 0.001$) and addition ($p < 0.001$). The ‘Error by List’ interaction ($\chi^2 = 33.60$; d. f. = 2; $p < 0.001$) was also significant: multiple comparisons revealed that the number of omissions was similar in the two lists but that the other two types of errors were modulated, with an increment of addition ($p < 0.01$) and a reduction of substitution ($p < 0.01$) errors in the EW list.

In both lists the number of visual errors is comparable in the P-ND+ and P+ND+ groups (Mann-Whitney tests. W list: $z = 0.57$, p = n.s.; EW list: $z = -0.15$, p = n.s.).

Examples of neglect reading errors made by patients in the W and EW lists are reported in Table IX.

Correlation Analyses

In the P+ND+ group, where differences among the three types of reading errors were found in the baseline condition, we investigated the relationship between substitutions (the most frequent type of error) and the other “negative” or “positive” symptoms in target cancellation tasks; the star cancellation test was used for this analysis, as it was the task in which more productive responses were elicited. Neither the correlation between substitution errors and the perseveration index in the star cancellation test (Pearson coefficient: $r = -0.16$; p = n.s.), nor the correlation between substitutions and the mean omission score (Pearson coefficient: $r = 0.17$; p = n.s.) were significant.

Table IX. Examples of reading errors in patients with neglect dyslexia.

Omissions		Substitutions		Additions	
Target	Patient's reading	Target	Patient's reading	Target	Patient's reading
POLMONITE	*NITE*	PARROCCHIA	**VE***CCHIA*	ASTA	**C***ASTA*
MISSILE	*SILE*	MANO	**S***ANO*	ERRORE	**T***ERRORE*
VOTO	*OTO*	INVIARE	**AV***VIARE*	APPELLO	**C***APPELLO*
EREMITA	*ITA*	VIOLONCELLO	**CA***NCELLO*	LETTORE	**DIR***ETTORE*
VISONE	*SONE*	FLUIDO	**G***UIDO*	EREMITA	**N***EREMITA*
MATITA	*TITA*	RUVIDO	**LI***VIDO*	RENDERE	**ATT***ENDERE*
SINDACATO	*DACATO*	VISONE	**B***ISONE*	CALARE	**RE***ALARE*

Italics: letters read correctly to the right of the neglect point. Bold: letters extraneous to the target. Underlined: letters added to the left of the neglect point, exceeding the length of the target.

Conclusion

Right-brain damaged patients showing neglect in target cancellation and line bisection tasks may misread letters in the contralesional part of a word. Not all USN patients present symptoms of the neglect dyslexia: in our sample approximately the half of the group makes reading errors in the left-side of the letter string.

A preliminary analysis demonstrate that ND+ patients have a more severe ipsilesional bias in both target cancellation and line bisection tests, supporting the view that a ipsilateral reading disorder may be present in patients with a greater attentional deficit. However there is no evidence of a difference in the severity of the symptoms between perseverating and non-perseverating participants in the ND+ group.

With respect to the number of errors made by neglect patients, results in the base words list show that perseverating patients produce more substitution than omission and addition errors, with substitutions indicating an active re-elaboration of the contralesional part of the verbal target. Nevertheless, the correlation between substitutions and perseveration indexes is not significant. On the other hand, this experiment does not find prevalence of any one type of reading error in patients who do not show perseveration responses in target cancellation tasks: in fact, the tendency of this group is to produce more omission errors.

Additions (Chatterjee, 1995) appear to be the type of reading error which occurs less frequently in both perseverating and non-perseverating patients. However this study demonstrated that the frequency of this pathological behaviour can be modulated: in a list eliciting addition responses, right-brain-damaged patients with neglect are more inclined to add letters to the left side of the stimulus, independently of the presence of perseveration behaviour in target cancellation tests. This phenomenon is absent in the neurologically unimpaired control participants.

REVIEW

Bodily delusion referring to the affected limbs: somatoparaphrenia

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- Review of the neuropsychological literature

A review of the cases of somatoparaphrenia published in the scientific literature was performed. We first used the PubMed database, entering the keywords *somatoparaphrenia*, *disownership*, *misoplegia*, *asomatognosia,* and successively we searched for earlier papers, quoted by PubMed retrieved articles. Secondly, the review works of Schilder (1935), Lhermitte (1952), Weinstein and Kahn (1955), Critchley (1953), Hécaen and Albert (1978), Bisiach (1995), and Braun et al. (2007) were considered.

Table X shows the demographical and neurological details of 56 brain-damaged patients with unilateral, or mainly unilateral, hemispheric lesions and somatoparaphrenic symptoms. Table XI reports some details of the phenomenology of the delusion concerning the contralesional side of the body, and associated relevant impairments.

The somatoparaphrenic descriptions refer to 25 (45%) male and 31 (55%) female patients, with the disorder being more frequent in female patients. Fifty-one out of 56 patients (91%) showed somatoparaphrenia for the left side of the body, associated with a right-sided lesion. Two patients (Ives and Nielsen, 1937, case #1; Roth, 1949, case #1) had also a lesion in the left hemisphere. Only five out of 56 patients (9%) (Schilder, 1935, case #2; Nielsen, 1938; Halloran, 1946; note however that the patient was left-handed; Miura et al., 1996; Schiff and Pulver, 1999) exhibited somatoparaphrenia for the right side of the body, associated with a left-sided lesion. In the vast majority of patients (50 out of 56, 89%) the aetiology of the lesion was vascular. Four patients had a brain tumour (Garcin et al., 1938; Roth, 1949, case #1; Weinstein and Kahn, 1950; Nightingale, 1982), and one patient carcinomatous metastases, a massive softening in the right hemisphere, and herniation of the right cingulate gyrus, disclosed post-mortem (Weinstein et al. 1954, case #1). In the right-brain-damaged patient of Biancone (1909, briefly mentioned by Lhermitte, 1952, p. 224) the aetiology was not specified.

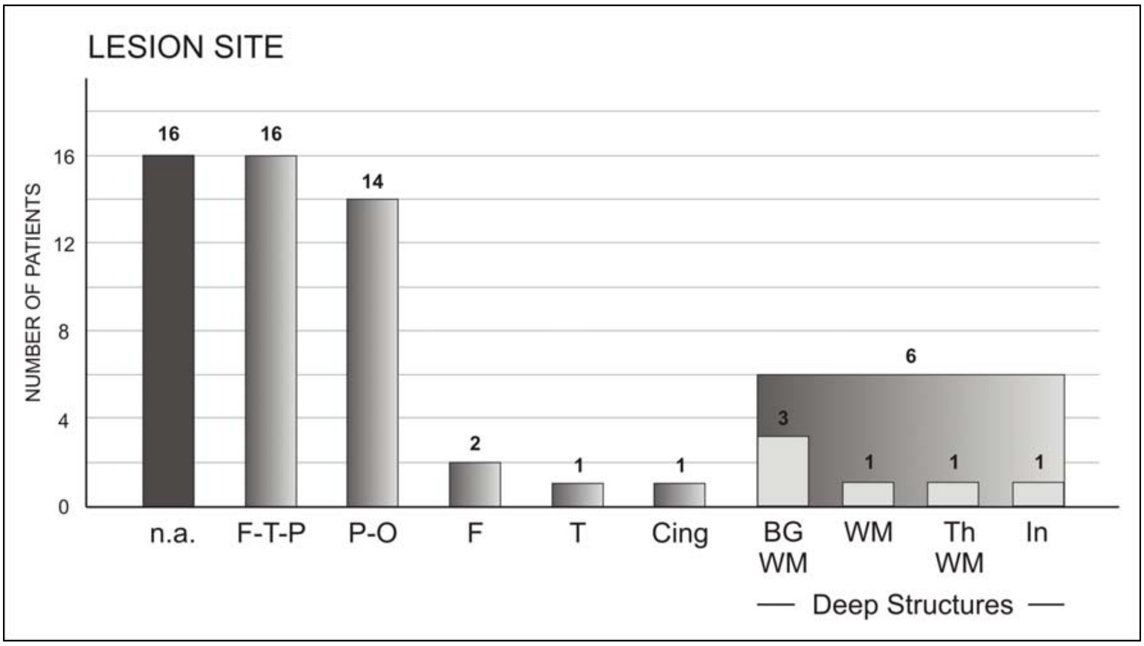
In 16 patients, no precise information about the localization of the lesion was available. When this information was reported, the damage resulted quite extensive in 16 patients, involving the fronto-temporo-parietal regions (Ives and Nielsen, 1937, case #2; Lhermitte and Tchehrazi, 1937; Wortis and Dattner, 1942; Roth, 1949, two cases; Frederiks, 1963; Verret and Lapresle, 1978; Assal, 1983; Berthier and Starkstein, 1987; Starkstein et al., 1990, case #2; Bisiach et al., 1991; Levine et al., 1991, case #4; Aglioti et al., 1996; Schiff and Pulver, 1999; Moro et al., 2004, two cases). It should be noted, however, that the available data concerning the site and the size of the lesion vary considerably across reports, ranging from the affected vascular territory to localization based on post-mortem examination, surgical exploration, or structural neuroimaging (CT, MRI). In other patients the lesion was more selective. Fourteen patients had lesions involving the posterior regions, including the parietal and occipital areas (Anton, 1893; Pötzl, quoted by Schilder, 1935, two cases; Garcin et al., 1938; Halloran, 1946; Sandifer, 1946; Nightingale, 1982; Bisiach et al., 1990b, patient PR; Richardson, 1992; Rode et al., 1992; Halligan et al., 1995; Miura et al., 1996; Daprati et al., 2000; Paulig et al., 2000).

The group study of Feinberg et al. (1990) indicated a damage to the right inferior-posterior parietal region (supramarginal gyrus), and to the underlying white matter, as a pathological correlate of asomatognosia (see also Feinberg et al., 2005).

The right posterior insula was selectively damaged in one patient with a transient somatoparaphrenic delusion (Cereda et al., 2002, case #4), and resulted a relevant lesion site in the 11 patients reported by Baier and Karnath (2008), who showed both anosognosia for hemiplegia (see Karnath et al., 2005), and somatoparaphrenia / asomatognosia. In the two patients reported by Levine et al. (1991) the insula was damaged, together with other cortical and subcortical regions: in case #4 the lesion was mainly posterior, involving the temporo-parietal region; in case #6 the damage was anterior, including the frontal lobe, and parts of the basal ganglia. Three patients had subcortical lesions of the basal ganglia (Healton et al., 1982; Halligan et al., 1993; Bottini et al., 2002). The thalamus was damaged in a number of patients (Anton, 1893; Pötzl's case #2, quoted by Schilder, 1935; Ives and Nielsen, 1937, case #1; Sandifer, 1946; Miura et al., 1996; Daprati et al., 2000; Paulig et al., 2000). In patient LA-O of Bisiach and Geminiani (1991) the subcortical white matter was damaged. Case #1 of Starkstein et al. (1990) had an ischemic lesion in the vascular territory of the right anterior cerebral artery, involving the cingulate gyrus, part of the supplementary motor area, and the outflow of the genu of the corpus callosum. The delusion of this patient was that the left limbs were "disjointed and separated" from the rest of his body, but there was no disownership of the contralesional limbs. An alien hand sign was also present. The other patient with a frontal damage (Levine et al., 1991, case #6) had a complex delusion of disownership, with the left upper limb being a leg, left in the bed by the patient's grandson.

A schematic representation of the cerebral structures damaged in neurological patients showing somatoparaphrenia is shown in Figure 16.

Figure 16. Lesion sites of the 56 patients with somatoparaphrenia.



n.a.: not available; F: frontal; T: temporal; P: parietal; O: occipital; Cing: cingulate gyrus; BG: basal ganglia WM: white matter; Th: thalamus; In: insula.

The manifestations of somatoparaphrenia are manifold, with a continuum between the various patterns of pathological verbal reports (confirming the suggestion of Critchley 1953). Table XI summarizes the patients' reports. Patients may feel a sense of estrangeness towards contralesional body parts (Anton, 1893; Pötzl's case #2, quoted by

Schilder, 1935; Roth, 1949, case #2). Body parts may be felt as separated from the patients' body (Pötzl's case #2, quoted by Schilder, 1935; Starkstein et al., 1990, case #1). Patients with a sense of estrangeness may sometimes wonder whether the affected limb belongs to another person (Roth, 1949, case #2). The more frequent manifestations of somatoparaphrenia, present in over two thirds of the patients, is a more or less definite sense of disownership, namely: the delusional belief that contralesional body parts do not belong to them, and that they belong to another person such as the doctor, the examiner, a relative, or an acquaintance. More complex delusional misidentification may occur, with, for instance, the affected limb being referred to as a "plank" (Ehrenwald, 1931), "a make-believe leg" (Levine et al., 1991, case #2), or "a baby in bed with the patient" (Richardson, 1992). Patients may misidentify the limbs of another person as their own (Garcin et al., 1938; Gerstmann, 1942, case #1).

These manifold manifestations may, admittedly oversimplifying, be summarized as follows: 1) feeling of estrangeness of the affected body parts, of separation from the patient's body, or both; 2) delusional beliefs of disownership of the affected body parts; 3) delusional beliefs that the affected body parts belong to another person; 4) more complex delusional misidentifications of the affected body parts; v) associated disorders, including supernumerary limbs, misoplegia, and personification. In the individual patient, these symptoms may fluctuate over time.

Feinberg and co-workers (2005) draw a distinction between: 1) "simple" misidentifications (i.e., patients disown the affected body parts, or attribute ownership to another person), that may be readily corrected when the error is pointed out by the examiner; 2) "delusional" misidentifications, that obdurately resist to the examiner's demonstrations. The somatoparaphrenic phenomena included in this review are likely to belong to Feinberg's "delusional" misidentification type, also considering their duration in time. In a comprehensive analysis of delusional misidentification, and reduplication syndromes (including asomatognosia), Feinberg et al. (2005), and Feinberg and Keenan (2005) suggest a main role of frontal damage, particularly in the right hemisphere, in bringing about these disorders. The present data, confined to misidentifications concerning body parts (i.e., somatoparaphrenia), suggest that an extensive cortical fronto-temporo-parietal network constitutes the neural underpinnings of the sense of ownership of the body. However, the finding that a number of patients have posterior temporo-parietal lesions suggests a particularly relevant role of these structures. The insular cortex may be also relevant.

In a few studies the ownership of objects closely related to the patient's disowned body part, such as rings, has been investigated. One right-brain-damaged patient recognized as her own a ring worn on her left hand (the delusion consisted in the belief that the hand belonged to the doctor), and commented: *"That's my ring, you have got my ring, doctor"* (Sandifer, 1946, p. 123). The conversation eventually led to the temporary dispersal of the somatoparaphrenic delusion. Similarly, another right-brain-damaged patient *"could not explain why her rings happened to be worn by the fingers of the alien [left] hand"* (Bisiach and Geminiani, 1991, case #1; see also in Aglioti et al., 1996, the unpublished related observation of a patient who recognized the disowned left hand as her own, only when her wedding ring was put on the hand itself). The patient of Garcin et al. (1938) explained the absence of his wedding ring on the female hand he misidentified as his own stating that he had taken it off. Further, the patient accounted for the presence of a wrist-watch saying that he had put it on. A more systematic study was made by Aglioti et al. (1996), whose right-brain-damaged patient recognized ownership of a ring, usually worn on her left (disowned) hand, only when worn on the right hand, or held by the examiner. A ring usually worn on the right hand, was, by contrast, recognized by the patient as her own, without hesitation. The findings of Aglioti et al. (1996) suggest the notion of an "extended body schema", that may include some objects, that are closely connected to body parts, having been worn for a long time, and are encoded both in the body schema, and in autobiographical episodic memory (see Schilder, 1935; Teitelbaum, 1941, for the view that some objects, such as clothes, may be closely associated to the representation of the body). The previous clinical observations by Sandifer (1946), Bisiach and Geminiani (1991), and Aglioti et al. themselves (1996, unpublished observation), suggest that this is not always the case, however.

The view that premorbid personality may play a more or less relevant role in the manifestations of the neglect syndrome characterized by unawareness of the neurological deficit (anosognosia) was fully developed in the 1950s, and is extensively summarized in the book "Denial of illness. Symbolic and physiological aspects" by Weinstein and Kahn (1955). The productive symptoms of somatoparaphrenia were less extensively explored in terms of psychological attitudes, but Guthrie and Grossman (1952, case #1) reported a 40-year-old female patient, with no evidence of focal and definite neurological disease, who denied the existence of the left side of her body. When asked to move her left side, the patient moved the right side, and denied ownership of her left hand. Interestingly, the patient recognized her wedding ring on the third finger of the left hand, but stated that the doctor must have taken her ring, since her delusional belief was that her left hand belonged to the doctor (see similar symptoms, but in neurological patients, in Sandifer, 1946, case #1; Bisiach and

Geminiani, 1991, case #1). Psychologically determined difficulties with body parts, including personal neglect, may be produced also by hypnotic suggestion (Teitelbaum, 1941). A perusal of the case reports summarized in Table XI, however, does not reveal any definite premorbid psychopathological pattern. The patients' medical history is typically uninformative in this respect, with a few exceptions: patient #4 reported by Rubinstein (1941) had a long-lasting psychosis; the patient reported by Nightingale (1982) had been suffering from generalized epilepsy.

- Somatoparaphrenia and neurological deficits

In most patients somatoparaphrenia is associated with a severe sensorimotor hemisyndrome. As shown in Table X, however, there are reports of somatoparaphrenic patients with no, or minor, motor and somatosensory deficits, and visual field defects may be definitely absent. Interestingly, position sense was defective in most cases, and the patients (Nightingale, 1982; Starkstein et al., 1990, case #1), in whom proprioception was reported to be spared, did not exhibit disownership of the left side.

The dissociation between somatoparaphrenia and deficits of tactile perception is further corroborated by a few studies assessing the effects, on somatoparaphrenia, of manoeuvres that bring about a temporary recovery of contralesional hemianaesthesia. In two right-brain-damaged patients, Moro et al. (2004) found that crossing the spatial position of the hands (namely, placing the left hand in the right-hand-side of egocentric space) reduced left somatosensory deficits, but did not affect disownership of the left hand (see a similar observation in the right-brain damaged patient reported by Aglioti et al., 1996). These effects of the spatial position of the hands on the ability to report somatosensory stimuli by right-brain-damaged patients (Smania and Aglioti, 1995;

Aglioti et al., 1999) may be accounted for by the hypothesis that the detection and report of somatosensory stimuli entail encoding in a spatial egocentric frame of reference (Vallar, 1997; Gallace and Spence, 2007; Vallar, 2007). Accordingly, in right-brain-damaged patients with left neglect, a location of the left hand in the non-neglected right-hand side of space provides the coordinate system appropriate for perceptual awareness to unconsciously processed tactile inputs.

The finding that the manipulation of the position of the hand ameliorates somatosensory processing, but not somatoparaphrenia, suggests that the somatosensory impairment is not a necessary component of somatoparaphrenia. This conclusion does not extend to proprioception. The appreciation of the overall position of the body, and of the relative position of body parts, is closely related to, and dependent on, movement, and may be a basic component of the sense of ownership. It should be noted, however, that also the deficit of position sense has a higher-order component, related to the neglect syndrome. The deficit of position sense is more severe in right brain-damaged patients with left neglect, and, as other manifestations of the neglect syndrome (Vallar et al., 1997; Rossetti and Rode, 2002; Kerkhoff, 2003), is temporarily improved by optokinetic stimulation with a leftward direction of the movement of the luminous dots (Vallar et al., 1993; Vallar et al., 1995).

