Visual deficit and cognitive aspects in the unilateral negligence syndrome: a qualitative review of the literature.

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Objective
The objective of this paper was to undertake a narrative review of the literature regarding main characteristics of the unilateral negligence syndrome.

Method
A literature search was performed to identify published full text original research articles documenting correlations between right brain damage and visual and cognitive deficit and to identify published systematic reviews/meta-analysis. The electronic databases comprised of Embase, Google, Google Scholar, Medline, PubMed, Science Direct, Scopus and Springer Link. An interpretative narrative synthesis was undertaken and emergent themes analysed and reported.

Results
Twenty studies and eight reviews were included in the final analysis. There were seven main themes which including: right brain damage, visual deficit, behavioral aspects, spatial attention, peripersonal and extrapersonal space, awareness, interventention.

Conclusions
In this review we have focused on clinical aspects of neglect. Recent findings emphasise that the neglect syndrome is a dramatic condition which impairs awareness of controlateral-sided events. It is characterized by the presence of different and specific deficits. The studies on the neglect confirm the modular interpretation of the neural circuits and the dissociation between many cerebral process. It would be correct thinking a specific rehabilitation in terms of what is the best way to treat a person with a specific cognitive deficit.

Introduction
Observations in neurological patients, jointly to modern studies of neuroimaging and to assessment with cognitive test they allow to draw some inferences on as brain represents personal, peripersonal and extrapersonal space and to draw characteristics of the neglect. It’s a complex and heterogeneous syndrome.

After an unilateral hemispheric lesion a consistent number of subjects fail to be aware of or acknowledge items on their contralesional side (the left side for patients with right brain damage) and attend instead to items towards the same side as their brain damage - their ipsilesional side. Elements of the neglect syndrome include hemi-inattention, extinction to double simultaneous stimulation, hemiakinesia, allesthesia, and hemispatial neglect. Hemi-inattention refers to a failure to respond or orient to stimulation on the contralesional side of the body. Hemiakinesia refers to failure or disinclination to use the contralesional limbs and even to extinguish movement with the contralesional limb when both sides of the body are tested for movement at the same time. Allesthesia refers to a misperception of which side of the body has been stimulated. Hemispatial neglect denotes the consistency with which neglect occurs on one side of space as defined by the midline of the body.

In the acute or transitory phase, immediately following a cerebral lesion, the most typical signs of severe unilateral neglect can be easily recognized. Patients with unilateral neglect have an obvious ipsilesional deviation of the eyes, the head, and the trunk [17]. The patients read only parts of a text, losing the ability to understand it, they ignore the people that are turned him by left, they don't succeed in autonomously feeding because they skip part of the food in the dish, they can also to deny that the limbs cut from lesion or
to affirm that the limbs of left don't belong to their body and, rather they show marveled for the presence in their bed of these extraneous limbs. It deals with examples related to the most frequent case of neglect for the left side due to right lesion, but left damages produce symmetrical deficit. These symptoms are typical of the acclaimed syndrome of neglect. Soon, however, in such subjects a process of recovery is established that, in some cases, can bring to the alloestesia: in this case the patient doesn't neglect the information anymore coming from the left space but attributes her to symmetrical positions of the right space. With the progress of the recovery can be revealed a light form called extinction: the subjects have only visual deficit related to the survey of stimuli following the simultaneous presentation of other stimuli in the right hemispace. Many subtypes or forms of neglect have been described. These are usually distinguished by their presumed underlying mechanism or type of behaviour. The various forms of neglect (i.e. attentional, motor-intentional, representational, personal, etc.) are not mutually exclusive and a patient may have one or more forms of neglect at the same time.

The redoubt tendency or the incapability to explore the space against side to the lesion and to answer to the stimuli from it deriving it produces a debilitating medical condition that behaves consequences in the daily life of the patient.

