Review article

Neglect Dyslexia in Relation to Unilateral Visuospatial Neglect: A Review

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Abstract: Unilateral visuospatial neglect and neglect dyslexia are neuropsychological syndromes in which patients exhibit consistently lateralised perceptual deficits. However, there is little agreement surrounding whether neglect dyslexia is best understood as a consequence of a domain-general visuospatial neglect impairment or as an independent, content-specific cognitive deficit. Previous case studies have revealed that neglect dyslexia is an exceptionally heterogeneous condition and have strongly suggested that not all neglect dyslexia patient error patterns can be fully explained as a consequence of domain-general visuospatial neglect impairment. Additionally, theoretical models which attempt to explain neglect dyslexia as a consequence of domain-general unilateral visuospatial neglect fail to account for neglect dyslexia errors which occur when reading vertically presented words, lack of neglect errors when reading number strings, and neglect dyslexia which co-occurs with oppositely lateralised domain-general visuospatial neglect. Cumulatively, these shortcomings reveal that neglect dyslexia cannot always be accurately characterised as a side-effect of domain-general visuospatial unilateral neglect deficits. These findings strongly imply that neglect dyslexia may be better understood as a content-specific impairment.

Keywords: stroke; unilateral visuospatial neglect; neglect dyslexia; visuospatial attention; reading
1. Introduction

Unilateral visuospatial neglect is a neuropsychological syndrome characterised by consistently lateralised perceptual deficits. Patients with neglect have unimpaired visual processing but are unable to respond or attend to stimuli presented on one side of their environment [1-5]. Although unilateral visuospatial neglect is most frequently associated with damage to the right temporo-parietal or ventro-frontal cortex, unilateral visuospatial neglect has been found to occur following a wide range of lesion patterns [6-8]. Mort et al. [9] conducted a lesion mapping analysis including 35 stroke survivors and concluded that damage to the angular gyrus and parahippocampal region was most strongly associated with unilateral visuospatial neglect. A meta-analysis of 22 lesion-symptom mapping studies of left visuo-spatial neglect concluded that egocentric deficits are associated with damage to perisylvian network structures including the right supramarginal, pre- and postcentral, and superior temporal gyri while allocentric deficits are associated with damage to the right angular, middle temporal, and middle occipital gyri [10]. We also note however, that other studies have identified cases of unilateral visuospatial neglect in patients with brain damage confined to the left-hemisphere [8, 11, 12], as well as reports of patients experiencing neglect after cerebellar lesions [13]. The heterogeneous pattern of lesions associated with unilateral visuospatial neglect may be accounted for by characterizing this condition as a symptom of damage to diffuse attentional regulation networks [14, 15].

Behaviourally, unilateral visuospatial neglect is most commonly characterized as an impairment which arises from a directional bias in spatial attention caused by an inability to distribute attention evenly over space [16, 17]. This attentional asymmetry can be reliably detected by standardized assessments which require patients to distribute attention evenly over space in order to attend to and respond to visual stimuli presented in both the left and right visual fields [18, 19]. When asked to copy line drawings or simple figures, patients with neglect will consistently fail to copy one half of presented stimuli [20]. When presented with simple object cancellation tasks, patients with neglect reliably fail to cross out any stimuli falling in the contra-lesional visual field [18, 19].

Patients with more general vision impairment such as visual disorientation and partial blindness may exhibit impairments when tested on these neglect assessment tasks, but neglect patients can be differentiated from these patients due to the consistent lateralization of neglect errors [18, 19]. Severe visual impairments can confound tests designed to detect unilateral visual neglect and patients with these confounding deficits are generally excluded from experiments intending to investigate unilateral visuospatial neglect [21].

Although the lateralized perceptual deficits seen in unilateral visuospatial neglect may seem similar to those exhibited by patients exhibiting hemianopia, visual extinction, or visual disorientation;
unilateral visuospatial neglect is a distinct and independent condition. Though patients with hemianopia commit consistently lateralized visual errors similar to those seen in patients exhibiting unilateral visuospatial neglect [22, 23], these errors can be attributed to impaired vision or complete blindness in one visual field while patients with unilateral visuospatial neglect have intact early visual processing [23]. Similarly, visual disorientation confined to a single visual field can cause difficulty localizing objects presented on one side of space [24, 25]. However, patients experiencing visual distortion maintain the ability to perceive objects presented in the affected visual field even if this perception may be inaccurate while patients with unilateral visuospatial neglect are entirely unable to perceive stimuli presented in the contralesional visual field [26]. Clinically, the most striking difference lies in the awareness of the problem and patients with hemianopia very quickly learn to compensate by saccading into the impaired field [27]. These distinctions further emphasize that unilateral visuospatial neglect is not a visual deficit, but rather is an impairment of attention and perception.

