A syndrome of spatial attentional spectrum

Neuropsychology of spatial neglect

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Summary

There is no consistency in the terms used to refer to the syndrome of spatial neglect, with different terms used to refer to the syndrome as a whole or one of its subtypes. There are hundreds of neglect tools available. However many are not able to differentiate presenting subtypes. It is important for clinicians and researchers to critically evaluate the neglect tools being used for the screening and diagnosis of neglect. The objective of this review is to capture the reported definitions for the subtypes of neglect after stroke and map the range of assessment tools employed for each neglect subtype.

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Clinical manifestations

Spatial neglect can be defined as a failure to perceive, process and orient to stimuli in the somatic and extrasomatic space that is contralateral to a focal brain lesion. Importantly, the symptoms of spatial neglect cannot be explained by primary motor or sensory disorders, nor by intellectual disorders [1]. It is a multifaceted cognitive disorder that manifests through different symptoms [2]. The percentage of stroke patients who experience spatial neglect varies widely and ranges from 15% to 85% during the acute stage (<20 days), and 30% to 40% after 3 months [33, 107]. More than 80% of patients screened with a detailed battery show some degree of neglect on at least one measure, and 36% show moderate to severe neglect across several measures [33].

Neglect cannot solely be explained by sensory disturbances, as impairments of perceptual processing are also noted in people with neglect. In the acute phase of the disorder, patients show a reproducible ipsilesional deviation of the head and eye [1]. Moreover, they may respond to stimuli coming from the contralesional side as if it was coming from the ipsilesional side [2]. Perceptual extinction is another symptom that cannot be explained by sensory disturbance and is present 23% of the time [111]. When two stimuli are presented simultaneously on each side, the stimulus on the contralesional side is not perceived. However, the same stimulus on the contralesional side is perceived when presented alone. The inability to orient to the contralesional side when presented with a competing stimulus in the intact side can be interpreted as a deficit in spatial attention [3–5] and is present 70% of the time [111].

Motor deficits are associated with spatial neglect and have an incidence of 33% [112]. Multiple studies have tried to distinguish motor deficits from perceptual deficits using different techniques. For instance, in a study by Husain et al. [6] participants had to move their hand, starting from different positions, to respond to a target light appearing on the right or left of a central fixation point. The findings of this study, coupled with findings from other similar studies [7, 8], suggest that patients with neglect may fail to initiate movements in the contralesional area in addition to failing to perceive contralesional visual stimuli. This symptom has been called "premotor neglect" [7]. Another aspect of motor neglect affects the limbs of patients with neglect and is termed "unilateral hypokinesia" [9]. This symptom is characterised by a reduction in spontaneous use and movement of the contralesional limb, without the presence of limb paralysis or weakness [10].

The complex and heterogeneous nature of spatial neglect arises not only from the multisensory modality of the disorder [11], as discussed above, but also from the different reference frames and sectors of space [1]. Moreover, adding to the complexity of the disorder, neglect can affect the mental representation of objects. This deficit can be measured using mental imagery tasks such as asking individuals to describe from memory elements of a familiar place or objects. Neglect patients may omit certain elements in the contralesional side of the setting or object [12].

Different frames of reference can define spatial neglect when left-right coordinates are considered. The contralesional portion of space that is neglected varies between different tasks and stimuli, and between patients. This frame of reference is defined as "egocentric" because it is relative to the midline of the body or head of the individual [108]. Studies have shown that individuals exhibit a biased perception of "straight ahead" by orienting to the right as a default position for their head [13, 14]. Neglect can also affect the left side of each individual object, regardless of their egocentric localisation. This frame of reference is defined as "allocentric" because it is object-centred neglect. Patients may eat food from one side of the plate, shave and apply cosmetics to one side of the face [15]. Moreover, patients may neglect letters during reading and spelling of words [16, 17]. Multiple studies have examined ob-

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ject-centred neglect by manipulating the orientation and nature of the stimulus presented [18–20]. Patients show worse neglect for the left side of an object presented in the right visual field than for the right side of an object presented in the left visual field, which shows the allocentric frame of reference of neglect.

