

The neurological basis of visual neglect

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Purpose of review

A recent study has confirmed the enormous impact of visual neglect on the health services of the western world. Neglect was present in 48% of a sample of 166 right hemisphere stroke patients, and the severity of neglect predicted the extent of functional disability and family burden more accurately than did the extent of brain damage. Given the medical significance of neglect and its tantalizing relevance to understanding human conscious experience, it is unsurprising that the neuropsychological literature concerning the syndrome continues to grow rapidly.

Recent findings

We include brief surveys of six topics currently attracting attention in the field: the anatomical focus of neglect; the visual input pathways implicated; impairments of spatial working memory; the nature of visual extinction; perceptual distortions in neglect; studies on healthy subjects using transcranial magnetic stimulation; and the use of prism adaptation for the rehabilitation of neglect.

Summary

There is steady progress in understanding the essential components of neglect and their brain localization. Every step towards clarity, however, seems to be matched by a new discovery of the inherent complexity of the syndrome. The clinical expression of neglect may reflect the interaction of a variety of spatially lateralized and non-lateralized impairments, not all of which are present in all patients. The quest for an effective technique for the clinical rehabilitation of neglect continues, with prism adaptation emerging as the most promising approach to date.

Keywords

extinction, inattention, neglect, neuropsychological, visuospatial

Abbreviations

LED	light emitting diode
PPC	posterior parietal cortex
STG	superior temporal gyrus
SWM	spatial working memory
TMS	transcranial magnetic stimulation

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Introduction

In order to deal with the cognitive problems that beset the lives of patients with neglect [1[•]], it is necessary first to understand their nature. Neglect has long been recognized as a multi-component syndrome. A notorious indication of this heterogeneity is that while two of the cardinal diagnostic tests – search/cancellation and line bisection – between them pick up most patients with neglect, double dissociations between the two tests can occur. Thus the two tasks cannot be measuring the same unitary cognitive deficit. One possible conclusion from this is that cancellation tasks tap into more central aspects of the syndrome than line bisection [2]: and indeed an impairment of space exploration would seem to correspond more closely to the readily observable clinical signs of neglect. The controversy is relevant to recent lesion overlap studies, which have questioned the traditionally accepted view of neglect localization. It is indisputable that the most frequently damaged region in patients with neglect lies around the parieto-temporal junction of the right hemisphere [3,4]. What is disputed is the common inference that this is therefore the critical area of damage in causing neglect. Specifically, in order to demonstrate that *X* is the critical area of damage for some disorder, one has to show not only that damage to *X* causes the disorder, but also that damage to *not-X* does not cause the disorder [5[•]]. In other words, one has to have a control group of patients who do not have neglect, and then carry out a subtraction of the lesions of these patients from those of a group of patients who do have neglect.

When this is done, the results of any given study seem to depend upon the diagnostic definition of neglect adopted. One recent study [6[•]], based on 140 patients with right hemisphere strokes of whom 78 had neglect (defined without use of the line bisection task), suggests that the right superior temporal cortex and insula, along with the basal ganglia, constitute the critical focus for neglect. A study that did include the line bisection task among the diagnostic criteria, however, placed the focus

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more posteriorly, in the right inferior parietal lobule [7]. The latest work has investigated the critical lesion for neglect on line bisection, subtracting the lesions of patients with neglect for cancellation but not bisection tasks from those of patients with neglect for both. This analysis placed the focus for neglect on line bisection tasks even more posteriorly, at the right lateral occipito-temporal junction [8**].

One important possibility, nonetheless, is that all neglect patients do share some common underlying disorder, but that the interaction of this with the presence or absence of other deficits (for example, in spatial working memory, or in spatial perception) may differentially impair performance of different diagnostic tests. Given that all tests are imperfect in the degree to which they measure a single cognitive process, cases of double dissociation may thus say as much about the nature of the tasks as they do about the nature of neglect.