In most cases the syndrome is a consequence of lesions that involve the parietal lobe, and precisely the inferior parietal lobule, but cases have been described in which the lesion is circumscribed to other areas as the frontal lobe and the subcortical structures, the thalamus and the basal ganglia. The reported incidence of Unilateral neglect varies widely from 10% to 82% following right-hemisphere stroke and from 15% to 65% following left-hemisphere stroke. Neglect is characterized by many component deficits and presumably determined by the exact location and extent of brain damage. An increasing number of articles have revealed that hemispatial neglect is heterogeneous, not only in the diversity of clinical manifestations, but also in the dispersibility and variety of the associated lesions.

Current knowledge concerning neural basis of spatial neglect comes from traditional anatomo-clinical correlation between site of the cerebral lesion and behavioural deficit and from more recently developed interference with the function of specific cerebral areas, induced by transcranialmagnetic stimulation (TMS), PET or fMRI (see next section). Not all the cerebral areas activated (or deactivated) by a given task are necessary to the execution of it, representing instead a more redundant neural network. The integration of lesion and activation findings will however reveal the complete functional neuroanatomy of spatial unilateral neglect and spatial cognition.

Neuroimaging data suggest that lesions of the posterior parietal lobe are the most frequent anatomical correlate of spatial unilateral neglect. The crucial area is the inferior parietal lobule (Brodmann’s area) at the temporo-parietal junction. Lesions localised more posteriorly in the occipital regions, or more superiorly in the superior parietal lobule bring about visual field deficits or a deficit of reaching (optic ataxia), without neglect. Other cerebral areas, damage to which can be associated with neglect, include the superior temporal gyrus, the lateral premotor cortex and a number of subcortical regions (thalamus, basal ganglia, white matter fibre tracts). Studies that have measured regional cerebral blood flow and metabolism in patients with neglect show that the extent of the cerebral dysfunction, as revealed by hypoperfusion or hypometabolism, is much wider than the cerebral areas destroyed by the lesion, and involves areas far removed but connected with the damaged regions. These findings indicate that the neural basis of neglect, and of spatial cognition, comprises a number of connected cortical and subcortical brain regions of neglect.
Experiments using TMS in normal subjects have recently corroborated the view that damage to right posterior parietal cortex is the main pathological correlate of spatial neglect. The most common lesion sites associated with the neglect syndrome include the posterior parietal cortex (PPC), inferior parietal lobe (IPL), and the temporo-parietal junction (TPJ; see Chechlacz et al., 2010; Leibovitch et al., 1998; Vallar, 2001; Vallar et al., 2003; Vallar and Perani, 1986; Verdon et al., 2010). Some studies also suggest that damage within the medial temporal lobe (the parahippocampus), the inferior frontal cortex (Husain and Kennard, 1996; Vallar, 2001; Walker et al., 1998) and the mid superior temporal gyrus (STG) can lead to neglect. Patients may have one type of neglect or a combination of neglect behaviors. Because neglect has a wide variety of clinical presentations, no single neuropsychological test can be used to identify the disorder or to provide a complete diagnosis. Some authors have recommended that assessment of neglect include a test battery. To ensure sufficient sensitivity, the battery should include measures for all types of neglect.

More important test are: (peripersonal space neglect) BIT Conventional Line crossing (BIT-C) Letter cancellation (BIT-C) Star cancellation (BIT-C) BIT Behavioural Picture scanning (BIT-B) Menu reading (BIT-B) Coin sorting (BIT-B) Card sorting (BIT-B) Bells test; (personal space neglect) Comb and Razor test Fluff test; (extrapersonal space neglect) Room description, Semi-structured ecological scale; (representational space neglect) Mental number bisection task, Motor functions, Motricity Index and trunk control test.

