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A UNIFIED PERSPECTIVE OF UNILATERAL SPATIAL NEGLECT

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A Unified Perspective of Unilateral Spatial Neglect

Submitted by Joel Gerafi to the University of Skövde as a final year project towards the degree of M.Sc. in the School of Humanities and Informatics. The project has been supervised by Judith Annett.

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I hereby certify that all material in this final year project which is not my own work has been identified and that no work is included for which a degree has already been conferred on me.

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Abstract

The aim of this review is to provide a unified perspective of unilateral spatial neglect (USN). USN is a neurological disorder frequently observed following damage or diseases to the brain. It is particularly associated with strokes to specific anatomical structures within the right hemisphere. Patients with USN fail to respond to or orient towards stimuli located in the hemispace contralateral to the lesion. They also show peculiar behavioral manifestations. There are several distinct subtypes of USN which can affect sensory or motor modalities, spatial representations, the range of space, or pure imagery. This disorder can appear in any sensory modality but the majority of studies have investigated the visual aspect of USN in these subtypes. Theoretical proposals are supported by empirical evidence deriving from neuroimaging which distinguish between these subtypes of USN. Thus, the heterogeneity of the disorder is evident and clinical assessment methods face great difficulties while prevalence rates vary. The neural pathways of spatial attention distinguish between the ventral and dorsal visual streams, both with distinct functional roles and anatomical bases. Prism adaptation (PA) is a common rehabilitation technique among many others and has shown positive effects on USN while having some limitations. A general discussion and concluding remarks are presented in the final section followed by future research suggestions.

Keywords: Attention, hemispace, hemisphere, unilateral spatial neglect, stroke

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A Failure of Spatial Representation & Attention

Our notion of experiencing the world around us as a coherent whole arises naturally, regardless of considering the complex neural mechanisms responsible for our spatial representation and attention. These mechanisms are essential for a unified experience. If they fail to function properly as a result from a brain injury (e.g., stroke, traumatic brain injury, or brain tumor, a neurological disorder termed unilateral spatial neglect (USN) can appear (Revonsuo, 2010). Further, neurodegenerative diseases such as Huntington's disease (Ho et al., 2003) and Alzheimer's disease (Ishiai et al., 2000) can also lead to USN, although rarely occurring. USN is typically caused by stroke (Corbetta & Shulman, 2011) which is why this review mainly focuses on USN post-stroke. The reported prevalence rates of USN following strokes have shown to vary substantially in general (Sunderland, Wade, & Hewer, 1987; Stone, Halligan, & Greenwood, 1993 as cited in Pierce & Buxbaum, 2002; Sunderland, Walker, & Walker, 2006; Stone et al., 1993 as cited in Ting et al., 2011) and also following right and left hemisphere strokes (Bowen, McKenna, & Tallis, 1999). However, several studies reported that nearly half of the right hemisphere stroke patients suffered from USN (Buxbaum et al., 2004; Ringman, Saver, Woolson, Clarke, & Adams, 2004) while the disorder is more rare after left hemisphere strokes (Bowen et al., 1999; Ringman et al., 2004).

USN causes parts of our perceptual space to completely vanish from our consciousness (Revonsuo, 2010). It can be defined as "the inability to respond to or to orient towards stimuli located in the hemispace contralateral to the lesion of one of the cerebral hemispheres, where these symptoms are not due to the primary sensory or motor deficits" (Tsirlin, Dupierrix, Chokron, Coquillart, & Ohlmann, 2009, p. 175). Corbetta and Shulman (2011) presented several common characterizations associated with USN, such as a decreased reaction speed when patients process stimuli during target detection tasks. A lower physiological arousal from stimuli has also been detected by measuring autonomic, electrophysiological, and behavioral activity. Ogden (1987) pointed out that USN can appear in any sensory modality and even in multiple modalities in the same patient. However, it is most frequently reported in the visual/visuospatial sensory modality. Corbetta and Shulman (2011) stated that although the visual cortex is intact with normal visual perception, a bias towards directing spatial actions to the same hemispace as the lesion is often observed in patients. Further, damage to cortical and subcortical areas often associated with USN are located in the right hemisphere, an idea generally shared by others (Buxbaum et al., 2004; Revonsuo, 2010). USN may also be related to the hypoperfusion (dereased blood flow) to several cortical areas not detectable by structural brain imaging, rather than due to the detectable lesions to the specific subcortical areas (Hillis et al., 2005). It can also relate with lesions extending to white matter pathways (Bird et al., 2006; Bortolomeo, Thiebaut, & Doricchi, 2007; Vandenberghe & Gillebert, 2009).

The term USN is used in literature together with various interchangeable terms due to the numerous existing subtypes of USN. The most common terms mentioned are; unilateral neglect, hemineglect, hemi-inattention (Bowen et al., 1999), hemispatial neglect, visual neglect, and visual inattention (Ting et al., 2011). Therefore, the term USN is broad and appropriate to be used consistently. In cases where the term neglect is used, it refers to USN. This may avoid confusion for readers since the meaning of all terms presented above is rather similar. Ogden (1987) pointed out that visual neglect is occasionally defined differently when it involves a pure visual field deficit after damage to the optic pathways or the visual cortex.

The purpose of this review is to provide a unified perspective of USN but mainly with respect to the visual aspect because that has been investigated in the majority of reported studies. The review will initially describe typical behavioral manifestations of patients suffering from USN and the close relationship between perceiving and conceiving the world around us. Reported prevalence rates post-stroke and several subtypes of USN are presented but mostly in regard to the visual aspect. The following section describes the different clinical assessment methods and those most commonly used. Next, the anatomical correlates of the USN subtypes are presented followed by the theory of a right hemisphere dominance of attention along with neuroimaging evidence either confirming or disconfirming this theory. Subsequently, the neural pathways of spatial attention will be described before presenting various rehabilitation methods for USN. This focuses particularly on PA, its effectiveness, and limitations because it is one of the most commonly used rehabilitation methods. The final section of the review is devoted to a general discussion which summarizes the main findings in above mentioned sections as well as providing concluding remarks and suggestions for future research.

Corbetta and Shulman (2011) argued for the importance to conduct research about USN primarily in order to establish a neurological model for our awareness, spatial cognition, and lateralization of the cerebral cortex. It is reasonable to agree with this proposal and suggest that these insights may provide a deeper understanding of how these neural networks, which are responsible for our perception of the world, operate. Thus, this knowledge may guide us towards improving individually suitable rehabilitation methods for patients suffering from USN, mainly since this disorder has several subtypes, a profound heterogeneity, and a multifactorial nature.

Behavioral Manifestations of Unilateral Spatial Neglect

Patients suffering from USN may show a wide range of peculiar behavioral manifestations following their loss of perceptual space (Revonsuo, 2010). As mentioned by Adair and Barrett (2008), patients may direct vision to one side when answering questions posed by an examiner, although the examiner is positioned on the other side. Some patients may ignore food on one side of the plate while eating only from the other side of the plate (Adair & Barrett, 2008; Revonsuo, 2010). Further, patients can also fail to see one side of their face in the mirror and therefore only shave or apply make-up to the other side of their face. Consequently, they can have an asymmetrical outward appearance because they do not see both sides of their face in the mirror (Becchio & Bertone, 2005; Revonsuo, 2010). Other cases reported that patients occasionally but unintentionally collide into objects located on one side (e.g., walls, door frames, or furniture) while not colliding with objects on the other side (Adair & Barrett, 2008; Becchio & Bertone, 2005).

It has also been shown that patients can have problems with imagining both sides of objects or scenes when attempting to describe or draw them from memory. However, these patients still seem to have the knowledge about the entire object or scene. They still have the ability to imagine themselves turning around in order to see the object or scene from another perspective (Revonsuo, 2010). Other common observations mentioned by Revonsuo (2010) concern patients instructed to use a pencil and paper to draw a clock or a flower simply by copying it. As a result, these pictures appear without having one side of the clock or the flower while only having details drawn on the other side (see Figure 1). Additionally, difficulties in reading have been recognized due to the inability to see the words on one side of the page, thus it becomes problematic for the patients to understand the whole content. Nevertheless, Becchio and Bertone (2005) pointed out that an extensive list of examples regarding different behavioral manifestations could be given.