Input pathways

Visual information arriving through the geniculostriate pathway passes to higher visual areas of the cerebral cortex principally along two bifurcating pathways, the 'dorsal stream', the cluster of visual cortical areas that culminates in superior parts of the posterior parietal lobe, and the 'ventral stream', which terminates in inferior temporal cortex. Current views link the dorsal stream to the dynamic visual control of goal-directed action, and ventral stream processing to the construction of perceptual representations [9,10]. Although functional magnetic resonance imaging studies [11,12] show that neither of these two cortical routes brings visual information directly to parieto-temporal regions, the disturbance of conscious perceptual experience that characterizes neglect suggests a disruption of a high-level system that would depend on perceptual inputs [9].

Several direct tests of visuomotor processing of the kind believed to be mediated by the dorsal stream have been carried out in neglect patients, and in the main these have shown a remarkable preservation of such behaviour (though see Marotta *et al.* [13]). Simple reaching to a visual target is unimpaired [14], as is the visual calibration of hand aperture during reaching to grasp objects of different sizes [15]. Reaching between potential obstacles, which is severely compromised following dorsal stream damage [16], is spared in almost all neglect patients [17*]. Furthermore, a patient with visual extinction steered his reaches between two obstacles in identical fashion on trials when he was or was not aware of the one on the left [18*]. The same patient was also able to adjust his reaching movements online using visual feedback from a light emitting diode (LED) on his left hand, just as well whether or not he consciously detected the LED [19*]. These results support the idea of a

functionally intact dorsal stream in neglect patients, operating independently of visual awareness. Nevertheless, it should be noted that they are all restricted to metrical aspects of spatial processing, rather than to spatial exploration.

Impairments of spatial working memory

As noted in the introduction, the apparent centrality of cancellation deficits to neglect does not mean that they reflect a unitary disorder. Like all of the traditional diagnostic tasks, cancellation is complex and involves many different cognitive sub-processes. The individual clinical expression of neglect probably reflects the interaction of both lateralized and non-lateralized impairments. In particular, an impairment of spatial working memory (SWM) may explain the tendency of some neglect patients to explore the same locations repeatedly during visual search. For example, one parietal neglect patient was required to press a button for each new target found during a visual search task while his gaze was monitored [20]. The patient re-fixated rightward targets repeatedly, producing high 're-click' rates while doing so, as if he did not recall having visited them before. It was proposed that a non-lateralized impairment of SWM following right parietal damage might interact with the lateral orienting bias of neglect to produce recursive searching of rightward locations, thereby exacerbating neglect of the left side.

Subsequent research has demonstrated that target cancellation tasks are more sensitive to neglect when the responses leave no visible mark, so that memory for previously visited locations becomes more critical [21*]. SWM impairments, even when assessed by non-lateralized tasks, have been reported to be common among neglect patients, especially those with parietal damage, and to be correlated significantly with the degree of behavioural asymmetry in cancellation [22*,23*]. Consistent with this, it has been observed that neglect patients with parietal damage, but not those without, are impaired in detecting changes in target location, relative to changes in colour or shape, at any horizontal location [24*]. Finally, a magnetic resonance imaging study found [25*] elevated re-click rates in patients with lesions of the intraparietal sulcus and of the inferior frontal lobe. Only in the parietal patients, however, did the probability of re-clicking upon a re-fixated target increase with time elapsed since the first fixation on that target. The behaviour of the parietal patients is consistent with a memory deficit, while the frontal pattern is more suggestive of a failure to inhibit responding.

One live issue is whether the SWM impairment apparent in neglect is a deficit of memory *per se*, or whether it may be better understood in terms of a disruption of spatial remapping processes in the parietal lobe that

normally support the experienced constancy of space across saccadic and attentional shifts [26]. Additionally, it remains to be seen how the proposed SWM impairment can be reconciled with the well-established symptom of representational neglect, in which patients neglect the left side of mental images. Recent evidence supports an interpretation of representational neglect as a lateralized impairment of SWM [27], a very different proposal.