Neglect can selectively affect different sectors of space that can be divided into personal, peri-personal and extra-personal space. The neglect of personal space is defined as the failure of the patient to investigate the contralesional half of their body [21]. To assess personal neglect, patients may be asked to use common objects such as combs, eyeglasses and razors. The symmetry of the task is assessed to determine the severity of personal neglect [22]. The neglect of peri-personal space is a deficit that concerns stimuli present within reaching distance of the patient. Peri-personal neglect is assessed using paper and pencil tasks that evaluate motor, perceptual and selective attention skills such as letter cancellation tests, barrage test and sentence reading test [1, 22, 23]. The neglect of extra-personal space affects stimuli that are present outside reach and in far space. Extra-personal neglect can be assessed using room descriptions and having patients utilise tools [24]. Each of these three subtypes is rarely seen alone, with personal and extra-personal neglect being the most frequent subtypes [22].

There are other types of neglect that are less evaluated and not as common. These include representational deficits and auditory neglect.

There are other types of neglect that are less evaluated and not as common. These include representational deficits and auditory neglect. Neglect of representational space was studied by Bisiach and Luzatti [113]. In their study, participants with visual neglect were asked to describe, from memory, a square in Milan. Consistent with visual neglect symptoms, the participants described the right side of the square and neglected to describe the left side. They were then asked to "turn around" in their mind and describe the square from the other side. This time, the participants were able to describe what had previously been to their left and neglect what was previously on their right. This demonstrates that long-term memory and mental representations are also affected in visual neglect. Auditory neglect is the inattention to stimuli that is presented on the controlesional space [114]. It is assessed by presenting the participant with two simultaneous verbal auditory stimuli in both ears, and then asking the participant to specify the best perceived stimulus. Auditory neglect is usually observed after lesions in the anterolateral parabelt and inferior parietal cortex, or the "where" pathway of the auditory cortex. It is also observed after lesions in the caudolateral parabelt and temporal cortex, or the "what" pathway [115].

It is worth noting that it is important to differentiate between visual neglect and hemianopia, a visual field defect. Hemianopia occurs from lesions to the optic tract and/or striate cortex and causes impairments to the primary perception of contralesional visual information [25]. Typically, patients who have hemianopia can still normally orient towards the contralesional side and do not present the same difficulties that neglect patients encounter in drawing and cancellation tasks. Whilst neglect patients exhibit a graded pattern of deficit from the impaired to the intact side, hemianopia patients display a sharp demarcation between the two sides [1]. However, it is sometimes difficult to differentiate between visual neglect and hemianopia [26, 27]. Although both deficits often occur independently of one another, neglect has been found to mimic hemianopia in severe cases. This "pseudo-hemianopia" is characterised by a complete failure to perceive stimulation in the contralesional visual field that cannot be explained by lesions in the optic tract or striate cortex [26].

Clinical assessment of spatial neglect

Spatial neglect can be described as highly heterogenous in its clinical manifestations and neuroanatomical correlates. The dissociations in symptom manifestations can be explained by different lesion sites and brain networks associated with neglect [28, 29]. These different aspects of the multi-component disorder are not always overtly evident and batteries that include several different tests are needed to measure and reveal their presence [30]. The observed dissociation in clinical symptoms can be traced back to the various domains affected by visual neglect. Using a factorial analysis, the study by Verdon et al. [28] revealed three main domains that explain 82% of the total variance across all neglect tests. Those three domains are related to the perceptive/visuo-spatial, exploratory/visuo-motor, and allocentric/object-centred aspects of spatial neglect. In this article, we chose to use Verdon's factorial analysis to classify the various tests used to assess visual neglect under one of those three different domains.

Perceptive and visuo-spatial component

Perceptive and visuo-spatial aspects of neglect refer to the ability to shift attention spontaneously to the contralesional side and maintain a stable attentional perception of the world over time and despite frequent eye