The dissociation between impairments of somatosensory processing and somatoparaphrenia is also suggested by the observation that the detection of touches delivered to the left hand of a somatoparaphrenic patient temporary improved, when the examiner stipulated with her that the touches were given to the hand of the patient's niece, and not to the patient's hand (Bottini et al., 2002). This "cognitive" manipulation improved detection of left somatosensory stimuli, capitalizing on the patient's delusion of disownership (namely, the belief that the patient's left hand belonged to her niece), that did not change, however.

As Table X shows, visual field deficits do not appear to be a necessary impairment for somatoparaphrenia to occur. In a few patients no contralesional hemianopia was found (Schilder, 1935; Ives and Nielsen, 1937, case #1; Von Hagen and Ives, 1937; Frederiks, 1963; Nightingale, 1982; Bisiach et al., 1991; Cereda et al., 2002; see also the recent series of Baier and Karnath, 2008). In other patients, the visual deficit was confined to extinction to double simultaneous stimulation (Hécaen et al., 1954; Starkstein et al., 1990; Daprati et al., 2000; Moro et al., 2004, case #2). Furthermore, the clinical fact of somatoparaphrenia, as noted by the early investigators of the symptom, is that patients fail to acknowledge the ownership of contralesional body parts also when these are moved on the body midline, in central vision (Barré et al., 1923; Pötzl's case #1, quoted by Schilder, 1935; Bisiach et al., 1990b).

- Somatoparaphrenia and spatial neglect

The close association between extrapersonal and personal neglect on the one hand, and somatoparaphrenia on the other hand, is apparent from the inspection of Table X, with most patients showing both manifestations of the syndrome. In three patients, however, mention is specifically made that no "hemisomatoagnosia" (Hécaen et al., 1954), or "personal neglect" (Bisiach et al., 1991; Halligan et al., 1993) were present. Accordingly, somatoparaphrenia appears to be independent of awareness of the contralesional side of the body (explicitly disowned as it is), as assessed, for instance, by requiring patients to reach for their body parts (Bisiach et al., 1986). Furthermore, one main feature of somatoparaphrenia is the obdurate denial of ownership of contralesional body parts, even when they are placed in the ipsilesional side, namely, in a non-neglected portion of space (see, for instance, patient PR, described by Bisiach et al., 1990b). Furthermore, the intracarotid amobarbital study of Meador et al. (2000) revealed double dissociations between asomatognosia, anosognosia, and personal neglect. In sum, these findings suggest that the spatial representation of body parts is largely independent of the processes concerned with their sense of ownership.

The closer association between somatoparaphrenia and extrapersonal neglect may reflect the fact that one main feature of somatoparaphrenia is a blurred distinction between corporeal (namely, the patients' body parts), and extracorporeal objects (namely, body parts of other persons, or other non-corporeal objects), that results in the delusional disownership of contralesional body parts, and, although less frequently, in the replacement of the patient's affected body parts by other objects (Ehrenwald, 1931), in contralesional hallucinations (Anton, 1893; see Zingerle, 1913 in Benke et al., 2004), and in supernumerary limbs (Ehrenwald, 1930; Hécaen et al., 1954; Frederiks, 1963; Starkstein et al., 1990, case #1; Halligan et al., 1993; Moro et al., 2004). This type of impairment may involve a disordered representation of objects in extrapersonal space, concerning another person's body parts.

Extrapersonal spatial neglect, however, is not a sufficient condition for somatoparaphrenia to occur, since most patients with left spatial neglect do not exhibit the disorder (Bisiach and Vallar, 2000). Interestingly, the patient reported by Garcin et al. (1938), who did not exhibit extrapersonal neglect, as assessed by drawing tasks, did not show disownership of the contralesional left upper limb, although a personal neglect for the left side of the body was present. The patient erroneously identified the arm of another person as his own arm, only when his own arm was covered, and he could not see it.

In one of the few experimental studies of somatoparaphrenia Daprati et al. (2000) found that their patient - who had recovered from the clinically apparent delusion of disownership of the left hand - was unable to recognize his left hand performing a movement, while looking at it on a screen, where either the patient's hand, or another person's hand, was shown. Specifically, the patients denied ownership of both his left hand, and, correctly, of another person's hand. Confabulatory comments (e.g., *"I saw a long needle"*, *"I saw nothing at all"*) were recorded. The patient was able to recognize his right hand acting on the screen, but mistook the examiner's hand for his own. In four neurologically unimpaired control participants, and in two neglect patients, the error of denying ownership of the participant's hand was much less frequent.

These results document experimentally the possibility that one pathological mechanism of somatoparaphrenia is the inability to discriminate between personal and extrapersonal (another person's) body parts. Impairments of position sense and of tactile perception (be they primarily sensory, a disorder related to spatial neglect, or with both lower- and higher-order components, see Vallar, 2007) may be a pathological, though not unique, factor contributing to the somatoparaphrenic delusion, depriving the patient's own body parts of a main distinctive feature, that allows discrimination from other persons' body parts and extra-personal objects.

The hypothesis that the deficit underlying somatoparaphrenic delusions has a spatial component is definitely supported by the observation in two right-brain-damaged patients, and in one left-brain-damaged patient, that vestibular stimulation - a manoeuvre that temporarily improves many manifestations of the neglect syndrome (Vallar et al., 1997; Rossetti and Rode, 2002) - ameliorates also the disownership of the left upper limb (Bisiach et al., 1991; Rode et al., 1992), and of the right hand (Schiff and Pulver, 1999). Rode and co-workers (1992) investigated in their patient the effects of vestibular stimulation on other manifestations of the neglect syndrome, finding also an improvement of extrapersonal and personal neglect, of anosognosia for hemiplegia, and of the motor deficit in the lower limb. The somatosensory impairment and hemianopia remained unchanged, and this finding strengthens the suggestion that sensory impairments are not a core pathological factor of somatoparaphrenia. Interestingly, the logorrhoea that accompanied the delusional speech disappeared immediately after the vestibular stimulation. These findings suggest that somatoparaphrenia shares with other manifestations of the syndrome of spatial neglect a disordered component (possibly a disrupted “spatial medium”, see Bisiach and Vallar 2000) that may be temporarily restored by vestibular stimulation. An early account of somatoparaphrenia in terms of a higher order spatial representational disorder (“dyschiria”) may be found in Bisiach and Berti (1987).

Table X. Demographical, neurological and neuropsychological data of 56 hemisphere-damaged patients with somatoparaphrenia.

Report	C	Sex/ Age	Aetiology/ Lesion side	Lesion site	Neurological deficit M	SS	PS	VF	Anosognosia	Spatial neglect extrapersonal	personal
Anton (1893)	C1	M/65	CVA/R	O, th [pm]	-	+	+	+	nr	+[1]	+[1]
Biancone (1909) quoted by Lhermitte (1952)	C1	F/62	nr/R	nr	+	+	nr	nr	nr	nr	nr
Zingerle (1913)	C2	M/45	CVA/R	nr	+	+	+	+	+M-SS	nr	+[1]
Kramer (1915)	C1	M/nr	CVA/R	nr	+	+	+	+	+M	+[1]	+[1]
Barré et al. (1923)	C1	M/60	CVA/R	nr	+	-[^^]	+§	+	+M	+[1]	+[1]
Barkman (1925)	C9	F/53	CVA/R	nr	+	+	+	+	+M	+[1]	+[1]
Ehrenwald (1930)	C1	M/59	CVA/R	nr	+	+	+	+	/+M/	nr	+[1]
Ehrenwald (1931)	C5	M/64	CVA/R	nr	+	+	+	+	+M	+[1]	+[1]
Pötzl quoted by Schilder (1935 , p. 29-30)	C1	M	CVA/R	ic, inf Pl [pm]	+	+	+	nr	+M	+[1]	+[1]
	C2	M	CVA/R	P, O, th [pm]	nr	nr	nr	+	nr	nr	+[1]
Schilder (1935, p. 309-12)	C2	F/48	CVA/L	nr	+	+	+	-	-	nr	nr

Table X. Continued.

Report	C	Sex/ Age	Aetiology/ Lesion side	Lesion site	Neurological deficit M	 SS	 PS	 VF	Anosognosia	Spatial neglect extrapersonal	 personal
Ives & Nielsen	C1	M/42	CVA/R(L)	th, ic,wm ant (L: T, crb) [pm]	+	+°	nr	-	-	nr	nr
(1937)	C2	M/66	CVA/R	F, P, T,O, ln [pm]	+	+	+	+	-	nr	nr
Lhermitte & Tchehrazi (1937)	C1	M/70	CVA/R	sylvian [pm]	+	+	+	+	+M	nr	+[1]
Olsen (1937, quoted by Nielsen 1938, p. 554-55)	C1	F/nr	CVA/R	nr	+	nr	nr	+	nr	nr	nr
Von Hagen & Ives (1937)	C1	F/48	CVA/R	nr	+	+	+u	-	+M	+[1]	+[1]
Garcin et al. (1938)	C1	M/64	N/R	T, P [pm]	+°	-	+	+	-	-	+
Nielsen (1938)	C8	F/57	CVA/L	nr	+	+^^	+	+	+M-l	nr	nr
Rubinstein (1941)	C4	F/63	CVA/R	nr	+	/+/	+	/+/	+M	+[1]	+[1]
Wortis & Dattner (1942)	C1	F/78	CVA/R	MCA [c]	+	+	+	+	+M°	+[1]	+[1]
Gerstmann	C1	F/48	CVA/R	nr	+	+	+	nr	+M	nr	-[1]
(1942)	C2	F/34	CVA/R	nr	+	+	+	+	+M-SS	+[1]	+[1]
Halloran (1946)	C1	M/70	subdural hematoma/L	inf. P, Th-P peduncle (compressed)	+	+u	+	nr	nr	nr	nr
Sandifer (1946)	C1	F/66	CVA/R	th, sup T, inf Pl [pm]	+	+	+	+	+M-SS-VF	+[2]	+[2]

Table X. Continued.

Report	C	Sex/ Age	Aetiology/ Lesion side	Lesion site	Neurological deficit M	SS	PS	VF	Anosognosia	Spatial neglect extrapersonal	personal
Roth (1949)	C1	F/61	N/R-(L)	R: pre-post Ce, inf-sup Pl, sup-post T, post wm (L: post Ce) [pm]	+	+°^^	+	+	+°M	+[2]	+[1]
	C2	M/51	CVA/R	ICA [pm]	+	+	+	+	+M	+[2]	+[2]
Weinstein & Kahn (1950)	C7	F/38	N/R	T [surg]	+	-	+§	nr	+M	nr	+[1]
Hécaen et al. (1954)	C1	F/66	CVA/R	nr	+	+	+	e	+M°	+[2]	-**
Weinstein et al. (1954)	C1	F/57	N-CVA/R	cing herniation [pm]	+	e^^	+	+	+M	+[1]	+[1]
Frederiks (1963)	C1	M/36	CVA/R	sylvian aneurysm [surg]	+	+	+	-	+M	nr	+[1]
Verret & Lapresle (1978)	C1	F/64	CVA/R	sylvian [SPET]	+	+	+	+	+M	nr	+[1]
Healton et al. (1982)	C1	F/75	CVA/R	p, ln, cn, ic, ec [pm]	+	+	+	+	+M	+[1]	+[1]
Nightingale (1982)	C1	M/46	N/R	P [CT]	+°	-^	-	-	nr	nr	+[1]
Assal (1983)	C1	F/86	CVA/R	sylvian [CT]	+	+^^	+	+	+M	+[2]	+[2]

Table X. Continued.

Report	C	Sex/ Age	Aetiology/ Lesion side	Lesion site	Neurological deficit M	SS	PS	VF	Anosognosia	Spatial neglect extrapersonal	personal
Berthier & Starkstein (1987)	C1	M/63	CVA/R	F, T, P [CT]	+	-[^^]	nr	+	nr	+[1]	+[1]
Starkstein et al. (1990)	C1	M/71	CVA/R	cing, F, cc [CT]	+l	e[^^]	-	e[^^]	+M	+[2]	+[2]
	C2	F/48	CVA/R	MCA [CT]	+	+°	+°	e	+M	+[2]	+[2]
Bisiach et al. (1990b)	PR	M/74	CVA/R	T, P, O [CT]	+	nr	nr	nr	+M	+[1]	+[1]
Bisiach & Geminiani (1991)	LA-O	F/65	CVA/R	wm [CT]	+	+	+	+	+M	+[2]	nr
Bisiach et al. (1991)	C1	F/84	CVA/R	F, P, T [CT]	+	+	+	-	+M	+[2]	-
Levine et al. (1991)	C4	F/78	CVA/R	pre-post Ce, inf Pl, post T, In, ic [CT]	+	+	+	+i	+M	+[2]	nr
	C6	M/60	CVA/R	F, In, ic, ln, cn, wm [CT]	+	+	+	+	+M	+[2]	nr
Richardson (1992)	C1	M/64	CVA/R	P, T, O [CT]	+	nr	nr	nr	nr	nr	nr
Rode et al. (1992)	C1	F/69	CVA/R	P, T, O, sub [CT]	+	+	+	+	+M-VF	+[2]	+[2]
Halligan et al. (1993)	C1	M/65	CVA/R	bg [CT]	+	+	+	/+/	-[#]	+[2]	-
Halligan et al. (1995)	C1	M/41	CVA/R	T, P [CT]	+	+	+	+	-	+[2]	/+[2]/
Miura et al. (1996)	C1	F/77	CVA/L	O, T, th, ic, cn [CT/MRI]	+	+	+	+	+M	+	nr

Table X. Continued.

Report	C	Sex/ Age	Aetiology/ Lesion side	Lesion site	Neurological deficit M	SS	PS	VF	Anosognosia	Spatial neglect extrapersonal	personal
Aglioti et al. (1996)	C1	F/73	CVA/R	F, P, T [CT]	+	+	+	+	+M-SS	+[2]	+[2]
Schiff & Pulver (1999)	C1	F/81	CVA/L	F, T, P, O [MRI]	+	nr	nr	+	nr	+[1]	+[1]
Daprati et al. (2000)	C1	M/50	CVA/R	th, T, P [MRI]	/+/	+	+	e	-[##]	+[2¥]	-[2¥]
Paulig et al. (2000)	C1	F/85	CVA/R	PCA, post th, T, P [nr]	+	+	+	+	+M	+[1]	+[1]
Bottini et al. (2002)	C1	F/77	CVA/R	ln, ic post, wm [CT]	+	+	+	+	+M-SS-VF	+[2]	+[2]
Cereda et al. (2002)	C4	F/75	CVA/R	In post [MRI]	-	+u	+§	-	nr	-	nr
Moro et al. (2004)	C1	F/62	CVA/R	F, T, P [CT]	+	+	+u	+	nr	+[2]	+[2]
	C2	M/66	CVA/R	F, T, P [CT]	+	+	+	e	-	+[2]	+[2]
Brugger[$]	C1	F/57	CVA/R	nr	+	+	+	nr	+M°	+[1]	+[1]

ABBREVIATIONS

C: case; M/SS/PS/VF: motor/somatosensory/position sense/visual field defect.

M/F: male/female; R/L: left/right; +/-: presence/absence of impairment; nr: not reported.

CVA: cerebrovascular attack; N: neoplastic lesion; MCA: middle cerebral artery; PCA: posterior cerebral artery; ICA: internal carotid artery; sylvian: lesion in the fronto-temporo-parietal areas surrounding the sylvian fissure; F: frontal; P: parietal; Pl: parietal lobule; T: temporal; O: occipital; In: insula; Ce: central gyrus; ic: internal capsule; ec: external capsule; th: thalamus; p: putamen; ln: lenticular nucleus; cn: caudate nucleus; bg: basal ganglia; sub: subcortical lesion; cc: corpus callosum; cing: cingulate gyrus; wm: white matter; crb: cerebellum.

ant/post: anterior/posterior; inf/sup: inferior/superior.

[c/pm/surg/CT/MRI]: clinical diagnosis/post mortem/surgery/Computerized Tomography/Magnetic Resonance Imaging.

[1]: conclusion based on the clinical report (e.g., for complete neglect: head and eyes deviated towards the ipsilesional side; for personal neglect, mention that the patient's (Pt) attention was preferentially oriented towards the ipsilesional side of the body); [2]: neuropsychological evaluation.

°: mild impairment.

§: vibration sense preserved.

[^]: L somatosensory inattention.

[^^]: mislocalisation of sensory stimuli from the contralesional to the ipsilesional side (allochiria).

e: contralesional extinction to double simultaneous stimulation.

u: upper limb only; l: lower limb only; i: inferior quadrant.

/ /: recovered deficit.

( ): additional lesion in the hemisphere ipsilateral to the side of the clinical deficit.

[**]: with closed eyes the Pt was unable to find her L hand.

[#]: no explicit evidence of anosognosia on Cutting's (1978) questionnaire, but the Pt believed that he could use the L hand to write his signature, and, requested to do so, he performed the signature using the R hand.

[##]: no anosognosia for left arm weakness, anosognosia for left spatial neglect on Cutting's (1978) questionnaire; the Pt was assessed when somatoparaphrenia had recovered.

[¥]: the formal psychometric assessment was performed after the Pt had recovered from somatoparaphrenia, a few weeks after stroke onset; in the acute phase a severe L visuo-spatial neglect was present.

[$] : courtesy of Dr. Peter Brugger: http://www.artbrain.org/phantomlimb/brugger.htm

Table XI. Summary report of the patients' somatoparaphrenic delusion.

Report	Duration of delusion	Body side	Description of delusion	Additional observations
Anton (1893)	w	L	Limbs foreign to the Pt.	Visual hallucinations, from the Pt's L side: daughter pursuing the Pt with love advances; wife sitting on the left edge of the bed, making love to the male nurses.
Biancone (1909, quoted by Lhermitte 1952)	nr	L	Limbs belonging to another person	Requested to indicate the foot of this stranger the Pt indicated her own foot.
Zingerle (1913)	2 w	L	A woman laying in the bed on the L side of the Pt's body.	Pt pointing leftwards, while reporting the delusion.
Kramer (1915)	nr	L	Hand belonging to the doctor.	-
Barré et al. (1923)	3 w	L	Hand belonging to the doctor.	-
Barkman (1925)	transient	L	When, by chance, the Pt's L-LLi was touched by her R-LLi, she asked if it was her husband's LLi [report from the Pt's husband].	-
Ehrenwald (1930)	2 m	L	A nest of hands in his bed.	Two months later the Pt, aware of hemiplegia, asked hands to be removed, and put in a bag with the remaining ones. The L hand was not the "right" one. New hand more voluminous, heavier,and fleshier, old one smaller and thinner.
Ehrenwald (1931)	6 m	L	Disownership of ULi, described as a monster; bodily transformation: in place of the L side of the body there was a plank, subdivided into compartments by other planks, with a hole in which the food fell.	-
Pötzl quoted by Schilder (1935, pp. 29-30)	nr	L	Disownership of the hand (probaby from the Pt nearby).	Disownership observed when the Pt's plegic arm was placed in front of him. Referred to as "so long and lifeless, and as dead as a snake".
	nr	L	Hand felt as estranged and separated from the Pt.	-
Schilder (1935, p. 309-12)	nr	R	Disownership of the hand and ankle (doubtfully).	Delusion about R ULi and LLi fractures. R Hand reported as too big and swollen.

Table XI. Continued.