Line bisection and perceptual distortions

Line bisection too may not be as simple a task as is often assumed. One proposal is that neglect patients make rightward bisection errors because they experience a laterally anisometric perception of space [28]. For example, the so-called landmark task [28,29,30] shows that many neglect patients judge the left half of a correctly bisected line as being shorter than the right half. This notion of an anisometry of perceived space in neglect has recently received support from several sources. In one study, neglect patients were required to localize a brief target at different eccentricities, and reported stimuli in the left visual field as closer to the midline than they actually were [31]. In a second study [32], a neglect patient was shown a stimulus moving leftwards or rightwards at different accelerations. His threshold for acceleration perception was much lower for leftward movements than for rightward movements, as if the units of distance traversed on the left were seen as shorter than those on the right. A third report examined patients suffering from neglect dyslexia, who typically misread individual words by ignoring or misreporting the initial letters. These errors virtually disappeared when the words were printed with the letters progressively more widely spaced towards the left [33], consistent with the idea that this would compensate for a perceptual distortion of space.

Although perceptual distortions may affect the conscious experience of many neglect patients, there are other processes at work in determining line bisection behaviour. In one radical new approach, the authors recorded the lateral position of the bisection response within the workspace and studied how this varied when the left and right endpoints of the line were manipulated independently [34]. Across 30 patients with neglect, responses were less affected by changes in the location of the left endpoint than by changes in the right endpoint; in several cases, responses were entirely uninfluenced by the left endpoint of the line. The authors show that the well-known effects of line length and spatial position can be predicted from this pattern of responding, without assuming that the patients are making a subjective midpoint judgement [34,35]. They further argue that the degree of asymmetry in the influence of the two endpoints may

provide a more sensitive measure of neglect than the traditional measure of bisection error.

Extinction to double simultaneous stimulation

In extinction, patients fail to detect brief contralesional stimulation accompanied by ipsilesional stimulation, despite being able to detect contralesional stimuli in isolation. Neglect and extinction often co-occur, but they can also dissociate, suggesting that they may have separate neural underpinnings. A lesion overlap study has reported that involvement of the right temporo-parietal junction distinguished cortically damaged patients with left visual neglect and extinction from those with neglect alone, which was associated with more anterior lesions, in the superior temporal gyrus (STG) [36]. It should be noted that neglect in this study was defined without line bisection as a diagnostic test, and that the focus identified for extinction lies close to that identified for neglect using line bisection tasks [8]. Thus a closer link may exist between extinction and line bisection errors than between extinction and cancellation impairments.

Just as the relationship between neglect and extinction will depend upon the criteria used to diagnose neglect, so will it depend upon those used to diagnose extinction. This point was illustrated in a psychophysical study that defined extinction as a disproportionate interference from ipsilesional stimuli on the processing of contralesional stimuli [37]. This was measured in an orientation discrimination task in which lateralized target gratings were presented briefly with and without distractor gratings in the opposite field. Stimuli were presented at 20 times the luminance threshold for orientation discrimination in each field. All 15 neglect patients showed asymmetrical interference, though only seven of them showed visual extinction in standard confrontation testing. Patients without neglect, even those who showed classical extinction, did not show asymmetrical interference effects. The authors conclude that visual extinction, when assessed by a sufficiently sensitive method that excludes low-level sensory factors, is not dissociable from neglect. It is worth noting that their diagnostic tests for neglect included line bisection, and that bisection deviation correlated significantly with an index of the asymmetry of distractor interference.

The study of extinction has in the past been handicapped by inadequately precise methods of analysis. This paper [37] (see also Geeraerts *et al.* [38]) takes a valuable step forward in applying rigorous psychophysical techniques, and by excluding low-level sensory artefacts. Other recent work has begun to apply signal detection analyses to extinction phenomena [39,40], which again should help refine our understanding of the disorder.