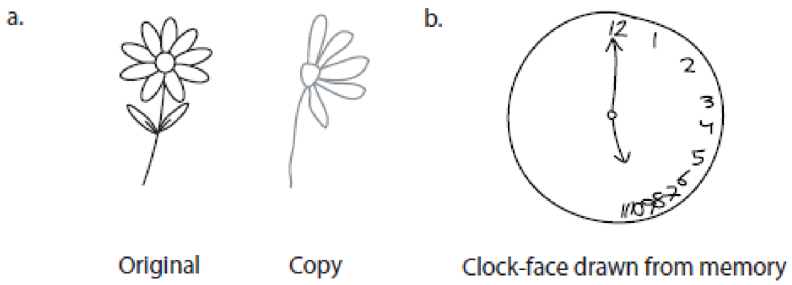

Figure 1. Neuropsychological tests that reveal neglect. **a.** Asked to draw a copy of a flower, a neglect patient leaves out the details on the left, thus producing only a half-flower. **b.** Asked to draw a clock-face, the patient will try to fit all the numbers and clock-hands into the right side of the clock. These tests dramatically reveal that neglect patients have lost the awareness of the left side of perceptual space. Modified from *Consciousness: The science of subjectivity* (p. 110), by A. Revonsuo, 2010, New York, NY: Psychology Press. Copyright 2010 by Psychology Press. Reprinted with permission.

Perceiving & Conceiving the World

It is important to realize the close relationship between perceiving and conceiving the world, especially with respect to USN patients. The different behavioral manifestations presented above by (Adair & Barrett, 2008; Becchio & Bertone, 2005; Revonsuo, 2010) indicated that the perceptual experience of the world for patients with USN comprises only a half world. The other half of their perceptual space do not exist and has never existed. Therefore, their perception of a half world is simultaneously conceived as the whole world (Becchio & Bertone, 2005). Revonsuo (2010) suggested that these patients do not realize that their simulated world in their consciousness only represents half of the world, mainly because the empty space do not exist and has not left any detectable empty space behind.

Prevalence Rates of Unilateral Spatial Neglect after Stroke

Approximately 3-5 million patients suffer from a stroke every year as reported by Ogourtsova, Korner-Bitensky, and Ptito (2010). Inconsistencies regarding prevalence rates of USN have been reported following right hemispheric strokes (Bowen et al., 1999). According to Bowen et al. (1999), this inconsistency is due to differences in subject selections between studies, the timing of assessment after onset of stroke, the choice of assessment tools, and differences in lesion location among patients. Ringman et al. (2004) further pointed out that increased age in patients, particularly with a stroke in the right hemisphere is associated with USN. Thus, age is another contributing factor to this inconsistency. The diagnostic assessment and effectiveness of rehabilitation methods are reliant on increased knowledge concerning the underlying mechanisms of USN, given the heterogeneity and disabling effects of the disorder (Ogourtsova et al., 2010).

An extensive study in the US included 1,281 stroke patients and assessed the presence and severity of USN both during the acute phase (within 1 week) and after 3 months. This was assessed accordingly with the NIH Stroke Scale (NIHSS) and by computed tomography (CT) scans. During the acute phase, results indicated a prevalence rate of USN in 43% of the patients following right hemispheric stroke, while occurring in 20% among the left hemispheric stroke patients (Ringman et al., 2004). After 3 months, the presence of USN was shown in 17% of the patients with lesions confined to the right hemisphere while only 5% had USN among the patients with lesions within the left hemisphere (Ringman et al., 2004).

A relatively similar prevalence rate was reported in a study by Buxbaum et al. (2004), showing that severe and persistent USN appeared in 48% of 166 patients with right hemispheric stroke. A wide range of behavioral test batteries were used for the assessment while lesion locations were assessed with both CT scans and T2/proton density magnetic resonance imaging (MRI). These recent studies by (Buxbaum et al., 2004; Ringman et al., 2004) presented relatively consistent prevalence rates of USN after stroke. However, earlier reported studies indicated wide ranging prevalence rates, ranging from 13% of stroke patients (Sunderland et al., 1987) to 81% (Stone, Wilson, & Wroot, 1991) (as cited in Pierce & Buxbaum, 2002). Additionally, other studies reported the prevalence rates to range even more widely, from 8% (Sunderland et al., 2006) to 82% (Stone et al., 1993), supporting the idea of inconsistencies among reported prevalence rates in studies (as cited in Ting et al., 2011).

Subtypes of Unilateral Spatial Neglect

There are several subtypes of USN with distinct classifications accordingly (Ting et al., 2011). Vallar (1998) conceptualized these subtypes of USN by classifying them in terms of three separate categories; modality (input/output), spatial representation, and range of space (see Figure 2). A fourth category has also been described and includes two subtypes of pure imagery neglect (see Figure 2) (Guariglia & Pizzamiglio, 2007; Ortique et al., 2003; Pizzamiglio, Guariglia, Nico, & Padovani, 1993).

The first category is modality and is separated into input and output. Sensory neglect concerns the input modality. This subtype of neglect is associated with the perceptual unawareness of sensory stimuli in the hemispace contralateral to the lesion. It can involve the tactile/somatosensory, the auditory, or the visual/visuospatial sensory modality. Premotor neglect concerns the output modality characterized by the inability to orientate the limbs towards the contralateral hemispace to the lesion, although awareness of the stimulus remains intact (see Figure 2) (Vallar, 1998).

The second category regards spatial representation, also referred to as the frame of reference. It involves a distinction between two subtypes of neglect; the egocentric (viewer-centered) and the allocentric (stimulus-centered) neglect. The former is described as the inability to spatially focus attention towards the hemispace contralateral to the lesion relative to the midline of the observer's body, head, or eye. The latter is a failure of the observer to focus attention towards one side of a stimulus, regardless of the stimulus position in relation to the midline of the observer's body, head, or eye (see Figure 2) (Adair & Barrett, 2008; Corbetta & Shulman, 2011; Vallar, 1998).

Further, the third category separates neglect into three different range of spaces (personal, peripersonal, and extrapersonal). This divide them into the space of the observer's body (personal), the space within the observer's arm's reach (peripersonal), and the space outside the observer's arm's reach (extrapersonal) (see Figure 2) (Vallar, 1998).

Representational & Perceptual Neglect

The fourth category includes two additional subtypes of neglect (Guariglia & Pizzamiglio, 2007; Ortique et al., 2003; Pizzamiglio et al., 1993) and is categorized as neglect of pure mental imagery. These two subtypes of neglect have distinct impact on spatial representations (Guariglia & Pizzamiglio, 2007) (see Figure 2). In order to put this into perspective, a study by Pizzamiglio et al. (1993) described a case with one patient (MC) having representational neglect and the other patient (BM) having perceptual neglect. Both patients were separately placed in the center of a room and asked to visually observe the four surrounding walls (including objects). Their verbal descriptions of the room were recorded in order to be compared to the recordings of their mental descriptions of the room, approximately one hour after while both patients were outside the room.

Results indicated a clear difference between both patients ability to perform memory recall of the room and its objects. Patient MC provided a detailed description of the whole room and its objects while visually observing it, but was only able to describe one side of the room when mentally describing it. Patient MB only described one side of the room while visually observing it, but was able to describe both sides of the room when mentally describing it. The important difference between these two subtypes of imagery neglect in these patients concerns the ability to navigate and build a cognitive map of an environment by forming a mental representation based on memory recall. While patient MC indicated a failure in constructing a mental map of the whole environment and thus being unable to recall it from memory, patient MB was successful in constructing this mental map of the entire room (Pizzamiglio et al., 1993). Guariglia and Pizzamiglio (2007) mentioned that many reports argued for a remarkable dissociation between the ability to visually represent an entire environment, while failing to mentally represent it entirely as in representational neglect. In perceptual neglect, this dissociation occurs vice versa as shown by Pizzamiglio et al. (1993).