Report	Duration of delusion	Body Side	Description of delusion	Additional observations
Ives & Nielsen (1937)	3 d[¥]	L	Limbs belonging to another person (the doctor, the Ex).	-
	5 d[¥]	L	Feeling of non-belonging of the ULi.	Someone substituted "this arm" for the Pt's arm
Lhermitte & Tchehrazi (1937)	1 m	L	Uli belonging to another Pt.	Belief that another Pt was scratching his chest with his ULi.
Olsen (1937) (1937, quoted by Nielsen 1938, p. 554-55)	nr	L	Limbs belonging to another person (the Ex, a person laying in bed with the Pt).	-
Von Hagen & Ives (1937)	15 d	L	Occasionally, Pt's hand belonging to the her brother-in-law; when the Pt touched her L elbow, she called it "someone's else knee".	L limbs called " That's an old man. Stays in bed all the time". "I do not want any spirits in bed with me".
Garcin et al. (1938)	8 d	L	With ULi covered, Pt misidentified another person's ULi as his own (female on some trials).	Confabulatory responses to account for the absence on the other person's ULi of his wedding ring and of the presence of a diamond –ring and a wrist-watch.
Nielsen (1938)	8 d	R	ULi belonging to another person, perhaps the Pt's daughter.	Not felt any other portion of the daughter's body. After recovery, Pt recalled the delusion as an "hallucination".
Rubinstein (1941)	15 d	L	Disownership of the hand, defined as a "reptile".	Acknowledgement of ownership after comparison of the L and R thumbs; Pt telling the nurse that "a corpse was lying in her bed at the left side", "a poor dead devil's arm" put in place of her own. Pt previously detained in mental hospitals with delusions of persecution, auditory and visual hallucinations (snakes and other reptiles biting her).
Wortis & Dattner (1942)	nr	L	Disownership of the hand and forearm. Pt lost her hand as a girl. Pt found the hand in the room and sewed it on.	Hand smaller and heavier than the R one, and attached to the Pt'elbow.

Table XI. Continued.

Report	Duration of delusion	Body Side	Description of delusion	Additional observations
Gerstmann (1942)	nr	L	At times, when the Ex's ULi was placed in front of the Pt's face or chest, not in contact with her, feeling that this was her own L paralysed ULi.	-
	5 d	L	Limb belonging to another person, a little girl, laying in bed with the Pt.	Girl's arm slipped into the Pt's sleeve.
Halloran (1946)	4 d	R	Hand belonging to the doctor.	Pt non-aphasic, L-handed. Acknowledgement of ownership of the foot.
Sandifer (1946)	3 d	L	Disownership of the hand (belonging to the doctor), of the leg, and the arm.	Pt's hand being near her L shoulder. Ownership of Pt's ring acknowledged. After repeated testing, temporary acknowledgment of ownership of the hand, and of hemiplegia.
Roth (1949)	4 m ½[¥]	L	Disownership of the hand.	Pt unable to find the hand, feeling that someone stole it.
	about 10 d	L	Limbs foreign to the Pt, asking whether ULi belonged to his wife.	Delusion not involving trunk or face.
Weinstein & Kahn (1950)	9 d	L	Occasionally Pt's ULi belonging to the Ex, or the nurse.	-
Hécaen et al. (1954)	5 ½ m[¥]	L	Hand belonging to the nurse, when viewing was prevented; super ULi on the L side of the body, described as a living ULi, belonging to the nurse.	M: Pt sometimes insulting the nurse, to whom the ULi belonged. Pt dictated a letter to the nurse, owner of the super ULi.
Weinstein et al. (1954)	1 m[¥]	L	Hand (identified as the "extra" super) belonging to a close friend, Mrs. D, a nurse, or, twice, to the doctor.	Super hand and part of the ULi ("heavier", "bigger", "fatter", "hot and heavy", "a no man's hand, hard working and well used").
Frederiks (1963)	15 d	L	Disownership of the L side of the body.	Super three arms and legs (Pt surprised by this experience).

Table XI. Continued.

Report	Duration of delusion	Body Side	Description of delusion	Additional observations
Verret & Lapresle (1978)	2 ½ m	L	Hand and ULi belonging to the doctor.	M: Pt hit her estranged L-ULi, and scratched her L-LLi, identified as “the doctor’s leg”. Hand ownership acknowledged with vision prevented, and tactile exploration by the R hand being used. In front of a mirror, with direct vision prevented, ownership of the L hand immediately acknowledged. With both mirror and direct vision deficit unchanged.
Healton et al. (1982	10 d[¥]	L	ULi belonging to Ex	-
Nightingale (1982)	2 y	L	L side different from R side, recognised as “self” and “good”: L side evil, controlled by external agents (the Devil, the Pt’s deceased father) attempting at inducing the Pt to perform evil acts.	Rarely, auditory and visual (usually, the Pt’sfather)hallucinations, emanating from the Pt’s L extrapersonal space. From the age of 30 generalized epilepsy.
Assal (1983)	nr	L	ULi belonging to the Pt’s husband, both with and without visual control. No deficit for the LLi.	Sometimes, in front of a mirror, Pt acknowledged the L-ULi as her own; the Ex’s hand, when moved from the Pt’s L side towards the R side, was attributed to her husband, or to a variable female relative.
Berthier & Starkstein (1987)	6 m	L	Three L-ULis: one of the Pt, one of his niece, the 3rd crossed over his chest.	Auditory, tactile and visual hallucinations; personification and M for the L hand.
Starkstein et al. (1990)	1 m	L	L limbs “disjointed and separated” from the rest of the Pt’s body; super strange limb laying beside the Pt’s L-ULi.	M: Pt hated his L upper limb and called it a “jerk”; L alien hand (mild motor deficit of the ULi).
	6 m	L	ULi belonging to a nearby person.	M: Pt disliked her L-ULi, hit it repeatedly(“it does not obey me”) and called it “zodoquio” (neologism).
Bisiach et al. (1990b)	2 w	L	Pt’s hand belonging to the doctor.	Placing passively L hand in the R side of space did not affect disownership.

Table XI. Continued.

Report	Duration of delusion	Body Side	Description of delusion	Additional observations
Bisiach & Geminiani (1991)	2 d	L	Hand belonging to another Pt (forgotten in the ambulance).	Ownership of L shoulder, and *inferentially* of arm and elbow. Placing passively L hand in the R side of space did not affect disownership. Limb weakness acknowledged, but referred to the *right* side.
Bisiach et al. (1991)	nr	L	ULi belonging to the Pt's mother.	Temporary remission through vestibular stimulation.
Levine et al. (1991)	nr nr	L L	Heavy weight on the Pt's chest identified as her husband's arm. ULi being a make-believe leg, left in the bed by the Pt's 3-year-old grandson, who had visited earlier	- -
Richardson (1992)	7 d	L	ULi being a baby in bed with the Pt.	Auditory and visual hallucinations. History of alcohol abuse.
Rode et al. (1992)	6 m	L	ULi belonging to the Ex. Pt's ULi "behind the door".	Temporary remission through vestibular stimulation.
Halligan et al. (1993)	7 m	L	Denial of ownership of the U and LLi; 3rd super ULi originating from the top L corner of the Pt's torso.	Belief that the L limbs had previously been amputated.
Halligan et al. (1995)	1 m	L	Non-belonging of the ULi, and the foot.	Doctors interested in amputating L limbs.
Miura et al. (1996)	2 ½ m	R	Hand belonging to the doctor.	-
Aglioti et al. (1996)	17 d	L	Denial of ownership of the hand, left in the Pt's bed by the doctors.	Denial of ownership of rings worn on her L hand; acknowledgement of ownership of a ring on the R hand, and of L rings moved to the R hand; right-sided (crossed) position of the L hand improved detection of touch, not disownership of the L hand and of objects related to it.
Schiff & Pulver (1999)	30 d	R	Denial of ownership of the hand	Temporary remission through vestibular stimulation. Aphasia.
Daprati et al. (2000)	transient	L	Hand likely belonging to the Pt's son.	-

Table XI. Continued.

Report	Duration of delusion	Body Side	Description of delusion	Additional observations
Paulig et al. (2000)	nr	L	L side described as Pt's handicapped nephew and a clumsy cat.	-
Bottini et al. (2002)	2 m	L	Hand belonging to the Pt's niece.	Touches to L hand reported, with verbal instructions coherent with the Pt's delusion (i.e., "Ex touches the niece's hand").
Cereda et al. (2002)	transient	L	Not recognizing own ULi.	Being touched by a stranger; a foreign body in the Pt's bed.
Moro et al. (2004)	5 w	L	Non-belonging of the hand and the wrist; shoulder and elbow recognized as her own. 3rd super ULi, not plegic, on the L side of the body, originating from the shoulder.	Right-sided (crossed) position of the L hand improved detection of touch, not disownership.
	nr	L	Hand belonging to another Pt, given to him by the doctors by mistake; no other disowned body part; 2-3 super LLi.	Hand-crossed-position effect as in case #1. M: Pt tried to push the super LLi out of the bed. Sense of disownership disappeared with closed eyes.
Brugger	10 days	L	In darkness, presence of the Pt's sister on the L side of her body, for three nights a welcome presence, as the Pt was less alone.	M: from the 4th night, the Pt reported that there was not enough space in the bed for two, became angry with her sister, and finally repeatedly bit the sister's R arm (actually, the Pt's L arm).

ABBREVIATIONS
U/LLi: upper/lower limb; ¥: delusion lasting till the patient was cooperative, before death; super: supernumerary; M: misoplegia; d/w/m/y: days/weeks/months/years. Ex: examiner. For other abbreviations see Table I.

"The left hand belongs to my son": somatoparaphrenic delusion in a neglect patient showing productive spatial symptoms

- <u>Case report</u>

JJ was a 97-year-old right-handed female patient, with 17 years of education, who sustained a right hemisphere stroke on September 16, 2009. The CT scan (see Figure 17) showed a right ischemic lesion with a hemorrhagic component, consisting in damage to the cortico-subcortical fronto-parietal area, including the insula cortex.

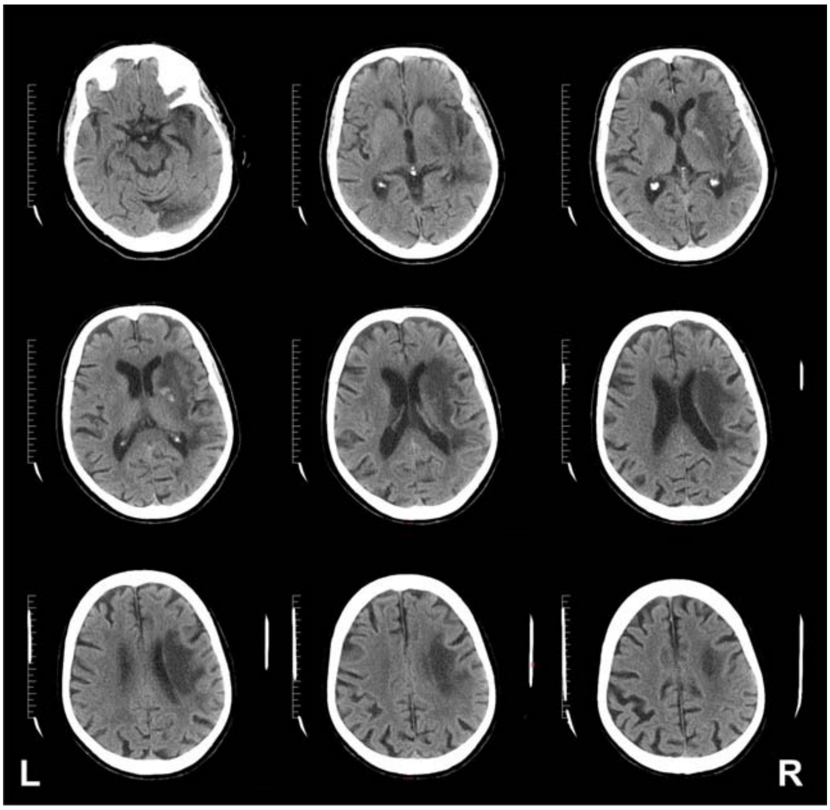


Figure 17. Patient JJ. CT scan images done on September 29, 2009. L = left; R = right.

Table XII. Results of JJ's neuropsychological evaluation (October 13, 2009).

TEST performance	Maximum score	JJ Score	Pathological
SPATIAL NEGLECT			
Line cancellation (Albert, 1973)	21	3	*
Letter cancellation (Diller and Weinberg, 1977)	104	1	*
Star cancellation (Wilson et al., 1987)	56	7	*
Bell cancellation (Gauthier et al., 1989)	35	0	*
Line bisection	-	+7.3mm	*
Sentences reading (Zoccolotti and Judica, 1991)	6	0	*
Copying a drawing:			
- Daisy	2	0.5	*
- Two daisies	4	0.5	*
(Halligan and Marshall, 1993)			
- Butterfly	2	0.5	*
- Complex drawing	10	0.5	*
(modified by Gainotti et al., 1972)			
Drawing from memory:			
- Clock	12	10	*
- Daisy	2	2	
- Butterfly	2	1	*
PERSONAL NEGLECT			
Body reaching (modified by Bisiach et al., 1986)	18	16	*
Body exploration (Cocchini et al., 2001)	15	8	*

The patient had no history of previous neurological or psychiatric disorders. One month after stroke onset she was given a neurological and neuropsychological evaluation, during which she was alert and cooperative. The neurological examination showed the presence of severe left hemiplegia, complete left hemianaesthesia and left hemianopia: the patient appeared completely unaware of these deficits (Bisiach et al., 1986).

The presence of USN was ascertained: the patient showed an attentional bias in all tests. In cancellation tasks she marked only few targets in the right extremity of the sheet: 3/21 lines (Albert, 1973), 1/104 letter (Diller and Weinberg, 1977), 7/56 stars (Wilson et al., 1987) and none of the 35 bells (Gauthier et al., 1989). The mean deviation score in the line bisection test was +7.3mm. Neglect dyslexia was detected by a sentence reading test (Zoccolotti and Judica, 1991): the patient made 5 omissions and one substitution. Her performance in copying the drawings was defective, as she omitted many contralateral elements. Her mental representation was slightly faulty. Personal neglect was also detected (Bisiach et al., 1986; Cocchini et al., 2001). The scores obtained in the neuropsychological battery are reported in Table XII.

During a neuropsychological interview the patient exhibited somatoparaphrenia for the left hand, denying repeatedly that it was hers. If the examiner insisted, she affirmed that it belonged to her son or, rarely, to her nephew. The transcription of the short interview is given below:

Examiner (E), pointing to the patient's right hand: *Whose is this hand?*

JJ: *It is mine.*

E, pointing to the left hand: *And whose is this one?*

JJ: *It is my son's hand.*

E: *Where is your son now?*

JJ: *He is in Vicenza, at work* (note that the patient was in Milan).

E: *And why is his hand here, with you?*

JJ: *He left his hand to keep me company.*

E, pointing to the left elbow*: Whose is this elbow?*

JJ*: It is mine.*

Occasionally, she also showed a delusional belief regarding her left leg, which she did not recognise as a body part but defined as a *"metal tube"*. She did not show any surprise that this should be so and she never manifested any aggressive behaviour toward the left side of her body.

She was checked for other productive symptoms. First the presence and the distribution of recurrent perseveration in the target cancellation tasks was assessed. She was requested to do the two versions of the star cancellation and the letter cancellation tests described in Experiment 2. JJ perseverated in the scattered version of the star cancellation test (eighteen recurrent perseveration marks in addition to the correct 8, perseveration index: 3.25) but not when the little stars were arranged in rows. No perseveration was recorded in the letter cancellation task when the stimuli were arranged in an orderly fashion; as she was not able to detect the presence of the stimuli in the scattered version of the test, it was impossible to evaluate perseveration (see Table XIII and Figure 18). Moreover she was unable to perform the Dual Task so it was not possible to measure her divided attention.

Table XIII. Neglect and perseveration scores obtained by JJ patient in the cancellation tasks.

	CANCELLATION TASKS			
	Star		Letter	
	scattered	in rows	scattered	in rows
Omission percentage	73.33%	76.77%	100%	98.08%
Perseveration Index	3.25	1	-	1

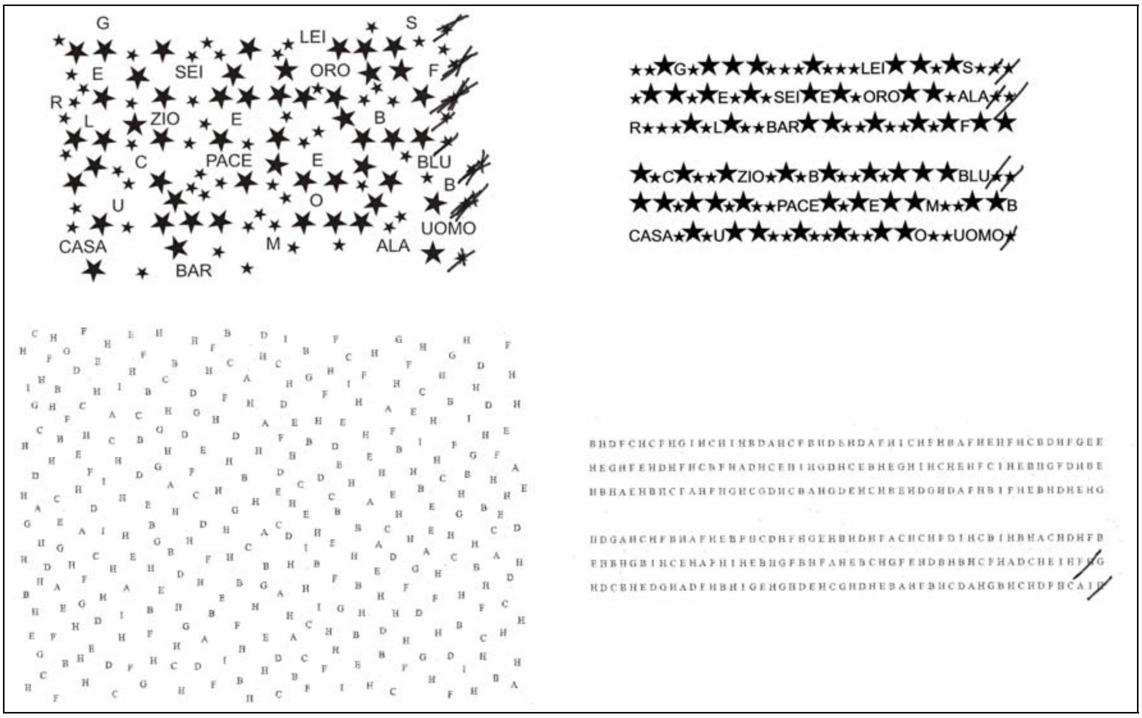


Figure 18. JJ’s performance on the four cancellation tests.

Then the presence of neglect errors in the word reading tasks was evaluated. JJ was asked to read the W and EW lists used in the Experiment 3. As shown in Table XIV, the patient produced five errors in the W list, of which one omission, two substitutions and two additions. In the EW list she made one omission, three substitutions and three additions.

In conclusion, this case suggests that productive symptoms related to extra-personal and personal space can co-exist after a vascular right brain lesion. JJ presented: 1) disownership of a body part contralateral to the brain damage, attributing possession to a relative; 2) recurrent perseveration in a target cancellation test, in which the target was non-verbal (star) and the stimuli were disposed randomly on the sheet; 3) more addition/substitution than omission errors in reading tasks.

Table XIV. Reading errors produced by JJ in the W and EW lists.

Omissions		Substitutions		Additions	
Target	Patient's Reading	Target	Patient's reading	Target	Patient's reading
VIOLONCELLO (W)	*NCELLO*	PILOTA (W)	**R***OTA*	VOTO (W)	**FIGLI***O*
LETTORE (EW)	*ETTORE*	CONO (W)	**S***ONO*	FLUIDO (W)	**LIQ***UIDO*
		SEGUIRE (EW)	**INT***UIRE*	MARE (EW)	**A***MARE*
		VOLTA (EW)	**AR***TA*	ARTE (EW)	**P***ARTE*
		CALARE (EW)	**D***ARE*	SOLARE (EW)	**PAR***LARE*

Italics: letters read correctly to the right of the neglect point. Bold: letters extraneous to the target. Underlined: letters added to the left of the neglect point, exceeding the length of the target. W = Word list; EW = Experimental Word list.

