

Current controversies

# The modular architecture of the neglect syndrome: Implications for action control in visual neglect

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## Abstract

In our recent review of action control deficits in hemispatial neglect we concluded that many patients with the disorder have deficits in visuomotor control [Coulthard, E., Parton, A., & Husain, M. (2006). Action control in visual neglect. *Neuropsychologia*, 44(13), 2717–2733]. This conclusion has been questioned and it has been argued instead that there are no action deficits in neglect [Himmelbach, M., Karnath, H.-O., & Perenin, M.-T. (2007). Action control is not affected by spatial neglect: A comment on Coulthard et al. *Neuropsychologia*, 45(8), 1979–1981]. We proposed that rather than being specific to the neglect syndrome, action control deficits are more likely to relate to lesion location. Although many of these impairments may contribute to the manifestation of neglect, they may also occur in brain-damaged patients without the condition. In this article, we explore this framework further, discussing how neglect behaviour may emerge from damage to a set of visuomotor or cognitive modules, or their connections. Central to our view is the idea that the critical combination of deficits leading to neglect varies considerably between cases, and that visuomotor or cognitive modules disrupted in the syndrome may not, in fact, be specific to neglect.

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The study of motor control in patients with neglect has produced a large amount of seemingly contradictory data. In our recent review (Coulthard et al., 2006), we sought to provide an overview and interpretation of the current evidence. We concluded that although many patients with neglect make abnormal visually-guided reaches, the pattern of deficits is highly variable, probably reflecting heterogeneity in lesion location across individual cases. Rather than being specific to the neglect syndrome, we suggested that abnormalities of reaching in these patients may correspond to the extent of damage to the visuomotor control system, involving critical regions in both the parietal and frontal cortex, the white matter tracts connecting them and subcortical regions. Thus, we consider the action control deficits present in neglect patients to consist of a range of impairments affecting multiple stages of the visuomotor control process.

In their response, Himmelbach, Karnath and Perenin (2006) Perenin argue that action control is not affected in neglect. Their

key point is that studies that have compared the behaviour of neglect patients only to healthy controls have little to offer because any impairment that is observed need not be specific to the neglect syndrome. In their view, the ‘decisive comparisons’ are between brain-damaged patients with and without neglect. In our review, we took great care to state explicitly the control groups used in the studies that we discussed, both in the text and in a detailed appendix, so that readers would be clear about the specificity of any inferences made regarding neglect. For example, we describe one study (Matingley, Bradshaw, & Phillips, 1992) that tested stroke patients both with and without neglect and found contralesional movement initiation slowing only in the neglect group. This study allowed us to infer that perhaps directional movement slowing does contribute to, or is closely associated with, the neglect syndrome. Therefore, even on the conservative criterion of Himmelbach et al., there is evidence for an action deficit in neglect patients.

Perhaps more important though is the wider issue raised by Himmelbach and his colleagues about the specificity of certain impairments to neglect. In their view, the critical point is to deter-

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mine whether deficits represent a specific impairment ‘caused by the presence of spatial neglect’. This proposal suggests these authors consider neglect to be a discrete, super-ordinate entity which influences other aspects of behaviour. Our view of the neglect syndrome is fundamentally very different (see Husain & Nachev, 2007; Husain & Rorden, 2003 for reviews). We consider neglect to emerge from the combination of a group of cognitive deficits. The exact combination of impairments may differ across patients depending upon lesion location, the capacity for recovery after brain-damage and pre-morbid capabilities. Moreover, none of these cognitive deficits need be specific to the neglect syndrome; they may exist in isolation in patients who do not have the disorder. But, when critically combined, they lead to the syndrome we designate as neglect.

This conclusion is based on a framework for understanding the neglect syndrome as a collection of component deficits, including spatial and non-spatial impairments (see Husain & Nachev, 2007; Husain & Rorden, 2003 for reviews). For example, abnormalities in directing attention (Husain, Shapiro, Martin, & Kennard, 1997; Posner, Walker, Friedrich, & Rafal, 1984), impaired spatial memory (Malhotra, Mannan, Driver, & Husain, 2004; Mannan et al., 2005), poor sustained attention (Robertson et al., 1997) and directional motor deficits (Husain, Mattingley, Rorden, Kennard, & Driver, 2000; Mattingley, Husain, Rorden, Kennard, & Driver, 1998) may each contribute to neglect behaviour in some but not all patients with the syndrome. These impairments may also be discernable in some patients who do not or no longer demonstrate neglect, as determined by bedside tests.

For example, the disengage deficit in directing attention first demonstrated by Posner et al. (1984), is clearly not specific to neglect patients; it has been documented also in patients without neglect, some of whom may have visual extinction (Friedrich, Egly, Rafal, & Beck, 1998). What may be more critical for the genesis of this deficit is the location of the lesion, rather than the presence or absence of neglect or extinction (Friedrich et al., 1998). Even the bias in straight ahead pointing, that is considered by some authors to reflect a shift of egocentric reference frame and a fundamental feature of neglect, appears to be neither exclusive to the syndrome nor to be present in all patients classified as having neglect (Bartolomeo & Chokron, 1999; Chokron & Bartolomeo, 1997; Farne, Ponti, & Ladavas, 1998). However, we would still consider it to be a contributory factor to the neglect manifest in some patients.