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movements that shift the location of objects [28, 31]. Patients demonstrate unilaterally reduced attention and the visuo-spatial neglect symptoms are usually the most obvious and the most impacted by neurorehabilitation [32]. Tasks that usually require little voluntary attentional and motor control are associated with the perceptive and visuo-spatial component of neglect [33]. In Verdon et al. [28] and the factorial analyses of Azouvi et al. [33] , this component was associated with reading, line bisection, clock drawing and identification of overlapping figures tasks that require visual scanning in a systematic manner. Reading tasks and line bisection tasks correlated the most with the perceptive and visuo-spatial component, with factor loadings of 0.87 and 0.86, respectively [28]. Recent studies have been increasingly looking at the correlation between performance in specific tests and different locations of cerebral lesions [34]. The perceptive and visuo-spatial aspect of neglect has been associated with lesions in the right inferior parietal lobule [28], which was long considered to be the only neuropathological correlate of neglect. Supporting this finding, multiple studies have used line bisection tasks to assess parietal function and the perceptive and visuo-spatial aspect of neglect and have found neglect to be associated with posterior parietal damage [35, 36], near the supramarginal gyrus [37]. Damage to the inferior parietal lobe of the posterior parietal cortex has been associated specifically with the perceptual, egocentric and exploratory components of neglect [38]. The representations of perceptual locations within parietal structures helps to promote the maintenance of previously explored locations in spatial working memory [116] and play a critical role in the spatial representations that are necessary to shift attention to contralesional locations. The spatial memory and the attention shifting are two abilities that usually impaired in neglect patients and could potentially be important in pinpointing the endpoints of a line or when returning to the next line in a text [28]. Overall, considering the lower factor loading (0.48) of drawing tasks [28], and previous literature on the link between performance on reading and line bisection tests and damage to posterior parietal cortex, we will consider those tasks as primary tools used to assess the perceptive and visuo-spatial component of neglect.

Reading tasks are used to assess neglect dyslexia, a symptom of spatial neglect where patients present with reading errors in the contralesional side of the text stimulus [39]. Various aspects of neglect dyslexia are reported, such as viewer-centred, stimulus-centred or word-centred neglect dyslexia and can present in multiple spatial scales [16]. Patients with neglect dyslexia might omit text on the entire left page of a book, a left text column, the left side of sentences or left letters in a word. The majority of reading tests used to assess neglect dyslexia are word-level assessments. Such tests might not give an accurate representation of the challenges faced by patients with neglect who encounter more than single words in isolation, in the real world [17]. A more recent study by Galleta et al. [39] used a functional reading task that reflects everyday world reading such as articles and menus. Their findings suggest that functional reading tasks are better at measuring neglect dyslexia severity than word-level assessments.

Line bisection tasks are some of the most commonly used pencil-and-paper tests to assess spatial neglect [2, 40]. Line bisection tasks are easy to administer, are less time-consuming than other tests, have a relative test sensitivity that ranges from 41.67% to 76.4% for spatial neglect and are therefore extensively used in clinical settings [41]. In the standard version of the task, patients are asked to mark the middle of a series of horizontal lines of different lengths with the centre of the lines aligned with the midsagittal plane of the individual's body [38]. Different versions of this task use different line length and number of lines. For instance, in the version of Schenkenberg et al. [42], 20 lines are used in a random arrangement with some on the right, some in the centre and some on the left of a piece of paper. The lines are 100, 120, 140, 160, 180, and 200 mm in length [40, 42]. In the version of Azouvi et al. [33], four lines 5 cm and 20 cm in length are used and are presented separately. Patients with spatial neglect set their mark with a rightward deviation, toward the ipsilateral end of the line [38]. Typically, the error is more pronounced for longer lines [43, 44]. Studies have shown that judging the left half of the line as shorter implies that the patient experiences a perceptual underestimation of contralateral extent and, therefore, this test has been shown to be effective in measuring the perceptive and visuo-spatial aspects of neglect [38, 45]. The landmark test [46] is a variant of the line bisection task that does not involve a motor response from the patient. It requires the individual to voice which half of a pre-bisected lines is longer or shorter [38]. Other line bisection tasks do not allow the distinction between the motor and the perceptual output, whereas the landmark test has been proven to be effective in separating those two components of spatial neglect [47].

The landmark test is a variant of the line bisection task that does not involve a motor response from the patient.

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Secondary tools used to assess the perceptive and visuo-spatial component of neglect include tasks mentioned by Verdon et al. [28] and the factorial analyses of Azouvi et al. [33], such as drawing tasks and the identification of overlapping figures test. On the basis of the lower factor loading (0.48) of drawing tasks [28], it was added as a secondary tool to access the visuo-spatial component of neglect. Additionally, a study by

The target cancellation task was used to identify the visuo-spatial network in awake craniotomies and prevent neglect postoperatively.