ANOSOGNOSIA
FOR NEGLECT SYNDROME

EXPERIMENT 4

Self-assessment of visuo-spatial performance:

(un)awareness in patients with unilateral spatial neglect

- Aim of the study

Previous studies on anosognosia for USN (Azouvi, 1996; Berti et al., 1996; Jehkonen et al., 2000) suggest that, even if unawareness of spatial attention deficits seems to be a pervasive component of the neglect syndrome, some neurological patients do show some form of insight regarding their spatial difficulties.

The Catherine Bergego Scale (CBS; Azouvi, 1996), which permits self-evaluation of ten routine everyday activities with four possible responses (range 0-4), is a useful tool for assessing presence and severity of unawareness, through it must be kept in mind that it is limited to measuring general problems occurring after cerebral damage, not specifically linked to an immediate performance. A generic subjective perception of the difficulties inherent in interacting with a part of space is also included in Jehkonen's study (2000). Anosognosia for specific performances is examined by Berti and colleagues (1996), but the authors use only two tasks (drawing and reading) and limit participants' feedback on the accuracy of the test to a direct answer (yes/no).

Recently Barrett and collaborators (2005) examine the presence of anosognosia in various cognitive domains in participants with probable Alzheimer disease (AD), through a pre- and post-task self-assessment using a vertical Likert scale. This scale is ideal for assessing the degree of impairment the patient considers s/he has; moreover, the comparison between the pre- and post-test evaluations provides important information about the possibility of modifying the awareness of the deficit.

We therefore evaluate the participants' performance on specific neuropsychological tests with a Likert scale to obtain a quantitative estimate of the presence of anosognosia for USN. The main objective is to verify if the patients' self-evaluation done prior to the test could be modified by watching a playback of their performance (post-test evaluation) or by an implicit rating, in which the question is addressed in the third person (Marcel et al., 2004). The stability of self-evaluation at 24 hours is also measured and the relationship between anosognosia for spatial attention and for motor impairment is considered.

- <u>Materials and methods</u>

Participants

Thirty-three patients (15 males, 18 females; mean age: 51 years, SD: ± 13.2, range: 34-75); mean education: 11 years, SD: ± 4.2, range: 2-18) with right hemisphere lesions participated in this study. The aetiology of the focal lesion was vascular in 31 participants (21 ischemic, 10 haemorrhagic) and neoplastic in two; the lesion site was assessed by CT or MRI scan.

Table XV. Demographic and neurological data of the 33 right-brain damaged patients.

	Sex/Age	Education (years)	Aetiology/ Lesion side	Neurological deficit M	SS	V	Associated deficit Anoso	Np	SP
P1	F/75	13	I / T	+	-	-	-	-	-
P2	M/74	12	I / Bg	-	-	-	-	-	-
P3	M/36	13	I / F-T-In	-	-	-	-	-	-
P4	M/38	13	I-H / T-P-In-Bg	+	-	-	-	-	-
P5	M/40	8	H / F-T-P	+	e	-	-	+	-
P6	F/65	13	I / Bg-ic	+	-	-	+M	-	-
P7	F/34	13	I / F-T-Bg	+	e	-	-	-	-
P8	M/46	17	I / Th-ic	+	e	-	-	-	-
P9	F/41	8	N / F	+	-	-	-	-	-
P10	F/52	8	I / Bg	+	-	-	-	-	-
P11	M/34	13	H / Bg-ic	+	+	-	+SS	-	-
P12	M/53	18	I / Sylvian region	-	e	+	-	-	-
P13	F/50	17	I-H / F	+	-	-	-	-	-
P14	M/48	11	I / F-T-In-bg	+	+	+	+SS-V	+	-
P15	F/58	5	H / F-T-In	+	+	+	+M-SS-V	-	-
P16	F/42	10	H / F-P	+	+	-	+SS	-	-
P17	F/44	13	I-H / Sylvian region	+	-	-	-	+	-
P18	F/44	2	H / F-T-P	+	+	-	+SS	-	-
P19	F/66	5	N / F-T	+	e	e	-	-	-
P20	F/38	13	I / F-T-O-In-ic	+	+	+	+SS-V	-	-
P21	M/51	10	H / F	-	-	-	-	+	-
P22	F/37	8	H / F-bg	+	+	+	-	-	-
P23	F/34	12	I-H / Sylvian region	+	+	+	+SS-V	-	-
P24	M/70	17	I / T-P-O	+	-	+	-	-	-
P25	F/29	11	H / s-cort	+	+	e	+SS	-	-
P26	M/71	18	I / Sylvian region	+	+	+	+SS	-	-
P27	M/54	17	I / bg-ic	+	+	+	+SS-V	+	-
P28	F/57	8	H / F-P-In-bg	+	+	e	+SS	-	-
P29	M/61	5	I / Sylvian region	-	-	+	-	-	-
P30	M/54	13	I / F-T-In	-	-	-	-	-	-
P31	F/73	5	H / F-s-cort	+	+	+	+SS-V	+	-
P32	F/50	13	I-H / In-bg	+	+	+	+M-SS-V	-	-
P33	M/60	8	I / T-O	-	-	+	-	-	-

I: ischemic lesion; H: haemorrhagic lesion; N: neoplastic lesion
F: frontal; P: parietal; T: temporal; O: occipital; In: insula; ic: internal capsule; bg: basal ganglia; s-cort: sub-cortical.
M: left motor deficit; SS: left somatosensory deficit; V: visual half-field deficit; e: extinction; ANOSO: anosognosia; Np: personal neglect; SP: somatoparaphrenia; +: presence of deficit; -: absence of deficit.

All participants were right-handed and had no history or neurological evidence of previous neurological impairments or psychiatric disorders. Global cognitive efficiency was assessed using the Mini Mental State Examination (Folstein et al., 1975) to exclude the presence of dementia. Contralesional motor, somato-sensory and visual-field defects were evaluated by the standard neurological examination; anosognosia for neurological deficits was also assessed (Bisiach et al., 1986). The patients' demographic and neurological data are reported in Table XV.

Twenty-three right-handed neurologically unimpaired participants, matched for age (mean: 55.5 years, SD: ± 16.1) and years of education (mean: 11.7 years, SD: ± 5), were tested as a control group (C).

Materials

The presence of USN was assessed by the following baseline evaluation:

- *Line bisection* (see Experiment 1).
- *Letter cancellation* (Diller and Weinberg, 1977) (see Experiment 1).
- *Star cancellation* (Wilson et al., 1987) (see Experiment 1).
- *Bell cancellation* (Gauthier et al., 1989). The patients' task was to cross out all of 35 bells (18 in the left-hand side and 17 in the right hand-side of the sheet), printed randomly on an A3 sheet, together with other shapes distracters. In neurologically unimpaired participants the maximum difference between omissions on the two sides of the sheet was four targets (Vallar, et al., 1994).
- *Sentence reading* (Zoccolotti and Judica, 1991). The participants' were given six sentences to read aloud, and the number of sentences read incorrectly was scored, in a range from 0 to 6, with reference to the "neglect point" scores (Ellis

et al., 1987). Neurologically unimpaired participants made no neglect errors in this test.

- *Drawing.* Copying of a complex figure with five elements (modified version of Gainotti et al., 1972), two daisies (Halligan and Marshall, 1993), one daisy, one butterfly; drawing from memory of a clock, one daisy, one butterfly.

The following tests were used in the experimental section, in which the participants were required to do a self-evaluation of their performance (see the Procedure below).

<u>Spatial neglect assessment</u>:

- *Line bisection* (see Experiment 1).
- *Star cancellation test* (modified version of the test by Wilson et al., 1987). The participants were instructed to draw a cross on each of the 60 small stars (30 in the left-hand side and 30 in the right hand-side of the sheet), printed randomly on an A4 sheet together with other distracters (big stars, letters, Italian words) (see the Scattered Star Test, in Experiment 2).
- *Copy of a complex drawing* (modified version of Gainotti et al., 1972) (see Experiment 1).
- *Drawing of a clock from memory* (see Experiment 1).
- *Sentence reading test*. Participants were given 12 sentences to read. Each sentence was printed horizontally in black uppercase letters (Arial, pt.14) in the centre of an A4 sheet and presented to the participants individually. The length of each string varied from 7 to 15 words.
- *Letter cancellation* (Diller and Weinberg, 1977) (see Experiment 1).

The mean bisection error for control participants was -0.64 mm (SD 3, range -6.2 / +5.8); the maximum difference between omission errors on the two sides of the sheet in the star cancellation task (omissions on the right – omissions on the left) was two and the maximum omission score in the complex drawing task was 0.5; the control group made no errors in the clock drawing and the sentence reading tasks. In the letter cancellation task the maximum difference between omission errors on the two sides of the sheet (omissions on the right – omissions on the left) was two, with reference to the available norms (Vallar et al., 1994).

<u>Cognitive test not assessing visuo-spatial functions</u>:

- *Phonemic verbal fluency* (Novelli et al., 1986) (see Experiment 1).

<u>Motor assessment</u>:

- *Direct movements of the upper limbs*. The participants were asked to raise their 1) right and 2) left arms, separately.
- *Unimanual tasks* (see Marcel et al., 2004). In this task the participants had to perform the following actions with one hand: 1) brush their teeth; 2) comb their hair; 3) drink a glass of water; 4) open a door; 5) sign their name.
- *Bimanual tasks* (see Marcel et al., 2004). In this task the participants had to perform the following actions with both hands: 1) shuffle a deck of cards; 2) separate two sheets glued in the center; 3) tie a bow on a cylindrical box; 4) put a key on a keychain; 5) open a tin.

Control participants executed these motor tasks perfectly.

Procedure

Seven days before the experimental sessions (-7D), neurological patients were given the neuropsychological battery in order to assess the presence of USN; they were classified as being affected by left USN syndrome (N+) if their performance on two of the target (letter, star and bell) cancellation tasks and/or on the line bisection test resulted pathological, with reference to the available norms or to the control group's performance. Participants who did not meet this criterion were classified as not affected by neglect (N-).

During the experiment, which was held during the following week, participants were asked to answer a series of questions, structured as follows:

- **Pre-test (PRE)**: *"In your present state, how well can you perform a task in which you have to… (e.g.: cross out all the small stars on the sheet)?"*.
- **Pre-test, implicit question (PRE-I)**: *"In your opinion, how well would a person in your present state be able to perform a task in which she has to … (e.g.: cross out all the small stars on the sheet)?"*.
- **Post-test (POST)**: *"How well have you performed this task, in which you had to… (e.g.: cross out all the small stars on the sheet)?"*.
- **Follow up after 24-hour (FU)**: *"In your present state, how well can you perform a task in which you have to… (e.g.: cross out all the small stars on the sheet)?"*.

This format was applied to all of the cognitive tests. In each spatial neglect assessment task when the examiner posed the first (PRE) question, s/he showed the test paper (or the first paper, in the line bisection and reading tasks) to the participants, in a central position, to facilitate their correct understanding of the type of task and evaluation of the spatial components. A supplementary condition was introduced for the letter cancellation task: after the POST self-evaluation, the examiner provided direct verbal feedback, informing the participants of the accuracy or inaccuracy of their performance, stating the approximate percentage of omission errors and specifying if they were located in the left-hand side of the sheet (for USN participants). Participants were then given an interfering verbal task for a few minutes and, subsequently, the following question was asked by the examiner:

- **After the examiner's feedback (PRE2)**: *"Imagine that you have to perform another task in which you have to mark all the Hs. How well could you do it in your present state?"*

Only a verbal example was provided in the phonemic fluency test.

Motor functions were evaluated only with the PRE, POST and FU questions. The following scores were assigned for execution of the motor functions: 0) perfect execution; 1) action performed with slowness and/or minimal clumsiness; 2) action performed with a great effort; 3) action impossible to perform.

Participants were given a vertical Likert scale on which to indicate their response (see Figure 19); the format used in this experiment was 18 cm in length overall, was centred on an A4 sheet, and was subdivided in seven points (indicated by coloured circles or squares), graduating in colour from the bottom (score = 1, red with a "minus" sign) to the top (score = 7, green with a "plus" sign), through white at the mid-point of the scale (score = 4). The examiner instructed the participants to indicate the point on the scale that best represented their ability to perform each task with the index finger of the right hand, considering that the bottom point represents *"Impossible to perform"*, the top *"Perfect performance"* and the intermediate point represents a neutral evaluation. Two test runs, in which the participants were asked how they would evaluate 1) losing or 2) winning a large sum of money, were made to help participants familiarize with the scale. Figure 19 shows the two versions of the Likert scale used.

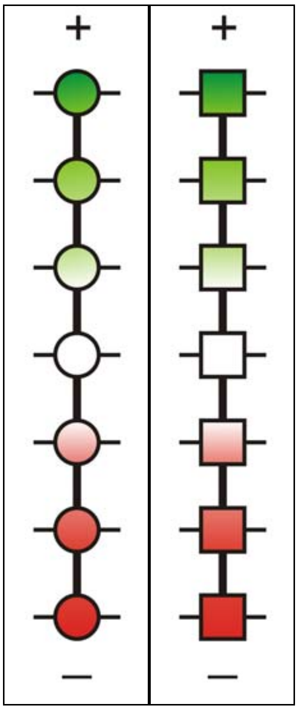


Figure 19: The two versions of Likert scale used: dots (on the left) and square (on the right).

The experiment schedule is summarized as follows:

- **Seven days prior to testing**: baseline evaluation to assess the presence of USN
- **Experimental phase: first day**
  - PRE evaluations for all neglect tests;

    PRE-I evaluations for all neglect tests;

    Neglect tests performed: line bisection, star cancellation, figure copying, drawing from memory, reading;

    POST evaluations after each neglect test performed;

    Letter cancellation task performed;

    POST evaluation of the letter cancellation task;

Verbal feedback on performance of the letter cancellation task;

Interference test;

PRE2 evaluation of the letter cancellation task.

- PRE evaluation of the verbal fluency test;

  PRE-I evaluation of the verbal fluency test;

  Verbal fluency test performed;

  POST evaluation of the verbal fluency test.

- PRE evaluations of all motor tasks;

  Execution of motor tasks;

  POST evaluations after each motor task.

- **Experimental phase: second day**
  - FU: PRE evaluation of neglect, verbal fluency and motor tasks.

Statistical analyses

Parametric analyses were conducted on the mean Likert evaluation scores of the groups to compare the participants' self-evaluations in different conditions. The relationships between self-evaluation and performances were explored with Pearson's correlation analysis.

- Results

Self-evaluation of neglect performances

The thirty-three neurological patients were divided in two groups, 18 without (18N-) and 15 with (15N+) USN, on the basis of the baseline assessments.

The week after the baseline assessment, the N+ group was divided into two subgroups for each experimental task, taking into account that neglect participants did not show neglect symptoms in every test. Therefore, for each task we classified N+ patients showing (N++) and not showing (N+-) neglect in that test, taking the control group's data or to the available normative values as a reference point. Subsequently, for each neglect task the self-evaluations of participants who performed the test well (C, N- and N+-) were compared to those of participants showing a defective performance (N++).

A series of ANOVA with 'Group' (four levels: C, N-, N+- and N++) as the 'between subjects' factor and 'Condition' (four levels: PRE, PRE-I, POST and FU) as the 'within subjects' factor were performed.

The analyses revealed that in the line bisection (N++ = 8) and the clock drawing (N++ = 5) tasks there were no significant differences between the groups (Line bisection: F = 1.9, d.f. = 3, p = n.s.; Clock drawing: F = 1.9, d.f. = 3, p = n.s.), between conditions (Line bisection: F = 1.3, d.f. = 3, p = n.s.; Clock drawing: F = 2.2, d.f. = 3, p = n.s.) or in interactions 'Group by Condition' (Line bisection: F = 0.8, d.f. = 9, p = n.s.; Clock drawing: F = 0.6, d.f. = 9, p = n.s.) (see Figures 20 and 21).

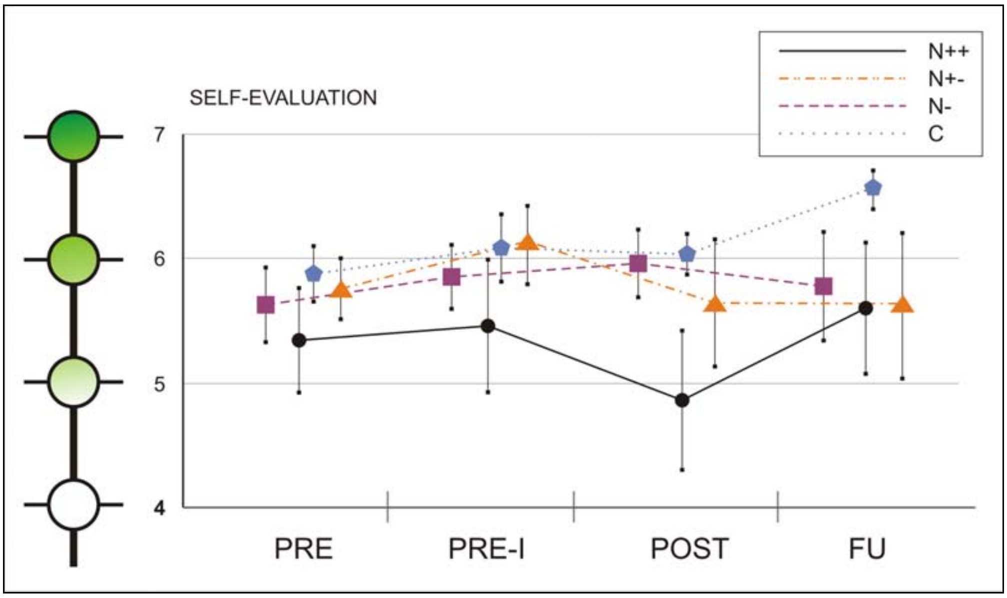


Figure 20: Evaluation scores (s.e.) in the line bisection task.

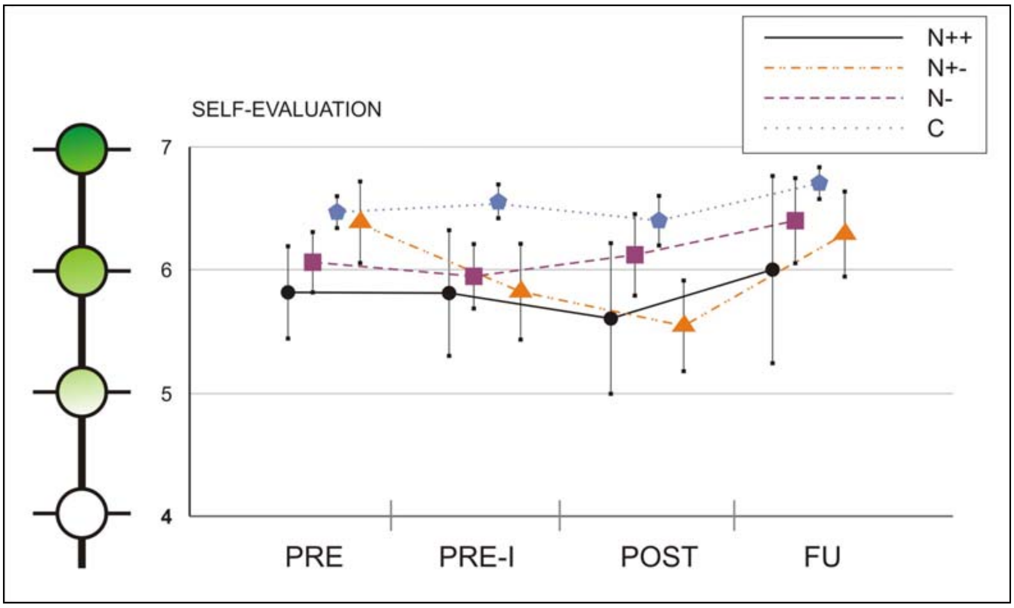


Figure 21: Evaluation scores (s.e.) in the drawing a clock from memory task.