A neural model developed by Byrne, Becker, and Burgess (2007) suggested that a deficit in translating visuospatial information from the egocentric to the allocentric reference frame (and vice versa) is related to representational neglect in regard to the failure of mentally navigating in an environment. Moreover, Ortique et al. (2003) suggested that representational and perceptual neglect have separate cortical systems. Additionally, damage to a system monitoring the egocentric frame of reference results in representational neglect (Rode, Rossetti, Perinin, & Boisson, 2004; Ortique et al., 2003).

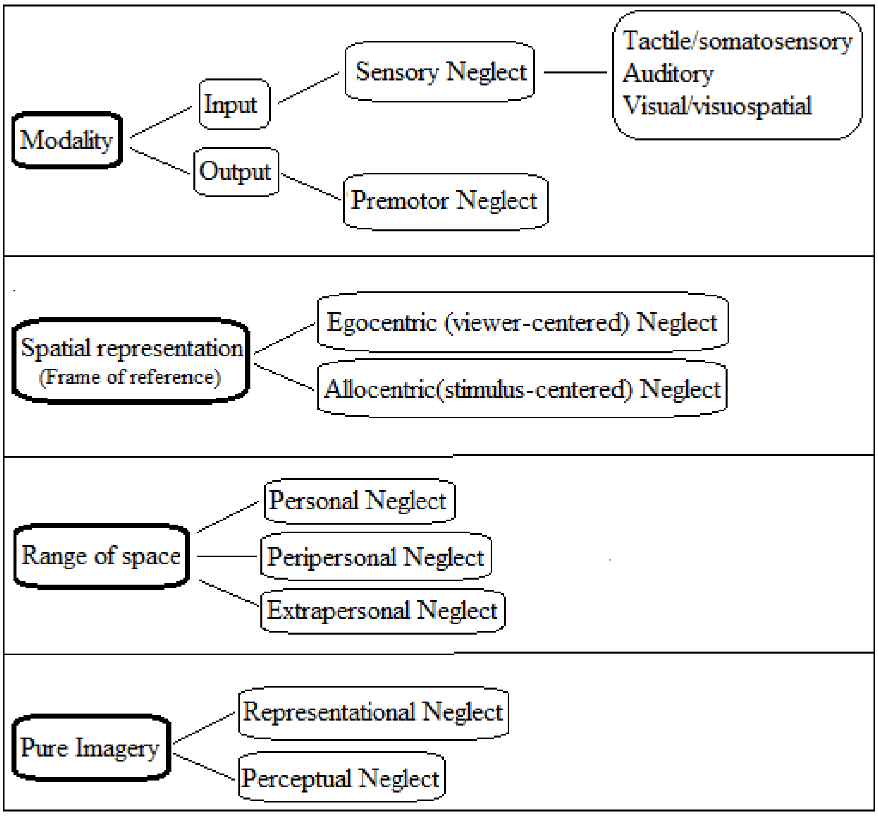

Figure 2. A conceptualization of the four main categories including the different subtypes of USN.

Clinical Assessment of Unilateral Spatial Neglect

Conventional Tests

There are various methods for the clinical assessment of USN. These methods are commonly divided into four main groups; pencil-and-paper tests, behavioral assessment tools, clinical observations, and recent virtual reality techniques (Ting et al., 2011).

The first group comprises conventional pencil-and-paper tests (Ting et al., 2011), such as cancellation tests, the line bisection test (LBT), and copying and drawing tests (Robertson, Tegnér, Tham, Lo, & Nimmo-Smith, 1995) often used for the assessment of USN (Kerkhoff, 2001). The aim of the cancellation tests is to instruct the patient to delete numerous identical visual targets on a paper sheet. The indication of USN can be assessed subsequently if the patient fails to detect and thus delete the targets on one side of the paper. Several modifications of the cancellation test frequently used are the star cancellation, letter cancellation, and the bell cancellation tests but having a similar purpose (Ting et al., 2011).

In the LBT, the patient is instructed to bisect a horizontal line as close to the midline as possible. This will indicate the potential orientation bias if the bisection is located further to the left or the right side relative to the midline of the horizontal line. The LBT is effective for assessing USN because it requires less time than the cancellation tests (Ting et al., 2011).

The copying and drawing tests ask patients to draw a copy of a picture (e.g., a clock, house, flower, or a face) in order to observe if only one side of the picture is drawn, thus indicating USN (Ting et al., 2011). These conventional pencil-and-paper tests are easy to administer but potential limitations are eminent. USN in extrapersonal space, auditory USN, and other subtypes of USN cannot be assessed. These tests may also not reflect essential everyday tasks occurring in the natural environment (Tsirlin et al., 2009). In addition, distinguishing between the sensory (input) and premotor (output) modality is difficult because these tests entail both visual attention and motor responses (Ting et al., 2011).

Non-Conventional Tests

The second group includes various non-conventional behavioral assessment tools. The most widely used tools are the behavioral inattention test (BIT) and the Catherine Bergego scale (CBS). The BIT contains six conventional paper-and-pencil tests (e.g., line crossing, letter cancellation, and star cancellation) and nine non-conventional behavioral tests (e.g., telephone dialing, article reading, and card sorting), altogether forming a 15-item checklist. However, the personal space is not properly assessed with the BIT. This is a serious limitation since USN can consist of several subtypes completely independent of each other, such as those affecting the range of spaces (Ting et al., 2011).

The CBS scale consists of a 10-item checklist and primarily aims to assess the performance of different daily activities rather than using test situations as in the BIT. This functional performance is assessed during activities that can be associated to all range of spaces (e.g., shaving the face (personal), eating food from a plate (peripersonal), or colliding into objects (extrapersonal)). Therefore, the CBS is rather to be used than the BIT, although both are recommended as behavioral assessment tools for patients indicating symptoms of USN (Ting et al., 2011).

Lindell et al. (2007) conducted a study including 31 healthy control participants and 34 patients with a right hemisphere stroke as confirmed with CT and MRI scans. Among the 34 stroke patients that were clinically assessed after 2-3 weeks post-stroke, 24 indicated symptoms of neglect in at least 1 of the 10 tests used. These tests included several conventional pencil-and-paper tests, non-conventional behavioral tests, among other tests. However, the primary aim of this study was to present the heterogeneity and multifactorial nature of neglect by showing that a wide range of different tests are needed in order to provide a sufficient clinical assessment of the disorder.

Clinical Observations

A third group of assessment method is also useful because USN in the acute phase can be elusive and thus difficult to detect. This method focuses on investigating the history of the patient by asking friends and family how the patient's behavior was prior to the stroke. Clinical observations are therefore important to include and can provide a more comprehensive understanding of the patient's deviant neglect behavior when it is compared to the patient's normal behavior (Ting et al., 2011).

Virtual Reality Techniques

Besides using conventional paper-and-pencil tests or non-conventional behavioral assessment tools as aforementioned, more recent promising virtual reality (VR) techniques have been developed. In regard for assessing USN patients, this fourth method produces virtual 3D worlds by simulating computer-generated environments (Tsirlin et al., 2009). Although VR techniques have been recently developed with respect to USN (Tsirlin et al., 2009), they can provide additional knowledge about the disorder by creating different virtual situations of daily tasks (Ting et al., 2011). Therefore, they can enhance conventional tests by incorporating them into VR versions, thus giving a more accurate and sensitive assessment procedure. They are not restricted to the patient's direct observation or search patterns as in a natural environment. Virtual reality based techniques can also create harmless environmental situations and can investigate functional performance in a variety of tasks in daily living (Tsirlin et al., 2009).