Chechlacz et al. [48] found an association between neglect, measured using a cancellation task, and damage to the right supramarginal gyrus, the intraparietal sulcus, the middle frontal gyrus and the superior temporal gyrus. These areas of the brain also correlate with this component of neglect [28]. The target cancellation task was used to identify the visuo-spatial network in awake craniotomies and prevent neglect postoperatively. This task proved to be useful in identifying visuo-spatial cortical and subcortical regions. However, target cancellation tasks do not solely target the interpretation of visual information, they also involve motor functions and therefore stimulation of the motor cortex. Thus, target cancellation tasks may not exclusively assess the visuo-spatial component of neglect and can also measure other components of neglect such as the motor component [49]. This applies to other tasks used to assess visual neglect. Owing to the nature of most of them, they target multiple areas of the brain, and thus assess multiple components of neglect. Very recently, virtual reality tools have been implemented in the assessment of visual neglect. this offers conditions closer to everyday life situations and detects more subtle symptoms of neglect that are not revealed by pencil and paper tasks [85]. Moreover, it addresses the limitations of paper and pencil tasks because it has better ecological validity, and it offers an environment closer to real-life situations [117].

Exploratory and visuo-motor component

The exploratory and visuo-motor aspects of neglect can be defined as the ability to direct attention and the motor skills used to perform a spatial neglect task [28]. In Verdon et al. [28] and the factorial analyses of Azouvi et al [33], this component was associated primarily with errors in cancellation tests including the Bells and Ota search tasks, and secondarily with errors in drawing tasks, such as landscape copy, reading tasks and line bisection tasks. Ota search and Bells cancellation tasks correlated the most with the exploratory and visuo-motor aspects of neglect, with factor loadings of 0.79 and 0.95, respectively. The landscape copy correlated to a lesser degree with the component, with a factor loading of 0.41 [28]. This component of neglect has been associated with right dorsolateral prefrontal cortex lesions. Regarding the exploratory aspect of the component, spatial neglect caused by right frontal lobe lesions is captured more prominently using cancellation and search tasks that include distractors. Frontal damage has been found to cause more severe attention biases in cancellation and search tasks than other lesions in the brain [50]. Moreover, the deficits noted on drawing tasks may be caused by the patient getting distracted by elements on the right side of the test display [51]. The attention problems and distractions could be explained by the essential role of the dorsolateral prefrontal cortex in the selection of target information and the inhibition of irrelevant distractors during search tasks [118]. Regarding the visuo-motor aspect of the component, damage to the frontal lobe and to the premotor cortex may cause deficits in motor planning as shown in line bisection, cancellation and drawing tasks [52]. Two peaks of frontal damage were noted using a voxel-based lesion-symptom mapping approach [28]. Both peaks were found to be involved in spatial attention and oculomotor control [30, 53]. Thus, dorsolateral prefrontal cortex lesions that cause deficits measured by cancellation, drawing and line bisection tasks, suggest attention and visuo-motor problems when exploring the contralesional space in a task. Moreover, pure motor neglect symptoms that affect the contralesional limbs without affecting the perception often arise after focal lesions in the anterior-lateral thalamus or the medial prefrontal cortex [119, 120]. Overall, on the basis of previous literature and the factorial analysis by Verdon et al. [28], cancellation tasks can be considered primarily tools to assess the exploratory and visuo-motor aspects of neglect, and drawing, reading, line bisection and eyetracking during free exploration tasks [121] can be considered secondary tools.