Visual extinction also involves lateralized perceptual deficits. Though some have suggested extinction to be a milder form of neglect [28], unlike unilateral visuospatial neglect impairments, visual extinction only occurs when stimuli are simultaneously presented in the ipsilesional and contralesional visual field [29, 30]. Patients are able to orient, interact and perceive items in their contralesional field without errors when presented in isolation.

Neglect as a syndrome has been shown to fractionate into a number of neglect-related cognitive deficits, such as allocentric (object-centred), egocentric (field-centred), representational, peripersonal, and extrapersonal neglect [1, 31-33]. These neglect-related cognitive deficits vary based on their respective centres of neglect or “neglect point” [34]. The centre of neglect represents the point in space which is the boundary between the space which a patient can perceive and cannot perceive [34]. For example, unilateral visuospatial neglect occurs in an egocentric frame of reference involving a centre of neglect located between the right and left visual fields while object-based neglect occurs in an allocentric frame of reference in which the centre of neglect varies with respect to the midpoint of each individual object a patient perceives [35-37].

Karnath and Rorden [38] proposed that unilateral visuospatial neglect is characterised by a core inability to distribute attention evenly throughout space and that this core deficit results in a series of lateralised spatial and attentional deficits, including syndromes such as object-based neglect, visual extinction, and neglect errors in reading. This model of unilateral visuospatial neglect asserts that neglect-related cognitive deficits are best understood as satellite components of a unitary syndrome, each resulting from a shared core impairment. However, it is not yet clear if all neglect-related deficits are best understood as components of a unitary, domain-general condition or a cluster of interrelated, content-specific deficits.

Neglect dyslexia is a neglect-related cognitive impairment in which patients commit consistently lateralised letter omission, addition, and substitution errors, specifically when reading individual words [34, 39-42]. Reported examples of omissions include reading ‘land’ instead of ‘island’ or reading ‘plane’ instead of ‘planet’. Examples of additions include reading ‘remembers’ instead of ‘members’ or reading ‘belongings’ instead of ‘belong’. Some often reported substitution errors include reading ‘measures’ instead of ‘treasures’ or reading ‘journey’ instead of ‘journal’ [42]. Like unilateral visuospatial neglect, neglect dyslexia patients have unimpaired early visual processing [43, 44]. This unimpaired vision differentiates neglect dyslexia from other reading impairments such as hemianopic alexia, which is caused by damage to early visual processes [43, 44]. Neglect dyslexia most frequently occurs following damage to right hemisphere areas [42]. Ptak et al. [45] found that neglect dyslexia was most strongly associated with damage to posterior cortical areas in the ventral stream of visual processing including the intraparietal sulcus and middle temporal gyri.

There is some disagreement surrounding the specific cognitive processes impaired in neglect dyslexia. Mozer and Behrmann [46] propose a connectionist account of neglect dyslexia in which this impairment is accounted for by damage to word recognition and spatial attention process. Caramazza and Hillis [47] assert that neglect dyslexia is best understood as an impaired ability to access spatial representations of words stored inside the orthographic lexicon. However, neglect dyslexia is generally classified as a peripheral dyslexia, a reading impairment resulting from general visual-feature analysis impairment [40, 41].

This classification of neglect dyslexia is based on the observation that patients with neglect dyslexia fail to identify the individual components of letter strings and are therefore unable to activate the corresponding mental representations of abstract letter units [42]. This impairment is present in both non-lexical and lexical reading processes, implying that neglect dyslexia involves an impairment which occurs in a process which is common to both routes [40-42]. This commonality and impairment of letter unit activation has led to the conclusion that neglect dyslexia is caused by a disruption of visual feature analysis processes. This classification explains neglect dyslexia as a side-effect of domain-general unilateral visuospatial neglect impairments rather than a content-specific cognitive deficit. Although this conclusion is consistent with much of the behavioural data collected from single-case studies of patients presenting with neglect dyslexia, it is not yet clear whether this classification of neglect dyslexia can fully explain all error patterns associated with this condition.

The purpose of the present review is to critically evaluate the classification of neglect dyslexia as a consequence of domain-general unilateral visuospatial neglect rather than a content specific deficit. This review aimed to consider findings from a range of neglect dyslexia and unilateral visuospatial neglect case studies in the context of the predictions of models which classify neglect dyslexia as a
side-effect of domain-general deficits. This analysis is based on a search of neglect dyslexia case studies and existing unilateral visuospatial neglect literature. Three online databases (Medline, PsychInfo, and Google Scholar) were searched to identify record of papers which investigated neglect dyslexia. The title, abstract, and keywords of these records were searched for “neglect dyslexia” or “unilateral visuospatial neglect”. This electronic search was last updated in May 2017.