In the sentence reading task (N++ = 11), the analysis showed that only the main factor 'Group' ($F = 9.7$, d.f. = 3, $p < 0.001$) reached significance, with none of the other factors or interactions being significant. A Newman-Keuls post hoc revealed that independently of the condition considered, N++ patients gave a lower evaluation of their performance than C ($p < 0.001$) and N- ($p < 0.01$) participants; however, the difference between N++ and N+- participants was not significant (see Figure 22).

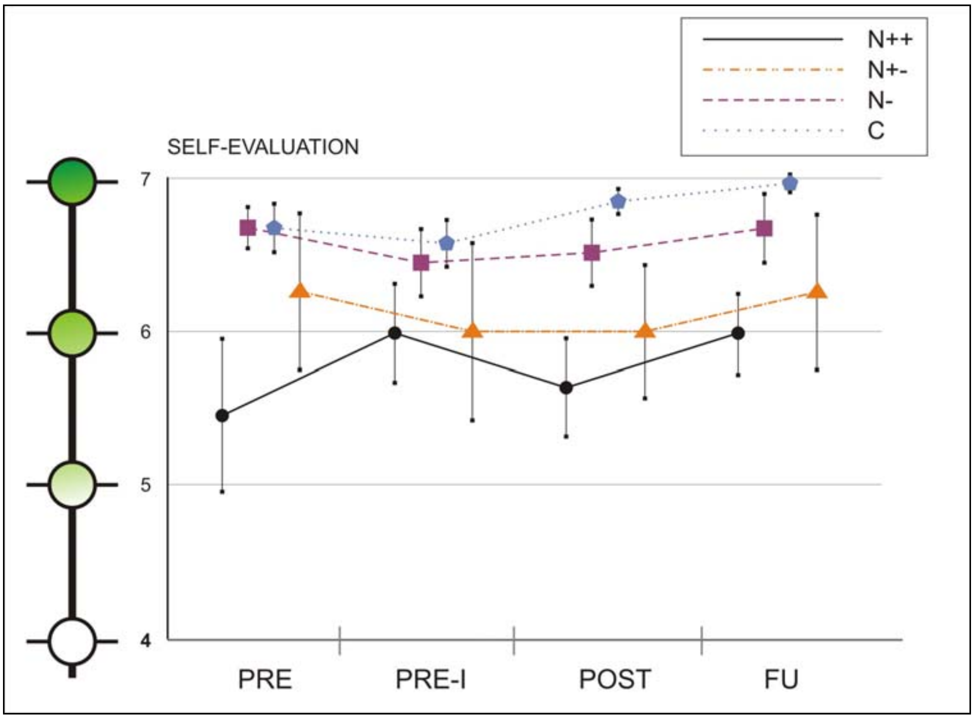


Figure 22: Evaluation scores (s.e.) in the sentence reading test.

A significant difference between groups ($F = 5.2$, d.f. = 3, $p = 0.003$) was found in the copying of a complex drawing task (N++ = 7); Newman-Keuls post hoc revealed that N++ patients gave a lower evaluation of their performance than C ($p < 0.001$), N- ($p < 0.01$) and N+- ($p < 0.01$) participants (see Figure 23).

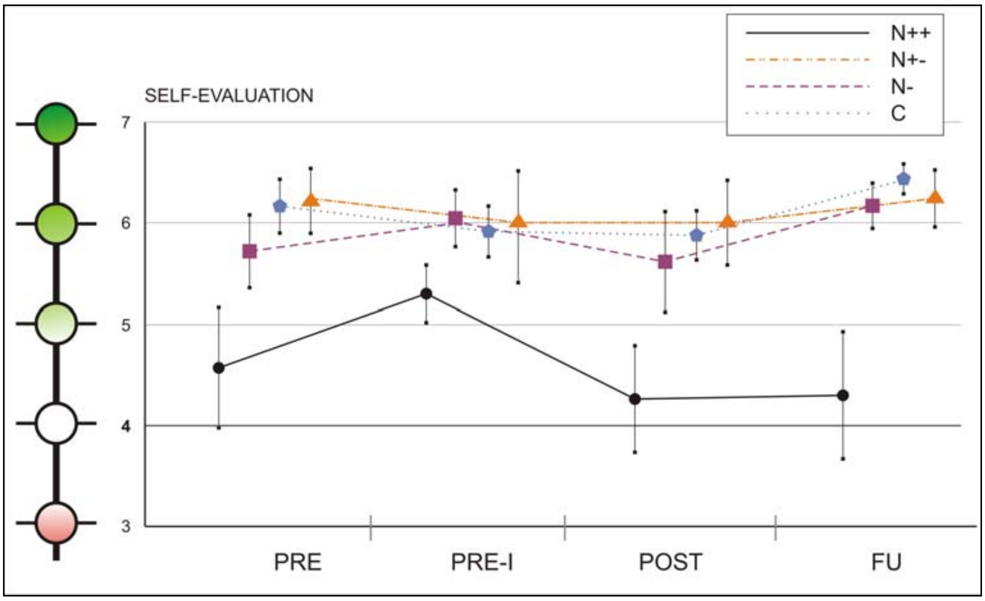


Figure 23: Evaluation scores (s.e.) in copying of a complex figure.

The influence of spatial constructional apraxia in the drawing task was evaluated performing an analysis of covariance. The following constructional apraxia (CA) scores were assigned to the drawings of the neurological participants: 2 points for each element correctly oriented and drawn; 1 point for each element distorted or badly oriented, but recognizable; 0 points for each element not recognizable and/or for the absence of the three-dimensional component in the "house" element. Possible differences in neglect severity (including N- and N+ participants) were removed by computing the proportion between the neglect and apraxia scores (CAp), with the CAp scores ranging from 0 (severe apraxia in all elements drawn) to 1 (no apraxia in the elements drawn). The CAp scores were then used as a covariate variable in the analysis of variance. A one-way analysis of covariance (ANCOVA) was performed on the PRE-test evaluation of the copying test, with 'Group' (three levels: N-, N+- and N++) as the 'between subjects' factor and the ‘CAp’ (the centred mean) scores as a linear and interactive covariate: the results showed that the main factor ‘Group’ was no longer significant (F = 2.1, d.f. = 2, p = n.s.), nor were the main factor ‘CAp’ (F = 1.9, d.f. = 2, p = n.s.) and the interaction ‘Group by CAp’ (F = 1, d.f. = 2, p = n.s.). A perusal of the individual CAp scores showed that N++ patients (mean CAp = 0.76) obtained more severe apraxic scores than N+- (mean CAp = 0.90) and N- (mean CAp = 0.94) neurological participants.

A significant difference between groups (F = 5.2, d.f. = 3, p = 0.003) was found in the star cancellation task (N++ = 7); Newman-Keuls post hoc revealed that N++ patients gave a lower evaluation of their performance than C (p < 0.001), N- (p < 0.001) and N+- (p < 0.01) participants (see Figure 24).

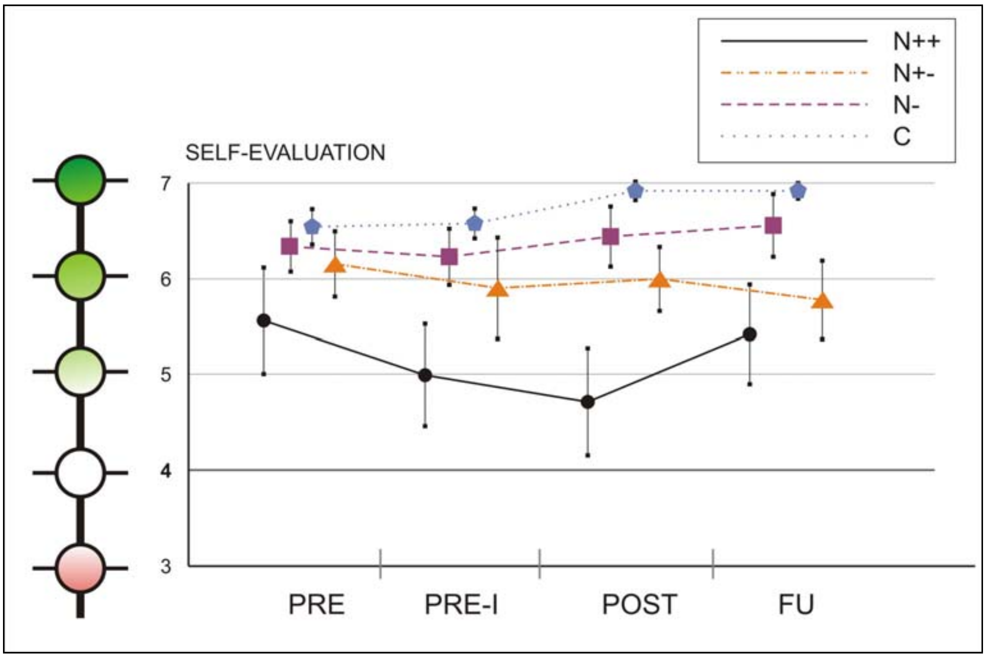


Figure 24: Evaluation scores (s.e.) in the star cancellation test.

Lastly an ANOVA with ‘Group’ (four levels: C, N-, N+- and N++) as the ‘between subjects’ factor and ‘Condition’ (five levels: PRE, PRE-I, POST, PRE2 and FU) as the 'within subjects' factor was run on the letter cancellation task (N++ = 7) evaluations (see Figure 25). The results were similar to those obtained in the star cancellation test: only the main factor 'Group' was significant (F = 18.2, d.f. = 3, $p < 0.001$), showing that N++ patients evaluated their performance differently compared to the other three groups (Newman-Keuls post hoc, with all $p < 0.001$).

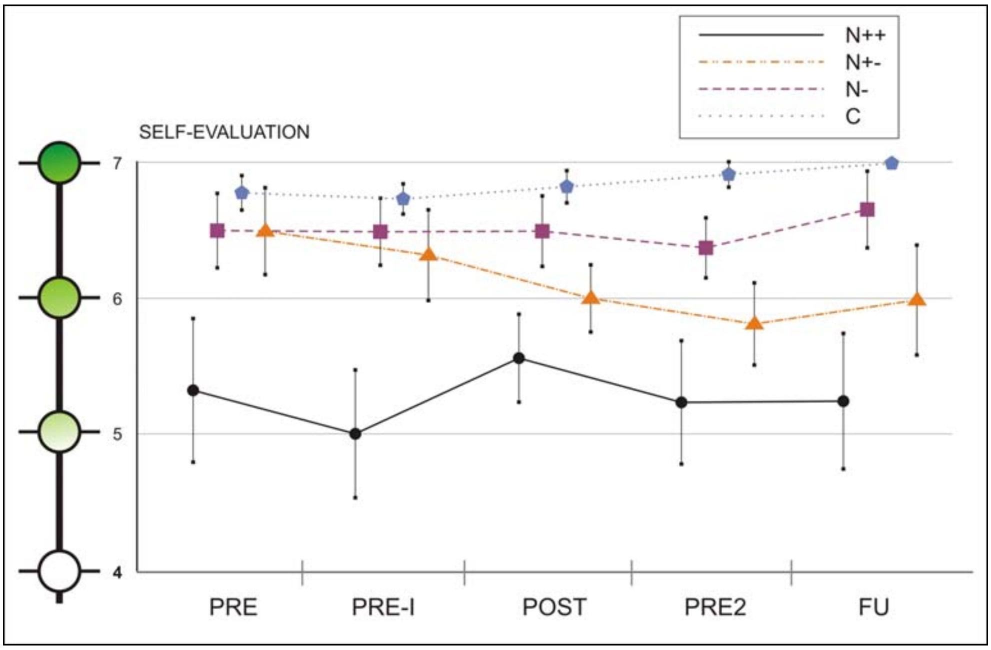


Figure 25: Evaluation scores (s.e.) in the letter cancellation test.

Self-evalutation of a non spatial cognitive task

Fifteen out of 18 N- participants (83.3%) obtained normal scores in the Phonemic verbal fluency test and were included in the analysis. The N+ group was subdivided into patients having (N++: n = 7; 46.7%) and not having (N+-: n = 8; 53.3%) a pathological performance (corresponding to PE = 0) in this cognitive task: both subgroups were included in the analysis. An ANOVA with 'Group' (four levels: C, N-, N+- and N++) as the ‘between subjects’ factor and ‘Condition’ (four levels: PRE, PRE-I, POST, and FU) as the ‘within subjects’ factor was run on the self-evaluation scores in the fluency test. Results showed the significance of the main factor ‘Condition’ ($F = 5.6$, d.f. = 3, $p = 0.001$): Newman-Keuls post hoc tests revealed that the mean POST evaluation was lower than the PRE ($p < 0.05$), PRE-I ($p < 0.05$) and FU ($p < 0.001$) scores. The main factor ‘Group’ was also significant ($F = 5.8$, d.f. = 3, $p = 0.002$); Newman-Keuls post hoc tests showed that the N++ group differed from the other three (all $p < 0.001$), indicating worse self-evaluations in participants with a pathological performance on this task (see Figure 26).

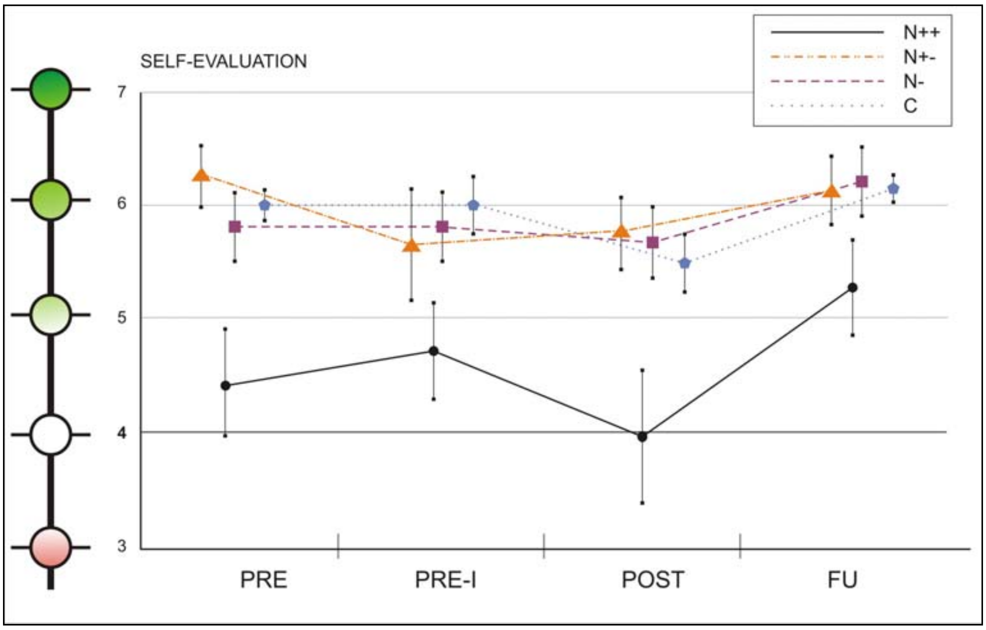


Figure 26: Evaluation scores (s.e.) in the Phonemic fluency task.

Correlation analyses

In neuropsychological (spatial and cognitive) tests in which a significant difference was found among the evaluations of the groups, particularly between evaluations made by neglect patients with (N++) or without (N+-) a defective neglect performance, further correlation analyses were performed.

A series of Pearson's correlation tests investigated the possible relationship between self-evaluations and real scores obtained by participants in the neglect group ($n = 15$). Since no effect of 'Condition' was found in the star and the letter cancellation task, only the correlations between the performance scores and the PRE evaluations were performed. The results showed no significant correlations between evaluation and performance in the star ($r = 0.188$, p = n.s.) and letter ($r = 0.093$, p = n.s.) cancellation tasks.

Both assessments were considered in the Fluency task, in which a significant difference between POST and PRE evaluations were found. The correlation was positive and significant ($r = 0.532$, $p = 0.041$) between the PRE evaluations and the raw scores (i.e., the number of words produced in one minute), but not significant when the PRE evaluations were compared to the corrected scores (adjusted for age and education; $r = 0.357$, p = n.s.) or to the equivalent scores ($r = 0.401$, p = n.s.). When the POST evaluations were included in the analyses, no significant results were found with raw ($r = 0.405$, p = n.s.) and equivalent ($r = 0.474$, p = n.s.) scores, but there was a slightly positive correlation between the POST evaluations and the fluency correct scores ($r = 0.509$, $p = 0.053$).

Self-evaluation of motor performances

- <u>Direct movements of the upper limbs</u>

  Control participants performed all tasks perfectly (execution score = 0), while N- and N+ participants showed various degrees of impairment in their motor performances. Preliminary analyses demonstrated that there was no difference between the evaluation scores of the tasks executed perfectly (score = 0) and with slowness and/or minimal clumsiness (score = 1); the same preliminary results were found when comparing the evaluation of tasks executed with great effort (score = 2) or not performed at all (score = 3). Therefore a mean evaluation score of the tasks well done (scores = 0 / 1) and of those badly done or not done at all (scores = 2 / 3) was computed for each neurological participant.

  The self-evaluations of the groups were compared for the well executed direct movement tasks (DM0-1). An ANOVA with ‘Group’ (three levels: C, N-, N+) as the ‘between subjects’ factor and ‘Condition’ (three levels: PRE, POST and FU) as the ‘within subjects’ factor was executed. The main factor ‘Group’ was significant ($F = 8.7$, d.f. = 2, $p = 0.001$): Newman-Keuls post hoc tests revealed that, independently of the condition, the mean evaluations of the N- ($M = 6.45$) and N+ ($M = 6.40$) patients differed from those of the controls ($M = 6.98$; all $p < 0.001$). The main factor ‘Condition’ was also significant ($F = 3.4$, d.f. = 2, $p = 0.039$), indicating that on average the Follow Up ($M = 6.73$) had higher mean scores than the PRE ($M = 6.54$) evaluations ($p < 0.05$).

The self-evaluations of neurological participants for the badly done/not done direct movements (DM2-3) were compared to those of the control group, who executed the motor actions perfectly.

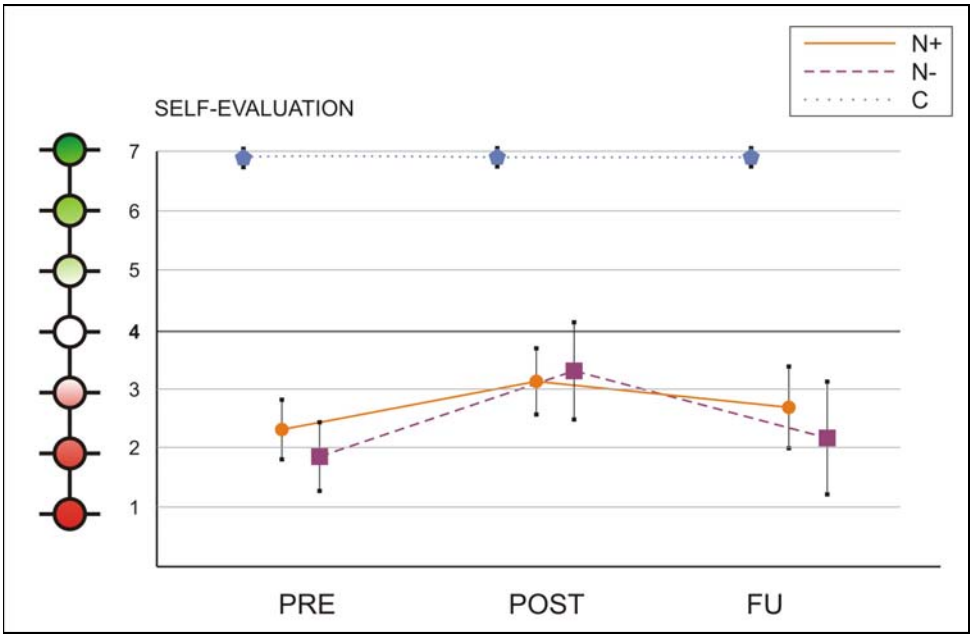


Figure 27: Evaluation scores (s.e.) in the DM tasks with patients' execution scores rated as 2/3 and C participants performing well on all tasks.