A study by Gupta, Knott, Kodgi, and Lathan (2000) investigated the spatial bias of vision in 2 USN patients and 4 healthy controls. A VR-Eye system was used consisting of a head-mounted display (HMD) which can track eye movements. The USN patients and the healthy controls performed two separate tasks. In the first task, they were instructed to name objects located in rows from left to right. In the second task, they observed an image of a clock and were instructed to identify the time. Results showed a significant difference between the USN patients and the healthy controls with respect to their performance in the two tasks. While the recorded eye movements of the healthy controls showed no signs of difficulty in the tasks and exhibited appropriate eye gaze, the USN patients directed eye movements only towards the contralateral hemispace to the lesion, thus not being able to use spatial vision properly and identify stimuli in both hemispaces.

Another study using VR technology was conducted by Tanaka, Sugihara, Nara, Ino, and Ifukube (2005). Eight stroke patients with left USN were included in the study after being scanned with CT or MRI, thus confirming lesions to different regions in the right hemisphere. Initially, the functional performance of various daily tasks was assessed, followed by two cancellation tests on paper sheets (line cancellation and star cancellation) as included in the BIT in order to assess neglect without using the HMD. Subsequently, a digital camera took pictures of the tests and presented them for the patients while using the HMD. These two special spatial tests consisted of a zoom-in condition and a zoom-out condition as altered by the digital camera and displayed accordingly in the HMD. The aim was to modify the visual input respectively. Results showed that patients focused more on the right side of the paper sheets during the two special spatial tests while using the HMD compared to when not using the HMD. Therefore, Tanaka et al. (2005) suggested that the symptoms of neglect in these patients can be aggravated by using a HMD due to the increased focus on objects, causing a stronger attention bias to the right side of the paper sheets during these tests.

Although the VR techniques are promising, there are some important limitations. This method of assessment is based on a virtual environment and may not correspond accurately to the natural environment. This has an impact on the performance of patients (Tsirlin et al., 2009). Another limitation is that most VR techniques mainly focuses on the visual deficit of USN and fail to investigate all three range of spaces, but instead only the peripersonal (Tsirlin et al., 2009; Ting et al., 2011) and rarely the extrapersonal space (Ting et al., 2011). Ting et al. (2011) pointed out the importance for future research of VR techniques to develop additional types of VR systems (e.g., auditory systems) in order to efficiently assess other aspects of the disorder.

Anatomical Correlates of Unilateral Spatial Neglect

Egocentric & Allocentric Neglect

USN is not only a disorder of spatial attention but also a disorder with a deficit for recognizing relevant objects among irrelevant ones in the neglected hemispace. This sensory distinctiveness is referred to as saliency. It primarily concerns the egocentric frame of reference (Corbetta & Shulman, 2002). This subtype of USN is more frequently observed than USN of the allocentric space (Ting et al., 2011). Several studies reported distinct neural mechanisms underlying these two subtypes of neglect concerning the spatial representation or also called the frame of reference (Ting et al., 2011). However, brain imaging methods such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have revealed that USN in general is commonly associated with damage to the angular gyrus (AG) and the temporoparietal junction (TPJ) posterior to the right inferior parietal lobe (IPL**)** (Heilman, Valenstein, & Watson, 2000; Hillis et al., 2005; Mort et al., 2003; Vallar & Perani, 1986), the right superior temporal gyrus (STG) (Karnath, Ferber, & Himmelbach, 2001; Karnath, Berger, Küker, & Rorden, 2004), and the right inferior frontal lobe (IFL) (Husain & Kennard, 1996). In addition, a disconnection between the frontal, the temporal, and the parietal cortex can lead to USN due to damage to the white matter pathways as identified by using diffusion tensor imaging (DTI). These potential lesions extend beyond the lesions identified by other structural imaging methods (Bird et al., 2006; Bortolomeo et al., 2007; Vandenberghe & Gillebert, 2009).

With respect to the anatomical correlates of egocentric and allocentric neglect, Hillis et al. (2005) conducted a study including 50 patients with acute subcortical infarcts (within 48 h of onset of neglect symptoms) within the right hemisphere (the basal ganglia, the thalamus, and/or the adjacent white matter). The purpose was to investigate how hypoperfusion in distinct cortical areas beyond detection of structural imaging (e.g., MRI) results in either egocentric or allocentric neglect, although subcortical infarcts are evident. The results indicated a strong relationship between egocentric and allocentric neglect and hypoperfusion to several cortical areas in 16 of the patients who matched the criteria for these two subtypes of neglect (11 with egocentric, 4 with allocentric, and 1 with both subtypes).

The patients with egocentric neglect had hypoperfusion to the right AG (Brodmann's area (BA) 39), the right supramarginal gyrus (SMG) (BA 40), the right posterior inferior frontal gyrus (IFG) (BA 44), and the right visual association cortex (BA 19). In contrast, patients with allocentric neglect had hypoperfusion to the right STG (BA 22) and the right posterior inferior temporal gyrus (ITG) (BA 37). Further, hypoperfusion to the right AG (BA 39) was most strongly associated with egocentric neglect while hypoperfusion to the right STG (BA

22) was most strongly associated with allocentric neglect. The single patient with both subtypes of neglect had hypoperfusion to all of the above mentioned BA's but with additional hypoperfusion to BA 4 and 6, except BA 19 (Hillis et al., 2005). These results are in line with previously mentioned studies of anatomical correlates of USN (Heilman et al., 2000; Husain & Kennard, 1996; Mort et al., 2003; Vallar & Perani, 1986; Karnath et al., 2001; Karnath et al., 2004) while also supporting (Ting et al., 2011) in that egocentric neglect is more common than allocentric neglect.

Personal, Peripersonal, & Extrapersonal Spatial Neglect

Other studies of stroke patients also identified separate neural mechanisms in the three different subtypes of neglect concerning range of space, indicating that peripersonal neglect occurs most frequently unaccompanied or together with personal neglect (Buxbaum et al., 2004; Lindell et al., 2007). However, clinical assessment of patients in earlier studies have often focused on the performance in peripersonal space regarding gradients in both lateral (left-right) and radial (near-far) space, indicating differences in attentional ability (Butler, Eskes, & Vandorpe, 2004). In this study, Butler et al. (2004) aimed to investigate the performance in both lateral and radial gradients not only in peripersonal space but also in extrapersonal space. The participants in the study were divided into three groups as follows: 7 right hemisphere stroke patients with neglect, 10 right hemisphere stroke patients without neglect, and 10 healthy subjects as a control group. Lesion locations were confirmed with CT scan together with a variety of clinical assessment tests (e.g., BIT) used as a neuropsychological baseline procedure in order to determine if neglect was present or not. All participants were then instructed to visually scan and verbally report stimuli located on a paper sheet, either in peripersonal or extrapersonal space.

Results showed that the right hemisphere stroke patients with neglect had increased lateral gradients regarding detection of the stimuli in both peripersonal and extrapersonal space as compared with the other two groups. In addition, results proposed distinct neural networks for perceiving and responding to stimuli in peripersonal and extrapersonal space. While peripersonal neglect was associated with lesions to areas of the dorsal stream, extrapersonal neglect was associated with lesions to areas in the ventral stream (Butler et al., 2004). However, these results deriving from the actual study by Butler et al. (2004) have been interpreted differently in a review by Adair and Barrett (2008), who stated that peripersonal neglect is associated with ventral stream lesions while extrapersonal neglect is associated with dorsal stream lesions. Nevertheless, Butler et al. (2004) reported that all neglect patients had lesions to the posterior parietal cortex (PPC) with additional lesions to other single cortical or subcortical areas. Lesions to specific areas in the frontal, the temporal, the parietal or subcortical structures were also observed in 5 of the 7 neglect patients. In contrast, the right hemisphere stroke patients without neglect had no lesions to the PPC but only lesions confined to single cortical areas, single cortical areas together with subcortical structures, or only to subcortical structures. These results supported the previous proposal that lesions to the PPC are often associated with USN (Buxbaum et al., 2004; Heilman et al., 2000; Hillis et al., 2005; Mort et al., 2003; Revonsuo, 2010; Vallar & Perani, 1986).