2. Evidence from neglect dyslexia case studies

The existing neglect dyslexia literature is dominated by single case studies. While these case studies provide detailed descriptions of error patterns in individual patients, the results of these studies have led to disagreement surrounding whether neglect dyslexia and unilateral visuospatial neglect represent dissociable conditions (Table 1).

<table>
<thead>
<tr>
<th>Case study patient</th>
<th>Neglect dyslexia tests and results</th>
<th>Domain-general impairments</th>
</tr>
</thead>
<tbody>
<tr>
<td>VB (Ellis et al. [34])</td>
<td>L S / L</td>
<td>Not dissociated</td>
</tr>
<tr>
<td>NG (Caramazza et al. [47])</td>
<td>R S, O ND (I) / R</td>
<td>(ND errors within a word-centered reference frame)</td>
</tr>
<tr>
<td>AH (Behrmann et al. [48])</td>
<td>L S, O, A / NT L</td>
<td>(viewer-centred error pattern, left UVN and ND)</td>
</tr>
<tr>
<td>MC (Savazzi [49])</td>
<td>L S, O, A ND1 NT L</td>
<td>(ND co-occurs with similarly lateralized UVN)</td>
</tr>
<tr>
<td>MO (Riddoch et al. [50])</td>
<td>L2 S, O, A NT NT /</td>
<td>(ND/UVN both present in limited exposure tasks)</td>
</tr>
<tr>
<td>JB (Riddoch et al. [50])</td>
<td>L2 S, O, A NT NT L</td>
<td>(ND only present in limited exposure tasks)</td>
</tr>
<tr>
<td>GG (Nichelli et al. [51])</td>
<td>L O ND (T) NT L</td>
<td>(ND errors within a word-centered reference frame)</td>
</tr>
<tr>
<td>NT</td>
<td>L S, O, ND1 / /</td>
<td>Dissociated</td>
</tr>
</tbody>
</table>

Table 1. An overview of different neglect dyslexia error types in published case studies.
(Friedman et al. [52])

<table>
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<tr>
<th>JOH (Costello et al. [53])</th>
<th>A</th>
</tr>
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<tbody>
<tr>
<td>L</td>
<td>S, A</td>
</tr>
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(ND occurs independently of UVN)
Dissociated

(ND/UVN occur in conflicting lateralizations)
Dissociated

AR (Cubelli et al. [54])

| L | S | NT | NT | R |

(ND/UVN occur in conflicting lateralizations)

1. Patients committed ND reading errors but the frequency of these errors was found to be significantly lower than the frequency of ND errors in horizontal words [49, 52]; 2. Impairment present in limited exposure conditions only [50]. ND: Neglect dyslexia; UVN: Unilateral visuo-spatial neglect; L: Left lateralized impairment; R: Right lateralized impairment; S: Substitution; O: Omission; A: Addition; T: Terminal letter errors; I: Initial letter errors; /: No impairment; NT: Not tested.

Ellis et al. [34] conducted a case study involving patient VB, a stroke survivor with left neglect dyslexia. When asked to read individual words, VB was found to reliably misread letters presented on the left side of words (e.g. River → “Liver”, Yellow → “Pillow”) (Table 1) [34]. VB also misread the initial letters in number strings, failed to read the left half of text passages, and exhibited severe left hemispatial unilateral visuospatial neglect. This investigation also found that VB was unimpaired when asked to read words which were printed vertically. This vertical presentation of words was intended to prevent any spatial biases caused by domain-general unilateral visuospatial neglect, and the findings that this modification prevented neglect dyslexia errors strongly supports the conclusion that VB’s neglect dyslexia represented a side-effect of a more domain-general neglect deficit rather than a content-specific deficit. Similar patterns of preservation of reading abilities vertical presentations have been identified in several other patients with neglect [42]. Although this specific pattern of behavioural impairment supports the conclusion that neglect dyslexia is best understood as a consequence of domain-general unilateral visuospatial neglect, other case studies have supported a view of neglect dyslexia as a content specific impairment, independent from unilateral neglect.

Caramazza and Hillis [47] conducted a case study involving NG, a stroke survivor with right unilateral visuospatial neglect and right neglect dyslexia. When asked to read individual words, NG was found to consistently misread the terminal letters of individual words. NG was also found to misread these terminal letters even when spatial bias was eliminated by presenting words vertically down the centre of each page [47]. Additionally, NG was able to name each individual letter in words, but still made end-word errors when asked to read the full words aloud [47]. These impairment patterns would not be expected if neglect dyslexia were merely a satellite symptom of a core domain-general unilateral visuospatial neglect syndrome [38]. Subsequent investigation revealed that NG also misread terminal letters when words were mirror-reflected so that the terminal letters (originally right-
lateralised) fell in the left visual field. This reversal of error lateralisation strongly suggests that NG’s neglect dyslexia errors cannot be fully explained by domain-general unilateral visuospatial neglect. Additionally, NG exhibited no impairment when reading strings of numbers, suggesting that neglect dyslexia may be a content-specific deficit. These findings support the conclusion that neglect dyslexia, in this case, was best understood as a content-specific cognitive deficit rather than a side effect of domain-general deficits. Additional case studies have successfully identified other neglect dyslexia patients who commit errors when reading vertically presented words [51, 55, 56] and were unimpaired when reading number strings [52]. Although the conclusion that neglect dyslexia is a content-specific deficit is consistent with these patterns of reading errors, the error patterns varied between patients and it is far from evident whether these findings are generalisable to all cases of neglect dyslexia.