Another ANOVA with 'Group' (three levels: C, N-, N+) as the 'between subjects' factor and 'Condition' (three levels: PRE, POST and FU) as the 'within subjects' factor was executed. Results showed that both main factors were significant ('Group': $F = 82.6$, d.f. = 2, $p < 0.001$; 'Condition': $F = 17.3$, d.f. = 2, $p < 0.001$), revealing that the N- ($M = 2.48$) and N+ ($M = 2.76$) participants evaluated their motor performances negatively and less favourably than the control participants (all $p < 0.001$); moreover data indicated that the POST ($M = 5.47$) mean evaluations were better overall than the PRE ($M = 5$; $p < 0.001$) and

FU ($M = 5.12$; $p < 0.05$) mean scores. The interaction 'Group by Condition' was also significant ($F = 6.9$, d.f. = 4, $p < 0.001$); Newman-Keuls post hoc tests showed that all evaluations were worse in N- participants (M PRE: 1.86; M POST: 3.43; M FU: 2.14) and N+ (M PRE: 2.39; M POST: 3.22; M FU: 2.67) compared to controls (PRE, POST and FU: $M = 6.98$; all $p < 0.001$), with no significant differences between the N- and N+ mean evaluation scores. Moreover significant differences were found between POST and PRE and between POST and FU scores both for N- (POST vs. PRE: $p < 0.001$; POST vs. FU: $p < 0.001$) and N+ (POST vs. PRE: $p < 0.01$; POST vs. FU: $p < 0.05$) (see Figure 27).

- <u>Unimanual tasks</u>

Both the control group and the neurological participants performed well (score = 0) on these motor tasks. An ANOVA with 'Group' (three levels: C, N-, N+) as the 'between subjects' factor and 'Condition' (three levels: PRE, POST and FU) as the 'within subjects' factor was executed on the mean self evaluations. The main factor 'Group' was significant ($F = 15.4$, d.f. = 2, $p < 0.001$); Newman-Keuls post hoc tests revealed that N+ patients ($M = 6.16$) evaluated their performances as being worse than those of N- ($M = 6.68$) and C ($M = 6.98$) participants (all $p < 0.001$); moreover N- participants also evaluated their performances as being worse than C participants ($p < 0.05$). The main factor 'Condition' was significant ($F = 16.3$, d.f. = 2, $p < 0.001$); Newman-Keuls post hoc tests indicated that PRE mean evaluations ($M = 6.52$) were lower than the POST ($M = 6.73$) and FU ($M = 6.73$) ones (all $p < 0.001$). Finally, the interaction ‘Group by Condition’ was also significant ($F = 5.4$, d.f. = 4, $p < 0.001$); Newman-Keuls post hoc tests showed that N+ participants attributed lower mean scores to their performance in the PRE evaluation phase ($M = 5.77$) compared to the N- ($M = 6.57$; $p < 0.05$) and C ($M = 6.97$; $p < 0.001$) participants; on the contrary POST (M C: 6.97; M N+: 6.33; M N-: 6.76) and FU (M C: 6.98; M N+: 6.38; M N-: 6.71) evaluations were similar in the three groups. In the N- group the PRE mean evaluations were lower and significantly different from the POST ($p < 0.01$) and FU ($p < 0.01$) ones; in the N+ group there was a significant difference between the PRE and POST ($p < 0.001$), the PRE and FU ($p < 0.001$) and also the POST and FU ($p < 0.05$) mean evaluation scores.

- <u>Bimanual tasks</u>

Control participants performed all bimanual tasks perfectly (execution score = 0), while N- and N+ participants showed varying degrees of impairment in their motor performances. A preliminary analysis showed that the evaluation scores of the tasks executed perfectly (score = 0) and with slowness and/or minimal clumsiness (score = 1) were similar: therefore, a mean evaluation score of the well executed tasks (scores = 0 / 1) was computed for each neurological participant. The preliminary analysis comparing the evaluation scores of tasks performed with great effort (score = 2) or not executed (score = 3) revealed significant differences: consequently the two results were maintained separate and a mean evaluation score of the poorly executed tasks (score = 2) and tasks not attempted (score = 3) was computed for each neurological participant.

A series of ANOVAs with ‘Group’ (three levels: C, N-, N+) as the ‘between subjects’ factor and ‘Condition’ (three levels: PRE, POST and FU) as the ‘within subjects’ factor was performed. The significance of the main factor ‘Group’ ($F = 10.3$, d.f. = 2, $p < 0.001$) emerged for the well executed bimanual tasks (BIM0-1); Newman-Keuls post hoc tests indicated that the mean evaluations of the control group ($M = 6.79$) differed from those of N- ($M = 5.29$; $p < 0.01$) and N+ ($M = 5.94$; $p < 0.05$) participants. The main factor ‘Condition’ was also significant ($F = 9.1$, d.f. = 2, $p < 0.001$), indicating that overall the PRE ($M = 5.94$) differed from the POST ($M = 6.36$; $p < 0.05$) and FU ($M = 6.33$; $p < 0.01$) scores. Finally, the interaction ‘Condition by Group’ was significant ($F = 2.7$, d.f. = 4, $p = 0.038$); Newman-Keuls post hoc tests revealed a significant difference in the N+ group between PRE ($M = 5.14$) and POST ($M = 6.32$; $p < 0.01$), as well as between PRE and FU ($M = 6.36$; $p < 0.001$) scores.

With regard to the bimanual tasks poorly executed by neurological participants (BIM2), the analysis revealed the significance of the main factor ‘Group’ ($F = 45.4$, d.f. = 2, $p < 0.001$), with the N- ($M = 3.67$) and N+ ($M = 3.92$) participants evaluating their bimanual performances as being worse than that of the control participants ($M = 6.79$), who were able to perform these tasks correctly (all $p < 0.001$). The main factor ‘Condition’ was also significant ($F = 6.8$, d.f. = 2, $p = 0.002$); Newman-Keuls post hoc tests indicated that the PRE scores ($M = 5.37$) were lower than the POST ($M = 5.89$) and FU ($M = 5.73$) ones (all $p < 0.05$).

Figure 28 shows the self-evaluation of the bimanual tasks that were not performed by neurological participants (BIM3). The ANOVA indicated a significant difference among the groups (F = 113.9, d.f. = 2, $p < 0.001$), with N- (M = 2.62) and N+ (M = 2.90) evaluations being significantly different from those of controls (M = 6.79; all $p < 0.001$). The main factor ‘Condition’ was significant (F = 8, d.f. = 2, $p < 0.001$), with the POST (M = 4.30) mean evaluations being lower than the PRE (M = 4.68; $p < 0.01$) and FU (M = 4.54; $p < 0.05$) ones. The interaction ‘Group by Condition’ was significant (F = 2.6, d.f. = 4, p = 0.041); Newman-Keuls post hoc tests showed that the N- (M PRE: 2.73; M POST: 1.47; M FU: 2.18) and N+ (M PRE: 3.04; M POST: 2.75; M FU: 2.92) mean evaluations differed from those of the control participants (M PRE: 6.72; M POST: 6.82; M FU: 6.83; all $p < 0.001$) but not from the other neurological participants. Moreover the POST evaluations (M = 1.47) were significantly lower in the N- group than the PRE (M = 2.73; $p < 0.001$) and FU (M = 2.18; $p < 0.01$) scores.

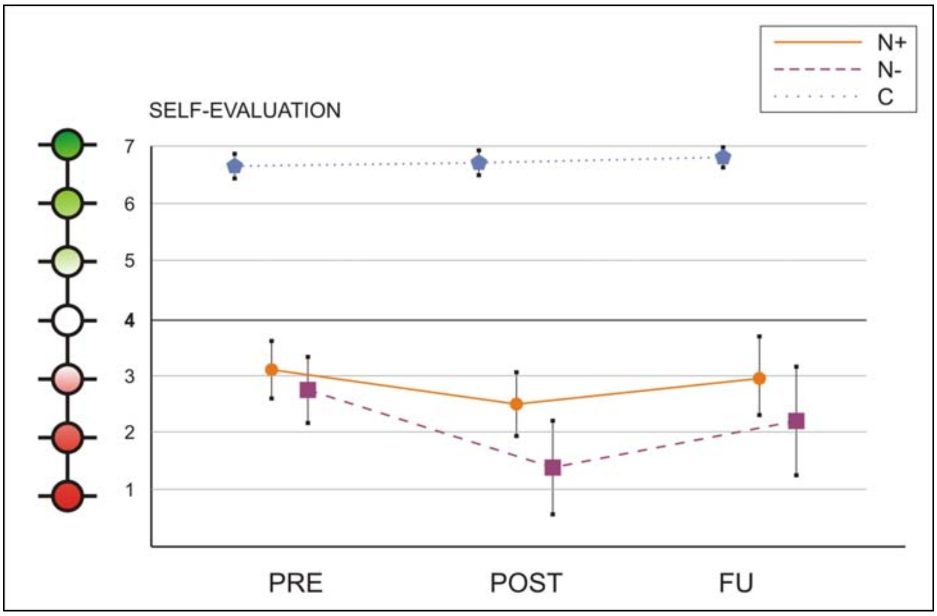


Figure 28: Evaluation scores (s.e.) in the BIM tasks with patients’ mean execution scores rated as ‘3’ and C participants performing well on all tasks.

- Conclusion

Right-brain-damaged patients with left USN may be aware of their spatial inattention, at least to a partial extent. Different tasks evoke different degrees of awareness: line bisection and representational tests do not elicit any awareness, while target cancellation tasks are the most sensitive, with the evaluation scores of N++ patients being significantly lower than those of the other groups of brain-damaged patients (N-, N+-) and neurologically unimpaired participants (C). The results of the copying and reading tests are less clear. In the copying task concomitant constructional apraxia disorders influence the patients' evaluation of their performance: when the constructional apraxia scores are introduced in the analysis as covariate, the differences between N++ patients and the other groups (N-, N+- and C) are no longer detected. In the reading task the evaluation of dyslexic and non-dyslexic neglect patients is comparable: a specific awareness for the reading disorder is not recorded. No modulations are found for USN tasks' evaluations.

Neurological participants evaluate their performance coherently in a cognitive test not measuring spatial attention and representation (i.e., a verbal fluency test): participants obtaining a pathological score consider their results as being worse than participants performing the Phonemic fluency task within the normal range of scores. Moreover, changes in performance evaluation triggered by the execution of the test are found in all participants, who evaluate their results negatively in the POST condition.

Correlation analyses in USN patients fail to reveal any relationship between evaluations made before the execution of the cancellation task and feedback on the performance scores. A slightly positive correlation between the PRE evaluations and the number of words generated is found in the phonemic test.

Brain-damaged patients (with or without USN) are seen to be aware of the motor disturbances consequent to the brain lesion. When unable to perform a task (either a direct movement or a bimanual test), patients evaluate their performance negatively and as significantly different from that of control participants. When neurological participants estimate direct movements of the upper limbs, the POST evaluations are better than the PRE and FU ones, although they always fall in the negative part of the Likert scale. Moreover, N- (but not N+) participants evaluate their performance after (POST) the execution of bimanual tasks as being worse than in the PRE and FU conditions. When a bimanual task is performed with difficulty, brain-damaged participants are able to modify their initial negative evaluation after executing the motor task, even if their self-assessment remains significantly lower than that of control participants. Finally, brain-damaged patients who execute a motor task appropriately underestimate their performance compared to the control group: in some cases their evaluation returns into the range of neurologically unimpaired participants after task execution.

GENERAL DISCUSSION

The experiments and the review reported in this doctoral thesis investigate a number of different aspects of monitoring disorders in patients with USN. The first section focuses on the occurrence and characteristics of productive symptoms, particularly perseveration in target cancellation tasks, and their association with other positive (e.g., perseveration in drawing tasks, reading errors in neglect dyslexia), and negative (e.g., omission errors) symptoms. The second section analyzes unawareness of USN symptoms, and their relationships with awareness for different cognitive and/or motor performances.

Perseveration and executive, mnestic and attentional deficits

A first result is that right-brain-damaged patients with left USN and perseverative behaviour do not show symptoms indicating an associated dysexecutive syndrome (Luria, 1966; Stuss and Benson, 1986): in Experiment 1 perseverating patients are not impaired in a subset of tasks (Phonemic verbal fluency, Stroop colour-word Interference test and Weigl's sorting test), assessing executive "frontal" functions. Perseverating patients obtain scores significantly lower than non-perseverating participants only in the Semantic fluency task. However, a perusal of the individual scores shows that only one out of the eight N+P+ patients has a pathological performance in this test and, remarkably, one N+P+ patient obtains the maximum equivalent score. These dissociations indicate that perseverating patients are not globally compromised in the Semantic fluency test, weakening the hypothesis of an association between these two impairments[1]. In line with our findings, a previous study (Nys et al., 2006) did not find any significant correlation between scores in verbal executive tasks (letter fluency, visual elevator) and perseveration responses in patients with contralesional USN.

Experiment 1 also indicates that productive phenomena in target cancellation tasks are not related to a deficit of visuo-spatial short-term memory. Compared with brain-damaged patients without USN, neglect patients without perseveration are impaired in the standard Corsi's block tapping task, while the memory scores of perseverating patients are similar to those of the other neurological groups (N- and N+P-). A deficit of spatial working memory does not appear then to be a necessary condition for perseveration to occur. Furthermore, compared with neurologically unimpaired control participants, patients with left USN are impaired in the vertical version of the Corsi's task but no difference is found among right-brain-damaged patients (N-, N+P- and N+P+). In a previous study (Nys et al., 2006) left- and right-brain-damaged patients with contralesional neglect and general inattention exhibited a defective performance in the Corsi's block tapping task, compared with control participants; however the relationships between perseveration responses and deficits of visuo-spatial short-term memory were not further explored. Overall, while deficits of spatial working memory may be associated with left USN, shape certain manifestations of the neglect syndrome, and possibly exacerbate the patterns of impairments (Wojciulik et al., 2004; Malhotra et

[1] It should be also noted that, while previous investigations suggest that damage to the frontal lobe is associated with perseveration, particularly in the right hemisphere (Na et al., 1999; Rusconi et al., 2002; Nys et al., 2006), defective semantic fluency appears to be more related to damage to the left temporal lobe than to the frontal lobe (Troyer et al., 1998; Henry and Crawford, 2004), although the issue is controversial (e.g., Baldo and Shimamura, 1998).

al., 2004), they do not appear to be a very relevant factor in eliciting perseveration responses. The behaviour of right brain-damaged patient G. K. studied by Husain et al. in 2001, who had suffered a parietal infarct sparing the frontal lobe, showed left spatial neglect and an associated deficit of visuo-spatial working memory, is relevant for this issue. In line with these conclusions, G. K. had a disproportionately high rate of re-fixations (i.e., the tendency shown by patients to revisit previously searched locations) and re-clicks (i.e., pressing a button in response to a target, erroneously judged as a new discovery) in visual search tasks, but did not make perseverative errors in paper-and-pencil cancellation tasks. Indeed, these two types of manifestations should be differentiated: the task used to reveal "revisiting" and "re-clickings" differs from the cancellation tasks in that in the former no visible marks are left on visited (and possibly on revisited and re-clicked) targets, while in the latter the repeated marks remain visible, suggesting that "revisiting" and "re-clickings", on the one hand, and perseveration in paper-and-pencil cancellation tasks, on the other, are largely independent disorders. Finally, in the original studies with the Corsi Block tapping test, showing an impairment of visuo-spatial short-term memory in both left- and right-brain-damaged patients with visual field deficits and posterior lesions, care was taken to include only patients who were able to explore the complete block tapping display, i.e., who did not exhibit contralesional USN in that particular task (De Renzi et al., 1977; De Renzi and Nichelli, 1975).

Another cognitive function that potentially influences the presence and severity of perseverative manifestations in target cancellation tests is the capacity to allocate attentional resources to different characteristics of the task at the same time. This aspect is investigated in Experiment 2. No differences are found between the Dual task performances of USN perseverating and non-perseverating patients, while perseverating patients' scores on two tasks carried out simultaneously are lower than those of neurologically unimpaired participants. It is well known that right-brain-damaged patients may present non-lateralized attentional disorders, such as sustained and divided attention deficits (Coslett et al., 1987; Wilkins et al., 1987; Hjaltason et al., 1996; Farnè et al., 2004; Husain and Nachev, 2007), but this does not appear to be crucial for recurrent motor perseveration to occur.

In conclusion, these findings indicate that the ability of right-brain-damaged patients showing perseverative motor behaviours to perform multi-task tests (i.e., a number of tasks simultaneously) may be reduced (Experiment 2), although these patients are not globally impaired in their executive functions (Nys et al., 2006) and visuo-spatial short-term memory (Experiment 1). However this deficit should be ascribed to characteristics other than the presence of productive phenomena, as indicated by the absence of differences in divided attentional scores between perseverating and non-perseverating patients.

Perseveration and omission errors

Neither Experiment 1 nor Experiment 2 show significant correlations between omission and perseveration errors, as found in previous reports (Rusconi et al., 2002; Vallar et al., 2006; Pia et al., 2009b). Other studies report such correlations as significant (Nys et al., 2006), or have computed them on the study by Rusconi et al. (2002; see the analysis in Toraldo et al., 2005). These significant correlations, however, make use of percentage perseveration indexes that relate omission and perseveration errors (e.g., number of targets with perseverative marks / numbers of targets cancelled x 100 as in Na et al., 1999; Nys et al., 2006), which are in turn correlated with omission errors. Interestingly, Nys et al. (2006), who made both types of correlations, found significant effects when the perseveration term was the percentage mentioned earlier (see Na et al., 1999), but not when the total number of re-markings was used (see Rusconi et al., 2002). In Experiment 1, using the perseveration score (Rusconi et al., 2002), our perseveration index and Na's (1999) perseveration percentage, no significant correlations are found between omission and perseveration; in Experiment 2 the same result is obtained using only the perseveration index, which appears to be the most sensitive tool for detecting the presence and severity of recurrent perseveration. The independence of omission and perseveration errors is definitely illustrated by the behaviour of a number of patients whose performance is summarised in Table II. N+P- patient P13 exhibits a severe USN in cancellation tasks, without any evidence of perseveration, while patient N+P+ P18 shows severe perseveration in the star cancellation task, in which, however, he makes no omission errors.