Studies on healthy subjects using transcranial magnetic stimulation

A powerful way of identifying anatomically separable aspects of the neglect syndrome is to isolate the impairment in normal subjects by the use of transcranial magnetic stimulation (TMS). In recent years it has been well established that applying TMS over the angular gyrus in the posterior parietal cortex (PPC) of the right hemisphere, causes a lateral shift in landmark judgements in the same direction as that seen in neglect patients. It also causes a deficit in the 'disengagement' of attention from an ipsilateral prime to a contralateral target, as is often observed in neglect patients [41]. PPC stimulation also causes an impairment in conjunction search tasks, which are impaired in neglect [42,43] and which resemble some of the cancellation tasks used to diagnose and study neglect patients. One recent study [44] was designed to address the current controversy over the critical anatomical focus for neglect, using both landmark [28,29,30] and search tasks in conjunction with TMS applied to either the right PPC or the right STG. No evidence was found for a critical involvement of the right STG in the landmark task, though the involvement of the right PPC was confirmed. Stimulation of the right STG, however, was found to have rather specific effects on visual search. Although a colour/form conjunction task was unaffected, a difficult single-feature search task was selectively disrupted by TMS of the right STG (but not of the PPC) [44]. These data provide independent support for the differential findings regarding the anatomy of cancellation and line bisection impairments summarized in the introduction to this review.

Prism adaptation and the rehabilitation of neglect

An enduring goal of research into visual neglect is the development of techniques for its rehabilitation. Several interventions have been devised, but the most exciting recent discovery is that visuomotor adaptation to rightward displacing prisms induces a temporary amelioration of many clinical signs of left neglect [45]. Adaptation develops quickly as the patient makes reaching movements to visual targets whilst wearing prism glasses. The beneficial effects are observed after removal of the glasses. Preliminary evidence concerning the long-term benefits of prism adaptation is encouraging [46]. This contrasts with a recent report that an alternative intervention, optokinetic stimulation, added no significant gain to traditional scanning training [47]. Results from the first trials of prism adaptation employing randomized controlled designs should become available within the next 2 years.

While reports of short-term benefits from rightward prism adaptation in neglect patients have continued to accumulate [48,49] (but see Morris *et al.* [50]), the evidence that neglect-like perceptual biases can be induced in normal

subjects by adaptation to leftward prisms has been less consistent. Effects of rightward prisms have been observed in normal subjects performing spatial estimation tasks requiring motor responses, both under visual and proprioceptive guidance [51], but two recent studies [49,50] assessing the effects of prism adaptation on the lateral distribution of spatial attention have failed to detect any influence.

The two major brain regions implicated in prism adaptation are the PPC and the cerebellum. Patient studies suggest that the cerebellum is necessary for normal adaptation, but the integrity of the PPC may not be [52]. The authors hypothesize that the PPC may participate in a strategic, conscious compensation, while the cerebellum is required for the unconscious sensorimotor realignment that underlies true prismatic after-effects [53,54]. If the strategic process is disrupted in neglect patients, the influence of sensorimotor realignment might be amplified, yielding extraordinary after-effects that generalize more widely. These speculations provide a valuable attempt to understand the apparent differences between prism adaptation in neglect and in healthy subjects [54].

Conclusion

Clarification of the anatomical and behavioural relationships between different aspects of the neglect syndrome will depend critically on how these aspects are defined and measured. A major source of confusion and disagreement has been, and remains, a reliance on traditional clinical tests, which do not tap unitary impairments. There are, however, promising advances in three major areas: cancellation, in which new measures have identified the role of spatial working memory impairments; line bisection, for which a new analysis shows that neglect on this task need not imply perceptual distortion; and extinction, for which advances in measurement offer a way to distinguish attentional from sensory factors. Ultimately, the goal is to pinpoint the core components of the neglect syndrome and, as far as possible, to develop pure measures of these. In rehabilitation, the usefulness of prism adaptation procedures is becoming clear, as are its limitations. Paradoxically, these advances owe little to our theoretical understanding of visual neglect, or of how the beneficial effects may be mediated.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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- This is a weighty literature review and analysis from two major contributors to the normal literature on prism adaptation. The argument is advanced that understanding the effects of prism adaptation in neglect will depend critically upon an appreciation of this literature. The theoretical proposals and suggestions for future research made here seem likely to have a major influence in this area.