The double dissociation model represents the gold standard neuropsychological approach for determining whether two cognitive processes can occur independently of one another [57]. According to this model’s logic, if two cognitive impairments can occur independently of one another, they cannot be dependent on the exact same underlying cognitive process [57]. It follows that if neglect dyslexia and unilateral visuospatial neglect are doubly dissociated, neglect dyslexia cannot be fully explained as a side-effect of domain-general unilateral visuospatial neglect deficits. However, previous case studies have produced conflicting results pertaining to the relationship between neglect dyslexia and unilateral visuospatial neglect, meaning that it is unclear whether neglect dyslexia and unilateral visuospatial neglect represent dissociated conditions (Table 1). There is a lack of evidence coming from standardised assessments to substantive samples of neglect dyslexia patients, precluding valid comparisons and conclusions about the deficit as a whole.

Like allocentric neglect and unilateral visuospatial neglect, neglect dyslexia and unilateral visuospatial neglect represent conditions which frequently co-occur [1, 42, 58]. This frequent comorbidity has led some to the conclusion that neglect dyslexia and unilateral visuospatial neglect must share a common cause [34, 41, 42]. However, a correlation between these two conditions does not necessarily provide evidence that these conditions share a common cause. For example, although allocentric and unilateral visuospatial neglect are highly comorbid, previous research has provided strong evidence that these conditions involve doubly dissociated, independent underlying cognitive deficits [59, 60]. Similarly, the frequent co-occurrence of neglect dyslexia and unilateral visuospatial neglect does not necessarily imply that neglect dyslexia can be fully accounted for by the same cognitive impairments which underlie unilateral visuospatial neglect.

While patients with unilateral visuospatial neglect do frequently exhibit impaired reading abilities, this reading impairment is not always neglect dyslexia. Many unilateral visuospatial neglect patients exhibit sentence level neglect, a reading impairment characterized by lateralized omissions of full
words when reading spatially presented passages of prose, but do not exhibit neglect dyslexia [35, 39]. Beschin et al. [61] assessed the reading abilities of thirty unilateral visuospatial neglect patients and identified a double dissociation between sentence level neglect and neglect dyslexia reading errors. Lee et al. [39] administered a battery of assessments designed to detect both unilateral visuospatial neglect and neglect dyslexia to a cohort of 138 acute stroke patients. This investigation identified 80 patients with severe unilateral visuospatial neglect and found that 37.5% of these patients also exhibited neglect dyslexia [39]. Additionally, Bisiach et al. [65] assessed a cohort of 39 patients with right hemisphere damage and identified two unilateral visuospatial neglect patients who committed no neglect dyslexia errors when reading text. These studies have illustrated a single dissociation between unilateral visuospatial neglect and neglect dyslexia. However, despite the numerous case studies demonstrating that neglect dyslexia and unilateral visuospatial neglect can be doubly dissociated, the specific relationship between these conditions remains unclear. In particular, it may be that neglect dyslexia co-occurs more frequently with unilateral visuospatial neglect, than the opposite pattern. Indeed, from the above group data, it is clear that the incidence of visuospatial neglect is high at 58% (see also e.g. Demeyere et al. [62] acute stroke neglect incidence of 49%). In contrast, the prevalence of neglect dyslexia in this same group was much lower at 27% and all patients also demonstrated unilateral visuospatial neglect (single dissociation only) [39]. Though many studies have reported cases with the opposite single dissociation of neglect dyslexia without unilateral visuospatial neglect (Table 1), the above evidence suggests an uneven dissociation, though this could also be partly explained by a lack of research into neglect dyslexia at a group level.

A neglect dyslexia classification can also be effectively evaluated by examining the predictions of models which classify neglect dyslexia as a consequence of domain-general unilateral visuospatial neglect impairments.