Cancellation tasks come in multiple versions. Generally, patients are asked to strike target items presented on a piece of paper [38]. In some versions of the tests, including the Bells task [54], several distracters are included amongst the targets. For example, in the Broken Hearts [55] or Circles test [56, 57], participants must mark completely shaped hearts or circles that are intermingled among distractor hearts or circles with gaps on the right or left side of the shape. In other versions of the tests, only targets are presented, such as in the line crossing test [58]. Tasks that include distracters are more effective at detecting neglect than tasks with only targets [59]. Cancellation tasks are scored by

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counting the total number of errors and the difference between the number of errors on the left- and right-hand sides of the test sheet. Cancellation tasks necessitate active exploration of the test sheet and patients must constantly shift attention between the different items on the piece of paper [60]. The Center of Cancellation developed initially by Binder and al. [131] and more recently Rorden and Karnath [132] provides an intuitive, continuous and robust measure of neglect severity. Patients with neglect with motor-exploratory deficits generally show neglect symptoms on the egocentric reference frame. They may, for example, eat food from plates that are on the right side of their body. Similarly, patients with motor-exploratory deficits will only detect targets on the right-hand side of the page on the cancellation task and will display a right-to-left horizontal scanning pattern that is consistent with exploratory, visuo-motor and egocentric deficits in neglect [61]. Patients with allocentric neglect exhibit different patterns on cancellation tasks, as discussed in the subsequent section.

Secondary tools used to assess the exploratory and visuo-motor aspect of neglect include drawing, reading, line bisection and eyetracking during free exploration tasks. Errors on drawing tasks may be caused by attention deficits that lead to the patient getting distracted by elements on the right side of the display and failing to explore the contralateral side [51, 28]. In this task, patients must draw a copy of a figure presented to them or from memory. The figures vary in complexity depending on the test used and more complex drawing tasks are more sensitive to neglect [1]. Some tasks include multiple figures to draw and patients with egocentric neglect fail to reproduce objects on the left-hand side of the paper. Moreover, drawing from memory tasks can provide information about visuomotor deficits. For instance, patients with left neglect will usually only draw on the right-hand side of the paper sheet [38]. Reading requires visuomotor and exploratory skills. Reading material encountered in real life situations, such as articles or menus, are more sensitive than word and phrase reading tasks in measuring spatial neglect. They involve left-to-right scanning which taps into exploratory skills and therefore are more efficient at detecting exploratory deficits [39]. Line bisection tasks and especially the version of Schenkenberg et al. [42] is the most sensitive when assessing the exploratory and visuo-motor aspect of neglect. It consists of three groups of lines, with one group drawn on the left, one in the center and one on the right-hand side of the sheet of paper [62]. The placement of those lines makes for a wide interactive field that is useful in detecting spatial exploration deficits [63]. Finally, eyetracking during free visual exploration is performed by testing the sensitivity of eye movement measurement while participants freely explore images of natural scenes or urban places [221]. This task aims to detect neglect in everyday behaviour. The study by Kaufmann et al. [221] found that this task detects significantly more patients with neglect than paper and pencil tasks. Overall, cancellation, drawing and line bisection tasks are the main tools that measure the exploratory and visuo-motor aspects of neglect [64].

Allocentric and object-centred component:

The third and final component of neglect is the allocentric and object-centred aspect that involves one side of the object in regard to its spatial coordinates [38]. It contrasts with the first two components, which both involve space based (egocentric) aspects [28]. Egocentric and allocentric symptoms can co-occur but can also manifest separately. Some studies suggest that those two aspects of neglect are independent [65, 66], but other studies argue that the two frames of reference are essentially egocentric [67, 68]. In the factorial analyses fo Verdon et al. [28], this component was associated mainly with allocentric errors on the Ota search task, with a factor loading of 0.9, and the compound word reading task, with a factor loading of 0.89. This component of neglect has been associated with right temporal lobe lesions [28]. Temporal lobe lesions associated with allocentric neglect have been found to be more ventral than those associated with egocentric neglect [69]. Another recent study by Pedrazzini et al. [60] has demonstrated that damage to the intraparietal cortex is a predictor of allocentric neglect but not egocentric neglect. Their findings suggest that the two frames of reference have distinct underlying processes that are nonetheless interdependent. Moreover, multiple studies found that even though the ventral stream of the temporal lobe is important for coding object shape, it also interacts with the dorsal stream of the parietal cortex, which is involved in the spatial coordinates of object representation and structure [70, 71]. For instance, the parietal cortex is involved in the mental transformation of objects such as rotating them [72]. Furthermore, a meta-analysis by Chechlacz et al. [73] found an association between allocentric symptoms and posterior lesions in the angular gyrus of the inferior parietal lobule. The studies mentioned above that examine allocentric neglect used different tests such

Certain versions of the cancellation task can distinguish between allocentric and egocentric neglect.