Other studies with PET (Weiss et al. 2000) and repetitive transcranial magnetic stimulation (rTMS) (Bjoertomt, Cowey, & Walsh, 2002) have reported additional support for distinguishing between the neural networks involved when perceiving and reporting stimuli in peripersonal or extrapersonal space. Weiss et al. (2000) conducted a PET study with 12 healthy participants asked to perform two independent tasks with a laser pointer; LBT and a second task pointing the laser towards appearing dots. Results showed that irrespective of the performance in the two tasks, dorsal stream activity was observed in the left dorsal occipital cortex, the left intraparietal cortex, the left ventral premotor cortex, and the left thalamus when participants performed these two tasks in peripersonal space. In contrast, a bilateral activity was observed in the ventral stream to areas such as the occipital cortex and the right medial temporal cortex when participants performed these tasks in extrapersonal space. These results are in line with the results by Butler et al. (2004) regarding the dichotomy between dorsal and ventral stream activity for peripersonal and extrapersonal space, while contradicting the proposal made by Adair and Barrett (2008).

In the study by Bjoertomt et al. (2002), rTMS was used in order to stimulate several brain areas in 6 healthy participants while performing a task from either a peripersonal or extrapersonal space. The purpose of the task was to determine and respond to whether the right or the left side was longer in a number of pre-bisected horizontal lines. Following this baseline condition, rTMS stimulated the right PPC and three areas in the occipital cortex (the right dorsal, the right ventral, and the left dorsal). Regarding stimuli in the peripersonal space, results showed that by stimulating the right PPC, the perceived left side of the pre-bisected horizontal lines appeared shorter than the right side as compared to the baseline condition. Regarding stimuli in the extrapersonal space however, results showed that stimulation of the right ventral occipital cortex (without the right dorsal or the left dorsal) lead to similar perceptions of the pre-bisected horizontal lines. These results provide further support to the studies made by (Butler et al., 2004; Weiss et al., 2000).

In contrast to the studies mentioned above by (Bjoertomt et al., 2002; Butler et al., 2004; Weiss et al., 2000) investigating anatomical correlates of peripersonal and extrapersonal space, Committeri et al. (2007) conducted a study in order to study the anatomical correlates of personal and extrapersonal space. The subjects in this study were 52 stroke patients divided into four groups; both extrapersonal and personal neglect, only extrapersonal neglect, only personal neglect, and a control group without USN. All patients were investigated with different advanced methodological approaches, (e.g., MRI, subtraction analysis, and voxelbased lesion-symptom mapping) together with appropriate clinical neuropsychological evaluation for confirming USN in personal or extrapersonal space.

Results showed that USN in personal space was associated with lesions to the right IPL (the post-central gyrus and the SMG) and adjacent white matter pathways. USN in extrapersonal space was instead associated with lesions to the right ventral premotor cortex in the inferior precentral gyrus (BA 6) together with the dorsolateral prefrontal cortex in the anterior and ventral regions of the middle frontal gyrus (MFG). In addition, further areas associated with extrapersonal neglect were the anterior and middle STG, the superior temporal sulcus and neighboring white matter pathways (Committeri et al., 2007).

Representational & Perceptual Neglect

In order to investigate the anatomical correlates of pure imagery neglect, Guariglia, Padovani, Pantano, and Pizzamiglio (1993) conducted a study with a patient who suffered from a stroke 16 months prior to the experiment. The CT scans showed lesions to the right frontal lobe and the anterior temporal lobe. In addition, single-photon emission computed tomography showed hypoperfusion to the right frontal lobe and the left cerebellum distant from the lesion. Several clinical neuropsychological tests were performed by the patient including conventional tests (e.g., line cancellation and letter cancellation) along with other assessments for range of space and motor neglect. The overall performance in these tests did not show any signs of USN. However the patient still showed representational neglect when required to describe several familiar places from various starting positions, thus only describing the right side in the familiar places. Guariglia et al. (1993) suggested an involvement of the frontal lobe in certain types of mental imagery since many patients often show neglect in extrapersonal space together with representational neglect. This patient failed to use memory recall in order to organize it into the egocentric space. This proposal is in line with the neural model previously mentioned by Byrne et al. (2007).

In another study by Ortique et al. (2003), a patient with pure representational neglect in extrapersonal space was investigated. In order to confirm this, clinical neuropsychological testing consisted of conventional tests (e.g., LBT, line cancellation, and letter cancellation) along with several other tests for assessing the different range of spaces. In one of these tests for assessing neglect in extrapersonal space, the patient was asked to perform two separate tasks; first imagining and describing a familiar place (a square in the city Geneva) from two opposite locations. In the second task, the patient was asked to imagine the map of France and recall as many cities as possible from two opposite locations (Paris and Marseille).

Nevertheless, this patient showed representational neglect in extrapersonal space with regard to the egocentric space and lesions to the right lateral temporo-occipital junction as confirmed with MRI. Ortique et al. (2003) argued that temporal areas associate with mental representations of extrapersonal space from an egocentric space. They additionally suggested that in cases where pure representational neglect appears in peripersonal space, it involves lesions to parietal areas rather than temporal areas. Therefore, the earlier proposals by (Bjoertomt et al., 2002; Butler et al., 2004; Weiss et al., 2000) regarding the anatomical dichotomy between peripersonal and extrapersonal space are in line with results from pure mental imagery neglect as shown in this study by Ortique et al. (2003). While parietal areas relate to the dorsal stream and peripersonal space, temporal areas relate to the ventral stream and extrapersonal space (Bjoertomt et al., 2002; Butler et al., 2004; Ortique et al., 2003; Weiss et al., 2000).

Right Hemisphere Dominance of Spatial Attention

As stated in the early study by Stone et al. (1993), stroke to the right hemisphere more frequently causes persistent and severe deficits compared to left hemisphere strokes. However, in regard to USN, lesions occurring in both hemispheres can indeed result in this disorder, despite occurring more frequently after stroke to the right hemisphere. This assumption is supported by a widely recognized theory in neurology, postulating for a right hemispheric dominance of attention (Heilman & Van Den Abell, 1980; Kinsbourne, 1977, 1987, 1993; Mesulam, 1981; Weintraub & Mesulam, 1987, 1988), sharing the idea that both hemispheres distribute spatial attention to the contralateral hemispace. However, this attentional distribution appears in a somewhat asymmetric manner. While the right hemisphere is capable of directing spatial attention to both left and right hemispaces, the left hemisphere is only capable of directing spatial attention towards the right hemispace. Consequently, spatial attention towards the right hemispace can be compensated by the right hemisphere when lesions are confined to the left hemisphere. However, damage to the right hemisphere cannot be compensated by the left hemisphere, thus impairing spatial attention towards the left hemispace (Heilman & Van Den Abell, 1980; Kinsbourne, 1977, 1987, 1993; Mesulam, 1981; Weintraub & Mesulam, 1987, 1988).

Evidence from Neuroimaging on Spatial Attention

Corbetta, Miezin, Shulman, and Petersen (1993) conducted a study with PET during a series of psychophysical measures. The aim was to investigate the neural mechanisms of spatial attention while cueing visual stimuli in the left and right visual field respectively. PET scans were performed during the psychophysical tasks to measure the regional blood flow. One group of 24 healthy subjects was initially tested while a second group of 6 healthy subjects was included in a pilot psychophysical experiment.

The PET data indicated that the same area in the left superior parietal lobule (SPL) was activated during spatial attention to both right and left visual fields, although a stronger activation in this area was observed during spatial attention to stimuli in the right visual field. However, stimuli presented to either the right or the left visual field activated two distinct areas in the right SPL. Thus, spatial attention to the left visual field is controlled by one of these two areas in the right SPL while attention to the right visual field is controlled by the second area in the right SPL together with the left SPL (Corbetta et al., 1993). According to Corbetta et al. (1993), this suggests that there are two distinct representations in the right SPL capable of directing spatial attention to both left and right visual fields. In contrast, the single representation in the left SPL is only capable of directing spatial attention to the right visual field.