3. Evidence from models of visual neglect and neglect dyslexia

Driver and Pouget [63] argue that neglect deficits like neglect dyslexia which seem to involve object-centred impairments can be explained in terms of “relative” domain-general unilateral visuospatial neglect. This argument characterises unilateral visuospatial neglect as a gradient of attention which is mediated by retinal position [63-65]. This inattention gradient is best illustrated as a skewed curve slanting from full attention on retinal positions in the non-neglected side of the visual field to complete inattention in retinal positions on the extreme side of the neglected visual field. Driver and Pouget [63] argue that this attentional gradient theory of visuospatial neglect means the neglected side of the visual field will always receive less attention than the non-neglected side of space regardless.
of retinal position. Driver and Pouget [63] asserted that this attentional asymmetry explains neglect dyslexia (and object-based or allocentric neglect) as a side-effect of unilateral visuospatial neglect and that these conditions should not be considered independent cognitive deficits. However, this attentional gradient theory cannot fully explain all error patterns which have been consistently documented in patients with brain damage.

A direct prediction of this model is that neglect dyslexia should only be found in patients who also exhibit domain-general unilateral visuospatial neglect, but previous research has found that this is not the case. Bisiach et al. [65] tested a cohort of stroke survivors on reading and visuospatial perception assessments and successfully identified 19 left neglect dyslexia patients. However, only 9 of these patients also exhibited domain-general unilateral visuospatial neglect deficits [65]. Patterson and Wilson [66] conducted an extensive case study involving a stroke survivor who reliably committed neglect dyslexia substitution errors when reading the initial letters of words and found that this patient exhibited no unilateral visuospatial neglect impairment when tested on a range of visuospatial neglect assessments. Similarly, Arduino et al. [67] also identified a single patient, RCG, who exhibited neglect dyslexia, but committed no domain-general neglect errors when tested on a series of assessments designed to detect unilateral visuospatial neglect. Friedmann and Nachman-Katz [52] also identified a case of neglect dyslexia in a 10-year-old child with no history of brain trauma. This child, NT, was found to reliably omit and substitute letters presented on the terminal ends of Hebrew words, but exhibited no domain-general unilateral visuospatial neglect impairment when tested on line bisection, object and letter cancellation, object drawing, picture copying tasks, and number-reading tasks [52]. A review of neglect dyslexia compiled by Vallar et al. [42] found that out of 46 neglect dyslexia patients assessed for domain-general neglect deficits in case studies, only 36 of these patients also exhibited unilateral visuospatial neglect. Additionally, three patients presenting both neglect dyslexia and unilateral visuospatial neglect were found to commit reading errors which affected the opposite lateralisation as their unilateral visuospatial neglect impairment (e.g. patients commit right-lateralised errors when reading and left-lateralised errors on line cancellation tasks) [42]. Behrmann et al. [68] employed a standardised clinical assessment battery to identify 9 patients with unilateral visuospatial neglect then tested these patients on a reading task in order to investigate the relationship between unilateral visuospatial neglect severity and neglect dyslexia. This investigation found that there was no relationship between the frequency of neglect dyslexia errors committed and the severity of unilateral visuospatial neglect in patients [68]. These findings suggest that neglect dyslexia and unilateral visuospatial neglect may represent doubly dissociated, independent cognitive impairments.

Additionally, if these conditions were simply a function of the same attentional gradient curve, these deficits would not be expected to occur in opposite lateralisation. In order for this to occur,
attention within each retinal location would have to be biased in the opposite direction as attention within the visual field as a whole, which does not seem plausible if all these attentional points can be summarised by the same curve of inattention. However, previous case studies have identified multiple patients in which unilateral visuospatial neglect and neglect dyslexia co-occurred in conflicting lateralisation. Katz and Sevush [55] identified a single patient, JM, who was found to commit left-lateralised substitution neglect dyslexia errors when reading but committed right-lateralised omission errors when completing unilateral visuospatial neglect assessments. Costello and Warrington [53] also identified a patient, JOH, who began consistently misread the initial letters of individual words following a craniotomy and partial removal of a left parieto-occipital mass. Although JOH’s neglect dyslexia was reliably left-lateralised, JOH was found to exhibit right-lateralised unilateral visuospatial neglect impairment when performing figure-copy and line bisection tasks. Similarly, Cubelli et al. [54] analysed cognitive assessment data from a single patient, AR, who committed reading errors which reliably affected the left side of individual words and sentences but committed right unilateral visuospatial neglect errors when copying arrays of geometric shapes and in clock-drawing tasks. This conjunction of conflicting lateralisation of errors cannot be explained by the attentional gradient model proposed by Driver and Pouget [63].

We note though that drawing tasks involve a wide variety of cognitive processes including planning, motor execution, visual object recognition, spatial coding, and spatial binding [69, 70]. This recruitment of diverse cognitive functions requires the cooperation of multiple discrete neural networks and the relative contributions of each of these networks is not yet well understood [69]. Reading involves a similarly complex set of abilities, where again visuospatial attention is a core aspect, alongside spatial coding, matching visual stimuli to orthographic representations, semantic content activation, and employing grapheme-phoneme correspondence rules [40].