Another important aspect, examined in Experiments 1 and 2, is the contribution of different types of cancellation tasks in eliciting perseveration behaviour. We used three cancellation tests in Experiment 1 to assess perseveration, compared to previous studies in which only a single task [line (Na et al., 1999), circle (Rusconi et al., 2002), star (Nys et al., 2006)], or the experimental manipulation of one task [star (Manly et al., 2002), lines (Bottini and Toraldo, 2003; Toraldo et al., 2005; Kim et al., 2009)] was used. Results demonstrate that neglect patients make more perseveration errors in star than in letter and line cancellations, whereas star and letter tests elicit comparable omission percentage scores. These findings i) provide further evidence to the effect that the mechanisms underlying omission (i.e., neglect) vs. perseveration errors are different, and ii) suggest the possibility that a scattered disposition of stimuli (a salient characteristic of the star but not of the letter cancellation tasks) may contribute to the patients' making more perseveration errors. The results of Experiment 2 corroborate the second point, showing that more perseveration errors are recorded when stimuli are scattered randomly over the paper. In line with these findings, a recent study (Pia et al., 2009b) also found a small number of neglect patients perseverating when the stimuli are neatly organized in rows, although the types of cancellation task compared (scattered lines and ellipses versus organized letters) differed from the ones we used. These results, which are also in line with previous studies on disorganized and unsystematic search patterns in neglect patients (Mark et al., 2004; Butler et al., 2009), suggest that re-marking target behaviour may be exacerbated by the difficulty of planning an efficient research strategy, which may be greater when stimuli are scattered. However, as demonstrated in Experiment 2, the higher attentional demands required by the complex organization of the visual search do not appear to be related to a general deficit of divided attentional resources, as indicated by the patients' pattern of performance in the Dual Task. Moreover, the results of Experiment 2 also reveal that the type of target to be cancelled is an important element to be taken into account in the production of recurrent perseveration. The scattered version of the letter cancellation task triggers less perseveration than the scattered version of the star task; hence it is important to evaluate a possible contribution of non-verbal stimuli in eliciting perseveration. The perseveration index is greater in the non-verbal vs. the verbal cancellation task, but only in the presence of scattered stimuli; when the stimuli are arranged in an orderly fashion, no differences between letter and star perseveration are found. This result indicates that when a more demanding task (i.e., scattered visual search) is required, the verbal target may reduce perseverative motor behaviour (or the non-verbal task increase it). In the recent work by Pia and colleagues (2009b), discussed above, all USN patients exhibited motor perseveration in the ellipse and line scattered cancellation tests, with only half of them perseverating in the letter cancellation task (but only the in-row target disposition was evaluated).

Complementary to these results, Experiment 2 also provides data of interest concerning the relationship between target disposition and frequency of the “negative” USN manifestations in target cancellation: our results reveal that neglect patients globally make more omissions when the test includes scattered stimuli. Experiment 2 examines four target cancellation conditions, assessing USN in both scattered and arranged versions of the star and letter cancellation tasks. Interestingly, the omission errors produced in the scattered-star versus letters-in-rows tests are comparable (scattered stars Experiment 2: 26.17%; letters in rows Experiment 2: 27.31%) confirming the results of Experiment 1, in which only these two tests are used, and similar omission percent scores are recorded. The star task may be globally easier than the letter cancellation task (dimension of area to be explored: A4 vs. A3; number of targets: 60 vs. 104): therefore, the scattered version of the less complex spatial test may elicit the same quantity of negative errors with respect to a task in which the area to be explored is more extensive, with more targets to be crossed out, but where the spatial organization of the stimuli facilitates research strategies (see the omission scores of scattered stars vs. letters in rows in both Experiment 1 and 2). However, this alleged greater simplicity of the star test does not impact on productive manifestations, as the great number of perseveration in the scattered version of this test reveals (Experiment 2).

Moreover, the percentage omission scores in the four tests provide some indication that more omissions may be elicited in the letter compared to the star cancellation tasks (trend which emerges, though not significant, from the statistical analyses, see also Figure 8)[2].

Taking the results concerning omission and perseveration errors together, in Experiment 2 we find that a scattered arrangement of the stimuli exacerbates both pathological manifestations, probably due to the difficulty encountered by neglect patients in formulating visual search strategies (Butler et al., 2009), that increase the ipsilesional attentional bias and, in patients with defective motor behaviour inhibition, elicits more recurrent perseveration marks. Nevertheless the target typology modulates “negative” and “positive” symptoms differently: patients perseverate more when stars are cancelled, while the omission percentage scores are statistically similar on letter and star targets; in fact, if there is a difference in omissions, it tends to be that letters elicit more neglect errors. This evidence further stresses the hypothesis that omissions and perseveration are independent, although frequently associated, phenomena (Na et al., 1999; Rusconi et al., 2002).

Patients showing recurrent perseveration in cancellation tasks also perseverate in drawing tasks, especially in drawing from memory (see Experiment 1). This finding is in line with the available clinical evidence, based on qualitative observations (Critchley, 1953; Gainotti and Tiacci, 1971), and suggests that perseveration in spatial neglect is a pathological phenomenon that may be found in different visuo-motor tasks with specific

[2] Previous studies recorded more neglect errors for verbal stimuli in visual (Heilman and Watson, 1978) and auditory (Eramudugolla et al., 2007) tasks, suggesting that a verbal target can activate the intact left hemisphere, increasing the attentional bias towards the right hemi-space (Kinsbourne, 1993). However support for this hypothesis was not provided by other investigators (Caplan, 1985; Gainotti et al., 2002; Weintraub and Mesulam, 1988).

features, such as cancellation and drawing. As shown in Figure 5, the memory condition evokes more perseveration errors in perseverating patients, with non-perseverating participants making no errors in drawing from memory. This task appears to be a sensitive tool for eliciting perseveration, possibly due to its additional cognitive demands (i.e., the retrieving and setting up of a representation of the object to be drawn), the lack of the graphic constraints posed by the model, and the obligatory continual comparison, when drawing, between the object to be drawn and its internal representation. However, the patterns of perseveration in the individual patients suggest a double dissociation between the copy and the memory conditions, with some patients showing more perseveration in copying, and others in drawing from memory. Similarly, patients with left neglect may make omission errors when copying, but not in drawing from memory (Halligan et al., 2003; see also Halligan and Marshall, 1997; Halligan and Marshall, 2001). Furthermore, even if no previous evidence is on record, the severity of perseveration errors may be as variable as that of spatial neglect itself, with patients showing remission periods, when tested at weekly intervals (Small and Ellis, 1994), but also variability of performance across the different trials of a single testing session (Anderson et al., 2000). The dissociation between omission and perseveration errors mentioned above is also apparent in some of the drawings shown in Figure 6. Patient P17 added a pine tree, the roots of the three pine trees, and a grass meadow below them. The USN of this patient, which emerged in the drawing task, was mild, involving a different part of the complex picture, with object-based (Gainotti et al., 1972; Halligan and Marshall, 1993) omissions on the left-hand side of the house, which was also spatially distorted. Patient P21 showed no USN in the clock drawing, but re-markings are apparent on both sides of the display.

These data indicate that perseveration emerges in tasks involving a complex set of visuo-motor skills: in line with this finding, our results contribute to the previous evidence indicating that re-markings and gratuitous productions in line bisection, a task that requires neither sequential actions nor target/non target discrimination and does not involve the monitoring of previously cancelled targets, are a rarely observed pathological phenomenon in right-brain-damaged patients with severe left spatial neglect (Bottini et al., 2002, patient FB; Evyapan and Kumral, 2001, three patients; Cantagallo and Della Sala, 1998, patient FF who suffered a right-sided temporo-parietal stroke).

Our results shed light on the available proposed interpretations of graphic perseveration in the USN syndrome. First, perseveration behaviour in right-brain-damaged patients with left neglect is not confined to cancellation tasks; however it cannot be traced back to a more general cognitive disorder, particularly of executive and spatial short-term memory functions. Interpretations in terms of allochiria (Manly et al., 2002; Bottini and Toraldo, 2003; Toraldo et al., 2005), namely the contra-ipsilesional transposition of part of the targets in the cancellation tasks, and of component parts of drawings, do not provide a complete account of the perseveration phenomena, even though allochiria may contribute to ipsilesional re-markings, and, more generally, to drawing in the ipsilesional side of the display (Grossi et al., 1995). More specifically, the patients' performance in drawings, such as those shown in Figure 6, does not reflect contra-ipsilesional transpositions. The addition, both contralesionally and ipsilesionally, of superfluous elements (Figure 6: A-P17) cannot be accounted for in terms of contra-ipsilesional allochiria. A similar argument applies to the bilateral re-markings and the contralesional repeated hours on the clock face drawn by patient B-P21 (Figure 6).

Moreover these observations are not compatible with general interpretations in terms of contralesional directional hypokinesia (Heilman et al., 1985; Heilman et al., 2003), namely the reluctance to plan and execute movements towards the neglected side inducing ipsilesional perseveration (see a discussion of this hypothesis in Toraldo et al., 2005). Furthermore, a group study by Nys et al. (2006) reported perseveration of comparable severity in both left- and right-brain-damaged patients, but re-markings show a contra-ipsilesional gradient only in the latter group, being higher in the right-sided positions, as found in previous studies (Na et al., 1999; Rusconi et al., 2002). To summarise, directional hypokinesia, as allochiria, may be a pathological factor contributing to perseveration, but does not appear sufficient to provide a complete account of the phenomenon.

Perseveration behaviour in patients with contralesional USN may be interpreted in the framework of a two-factor theory, which can be more or less brain-based. In the past a functional two-factor theory was proposed to account for anosognosia and other delusions (Davies et al., 2005). Denny-Brown’s (1958, p. 22) distinction between two impairments of exploratory behaviour, “frontal or magnetic apraxia” and “parietal or repellent apraxia” may be considered to be an early example of this approach. According to Denny-Brown the magnetic exploratory aspect of behaviour, involving “perseveration of all contactual reactions”, is managed by the parietal cortex, and released by frontal and temporal lesions. The repellent, negative, bias is determined by the premotor, cingulate and hippocampal regions, and released by parietal lesions. With reference to Denny-Brown, we can presuppose the presence of the first pathological factor underlying perseveration, releasing the complex motor activity, and the concomitant presence of contralesional USN, as the second factor. This is minimally defined as an ipsilesional bias of spatial attention and representation [according to some studies, disproportionately facilitating ipsilesional responses (Làdavas et al., 1990; Natale et al., 2005; Natale et al., 2007)], that may trigger perseveration with an ipsi-contralesional gradient. This two-factor hypothesis explains the association between perseveration and contralesional neglect, since the second factor (USN) releases and facilitates the manifestation of the first. It also accounts for the double dissociation between perseveration and USN in patients where only one pathological factor is present. Thirdly, since the second factor (USN) has different components, all involving an ipsilesional bias (Vallar, 1998), the perseveration behaviour of different patients may be shaped by contra-ipsilesional allochiria, contralesional directional hypokinesia (Toraldo et al., 2005), and, possibly, contralesional hyperschematia (Rode et al., 2006).

Anatomical correlates of perseveration

In Experiment 2 the anatomical lesion maps of patients showing recurrent perseveration provide evidence for the role of the right insula in the origin of perseverative phenomena. Previous studies focused on the involvement of frontal regions and basal ganglia in the right hemisphere (Na et al., 1999; Rusconi et al., 2002; Nys et al., 2006; Vallar et al., 2006; Pia et al., 2009b): in Experiment 2 the maximum overlap of N+P+ patients is on the right insula and right putamen, but comparing perseverating vs. non-perseverating neglect patients the insula is the region mainly implicated in the motor productive phenomenon.

The insula cortex is a multimodal area which plays a fundamental role in a wide range of functions (see Craig, 2009 for a review). Regarding the theme of our research, recent studies demonstrate that the anterior portion of the insular regions is implicated in error awareness, with mainly the right insula cortex being activated when erroneous responses are given and the error feedback provided (Klein et al., 2007; Ullsperger et al., 2010). Another interesting corpus of evidence underlines the role of this region in the intentional stopping of an action: when a decision is made intentionally to interrupt an intended action, the anterior insula is activated (Brass and Haggard, 2007; Campbell-Meiklejohn et al., 2008; Khun and Brass, 2009). One explanation is that the insula plays an evaluative role of the consequences of performing/stopping a voluntary action, integrating the information on intention and outcome (Brass and Haggard, 2010). Moreover it is well known that the activity of the right insula is related to action control experience (Farrer et al., 2003), and damage to this area is associated with incorrect evaluations of the outcome of movement in neurological patients with anosognosia for hemiplegia (Karnath et al., 2005). On the basis of this evidence, lesions affecting the right insula may contribute to the presence of recurrent perseveration, possibly due to failure of the inhibition of a motor action (i.e., crossing out targets that have already been marked), resulting in a defective evaluation of the action outcome (i.e., the incorrect execution of a task, in which only one mark for each stimulus is required). In addition, perseverating patients might show an associated lack of awareness about the errors made, possibly due to a failure to process the negative feedback on the performance (i.e., the visible second mark). In fact, the observation of the patients' behaviour during the cancellation tasks does not indicate that they consider perseveration as an error or a pathological behaviour, with the consequence that no modulation and correction of the inappropriate motor behaviour is elicited over time.

Considering that the insula is anatomically connected to the other cortical and subcortical structures (Augustine, 1996; Craig, 2009; Kalani et al., 2009), our data may be integrated with previous evidence suggesting the presence of a cerebral network in the right hemisphere involving insula, frontal cortex and basal ganglia, playing a key role in the occurrence of motor perseveration in USN.

Perseveration and reading errors: productive symptoms in dyslexic neglect patients

To the best of our knowledge, the results of Experiment 3 represent the first attempt to jointly analyze different productive manifestations in USN. We found an association between two symptoms in perseverating patients showing left neglect dyslexia: recurrent motor perseveration in the target cancellation task on the one hand, and substitution errors in the word reading task on the other. Addition errors are considered as the productive symptoms of neglect dyslexia by some investigators (Chatterjee, 1995; Vallar et al., 2006): from this point of view, Experiment 3 fails to find an association between productive manifestations in reading and cancellation tests. However it is important to note that substitutions also refer to an active modification of the contralesional part of the letter string; we therefore suggest that substitutions, as well as additions, can be considered as a productive reading symptom. In the view of Ellis and collaborators (1987), a substitution error corresponds to a paralexia produced by USN patients with a less severe spatial deficit, who present a defective encoding of contralesional letter identity, associated to preserved encoding of position (see also Arduino et al., 2002 for a similar account). An alternative explanation, based on our data and never proposed before, is that substitution (and not only addition) errors reflect a defective inhibitory mechanism that occurs in the oral re-elaboration of the verbal target. Our results show the co-occurrence of productive symptoms referring to the extra-personal space in USN patients, as indicated by the majority of substitution errors versus omission/addition reading errors in the perseverating group. No correlation was found between substitution and perseveration errors. This negative finding, which, as such, should be interpreted with caution, may reflect both the differences between the domains of reading and visuo-motor exploration in target cancellation, and the low number of patients in this study group.

There are no effects of error list in P-ND+ patients during the baseline word reading task, although most of the errors produced in this group are omissions. More data must be collected to verify this tendency.

To summarise, it appears that perseverating patients make more substitution errors in word reading tasks while non-perseverating patients do not make specific reading errors, or at most they make more omissions. These findings seem to indicate that omission and substitution errors in right-brain-damaged patients are not related to different degrees of severity of the same (i.e., defective spatial attention) pathology, with omissions and substitutions being symptoms of a continuum, ranging from severe (no information encoded) to mild (information encoded) spatial neglect (Ellis et al., 1987; Behrmann et al., 1990), but suggest that “positive” (perseveration and substitutions) pathological behaviours in USN patients tend to be related. In support of this view, in Experiment 3 we do not find statistical differences in the severity of neglect between patients mainly producing substitutions and the group of dyslexic patients not showing perseveration in target cancellation tasks.

A recent study (Martelli et al., 2010) tests the hypothesis that omissions and substitutions in neglect dyslexia reflect two independent mechanisms: the first visuo-spatial attentional, responsible for the presence of omission errors; the second perceptual (i.e., crowding) and independent of USN, responsible for the presence of substitution errors. Their results reveal that omission (but not substitution) errors are related to the performance in tests assessing USN and that increasing the space between letters in a word reading task augments the number of omission errors, without affecting the number of substitutions (which confirms the independence of the two reading disorders). Considering that the amount of substitutions produced by their dyslexic group is not significantly reduced in the spacing condition (the reduction of substitutions is present only in two out of six patients), as predicted by crowding, the perceptual phenomenon is found not to be the mechanism completely explaining the presence of this paralexic reading error. The results of Experiment 3, supporting the independence of omission and substitution errors, also suggest an alternative explanation for the presence of the substitution reading disorder, ascribing it to a productive (and not perceptual) manifestation, namely the active re-elaboration of the contralesional part of the verbal target.

In the second part of Experiment 3 we examined the occurrence and modulation of addition errors. Results show that additions are rare in both perseverating and non-perseverating patients in the base condition (W list). However the data of the experimental list (EW) indicate that the occurrence of additions can be modulated. In the original study by Ellis et al. (1987), in which a similar experimental investigation was performed, only one addition was elicited in a patient producing mainly substitutions. Coherently with the hypothesis that productive manifestations may co-occur in USN, we would expect an increase in addition errors only in the perseverating group in the EW list of Experiment 3. Results demonstrate that both perseverating and non-perseverating dyslexic patients are susceptible to a left-side letter addition phenomenon during a reading task designed to elicit this behaviour, while this manipulation does not influence reading performance in neurologically unimpaired participants. We conclude that addition errors are “positive” manifestations that, like other productive symptoms (Rusconi et al., 2002), may be elicited in right-brain-damaged patients with neglect; however they are rare in tasks which do not specifically trigger this behaviour. Further investigation should be directed to selectively examine the range of symptoms in neglect patients who mainly produce additions, investigating if perseverative behaviours in target cancellation tasks also occur.

Finally, Experiment 3 examines the relationship between USN and neglect dyslexia. In our sample, the spatial neglect diagnosed in patients with neglect dyslexia is more severe than in neglect patients without reading disturbances, which is in line with a recent large group study (Lee et al., 2009). The severity of USN is assessed by tasks requiring a visuo-motor activity, such as target cancellation and line bisection tests, which require a perceptive and motor response different to the verbal response solicited by the reading tasks; therefore this neglect group includes patients with multiple-component spatial impairments, affecting a wide range of neglect manifestations. Moreover, it must be kept in mind that we selected patients with neglect dyslexia in a word (as opposed to a sentence) reading task for our experiment: considering the reduced spatial horizontal component of a word (maximum length being 12 letters), therefore it is possible that the reading deficit is evident only in patients with severe spatial neglect in this study.

A personal productive symptom: somatoparaphrenia

This thesis includes an exhaustive review of patients affected by somatoparaphrenia.

The definite asymmetry that characterizes somatoparaphrenia indicates that the internal representations of the body concerned with ownership of body parts, emotional and motivational attitudes towards them and their perceived appearance, are largely supported by neural processes based in the right cerebral hemisphere. The close association with extrapersonal neglect, and the observation that somatoparaphrenia, as other aspects of the neglect syndrome, is temporarily improved by caloric vestibular stimulation (Bisiach et al., 1991; Rode et al., 1992; Schiff and Pulver, 1999) suggest that these processes concerned with body awareness and ownership include a spatial reference frame, that is also largely right-hemisphere-based (Bisiach and Vallar, 2000).