In regard to USN, a review by Riddoch et al. (2010) stated that these PET results by Corbetta et al. (1993) provide supporting evidence for the theory of a right hemisphere dominance of attention. However, as specifically claimed in the actual study by Corbetta et al. (1993), these results do not provide supporting evidence for the theory but rather a potential explanation derived from neuroimaging evidence regarding how spatial attention is distributed asymmetrically between the two hemispheres. Nevertheless, Corbetta et al. (1993) pointed out a possible confounder for this interpretation. The asymmetry in the parietal cortex activation could be due to a visuomotor interaction since all subjects responded to the stimuli in either visual field by using their left hand. Thus, spatial attention to the left visual field was processed by the right visual and motor cortices in an intra-hemispheric manner. However, spatial attention to the right visual field was processed by left visual cortex and the right motor cortex in an inter-hemispheric manner. The increased bilateral activation of the parietal cortex after spatial attention to the right visual field may therefore be due to the inter-hemispheric processes transferring information through corpus callosum.

Other recent studies by (Mevorach, Humphreys, & Shalev, 2006; Hodsoll, Mevorach, & Humphreys, 2009) have used transcranial magnetic stimulation (TMS) while healthy participants were instructed to perform several visual search tasks. After applying rTMS to the left and right PPC, results yield additional support for the argument that spatial attention is driven by the right hemisphere activation to salient stimuli as previously stated (Corbetta & Shulman 2002).

Neural Pathways of Spatial Attention

Ventral & Dorsal Visual Streams

As briefly described earlier, there seems to be two distinct attentional networks for processing visual information; the ventral stream and the dorsal stream. The ventral stream connects the visual cortex with the inferior temporal cortex and processes conscious perception and identification of objects. In contrast, the dorsal stream links the visual cortex with the SPL and the IPS and subconsciously integrating incoming visual information in order to create a spatial representation and thus perform visually guided movements towards objects (Goodale & Milner, 1992).

More recently, a different proposal was made by Corbetta and Shulman (2002) suggesting that these two attentional networks correspond to a ventral and a dorsal frontoparietal network rather than a ventral occipito-temporal and a dorsal occipito-parietal network as proposed by Goodale & Milner (1992). According to Corbetta and Shulman (2002), the ventral stream is strongly lateralized to the right hemisphere and connects the right TPJ (IPL and STG) and the right ventral frontal lobe (IFG and MFG). The role of this stream is to recognize and identify salient objects in a bottom-up manner. The dorsal stream however, is bilateral and connects the SPL/IPS with the dorsal frontal lobes (frontal eye fields (FEF). This stream operates in a top-down manner by using prior knowledge of what to search for in order to subsequently guide visuospatial directed movements towards that goal. Thus, there is a close interaction between bottom-up and top-down factors in regard to visual attention. Therefore, the suggestion by Corbetta and Shulman (2002) regarding how these two streams interact is that the ventral stream detects relevant stimuli while the dorsal stream spatially locates that stimulus. Another suggestion is that the ventral stream (particularly the right TPJ) disrupts the ongoing cognitive activity by interacting with the dorsal stream (particularly the bilateral SPL/IPS) when a salient stimulus is detected. The subject is therefore required to adopt a new attentional set based on the salient stimuli (see Figure 3).

In regard to USN, Corbetta and Shulman (2002) further pointed out that the neural localization of USN corresponds more closely with the strongly lateralized ventral stream than to the bilateral dorsal stream although USN is caused by a disruption in both of these two interacting attentional networks. These results derived from fMRI evidence support the theory of a right hemisphere dominance of attention previously discussed as well as providing a potential explanation for the higher prevalence rates of USN following lesions to the right PPC (see Figure 3).

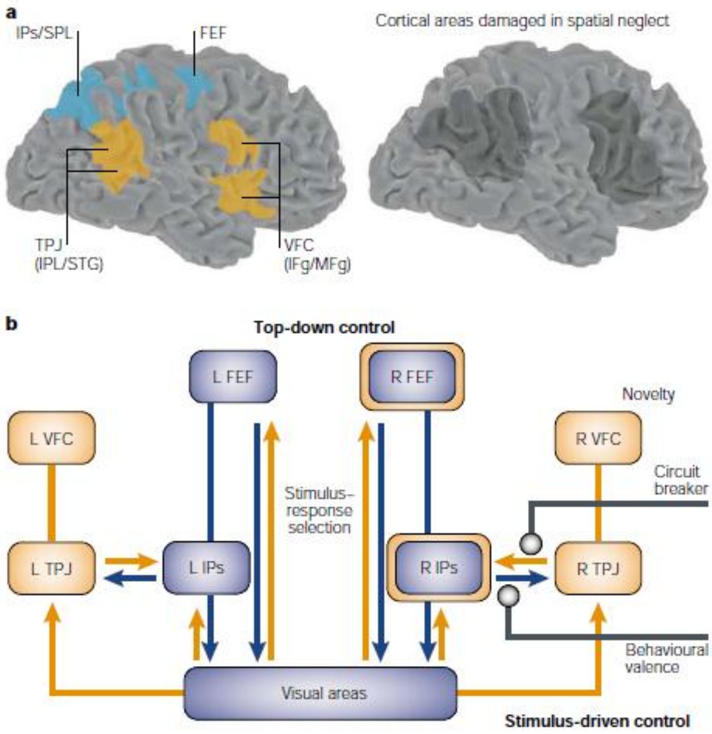

Figure 3. **Neuroanatomical model of attentional control. a** | Dorsal and ventral frontoparietal networks and their anatomical relationship with regions of damage in patients with unilateral neglect. Areas in blue indicate the dorsal frontoparietal network. FEF, frontal eye field; IPs/SPL, intraparietal sulcus/superior parietal lobule. Areas in orange indicate the stimulus-driven ventral frontoparietal network. TPJ, temporoparietal junction (IPL/STG, inferior parietal lobule/superior temporal gyrus); VFC, ventral frontal cortex (IFg/MFg, inferior frontal gyrus/middle frontal gyrus). The areas damaged in neglect (right) better match the ventral network. **b** | Anatomical model of top-down and stimulus-driven control. The IPs–FEF network is involved in the top-down control of visual processing (blue arrows). The TPJ–VFC network is involved in stimulus-driven control (orange arrows). The IPs and FEF are also modulated by stimulus-driven control. Connections between the TPJ and IPs interrupt ongoing top-down control when unattended stimuli are detected. Behavioural relevance is mediated by direct or indirect (not shown) connections between the IPs and TPJ. The VFC might be involved in novelty detection. L, left; R, right. Reprinted from "Control of goal-directed and stimulus-driven attention in the brain," by M. Corbetta and G. L. Shulman, 2002, *Nature Reviews Neuroscience, 3,* p. 212.

Rehabilitation Methods of Unilateral Spatial Neglect

Numerous rehabilitation methods have been developed with respect to patients with USN (see Figure 4). These methods can be separated into three categories; compensatory, substitutive, and restitutive (Kerkhoff, 2000). The first category concentrates on the remaining intact brain functions (Kerkhoff, 2000) by using (e.g., visual scanning therapy, optokinetic stimulation, neck muscle vibration, body rotation, or caloric stimulation). The aim is to manipulate the sensory input (e.g., visual, tactile/somatosensory, or the vestibular system) (Ting et al., 2011). The second category relies on methods such as optic devices (e.g., PA) (Kerkhoff, 2000; Ting et al., 2011) where improvements of neglect have been documented (Kerkhoff, 2000). The purpose of the third category is to use methods such as mental imagery, TMS, or VR-techniques (Ting et al., 2011) in order to retrain the impaired function (Kerkhoff, 2000). A study by Smania, Bazoli, Piva, & Guidetti, (1997) has shown that this mental imagery technique can result in positive long-term effects (6 months) in cases where patients show representational neglect of pure imagery.