A recent study examined the prevalence and neuropsychological correlates of perseverative responses in 206 subacute stroke patients and 63 healthy controls. Perseverative responses were considered present when there was at least one re-marking on the Star Cancellation, and both the degree and spatial distribution of re-markings were examined. A distinction was made between hemi-neglect and non-lateralized inattention. Spatial and verbal working memory were assessed with the Corsi Block Span and the Digit Span. Verbal and non-verbal executive function was assessed with the Visual Elevator and Letter Fluency. Stroke patients without inattention demonstrated remarking that were related to executive performance, and the degree of perseveration was equally distributed across the sheet. Hemi-neglect patients but not patients with generalized inattention demonstrated more remarking than controls, suggesting that a lateralized spatial attention bias triggers the perseverative responses.

Another contribution of search has used different methodological approaches to the anatomo-functional correlation to study both the neglect for the visual extrapersonal space that for the personal or bodily space, in an ample number of patients with cerebral lesions. A champion of 88 patients with presumed hemispheric right lesions has been submitted to examination for the evaluation of the extrapersonal neglect and to an examination of structural (MRI) magnetic resonance to tall definition (MPRAGE, 1x1x1 mm). After the application of a series of criterions of exclusion (to es., presence of bilateral lesions), the final champion results of 52 patients. The lesions, manually draw on the images MRI and normalize in a standard common space, besides the classical overlaps and subtractions, they have been submitted to statistic analysis to regional level and of single voxel, these last through the technical VLSM (Voxel-based Lesion-Symptom Mapping: Bates et al, 2003). The results of the different techniques of employed analysis have shown a clean separation among the critical regions for the two troubles, with those related to the neglect more extrapersonal rostralis and ventral and those relative to the more personal neglect caudalis and backs. The white substance to level of the central furrow together with the back insula and to the perysilvian area, results involved in the genesis of both the types of neglect, even if in smaller measure clearly in
comparison to the aforesaid regions, suggesting the possibility of a common base of parieto-frontal disconnection.

In the end such contribution strongly supports how much thin to now suggested only by studies on single cases: the necessary areas for an awareness suitable of the visual space extrapersonal and personal dissociate (both from a functional point of view and anatomical) in the brain of the man, in accord with how much observed in the non human records. The awareness of the space extrapersonal involves frontal regions and storms that are part of a circuit recently described for the allocation of the attention and for the re-orientation of the attention in the space. The deficit of the awareness for the personal space, seems instead due, to inferior wall lesions and to the functional disconnection among the somato-sensory coding and the more abstract egocentric representations of the body in the space.

Often unilateral neglect extends its to auditory, tactile and olfattive information. The syndrome manifests in absence of primary deficit and can have non visual components, for example motor or representative problems. An interesting study of Bruce Volpe (1979) has shown that the patients affections from spatial negligence would be able to formulate accurate judgments of peer / different in comparisons among item in the intact field and in that neglected and, therefore, that the information on the neglected side can suffer an elevated degree of analysis although the patient is not aware of it.

In Italy a demonstrative study of the fact that spatial negligence is not worth only for the items of the world sensorial external have conducted, but also for those of the visual memory during the recollection of a known scene. The researchers studied patient affections from neglect that, having spent big part of their life in the same city, they had familiarity for the most important places, particularly for the principal plaza. To the subjects researcher had asked to imagine to be in a particular point of the plaza and to describe what they saw around them. In their memory description, the patients omitted what it was found on the side against side to the lesion.

The most interesting aspect is that when the researchers asked to imagine to be in an opposite side to the precedent, they reported what in precedence they had skipped omitting the side of the first plaza described. The negligence of the objects on the side against damage could not be attributed it not to remember those scenes, on the contrary the fact that the wall lesion influenced the attention applied to parts of the image recalled by the memory reflected.

We also know that at times the subjects introduce troubles of the attention in the coordinates centered on the objects and not only in those they center on the eyes, the head or the body. To the attentional and representative of the left space, with consequent hyperactivation of the right space, deficits of representation of the quantity are accompanied, of the time, deficit of visual-spatial memory and limited awareness or indifference for the trouble, therefore if questioned the subjects they don't bring to have exploratory difficulty or they attribute their to other causes.