In our view, the cognitive and visuomotor modules that may be disrupted in neglect depend critically upon the precise extent of the lesion (see Fig. 1). Cortical lesions may destroy several modules in either anterior or posterior brain regions, or both. Moreover, different combinations of cognitive and visuomotor control modules may be affected in different patients. The recent large-scale study conducted by Buxbaum et al. (2004) on 166 patients with right hemisphere stroke confirms how widely variable such combinations of deficit can be. Even small subcortical lesions, if located in critical regions where several antero–posterior connections traverse (Fig. 1), may be sufficient to disconnect or disrupt widespread cortical modules in both frontal and parietal zones (Bartolomeo et al., 2007). Unilateral

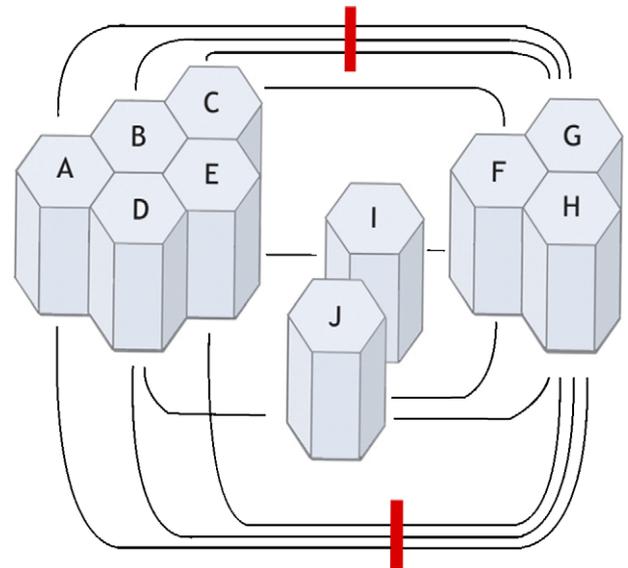


Fig. 1. Modular architecture of the neglect syndrome. In our view, neglect may emerge from damage to a combination of cognitive and visuomotor control modules, labelled A–J for illustrative purposes here. These modules are present in anatomically distant regions, for example, in parietal, frontal and subcortical regions. Stroke lesions may damage different combinations of critical modules in different neglect patients. None of the deficits that might arise from damage to a module need be specific to the neglect syndrome, but when critically combined, they may lead to the behavioural syndrome we classify as neglect. Even small lesions in white matter connections (marked by solid vertical bars) between these modules may suffice to disconnect or lead to widespread disruption within this architecture.

damage to a module which is represented in both the left and right hemisphere would be expected to lead to an ipsilesional bias because of unopposed activity of the intact module in the contralesional hemisphere. More critically, damage to modules that are present only in the right hemisphere, e.g. those involved in sustaining attention, would lead to a generalized deficit that might nevertheless interact with ipsilesional biases (Husain & Nachev, 2007).

Of course, not every deficit observed in a neglect patient need necessarily contribute to the syndrome. However, the argument that impairments found only in neglect cases but not in non-neglect cases are the key indicators of what underlies neglect is, in our view, incorrect. Our reading of the literature (Coulthard et al., 2006) is that there is evidence for ipsilesional biases in both initiating and executing reaches in neglect patients. The data also show differences in the reaching performance of neglect patients with parietal and frontal lesions (Husain et al., 2000; Mattingley et al., 1998). Importantly, the evidence is also consistent with interactions between contralesional action deficits and perceptual ones. Right parietal neglect patients are slower to initiate leftward reaches, but only to targets in left space. So both reach direction and target location are critical for this group of neglect patients (Husain et al., 2000; Mattingley et al., 1998).

The second contention of Himmelbach et al. concerns our discussion of optic ataxia, a syndrome which may also comprise several component deficits. In our review, we presented two new cases: one with a small lesion in the superior parietal

lobe (SPL) with optic ataxia, and a second patient who had a much larger lesion with optic ataxia and neglect (Coulthard et al., 2006). We included these cases partly to question a recent group study by Karnath and Perenin of optic ataxics and control patients which suggested there was “no evidence for the assumption that optic ataxia in humans is associated with a lesion typically centering on the SPL” (p. 1564) (Karnath & Perenin, 2005).

Our single case shows that a small lesion within the SPL is sufficient to cause optic ataxia, without extension of brain-damage to the inferior parietal lobe. Although group contrasts are an important way to investigate localization of syndromes, it is also important, in our view, to study single cases with highly focal lesions such as the case we described. From the response of Himmelbach et al., we seem now to be in agreement that the lesion location of the patient we presented is a critical region which, when damaged, leads to optic ataxia.