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as drawing, cancellation, single-word reading, and line bisection tasks. Overall, on the basis of previous literature and the factorial analysis by Verdon et al. [28], cancellation and single-word reading tasks would be considered primarily tools to assess the allocentric and object-centred aspect of neglect, and line bisection and drawing would be considered secondary tools.

Certain versions of the cancellation task can distinguish between allocentric and egocentric neglect [56, 74]. In the study of Verdon et al. [28], Ota's search task was used and allocentric neglect was measured by counting the omissions of targets with gaps on their contralesional side regardless of their location on the test sheet. When measuring egocentric neglect, the test is scored by counting the number of errors on the contralesional part of the test sheet [1]. In another version of the cancellation task, targets are grouped into two different clusters in such a way that they form two large targets made of smaller targets. Allocentric neglect is measured by counting omissions of targets on the contralesional part of each cluster, while egocentric neglect is measured by counting omissions on the contralesional part of the test sheet [74]. Finally, figurative discrimination tasks such as the Apple cancellation task and the Sensitive Neglect Test [75, 110] are more specialised at assessing both allocentric and egocentric neglect in one test and distinguishing between the two frames of reference [76]. In real word settings, this allocentric neglect may translate into eating food on the right side of each plate while still attending to plates on both sides of the body [61, 78].

Multiple studies have confirmed the efficacy of single-word reading in measuring allocentric neglect [70, 71, 79]. In single-word reading tasks, patients are asked to read right-side-up and upside-down words placed in the centre of a page [61, 80]. Typically, left-sided omissions and substitutions of letters, regardless of the modality, order of presentation and spatial location, are the types of errors seen when measuring allocentric neglect by using single-word reading [1, 61]. Single-word reading requires allocentric processing because single target parts have to be integrated to identify the whole word [60].

Secondary tools used to assess the allocentric aspect of neglect include line bisection and drawing tasks. In line bisection tasks, patients with neglect will mark the line far right of the centre [61]. This error might be the result of neglect of the left half of the body (egocentric) or left half of the object, in this case, the line [81]. To distinguish between the two frames of reference, smaller lines of 5 cm length can be used to assess allocentric neglect. The smaller line may be more precise in helping view the line as an object regardless of its location on the test sheet. Moreover, line bisection tasks can be combined with other tasks such as cancellation tasks to distinguish between the two types of neglect [61]. A study by Golay et al. [82] found that a patient with allocentric neglect shows impairment in line bisection tasks but not cancellation tasks, whereas patients with egocentric neglect demonstrate impairment on cancellation tasks but not line bisection tasks. On a neuroanatomical level, the errors observed in line bisection tasks have been suggested to be due to the activation of the allocentric ventral visual system [83]. Overall, line bisection tasks require object-based processing because the dimension of the line has to be judged [60].

Copying and drawing tasks can measure both allocentric and egocentric neglect [1]. An individual with neglect may fail to reproduce objects on the left-hand side of the paper (i.e., egocentric neglect), as previously discussed [38], but also fail to reproduce the left-hand side of each object (i.e., allocentric neglect). Overall, cancellation, single-word reading, drawing and line bisection tasks require object-based processing and are all important tools to measure the allocentric aspect of neglect [60].

Treatment of spatial neglect

We can distinguish between three main types of interventions: behavioural rehabilitation, noninvasive brain stimulation techniques and neurofeedback techniques. Behavioural rehabilitation techniques include pencil and paper tasks and more recently virtual reality (VR). Such an approach is called a top-down approach because it targets the individual's higher level cognitive processes by aiming to correct the perceptual and behavioural biases [84]. Some of the most common tests used are drawing, digit detecting, reading, visual exploration and writing. During those tests, visual scanning training is used, and the patient is instructed to explore the contralesional portions of space [29]. Very recently, VR tools have been implemented in the rehabilitation of visual neglect. It offers conditions closer to everyday life situations and detects more subtle symptoms of neglect that are not revealed by pencil and paper tasks [85]. Moreover, it offers the possibility to control for head, eye, limb and postural movements [86]. Some VR tasks incorporate the use of serious games and immersive virtual reality to enhance training motivation in people with visual neglect [117, 122]. Multiple studies have used VR and compared it with patients undergoing pencil and paper training and found great improvement inn visual neglect assessment tasks, such as cancellation tests, compared with the control group, but also decreased visuo-spatial deficits and improved daily life activities [87-90]. Moreover, a study by Knobel et

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al. [122] found that VR tasks that incorporate the use of games and immersive virtual reality were rated as a motivating and entertaining tasks, and can be used by different populations with different levels of skills, including individuals with cognitive impairments. Using VR systems may prove to be essential in visual neglect rehabilitation [91].