The principal characteristics of the neglect syndrome is the troubles of the cognitive elaboration and of the related to the space behavior. To these the characteristic aspects of the anosognosia or the lack of recognition of the deficit are added. The substantial literature, which we have already made reference, underlines that differences emisferiches exist in the emotional control, suggesting that the two hemispheres have a different role in the expression of positive and negative emotions. Quite a lot researchers have underlined the bond between right hemisphere and emotional trials considering the anosognosia as an abnormal emotional reaction, because of a deficit to the area of the brain mainly involved in the emotional behavior.
Furthermore, unilateral neglect can limit the effectiveness of rehabilitation, often to a greater extent than more obvious motor, sensory, and speech deficits. Some patients with unilateral neglect may be unaware of or deny their deficits. This phenomenon has been called “anosognosia”. Anosognosia, or denial of deficit, is a remarkable neuropsychological disorder, which bears on important conceptual issues such as self-deception.

Neurological patients with anosognosia would seem show reduced awareness of their disability its because of an absence of negative emotions. As Turnbull and Jones sustain (2005) recent evidences show that the anosognosics subject have an implicit awareness of their deficits and that the negation is due to the hostile emotional consequences that the full awareness could involve (Turnbull, Jones et Reed-Screen 2005).

Many treatments for unilateral neglect syndrome have been developed since the first years of the XXth century: Caloric vestibular stimulation (CVS), Optokinetic stimulation (OKS), Trunk orientation (TO), Neck muscle vibration (NMV), Transcutaneous electrical neural stimulation (TENS), Sustained attention training (SAT), Space remapping training, Feedback training Mental imagery training Fresnel, prisms Eye patching, Repetitive transcranial magnetic stimulation (rTMS), Transcranial direct current stimulation (tDCS), electric stimulation (FES),Pharmacological treatment with dopaminergic agonists, Pharmacological treatment with noradrenergic agonists.

Studies employing combined techincs Rehabilitation treatments for unilateral spatial neglect. Literature’s review and description of functioning Visual Scanning Training (VST) Limb Activation Treatment (LAT) Prism Adaptation (PA) has clinically relevant long-term benefits. A new perspective is to develop and combine new techniques targeting the different cognitive processes contributing to the clinical manifestations of visuo-spatial neglect such as spatial and non-spatial attention, intention,global-local processing, working memory, mental representation.

The frequent association and inter-relation of visuo-spatial neglect with motor, somato-sensory, visual and/or other cognitive impairments may explain in part this limitation. It is indeed difficult, in a rehabilitation context, to distinguish clearly the components of disability that are specifically attributable to visuo-spatial neglect [11].

This syndrome has been shown to constitute a substantial impairment for functional recovery. Although some spontaneous recovery occurs in the majority of patients after a stroke, left visuo-spatial neglect remains severe in many patients and may persist chronically.

Recent findings show that spatial attention deficits partially improve during the acute phase of the disease in less than half the patients investigated. There was an improvement in left visuospatial neglect at a later, chronic stage of the disease, but this recovery was not complete [6].

The heterogeneity of the population targeted, the lack of a clear patho-physiological understanding, and the variability of spontaneous recovery, requires well designed studies to investigate the effectiveness of any treatment procedure for left visuo-spatial neglect.

CONCLUSIONS

Neglect is a complex and heterogeneous condition with different combinations of deficit occurring in different patients. Treatments for neglect are unlikely to be successful unless they are tailored to the underlying cognitive deficits in individual patients. We cannot generalize and reduce the terminology in “effective” or “ineffective” terms. Probably, it would be more correct thinking about cognitive rehabilitation in terms of what is the best way to treat a person with a specific cognitive deficit. More specific is the cognitive deficit, more specific should be the cognitive intervention.
Promising new developments using behavioural and drug interventions have begun to offer some new hope for this common debilitating condition.

REFERENCES