We thank Himmelbach, Karnath, and Perenin for the stimulating response to our original article and hope that the present paper makes plain our views regarding the action control deficits which exist in patients with neglect.

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### References

- Bartolomeo, P., & Chokron, S. (1999). Egocentric frame of reference: Its role in spatial bias after right hemisphere lesions. *Neuropsychologia*, *37*(8), 881–894.
- Bartolomeo, P., Thiebaut de Schotten, M., & Doricchi, F. Left unilateral neglect as a disconnection syndrome. *Cereb Cortex*, 2007, Jan 31; [Epub ahead of print] PMID: 17272263.
- Buxbaum, L. J., Ferraro, M. K., Veramonti, T., Farne, A., Whyte, J., Ladavas, E., et al. (2004). Hemispatial neglect: Subtypes, neuroanatomy, and disability. *Neurology*, *62*(5), 749–756.
- Chokron, S., & Bartolomeo, P. (1997). Patterns of dissociation between left hemineglect and deviation of the egocentric reference. *Neuropsychologia*, *35*(11), 1503–1508.
- Chokron, S., Colliot, P., Bartolomeo, P., Rhein, F., Eusop, E., Vassel, P., et al. (2002). Visual, proprioceptive and tactile performance in left neglect patients. *Neuropsychologia*, *40*(12), 1965–1976.
- Coulthard, E., Parton, A., & Husain, M. (2006). Action control in visual neglect. *Neuropsychologia*, *44*(13), 2717–2733.
- Duncan, J., Bundesen, C., Olson, A., Humphreys, G., Chavda, S., & Shibuya, H. (1999). Systematic analysis of deficits in visual attention. *Journal of Experimental Psychology: General*, *128*, 450–478.
- Farne, A., Ponti, F., & Ladavas, E. (1998). In search of biased egocentric reference frames in neglect. *Neuropsychologia*, *36*(7), 611–623.
- Friedrich, F. J., Egly, R., Rafal, R. D., & Beck, D. (1998). Spatial attention deficits in humans: A comparison of superior parietal and temporal-parietal junction lesions. *Neuropsychology*, *12*(2), 193–207.
- Himmelbach, M., Karnath, H.-O., & Perenin, M.-T. (2007). Action control is not affected by spatial neglect: A comment on Coulthard et al. *Neuropsychologia*, *45*(8), 1979–1981.
- Husain, M., Mattingley, J. B., Rorden, C., Kennard, C., & Driver, J. (2000). Distinguishing sensory and motor biases in parietal and frontal neglect. *Brain*, *123*, 1643–1659.
- Husain, M., & Nachev, P. (2007). Space and the parietal cortex. *Trends in Cognitive Sciences*, *11*, 30–36.
- Husain, M., & Rorden, C. (2003). Non-spatially lateralized mechanisms in hemispatial neglect. *Nature Reviews Neuroscience*, *4*(1), 26–36.
- Husain, M., Shapiro, K., Martin, J., & Kennard, C. (1997). Abnormal temporal dynamics of visual attention in spatial neglect patients. *Nature*, *385*(6612), 154–156.
- Karnath, H.-O., & Perenin, M.-T. (2005). Cortical control of visually guided reaching: Evidence from patients with optic ataxia. *Cerebral Cortex*, *15*, 1561–1569.
- Malhotra, P., Jager, H. R., Parton, A., Greenwood, R., Playford, E. D., Brown, M., et al. (2005). Spatial working memory capacity in unilateral neglect. *Brain*, *128*, 424–435.
- Malhotra, P., Mannan, S., Driver, J., & Husain, M. (2004). Impaired spatial working memory: One component of the visual neglect syndrome? *Cortex*, *40*, 667–676.
- Mannan, S., Mort, D., Hodgson, T., Driver, J., Kennard, C., & Husain, M. (2005). Revisiting previously searched locations in visual neglect: Role of right parietal and frontal lesions in misjudging old locations as new. *Journal of Cognitive Neuroscience*, *17*, 340–354.
- Mattingley, J. B., Bradshaw, J. L., & Phillips, J. G. (1992). Impairments of movement initiation and execution in unilateral neglect. Directional hypokinesia and bradykinesia. *Brain*, *115*(Pt 6), 1849–1874.
- Mattingley, J. B., Husain, M., Rorden, C., Kennard, C., & Driver, J. (1998). Motor role of human inferior parietal lobe revealed in unilateral neglect patients. *Nature*, *392*(6672), 179–182.
- Posner, M. I., Walker, J. A., Friedrich, F. J., & Rafal, R. (1984). Effects of parietal injury on covert orienting of attention. *Journal of Neuroscience*, *4*, 1863–1874.
- Robertson, I. H., Manly, T., Beschin, N., Daini, R., Haeske-Dewick, H., Homberg, V., et al. (1997). Auditory sustained attention is a marker of unilateral spatial neglect. *Neuropsychologia*, *35*(12), 1527–1532.