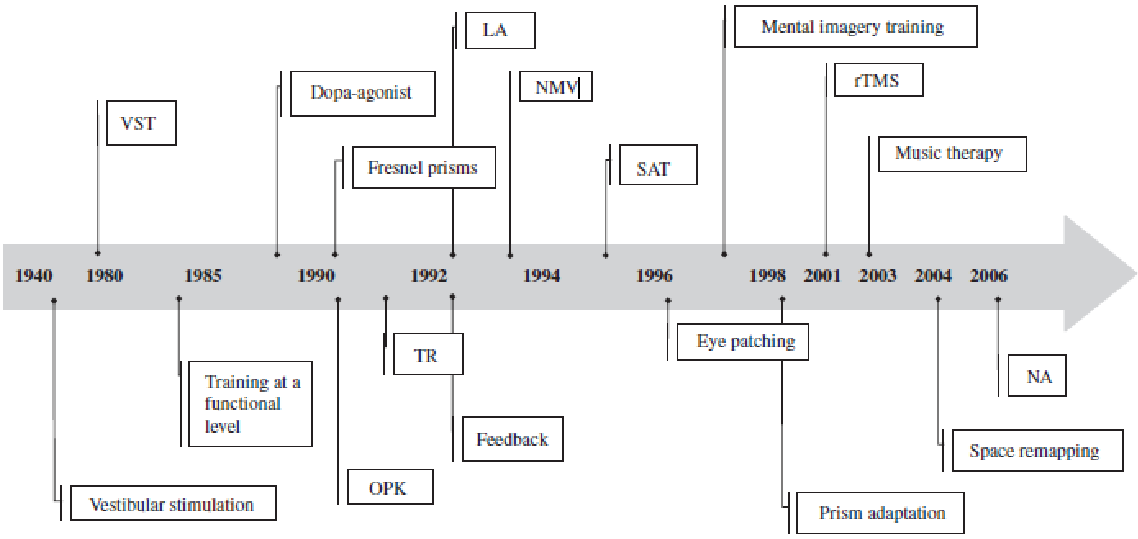

Figure 4. Time-line of the first publications for the 18 different attempts to remediate visuo-spatial neglect. *Abbreviations:* VST: visual scanning therapy; LA: limb activation; rTMS: repetitive transcranial magnetic stimulation; SAT: sustained attention training; OPK: optokinetic; NMV: neck muscle vibration; TR: trunk rotation; NA: noradrenergic agonist. Reprinted from "Visuo-spatial neglect: A systematic review of current interventions and their effectiveness," by J. Luauté, P. Halligan, G. Rode, Y. Rossetti, and D. Boisson, 2006, *Neuroscience and Biobehavioral Reviews, 30,* 961-982. Copyright 2006 by Elsevier Ltd. Reprinted with permission.

Prism Adaptation

One of the most common rehabilitation techniques for USN is PA. This inexpensive technique is relatively easy to use and has shown positive results among studies (Arene, & Hillis, 2007; Farne, Rossetti, Toniolo, & Làdavas, 2002; Frassinetti, Angeli, Meneghello, Avanzi, & Làdavas, 2002; Luauté , Halligan, Rode, Rossetti, & Boisson, 2006; Rossetti et al., 1998; Ting et al., 2011). If healthy participants wear prisms, they shift the vision in one direction (e.g., 10 degrees to the right) so that the patient fails to reach an object accurately. If this training is repeated during several trials, the participant eventually learns to reach towards the opposite direction (left) in relation to the rightward shift modified by the prisms. Subsequently, when the prisms are removed, a so called after-effect is seen which means that the participant still fails to reach the object, thus reaching towards the opposite direction (left) in relation to the objects actual location. This indicates that the motor system has adapted to the new visuomotor coordinates (Redding & Wallace, 2006).

The effectiveness of prism adaptation. Rossetti et al. (1998) conducted an initial study showing the positive effects of PA. In this study, 16 USN patients participated having a right hemisphere stroke as confirmed with CT scan. During the first experiment, a group of 8 neglect patients and 5 normal controls were required to point straight ahead towards a midline during 10 trials while blindfolded. While neglect patients pointed towards the right side, the normal controls accurately pointed towards the midline in relation to their egocentric reference frame. Subsequently, both groups performed 10 trials again while wearing prisms with a right optical shift of 10 degrees to the right. In these trials, objects appeared either to the left or the right in relation to their egocentric reference frame. After this PA exposure, the prisms were removed and both groups were blindfolded again. The results demonstrated that the neglect patients were more affected from the PA than the healthy controls. This was shown by greater leftward pointing after PA from the neglect patients compared to the healthy participants.

In the second experiment, 12 of the neglect patients were divided into a prism group and a control group. The prism group wore prisms with a right optical shift of 10 degrees while the control group wore neutral prisms without an optical shift. After the pointing session similar to that in the first experiment, both groups removed the prisms and performed five clinical assessment tests; LBT, line cancellation, a copying and drawing task, drawing from memory task, and reading a text in which they had performed prior to the PA exposure. The prism group showed great improvements in these tests compared to the control group who did not show a significant improvement. This improvement was seen during 2 hours after PA training and showed that this method can have positive results in future rehabilitation programs of neglect (Rossetti et al., 1998).

Other studies have also documented positive effects following PA (Farne et al., 2002; Frassinetti et al., 2002). In the study by Farne et al. (2002), 6 USN patients but also affected by the rare phenomena neglect dyslexia showed a right hemisphere stroke as confirmed with CT or MRI scans. In order to assess the severity of neglect, several visuospatial tests were used (e.g., line cancellation, bell cancellation), two tests from the BIT (letter cancellation and the LBT), and other visuoverbal tasks. They were then exposed with a short session of PA while pointing towards visual targets. Results showed long-lasting improvement of neglect (at least 24 h) after the PA session when performing the above mentioned visuospatial and visuoverbal tasks again.

In addition, Frassinetti et al. (2002) investigated 7 neglect patients with a right hemisphere stroke confirmed with CT scans. The assessment involved a wide range of tests in addition to the standard neuropsychological tests commonly used such as the conventional tests. Therefore, besides conventional pencil-and-paper tests, room description and object reaching tests were also used in order to assess everyday situations. Further, the BIT involving the conventional and non-conventional tests (e.g., picture scanning, telephone dialing, and article reading) were used. Another important aim of this study was to investigate the effects of PA (after performing pointing tasks) in the different range of spaces and to see if long-term improvements of neglect could be observed in these tests, in contrast to the short-term improvements presented in the earlier by Rossetti et al. (1998).

The 6 other neglect patients were included as a control group and performed the same clinical assessment tests as the 7 neglect patients in the experimental group. The control group however, was not exposed with PA. Results showed a difference in performance between both groups in all of the above mentioned clinical assessment tests after PA. Thus, PA training twice a day during a 2 week period increased performance significantly and improved neglect for the patients in the experimental group. This effect sustained for 5 weeks while this was not seen in the control group not performing PA training (Frassinetti et al., 2002).

Limitations of prism adaptation. There are some general limitations to PA worth to consider (Striemer & Danckert, 2010), although this technique has shown not only short-term improvements (Rossetti et al., 1998) but also long-term improvements of neglect (Farne et al., 2002; Frassinetti et al., 2002). Striemer and Danckert (2010) argued that PA influences anatomical structures related to the visuomotor pathways in the dorsal stream while the ventral stream concerned with perceptual saliency detection of objects is not influenced to the same extent. Another limitation raised by Striemer and Danckert (2010) is that PA studies often include few patients and visuomotor responses during PA are often performed with the same hand as during the measured performances in the subsequent tests (e.g., conventional, non-conventional tests). This technique may also show improvements of neglect in some patients while not in others. However, Adair and Barrett (2008) pointed out that PA has shown beneficial effects and a promising technique for neglect rehabilitation. Striemer and Danckert (2010) suggested that future research is required to investigate to what extent it influences the ventral and the dorsal streams to avoid these limitations.