The singular underlying mechanism model predicts that patients should exhibit similar neglect errors for all stimuli presented in the same location on the attentional gradient curve, regardless of stimuli content [63]. Although number strings are processed serially and lack the parallel word-form processing and reliance on orthographic lexicon access which are employed when reading, both number and word reading are dependent on an ability to accurately perceive the spatial presentation of each stimulus [40]. This suggests that if unilateral visuospatial neglect is the cause of the reading errors in neglect dyslexia, similar neglect errors could be expected when patients read number strings because performance on both of these tasks would be limited by the same spatial-attentional impairment. However previous research has identified a series of neglect dyslexia patients who committed no errors when reading numbers and strings of non-alphanumeric characters [47, 52].

Additionally, if neglect dyslexia could be fully explained by this attentional gradient theory
vertical presentation of words would be expected to prevent the occurrence of neglect dyslexia reading errors in all patients. Driver and Pouget's [63] characterisation of neglect dyslexia would predict that this modification would prevent attentional bias differences between words’ terminal and initial letters because each letter would be presented at the same level of attention. However, previous studies have identified a series of patients who reliably commit neglect dyslexia errors even when reading words which have been printed vertically. Patient JM was found to commit left-lateralised neglect dyslexia when reading spatially presented words and to reliably omit the first letter of words which were presented vertically [55] and patient NG was found to exhibit right neglect dyslexia and consistently misread the terminal letters of vertically presented words [47]. Similarly, Nichelli et al. [51] identified a single patient, GG, who exhibited neglect dyslexia for left-letters in horizontally presented words and for the lower-letters appearing in vertically presented words. These neglect dyslexia characteristic errors when reading vertically presented words cannot be fully accounted for by the attentional gradient theory.

The attentional gradient theory also predicts that the spatial deficits seen in neglect dyslexia would occur relative to a viewer-centred frame of reference rather than word-centred reference frame. Viewer-centred spatial deficits effect the same spatial lateralisation, regardless of how each word is rotated. This means that a patient with left neglect dyslexia would be expected to fail to report letters which appear on the left-most side of each individual word when words are presented normally, to commit no errors when words are presented vertically, and to neglect the left-most letters when words are mirror reflected so that the letters which were originally presented on the right now fall in the left side of space [47]. Conversely, the lateralisation of word-centred neglect dyslexia deficits would be expected to change depending on presentation of individual words. For example, a patient with word-centred right neglect dyslexia would be expected to neglect the terminal letters in standardly presented words, in words which are presented vertically, and in words which are mirror reflected so that the terminal letters now fall on the left side of space. However, case studies reporting patients who commit neglect dyslexia errors when reading vertically presented words have provided strong evidence against the characterisation of neglect dyslexia as a viewer-centred deficit (Table 1). Similarly, findings that the lateralisation of some patients’ neglect dyslexia errors is dependent on word rotation further support a ‘word-centred’ characterisation of this impairment [47, 51, 55].

Considered cumulatively, evidence from various case studies investigating neglect dyslexia strongly suggests that Driver and Pouget's [63] model cannot fully explain the full pattern of behavioural deficits associated with neglect dyslexia. Neglect dyslexia has been shown to occur independently of unilateral visuospatial neglect [42, 52, 65-67], in opposite lateralisation of unilateral visuospatial neglect [42, 53-55], and when reading non-lateralised, vertical words as well as to be
specific to words and not to other stimuli such as numbers [47, 52]. These inconsistencies strongly suggest that neglect dyslexia is not best characterised as a consequence of relative domain-general unilateral visuospatial neglect deficits.

A second theory which attributes neglect dyslexia deficits to a domain-general deficit proposes that neglect dyslexia is best understood as a form of stimulus density-sensitive unilateral visuospatial neglect [41, 71, 72]. This model of neglect dyslexia is based on the observation that patients with unilateral visuospatial neglect frequently tend to exhibit more severe deficits when performing tasks with high stimulus density compared to tasks with low stimulus density [71, 72]. For example, a systematic manipulation on the number of distractors in a cancellation task demonstrated a shifting of the ‘centre of cancellation’, with denser displays resulting in more lateralisation of attentional bias parameters [71].