Noninvasive brain stimulation or neuromodulator techniques include caloric vestibular stimulation (CVS), galvanic vestibular stimulation (GVS), transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), prismatic adaptation (PA), and optokinetic stimulation (OKS). In CVS, water irrigators are used to cool the contralesional auditory canal or warm the ipsilesional one. This procedure elicits horizontal nystagmus and has shown benefits in treating visual neglect [92]. GVS is a noninvasive procedure that requires application of a weak direct percutaneous current to stimulate the vestibular system [29]. TMS is a procedure that uses magnetic fields to stimulate nerve cells in the brain. Research has shown significantly higher cortical excitability in neglect patients compared with healthy controls. This degree of excitability can be reduced by TMS [123, 124]. In fact, studies have suggested that using inhibitory TMS on the intact left parietal cortex can reduce the left hemisphere activity, which rebalances interhemispheric activity and improve visual neglect symptoms [93–95]. More recently, continuous theta burst stimulation has been introduced as a new protocol. It has inhibitory effects on brain activity and can induce long-term depression in patients with neglect [125]. This protocol leads to significantly longer inhibitory effects on neglect symptoms than TMS and it helps improve and accelerate neglect recovery [126]. Moreover, recent studies have looked at the efficacy of using tDCS on neglect patients. Most of them found an improvement in activities of daily living when inhibitory and excitatory stimulation were used on the left and right posterior parietal cortex, respectively [96–98]. Prismatic adaptation is a technique that consists in producing a visual shift by making the patient wear prismatic googles and take part in different tasks [29]. This procedure has had mixed results, with some studies demonstrating its effectiveness [99] and some finding no beneficial outcomes [100, 101]. This effectiveness seems to be dependent on the location of the lesion [102] but also on the type of task [103]. Finally, optokinetic stimulation (OKS) is a sensory stimulation technique that helps modulate many facets of visual neglect. It leads to the activation of multiple brain regions such as the temporo-parietal cortex and the basal ganglia that are involved in visual space coding [127].

More recently, neurofeedback techniques have been used, a patient can learn to voluntarily control brain activity by learning mental strategies. In a recent paper [104], the authors show that patients with visual neglect were taught how to increase their right primary visual cortex activity using neurofeedback in functional magnetic resonance imaging (fMRI) [105] or with the electroencephalogram (EEG), the acute or chronic patients' improvement in visuo-spatial performance on tests, seem to be very promising [104].

Conclusion

Visual neglect is a complex cognitive disorder that involves multiple factors which can be grouped into three major domains: the perceptive and visuo-spatial, the exploratory and visuo-motor, and the allocentric and object-centred aspects. These three domains correlate with different lesion sites in the brain network [29], that lead to different clinical manifestations that are captured by various tasks. Ideally, multiple assessment tests should be used to fully capture the complex nature of the multi-component syndrome and the various symptoms that may manifest in association or in isolation [38]. Some of the most important tests that should be routinely used include Schenkenberg's line bisection test [42], target cancellation tasks such as the Bell's Test [54] or Ota's search task [56], and drawing tasks such as the Clock Drawing Test [106]. The future evaluation should include VR [128] but also with the EEG [129,130]. Concerning the future of rehabilitation, three main types of interventions are available to treat visual neglect: behavioral rehabilitation, noninvasive brain stimulation techniques and neurofeedback techniques. VR tools are very promising to treat visual neglect have because they offer conditions closer to everyday life situations and are accessible for people with cognitive impairments. More research needs to be done on the efficiency of VR therapy. Overall, considering the multi-factorial and complex nature of this disorder that affects the spatial attention of the patient, we deem it accurate to speak of a spatial attentional spectrum when referring to the syndrome.

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