Discussion

Brain injuries have shown to frequently result in USN (Revonsuo, 2010), although stroke is the most commonly reported cause (Corbetta & Shulman, 2011). Neurodegenerative diseases such as Huntington's disease (Ho et al., 2003) and Alzheimer's disease (Ishiai et al., 2000) have also shown to cause this disorder. Following stroke, mechanisms of spatial representation and attention can be damaged. These mechanisms are essential in order to experience the external world as a coherent whole. Therefore, these patients experience a half world since half of their perceptual space does not exist (Revonsuo, 2010). They also show peculiar behavioral manifestations affecting their functional performance in everyday life negatively (Adair & Barrett, 2008; Becchio & Bertone, 2005; Revonsuo, 2010).

USN following stroke to the right hemisphere appears more often (Buxbaum et al., 2004; Ringman et al., 2004; than stroke to the left hemisphere (Bowen et al., 1999; Ringman et al., 2004). The heterogeneity of USN affects reported prevalence rates (Bowen et al., 1999; Ogourtsova et al., 2010). This inconsistency is due to differences in subject selections between studies, the timing of assessment after onset of stroke, the choice of assessment tools, differences in lesion location among patients, and age differences (Bowen et al., 1999; Ringman et al., 2004). The theory of a right hemisphere dominance proposed that the right hemisphere is capable of directing spatial attention towards both hemispaces. In contrast, the left hemisphere is only capable of directing spatial attention towards the contralateral hemispace (Heilman & Van Den Abell, 1980; Kinsbourne, 1977, 1987, 1993; Mesulam, 1981; Weintraub & Mesulam, 1987, 1988).

Various interchangeable terms of USN are used in the literature, mainly due to the various subtypes of USN that exist (Bowen et al., 1999; Ting et al., 2011). These subtypes of USN are divided into four main categories (see Figure 2) (Guariglia & Pizzamiglio, 2007; Ortique et al., 2003; Pizzamiglio et al., 1993; Vallar, 1998). However, the majority of reported studies have investigated the visual aspect in these subtypes of USN. Therefore, these terms primarily refer to this aspect of USN, although they are all used widely in the different studies presented. It is reasonable to argue that it can be confusing to use several terms with a similar meaning. Thus, narrowing them down could perhaps clarify this issue of inconsistency.

A wide range of clinical assessment tests are often used to assess USN. These include both conventional paper-and-pencil tests and non-conventional behavioral tests (Ting et al., 2011). Ting et al. (2011) pointed out the importance of using a third assessment method called clinical observations. However, the reported studies in this review did not use this assessment method. Nevertheless, Tsirlin et al. (2009) pointed out that promising VR-techniques have been developed recently but not used to the same extent yet. Future research of VR may provide more sufficient assessment for the disorder because the heterogeneity of USN makes it difficult for these common clinical assessment methods to sufficiently assess all subtypes of the disorder.

Neuroimaging such as fMRI and PET have revealed common anatomical correlates of USN following damage to the right hemisphere. Damaged areas are often observed in the right AG and the right TPJ in the right IPL (Heilman et al., 2000; Hillis et al., 2005; Mort et al., 2003; Vallar & Perani, 1986), the right STG (Karnath et al., 2001; Karnath et al., 2004), the right IFL (Husain & Kennard, 1996), or damage to the white matter pathways extending beyond these structural lesions (Bird et al., 2006; Bortolomeo et al., 2007; Vandenberghe & Gillebert, 2009).

Regarding the spatial representation (frame of reference), different anatomical correlates have been observed in patients with hypoperfusion to distinct cortical areas beyond the detected subcortical infracts. Hypoperfusion to the right AG (BA 39), the right SMG (BA 40), the right posterior IFG (BA 44), and the right visual association cortex (BA 19) associated with egocentric neglect. Patients with allocentric neglect had hypoperfusion to the right STG (BA 22) and the right posterior (ITG) (BA 37) (Hillis et al., 2005). Further, differences in anatomical correlates were also reported in patients with USN in the different range of spaces. Peripersonal neglect was associated with lesions to areas in the dorsal stream while extrapersonal neglect was associated with lesions to areas in the ventral stream (Bjoertomt, et al., 2002; Butler et al., 2004; Weiss et al., 2000).

A different study by Committeri et al. (2007) showed that lesions to the right IPL (the post-central gyrus and the SMG) and adjacent white matter pathways were associated with personal neglect. Instead, extrapersonal neglect was associated with lesions to the right ventral premotor cortex in the inferior precentral gyrus (BA 6) together with the dorsolateral prefrontal cortex in the anterior and ventral regions of the MFG, the anterior and middle STG, the superior temporal sulcus, and adjacent white matter pathways.

In regard to neglect of pure imagery, Ortique et al. (2003) suggested that representational neglect for extrapersonal space in the egocentric space associated with lesions to temporal areas such as the right lateral temporo-occipital junction while representational neglect when appearing in peripersonal space associated with lesions to parietal areas. These results are in line with other studies (Bjoertomt, et al., 2002; Butler et al., 2004; Weiss et al., 2000), although this study investigated pure imagery neglect (Ortique et al., 2003).

There are two distinct but interacting attentional networks for processing visual information (Corbetta & Shulman, 2002; Goodale & Milner, 1992). However, Corbetta and Shulman (2002) recently proposed a ventral and dorsal frontoparietal network in contrast to the network proposed earlier by Goodale and Milner (1992) arguing for a ventral occipito-temporal and a dorsal occipito-parietal network. According to Corbetta and Shulman (2002), the ventral stream is lateralized to the right and involve structures such as TPJ (IPL and STG), and the right ventral frontal lobe (IFG and MFG). This stream detects objects and their relevance. The dorsal stream is bilateral and links the SPL/IPS with the dorsal frontal lobes (FEF). This stream guides visuospatial directed movements towards the object detected by the ventral stream. Both of these networks are crucial due to their interaction, although it is argued that the damaged areas causing USN are mostly related to the ventral stream.

PA is one of the most common rehabilitation methods for USN, although many others have been developed throughout the years (see Figure 4). Several studies show positive results following this method (Arene, & Hillis, 2007; Farne et al., 2002; Frassinetti et al., 2002; Luauté et al., 2006; Rossetti et al., 1998; Ting et al., 2011). Short-term improvement of neglect was shown by Rossetti et al. (1998) conducting the first study with PA. However, long-term improvements of neglect have also been reported by others (Farne et al., 2002; Frassinetti et al., 2002). One important limitation of PA is that it may affect visuomotor pathways associated with the dorsal stream to a more extent than the perceptual detection of objects associated with the ventral stream. Other limitations are that PA studies often include few patients and that the visuomotor responses during PA training are typically performed with the same hand as when performing the conventional and non-conventional tests for measuring its effectiveness after the PA exposure (Striemer & Danckert, 2010).

Conclusion

It is difficult to investigate USN mainly because its heterogeneity. This disorder is most often caused by stroke to specific anatomical structures in the right hemisphere. However, distinct anatomical correlates have also been confirmed in regard to the several subtypes of USN. Dividing the disorder into several subtypes and investigating them separately with neuroimaging methods is crucial because patients can suffer from one or more subtypes of USN simultaneously. Clinical assessment and rehabilitation methods are specifically reliant on this increased knowledge in order to be further developed. While continuing with PA methods in rehabilitation, future research should attempt to focus on recent VR-techniques. Incorporating these techniques into conventional and non-conventional tests may provide a less restricted approach by avoiding these natural environments. Thus, perhaps additional subtypes of USN can be investigated more sufficiently. In addition, further investigation of the distinct neural pathways of spatial attention and their interaction is needed. This may provide potential explanations about its relation to the different subtypes of USN. It may also increase understanding of how the brain operates to fully experience the world as a coherent whole.

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