Many patients who exhibit a spatial bias when completing complex, visually demanding tasks have been found to be unimpaired when tested on simpler, less cognitively demanding assessments [71, 72]. Similarly, patients who exhibit no unilateral visuospatial neglect impairments when tested with standard clinical assessments have been found to exhibit neglect deficits when these assessments were made more cognitively demanding by reducing exposure time or increasing attentional demands. Bonato et al. [73] identified a cohort of ten stroke patients who exhibited no neglect errors when tested on simple paper-and-pencil cancellation tasks but exhibited severe unilateral visuospatial neglect when tested on a series of more attentionally demanding computerized tasks in which they were required to orally report the lateralization of target presentations. These patients were also found to commit significantly more unilateral visuospatial neglect errors when the attentional demand of this computerized task was increased in a dual-task condition which further tasked attentional resources by requiring patients to respond to additional auditory or visual stimuli in addition to reporting target locations [73]. Additionally, Russell et al. [74] demonstrated that higher attentional load demands result in restriction of the visual field in both healthy and brain-lesioned individuals, by shrinking the attentional window, leading to stimuli in the periphery being missed, though in patients with unilateral visuospatial neglect this reduction was clearly lateralised [75]. These findings suggest that the level of attentional demand can modulate the apparent severity of unilateral visuospatial neglect impairment and additional research has suggested that this attentional demand may also modulate error frequency in neglect dyslexia [50].

For example, Riddoch and colleagues [50] identified a single patient, MO, who was unimpaired when reading under normal conditions but was found to commit left-lateralised neglect dyslexia errors when words were presented in limited exposure conditions. Similarly, Ellis et al. [34] found that patient VB’s frequency of neglect dyslexia errors rose from 6%-8% to 15% when exposure time for individual
words was limited to 2 s. Reading is a particularly visually demanding task [40]. Successful reading requires the identification and analysis of many letters presented in a very dense configuration. This implies that patients with unilateral visuospatial neglect are significantly more likely to commit lateralised errors when reading than when completing less visually demanding tasks and that many patients who commit lateralised reading errors may not necessarily appear to be impaired when completing lower density cancellation or neglect assessment tasks [41]. These implications may categorise neglect dyslexia reading errors as a side-effect of domain-general unilateral visuospatial neglect rather than an independent cognitive deficit, though evidence is lacking to determine whether these stimulus-density models can fully explain the behavioural impairments seen in neglect dyslexia.

One clear advantage of stimulus-density models is that these models provide a plausible explanation for committing neglect errors when reading. These models assert that patients who commit neglect errors when reading but show no impairment on other clinical assessments may do so simply because reading is a far more demanding visual processing task than the object cancellation, line bisection, and figure copy tasks which are commonly used to detect unilateral visuospatial neglect [41]. Additionally, stimulus-density models can account for why patients with neglect dyslexia generally commit neglect dyslexia errors with a greater frequency when reading longer words compared to shorter words [42]. Longer words require more letters to be analysed than shorter words, meaning that this difference in neglect dyslexia error frequency can potentially be explained by differences in visual processing loads. Although stimulus-density models of neglect dyslexia as a satellite symptom of a core underlying unilateral visuospatial neglect do successfully provide an explanation of many behavioural impairments seen in neglect dyslexia, these models fail to fully explain several consistently documented neglect dyslexia error patterns.

One such pattern is where neglect dyslexia has been shown to co-occur with oppositely lateralised unilateral visuospatial neglect. While stimulus density manipulations have frequently been found to influence the severity of neglect deficits, these manipulations have never been found to produce error lateralisation reversals [71, 72]. These findings strongly suggest that patients would not be expected to commit unilateral visuospatial neglect errors in opposite lateralisation when presented with tasks of varying stimulus density. However, many previous case studies have successfully identified cases of left neglect dyslexia in patients with right lateral visuospatial neglect [53-55]. Similarly, stimulus density-sensitive models of neglect dyslexia as a consequence of domain-general lateral visuospatial neglect fail to account for why stimulus manipulations have been found to affect the lateralisation of neglect dyslexia reading errors. Like the attentional gradient theory, this model asserts that neglect dyslexia is best explained as a satellite symptom, and would predict that neglect dyslexia errors should occur within a viewer-centred frame of reference. Yet previous research has illustrated that some
patients commit lateralised word reading errors which occur relative to a word-centred frame of reference patients [47, 76], suggesting a content-specific impairment in neglect dyslexia.

Caramazza and Hillis [47] proposed an alternative model of neglect dyslexia which characterises this syndrome as a content-specific cognitive deficit. Other forms of acquired dyslexia have been found to selectively damage specific components of the reading process, and Caramazza and Hillis [47] assert that neglect dyslexia involves a similar, reading-specific impairment [40]. Reading requires patients to access stored information about the spatial features of words which specify the order and identity of each letter in an individual word [40]. According to Caramazza and Hillis [47], patients with neglect dyslexia exhibit an impaired ability to access these orthographic representations of words, resulting in systematic reading errors. This account of neglect dyslexia is supported by Reznick and Friedmann's [77] findings that the morphological role of letters in the neglected portion of individual words influences the frequency of errors in Hebrew-reading neglect dyslexia patients. This study found that letters were significantly less likely to be neglected if they were part of a word’s root than when they were part of a derivational affix specifying the gender, number, or possessive content of the root [77]. If neglect dyslexia represented a domain-general impairment, the morphological role of letters would not influence their likelihood of being neglected [42]. These findings further support the conclusion that, at least in some cases, neglect dyslexia may be an impairment of representations of word spatial information generated in the orthographic stage of word analysis.