The representations concerned with ownership of body parts may be distinguished from those supporting awareness of somatosensory stimuli, and of the body as an object-in-space. Moving the disowned left hand to the attended (not neglected) right-hand-side of space may improve left somatosensory deficits, but does not affect disownership (Moro et al., 2004). Similarly, more “cognitive” manipulations, whereby a tactile stimulus is delivered not to the patient, but to the owner (in the patient’s delusional belief) of the patient’s left hand, again ameliorate left hemianaesthesia, but not disownership of the left hand (Bottini et al., 2002). The observation that vestibular stimulation may improve somatoparaphrenia, while somatosensory and visual half-field deficits are not improved by the manoeuvre (Rode et al., 1992), conjures up a double dissociation between somatoparaphrenia and sensory impairments. Finally, personal neglect is absent in a few patients (Gerstmann, 1942, case #1; Bisiach et al., 1991; Halligan et al., 1993; see also Meador et al., 2000). These double-dissociated effects - together with the traditional neurological wisdom that primary sensorimotor neurological deficits may occur without any associated neuropsychological disorder (but see Sterzi et al., 1993, for a partly higher-order account of "primary" sensorimotor impairments; Halligan and Marshall, 2002; Vallar, 2007) - also suggest that somatosensory impairments are surely not sufficient, and perhaps not necessary, to bring about somatoparaphrenia. This conclusion applies more definitely to visual half-field deficits, that may be absent in patients with somatoparaphrenia. These findings (particularly the data showing that the sensorimotor deficits of brain-damaged patients may be themselves a manifestation of a higher-order disorder, namely the USN syndrome) suggest that an account of somatoparaphrenia (and of anosognosia) in terms of a two-factor deficit (1-lower-level impairment: the left-sided motor and perceptual deficits; 2-higher-level impairment: a deficit in the belief revision system) (Davies and Coltheart, 2000; Davies et al., 2005) may need some reconsideration, with most of the involved pathological factors being higher-level, and related to spatial neglect. Proprioceptive impairments are closely associated with somatoparaphrenic phenomena, and, particularly, with disownership of the patient's own body parts. The appreciation of the positions of body parts, and of their changes as movements occur, appears to provide an important contribution to the sense of ownership, supporting the discrimination between one's own body parts and those of another person. In right-brain-damaged patients tactile and visual impairments appear to have a higher-order component also, related to the disruption of spatial reference frames.

In most patients somatoparaphrenic symptoms are present in the context of a fully-fledged USN syndrome. There are, however, a few patients in whom somatoparaphrenia has been found without anosognosia for neurological impairment (see a transient anosognosia in Ehrenwald's patient, 1930; Schilder, 1935; Halligan et al., 1995; Moro et al., 2004, case #2). A double dissociation between asomatognosia and anosognosia was shown by Meador et al. (2000), using intracarotid amobarbital inactivation. These rare observations of patients with somatoparaphrenia, together with Meador et al.'s (2000) intracarotid amobarbital inactivation results, indicate - at variance with Gerstmann's (1942) original suggestion of a close relationship between anosognosia and somatoparaphrenia - that the processes concerned with the monitoring of sensorimotor functions may be independent of those concerned with awareness of the body, and ownership of body parts (see Vallar and Ronchi, 2006, for a discussion of the dissociation between anosognosia for hemiplegia and personal neglect).

The neuropsychological data reviewed in Table X (although it should be noted that many patients had extensive fronto-temporo-parietal lesions), together with the group studies by Feinberg and co-workers (1990; 2000), suggest a role of the posterior cerebral regions (temporo-parietal junction), in agreement with classical views (Nielsen, 1946; review in Critchley, 1953). The relevant neural circuitry, however, may be more extensive and include deep cortical regions such as the posterior insula (Cereda et al., 2002; Baier and Karnath, 2008), and subcortical structures such as the basal ganglia (Healton et al., 1982; Halligan et al., 1993; Bottini et al., 2002). The finding that damage to the insular cortex (Karnath et al., 2005; Baier and Karnath, 2008) is shared by both anosognosia for hemiplegia and somatoparaphrenia (but see Feinberg et al., 1990) has been taken as evidence of a substantial overlap between the two disorders, in agreement with Gerstmann's (1942) original suggestion. However, anosognosia for hemiplegia and asomatognosia (i.e., somatoparaphrenia) are dissociated disorders (Meador et al., 2000). Furthermore, a lesion correlate of anosognosia for left hemiplegia is damage to the right premotor cortex (Berti et al., 2005), which may be contrasted with the more posterior damage that characterizes somatoparaphrenia. These data support the view that anosognosia for hemiplegia and somatoparaphrenia are independent, though often associated, disorders.

The present review is confined to neuropsychological data from brain-damaged patients, but the so-called "rubber hand illusion" (a phenomenon whereby neurologically unimpaired participants, after repeated synchronous touches applied to their own hand, and to a rubber hand, experience the perception that the rubber hand is their own hand and that the rubber hand "senses" the touch, see Botvinick and Cohen, 1998) deserves a brief mention. The illusion provides evidence that multisensory integration may be a mechanism for bodily self-attribution, with the rubber hand phenomenon being explained by a predominance of vision over somatosensory signals (see Tsakiris et al., 2006; Schwabe and Blanke, 2007; Tsakiris et al., 2007b, for a more general discussion of the relationships between agency and ownership). The neural bases of this illusion include the premotor cortex bilaterally (Ehrsson et al., 2004). Two recent rubber hand illusion studies with neurologically unimpaired participants suggest a role of the right temporo-parietal junction (Tsakiris et al., 2008, using Transcranial Magnetic Stimulation), of the right posterior insula, and of the right frontal operculum (Tsakiris et al., 2007a, using PET), for the sense of ownership of body parts, as distinct from external non-corporeal objects. Interestingly, the measure of body ownership in these studies is proprioceptive, and this review suggests, from the vantage point of somatoparaphrenia, a role of position sense deficit as a pathological factor. We can then consider the possibility that defective multisensory integration, which is supported by a network including the frontal premotor and the posterior parietal cortices, as well as certain subcortical structures such as the thalamus, the basal ganglia and the superior colliculus (review in Vallar and Maravita, 2009) as opposed to the impairment of specific sensory modalities, may be a relevant somatoparaphrenia mechanism, together with a disordered, mainly right-hemisphere-based, spatial representation of the body.

Patient JJ, who participated in our experiments (see the case report), provides an example of delusional belief about the ownership of a contralesional body part and associated spatial and personal neglect. Remarkably, her performances in target cancellation tasks reveal a great presence of recurrent perseveration confined to the scattered version of the star test; moreover, coherently with the data on the productive extra-personal symptoms discussed previously, she makes more “positive” (substitution and addition) than “negative” (omission) reading errors. This was also the case for Bottini et al. (2002)’s somatoparaphrenic patient, where perseverative (simple and complex) manifestations were recorded on a scattered line cancellation task (unfortunately the reading performance was not evaluated). This is evidence that a set of personal and extra-personal productive USN manifestations (Vallar, 2001) can co-exist.

Anosognosia for left spatial neglect

Experiment 4 of this thesis investigates the occurrence of awareness of the neglect syndrome. Despite its clinical relevance, this feature has been essentially “neglected” in the scientific literature and only few studies (Azouvi, 1996; Berti et al., 1996; Jehkonen et al., 2000) have analyzed the problem of anosognosia for spatial inattention. To the best of our knowledge, this is the first study that extensively investigates unawareness of USN, with quantitative measures and a wide range of tasks. In addition we also investigate the possible modulations and stability over time.

The main result is that anosognosia for USN is not a monolithic disorder, as neglect patients evaluate their performance in various tasks in different ways. In fact in two of the six tests used to assess spatial neglect (i.e., line bisection and clock drawing), the mean self-evaluations of N++ patients are comparable to those of the three control groups: in particular, in these tasks the critical comparisons between neglect patients showing neglect compared to those who do not do not reveal any differences in the evaluation scores. Possible reasons for this unawareness may be found in the characteristics of the two tasks.

In the line bisection test the visual-spatial feedback about the performance is limited and the information available regarding performance inaccuracy may not be sufficient for processing and eliciting awareness in any form. The other task in which no awareness emerges is drawing a clock from memory, which suggests the absence of insight for representational neglect. The main difference between this task and the other spatial tests used is that when drawing the clock patients have to compare their graphic output with an internal representation, which can be defective (Bisiach et al., 1981; Beschin et al., 1997; Lepore et al., 2004). Results suggest that patients with a flawed mental representation do not perceive any discrepancies between an imagined clock and their drawing, and consequently the evaluation score is steadily positive and similar to that of the other groups. However a motor component is also present in this task and the drawing can be influenced by the presence of directional hypokinesia (Heilman et al., 1985), with difficulty in performing movements towards the contralesional space and the consequent transposition of elements from the left hand side to the right: therefore to control the potential effect of additional motor components, the hypothesis of a global unawareness related to representational neglect must be confirmed using pure representational tests, such as the description of well-known places from memory [e.g., the Piazza del Duomo in Milan (Bisiach and Luzzatti, 1978), the map of France (Rode et al., 2004)].

In the copying a complex drawing task, neglect patients evaluate their performance more negatively than the other three groups (neurological: N-, N+-; control: C); however the significant difference between the evaluation scores of N++ patients and those of the other participants disappears when constructional apraxia is considered. Constructional apraxia (Kleist, 1934; Gainotti, 1985) is a pathological symptom consisting in the lack of accurate spatial relations between elements of objects, as assessed by drawing and assembly tasks. Constructional apraxia can be found in neurological patients following left and right-hemisphere strokes (Gainotti and Tiacci, 1970; Hier et al., 1983a and 1983b; Russell et al., 2010). Although results indicate that the self-evaluations of neglect patients are influenced by the presence of constructional apraxia, the lack of significance of the covariate main factor suggests that the drawing evaluation scores by neglect patients are not totally affected by this associated symptom. A recent study (Rinaldi et al., 2010) investigated the presence of anosognosia for constructional apraxia in five right-brain-damaged patients without signs of spatial neglect: their data indicate the presence of various degrees of unawareness, with three patients being totally unaware of their constructive performance while the remaining two presented a mild degree of unawareness. On the other hand, in the only study investigating anosognosia for neglect drawing performances (Berti et al., 1996), approximately half of the patients were unaware of their neglect drawing symptoms. Given that both anosognosia for constructional apraxia (Rinaldi et al., 2010) and for neglect drawing (Berti et al., 1996) are recorded in right-brain-damaged patients, our data suggest that the presence of only one of these two pathological symptoms is not sufficient to explain the patients' evaluation of the defective drawing performance, but it is possible that a combined effect of spatial and constructive deficits contributes to the lower self-evaluation scores of N++ patients.

Although anosognosia for neglect dyslexia was found in a previous study (Berti et al., 1996), our results suggest the absence of specific awareness for neglect reading errors. In Experiment 4 neglect patients with neglect dyslexia evaluate their ability and performance on a reading task more negatively than do C/N- participants: however we find no difference between N++ and N+- patients, suggesting that the evaluations of neglect patients with neglect dyslexia reflect a more generic knowledge about the presence of spatial difficulties, not specifically linked to the reading task. However this result should be considered with caution, given the limited dimension of the N+- group.

Awareness of USN in target cancellation tests is present. There is a clear difference between N++ patients and the other groups (N-, N+- and C) in the two cancellation tasks: as Figures 24 and 25 show, neglect patients omitting stimuli in the left-side of the sheets evaluate their capacity to perform these tasks and their outcome more negatively than the other participants. Target cancellation tasks are useful and sensitive tools for assessing the presence of USN (Ferber and Karnath, 2001). Our evidence demonstrates the presence of a specific awareness in neglect patients for this type of test, which requires a complex set of visuo-motor sequential actions as well as the distinction between targets/non-targets. A major visuo-motor feedback is available in cancellation tests compared with the other neglect tasks in which no (or partial) awareness is elicited and possibly processed by USN patients. However these evaluation scores are not correlated to the severity of the spatial performance, which suggests that a "grosgrain" awareness about the spatial difficulty (without, however, precise knowledge of the degree of the impairment) is present in these tasks.

To summarize, the data indicate that neglect patients are not completely anosognosic about their spatial symptoms and that some form of awareness is present. In particular, dissociation has been recorded between neglect performance in line bisection and cancellation tests (Halligan and Marshall, 1992; Marshall and Halligan, 1995), and dissociation in the awareness of performance in these two types of task has also been found.

In Experiment 4 we find a clear stability in the evaluations of spatial tasks: the N++ estimation scores span across all the conditions taken into consideration without any modulation by an implicit question, direct feedback of the task performed or follow up assessment. Previous experimental evidence emphasizes the presence of implicit awareness for motor deficits, comparing first person (i.e., how patients perform the various tasks) to third person (i.e., how would the examiners have performed these tasks if they had been in the patients' condition; Marcel et al., 2004). These data suggest that hemiplegic patients may have an implicit knowledge of their motor impairment, with this awareness becoming evident when an indirect question is made about motor ability. Other evidences of implicit awareness of motor deficits emerging in hemiplegic patients are on record (Fotopoulou et al., 2009 and 2010; Cocchini et al., 2010). In Experiment 4, differently from the previous findings about motor competencies (Marcel et al., 2004), no modulation by the implicit question is found in neglect evaluation, in tasks in which complete anosognosia for neglect is recorded (see the pre-testing evaluation scores in the line bisection and clock drawing tasks) or in tasks in which first person questions already evoke a form of awareness (target cancellation tasks). Moreover, similar self-evaluations are made by patients before and after the task execution. While the patients had already performed all these tests in the baseline assessment, it is possible that the evaluation made by neglect patients prior to task execution is influenced by their generic knowledge of their abilities, stored in memory representations in the pre-morbid condition; on the contrary, failure to perform the task may elicit a (more or less stable) update of their actual abilities, leading to a more accurate judgment (on this subject see evidence regarding motor impairments in Berti et al., 1996; Cocchini et al., 2002; Marcel et al., 2004). Possible consequences of the direct visible feedback could be that patients become aware (line bisection and clock drawing tests) or improve their judgement (target cancellation tasks). In the study conducted by Barrett and collaborators (2005) the pre-testing overestimation of the visuo-spatial abilities in patients with probable Alzheimer disease was reduced in the post-testing condition, while the memory evaluation was less accurate after the test execution, with Alzheimer patients presenting anosognosia for amnesia only in the post-testing condition. Ansell and Bucks (2006), on the contrary, found that patients with mild Alzheimer disease made a more precise evaluation of their memory competences after exposure to a memory task. In Experiment 4, which investigates the awareness of spatial abilities in neglect patients, no differences are recorded between evaluations made before and after task execution in any of the neglect tests. Thirdly, in Experiment 4 we find no modulation of the time assessment (follow up): while the temporal variability of spatial neglect performances has been demonstrated (Anderson et al., 2000), it does not extend to performance evaluations, which remain stable for at least 24 hours. Finally, patients do not modify their performance evaluation even on the basis of the feedback offered verbally by the examiner after the execution of the letter cancellation task. All these data regarding possible modulations of neglect performance evaluations are suggestive of the stability and inalterability of the patients' estimation of spatial competences, independent of the presence/absence of awareness of USN.

Results of Experiment 4 also indicate that anosognosia for USN, when present, is a specific, and not pervasive, monitoring deficit. In fact neglect patients correctly estimate their cognitive competences in a cognitive task that is not intended to assess visuo-spatial functions. In our sample, seven out of 15 (47%) neglect patients show a pathological performance in the Phonemic fluency test, in line with previous evidence indicating that verbal fluency competences can be defective in patients with right-brain lesions (Ramier and Hécaen, 1970; Davidson et al., 2008). While Marcel et al. (2004) found the presence of overestimation of the fluency deficits in some right-brain damaged patients, our results show that the self-estimation of the verbal fluency performance in neglect patients is adequate, both when defective and when preserved; in addition, the significant positive correlation between evaluation and fluency scores is indicative of a precise knowledge of different fluency competences. In our study, a modulation of the post-testing condition is also found in all groups, with self-evaluation scores decreasing after task execution: this could be accounted for by the difficulty in evaluating the outcome of this executive verbal test precisely, as no maximum score and no visual feedback are available (in contrast to the visual-spatial task assessing neglect symptoms). Therefore it is possible that the subjective perception of the participants is that "they can do better", with a consequent slight underestimation of their performance (see also data regarding the evaluations by neurological unimpaired participants of their performance on a semantic fluency task in Leicht et al., 2010). To sum up, the capacity to evaluate cognitive abilities and the modulation by different experimental conditions is not globally compromised in right-brain-damaged patients with neglect, as the results of linguistic self-evaluations show.

On the basis of this corpus of evidence, Experiment 4 demonstrates that awareness of USN can be found, though specifically related to certain tests. Neglect self-evaluation scores cannot be accounted for by either an aspecific effect of the brain lesion (see comparison with N- patients), or a compromised capacity to judge cognitive performance correctly (see evaluation scores in the Phonemic fluency test). Moreover, results reveal that a set of tasks involving heterogeneous components of spatial neglect are evaluated differently, demonstrating that awareness of neglect is not triggered by the pervasive presence of USN (with the exception of the sentence reading test, discussed above). Data collected in Experiment 4 indicate that, under certain test-conditions, monitoring processes concerning defects in cognitive performance are efficient and able to recognize and understand the spatial impairment. In line with previous evidence regarding selective manifestations of unawareness for neurological and cognitive deficits (Von Hagen and Yves, 1937; Nielsen, 1938; Berti et al., 1996; Marcel et al., 2004; Barrett et al., 2005; Leicht et al., 2010), we also found anosognosia for specific components of the USN syndrome, suggesting that also with regard to neglect tasks a monitoring system of the cognitive performance should not be conceived as unitary but rather as comprising a number of discrete modules. In addition, our findings indicate that evaluations of spatial neglect are stable and not easy to modulate.

Finally, our study also analyzes the presence of associated anosognosia for hemiplegia in the upper limbs. Results show that neurological patients (with and without neglect) appear to be aware of their motor capacities. When they are unable to perform the set of tasks, their evaluations are strongly negative and differ from those of the control group, whereas, in the case of motor tasks that can be performed by patients with mild motor impairments or the occurrence of control conditions (e.g., to raise the ipsilesional arm, to perform a unimanual task), motor abilities are sometimes underestimated, even if the action execution feedback is positive and could justify modification of the evaluation (e.g., in the bimanual tasks). Motor awareness is present in both direct questions and bimanual self-estimations, while data in literature show that dissimilar degrees of awareness can emerge when using different instruments (Marcel et al., 2004; Nimmo-Smith et al., 2005; Orfei et al., 2007; Cocchini et al., 2010; Starkstein et al., 2010). Our patients' knowledge of their motor inabilities is perhaps triggered by repeated failure on motor tasks, both in daily life and, especially, during physical rehabilitation; it should be noted that, at the time of testing, our neurological patients had not started USN cognitive rehabilitation. Neglect and anosognosia for hemiplegia following right-hemisphere damage can be associated disorders (Rode et al., 1992; Starkstein et al., 1993; Rode et al., 1998; Bottini et al., 2002), but dissociation between these two deficits (Berti et al., 2005; Appelros et al., 2007; Kortte and Hillis, 2009) and between anosognosia for neglect and for hemiplegia (Jehkonen et al., 2000) are on record and confirmed by our data.

To conclude, right-brain-damaged patients with left spatial neglect may show a range of behavioural monitoring disorders. Different productive symptoms are examined, including recurrent perseveration errors, which are most frequent when the task requires complex visuo-motor exploration and monitoring (e.g., the cancellation of targets scattered among distracters) and when a non-verbal stimulus (e.g., a star) is used (Experiments 1 and 2). Productive phenomena in target cancellation tasks do not appear to be associated with a dysexecutive syndrome, visuo-spatial memory impairment (Experiment 1) or divided attentional deficit (Experiment 2). The contribution of the right insula in error awareness and interruption of an inappropriate motor action is to be considered in the genesis of this “positive” motor symptom (Experiment 2). Perseveration seems to be mainly associated with substitution errors in patients with neglect dyslexia (Experiment 3): substitution may be considered a paralexic “producitve” reading disorder, in which an active modification of some letters of the target is made. There are no differences in the types of reading error produced in patients who do not show perseveration. Finally the monitoring processes of spatial performance have been found to be partially preserved in neglect patients (Experiment 4): in target cancellation tasks patients with USN appear aware about their defective performance. The presence/absence of awareness for visuo-spatial deficits seems to be stable over time and not susceptible to experimental modulations, unlike motor and linguistic performance evaluations, suggesting that the modulatory system of monitoring processes is not overall compromised.

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