This explanation of neglect dyslexia as a content-specific deficit provides a possible explanation of why neglect dyslexia has been found to occur independently of unilateral visuospatial neglect, since this model proposes that these two impairments’ underlying deficits would be independent. Similarly, the lateralisation of reading errors would also be expected to be influenced by word-orientation manipulations, as neglect dyslexia in this model occurs with respect to a word-centred frame of reference rather than a viewer-centred reference frame [47, 76]. Finally, this classification may explain why some neglect dyslexia patients were unimpaired when reading number strings, since reading these number strings does not involve accessing the orthographic lexicon and constitutes instead a sequential process [47, 52]. This characterisation of neglect dyslexia as a content-specific impairment may capture the heterogeneous pattern of reading errors observed in many neglect dyslexia patients more thoroughly than models which assert that neglect dyslexia is a consequence of a more domain-general unilateral visuospatial neglect deficit.

Although models which characterise neglect dyslexia as a content-specific impairment seem to provide the most complete explanation of the wide range of reading errors associated with this syndrome, it is not clear whether this model provides the best explanation for all cases of neglect dyslexia. The majority of documented cases of neglect dyslexia have been found to co-occur with
similarly lateralised unilateral spatial neglect, and cases of neglect dyslexia which occur independently of these domain-general deficits are comparatively rare [42]. Many patients (e.g. VB [34], MO [50]) seemed to commit reading errors which may be better accounted for as a side-effect of domain-general neglect deficits. However, it important to note that at least some previously documented cases of neglect dyslexia cannot be explained by these models. This strongly suggests that neglect dyslexia is not always a mere satellite symptom of a core unilateral visuospatial neglect. Previous research has demonstrated that unilateral visuospatial neglect fractionates into a number of dissociated syndromes which can independently impair perception in object-centred and field-centred frames of reference [1]. It seems likely that neglect dyslexia may represent a similarly heterogeneous condition which may also contain a number of behavioural subsets which much be teased apart before the syndrome as a whole can be understood.

Future research should aim to address this issue by assessing large groups of neglect dyslexia patients on standardized assessment batteries and specifically designed experimental manipulations to thoroughly evaluate visuospatial perception (e.g. the Behavioural Inattention Test [78]), including tests for object-centred neglect [60] and the Hearts Cancellation of the Oxford Cognitive Screen [79, 80] and imagery, word and non-word reading with systematic levels of word length (from e.g. the PALPA tests [81]), and rotated word reading. This approach aims to facilitate comparisons between the behavioural impairments seen in different neglect dyslexia patients in order to precisely identify behavioural subsets and to more accurately determine the rates of occurrence of neglect dyslexia which involves a content-specific cognitive impairment. The findings of this research promise to facilitate the development of more effective diagnostic tools and criteria, as well as inform rehabilitation strategies for neglect dyslexia patients. Furthermore, longitudinal studies including several time-point measurements post injury will further our understanding of the functional impact and natural recovery trajectory of neglect dyslexia and visuospatial neglect.

4. Conclusion

Critical evaluation of the existing neglect dyslexia literature reveals that many models which characterise neglect dyslexia as a consequence of a domain-general unilateral visuospatial neglect fail to account for many error patterns which have frequently been reported in patients. These models cannot account for neglect dyslexia errors which occur when reading vertically presented words, the absence of lateralised reading errors when reading number strings, and neglect dyslexia co-occurring with oppositely lateralised unilateral visuospatial neglect. These error patterns are more thoroughly explained by models which characterise neglect dyslexia as a content-specific impairment involving
an inability to access the orthographic lexicon. This suggests that at least some cases of neglect dyslexia are best understood as content-specific cognitive impairments. However, this is a highly heterogeneous condition and further research is needed to determine whether all cases of neglect dyslexia are best understood as content-specific impairments, or whether some indeed do result from a more general unilateral visuospatial neglect deficit. The existing neglect dyslexia literature is dominated by single case studies, precluding valid comparisons about the disorder as a whole. Future research is needed in order to conduct standardised assessments of large cohorts of patients in order to allow conclusions to be drawn about the disorder as a whole. Despite these limitations, we suggest that a core spatial deficit in unilateral visuospatial neglect cannot fully account for the pattern of neglect reading errors seen in patients with neglect dyslexia.

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Conflict of Interest

All authors declare that there are no conflicts of interest in this paper.

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