CHAPTER 15

Reaching between obstacles in spatial neglect and visual extinction

A. David Milner* and Robert D. McIntosh

Cognitive Neuroscience Research Unit, Wolfson Research Institute, University of Durham, Queen's Campus University Boulevard, Stockton-on-Tees TS17 6BH, UK

Abstract: The aim of the present studies was to investigate whether 'perception' and 'visually guided action' could be dissociated with regard to two different aspects of the neglect syndrome. In the first study we tested a group of patients with neglect in two tasks, both within the same experimental setting. One task was to bisect a space between two objects, while the other required subjects to reach between the same pair of objects en route to a target area, so that the objects became potential obstacles to the reach. In the second study we tested a patient with visual extinction to double simultaneous stimulation, using a similar reaching task. Our aim was to determine whether visual awareness of obstacles in the workspace was necessary for successful navigation. In both studies we found evidence that reaching responses took normal account of the presence and location of obstacles on the left side, despite the tendency to neglect such left-sided information in more explicit perceptual tasks. We interpret both sets of results within a theoretical framework that identifies on-line visuomotor control with the occipito-parietal 'dorsal stream' (along with associated premotor and subcortical structures), and visual perception with the occipito-temporal 'ventral stream', plus associated temporo-parietal areas.

Introduction

The neglect syndrome is a complex and multi-faceted group of symptoms (Heilman et al., 2002), some of which hang together better than others. The brain lesions that cause neglect symptoms vary widely, though there is a region around the parieto-temporal junction, particularly in the right hemisphere in cases of left-sided neglect, that is included in the majority of cases (Vallar, 1993; Vallar et al., 1994; Karnath et al., 2001). Perceptual extinction to double simultaneous stimulation is traditionally included as one of the cardinal symptoms of the neglect syndrome (Heilman et al., 2002), though it frequently occurs in the absence of other signs of neglect, and several authors have argued that it may be causally independent (e.g. Milner, 1987, 1997). Extinction can be characterized as a lateral bias of spatial attention occurring in the context of a reduced attentional capacity (e.g. Driver et al., 1997), whereby a stimulus on the ipsilesional side briefly attracts attention to the exclusion of simultaneous (or near-simultaneous) stimuli located in more contralesional locations. Other symptoms of neglect, such as rightward errors in line bisection, and left-sided deficits in visual search tasks, are generally regarded as more central to the essence of spatial neglect, though theories as to their causation range widely.

The present chapter is concerned with exploring the phenomena of visual neglect and extinction from an unconventional starting point, by asking whether these conditions affect a person's ability to guide their hand to a desired location while avoiding intervening obstacles lying on the right and

*Corresponding author. Cognitive Neuroscience Research Unit, Wolfson Research Institute, University of Durham, Queen's Campus University Boulevard, Stockton-on-Tees TS17 6BH, UK. Tel.: +44-1642-333850; Fax: +44-1642-385866; E-mail: a.d.milner@durham.ac.uk

PROGRESS IN BRAIN RESEARCH
VOLUME 144 ISSN 0079-6123
DOI: 10.1016/S0000-0000(00)00000-0

left of the workspace. The logic of this approach derives from the visual processing model set out by Milner and Goodale (1995). They argued that a distinction should be drawn between visual processing for perception and visual processing for action. According to the model, the former is embodied in the occipito-temporal 'ventral stream' of cortical processing, while the latter is embodied in the occipito-parietal 'dorsal stream' (Glickstein and May, 1982; Ungerleider and Mishkin, 1982). Although all visual processing can ultimately be expressed in the form of overt behavior (and indeed that is why it exists) the dorsal stream is thought to interact directly with premotor cortex and brainstem structures to transform visual information into motor coordinates, while the ventral stream can only influence action indirectly. What the latter route loses in immediacy, of course, it gains in flexibility.

We have suggested (Milner and Goodale, 1995; Milner, 1997; Milner and McIntosh, 2002) that the temporo-parietal region of the right hemisphere that is most heavily implicated in the causation of neglect probably functions in good part as a high-level representational system that is fed principally by visual inputs arising from the ventral stream. The region can perhaps be regarded as the endpoint of the perceptual processing pathway, where the ever-changing contents of our visual consciousness are represented, operating under the flexible control of attentional and executive systems located in superior parietal and prefrontal regions (Driver and Mattingley, 1998; Driver and Vuilleumier, 2001). Of course there is no doubt that overt behavior is affected by neglect, not just the patient's inner experience. Nonetheless, the hypothesis is that much of this abnormal behavior is driven by the indirect 'perceptual' route, rather than by the direct 'visuomotor' route. In other words, it is an expression of the distorted and disrupted perceptual experience of the patient rather than a direct result of a damaged visuomotor control system in the dorsal stream. Indeed, even some apparently pure motor manifestations of neglect, such as biased ocular exploration in darkness (e.g. Hornak, 1992; Karnath et al., 1998), might derive from a distorted internal representation of external space. A strong prediction of this hypothesis is that, in many cases of neglect, visual processing for direct action should be free from the pronounced perceptual biases that characterize the syndrome. It is this proposal that we aimed to test in the present studies.

It is necessary to distinguish this proposal of dissociated perceptual and visuomotor processing in neglect from the more familiar concept of a division between perceptual and motor contributions to neglect. Traditionally, there has been an assumption that the symptoms of neglect arise from spatial biases either in the processing of sensory input or in the programming of motor responses. A number of attempts have been made to distinguish between input- and output-related biases in neglect, though the validity of many of these studies has been questioned (see Mattingley and Driver, 1997 for a review). In contrast to this serial input–output distinction, however, the model of Milner and Goodale (1995) is concerned with a distinction between parallel visual processing systems, respectively underlying conscious perceptual awareness and automatic goal-directed actions. In relation to neglect symptoms, this model proposes that the expression of spatial biases in visual processing should depend upon the behavioral context in which the visual processing takes place. Specifically, the symptoms of neglect should be more often linked to the visual processing subserving perceptual awareness than to the processing underlying the guidance of automatic goal-directed actions.

Whether on not the visual guidance of simple direct actions in neglect patients is subject to lateral spatial biases has been a matter of some debate. Goodale et al. (1990) and Jackson et al. (2000) reported rightwardly curved trajectories in the pointing movements of recovered left neglect patients, and Harvey et al. (1994) observed a similar effect in right hemisphere damaged patients without neglect. Such effects, however, are not ubiquitous. For instance, Chieffi et al. (1993) observed no abnormal curvature in the pointing movements of a recovered left neglect patient to isolated visual targets. More importantly, these phenomena have not been substantiated by direct tests of patients with full left neglect. Perenin (1997) failed to observe any directional skewing of visually guided (open-loop) pointing movements among four neglect patients. Similarly, Karnath and colleagues (1997) reported accurate open- and closed-loop visual guidance in five chronic neglect patients, both in terms of terminal accuracy and hand trajectories, a result replicated recently by Harvey et al. (2002) in four neglect patients performing a simple grasping task. On the basis of such findings, Karnath et al. (1997) have argued that ipsilaterally curved movement trajectories are not characteristic of patients with neglect, although they may be characteristic of optic ataxia (Perenin, 1997).

The evidence for a systematic spatial bias in the visually guided actions of neglect patients is therefore not strong. However, at least two published studies have claimed to observe specifically visuomotor manifestations of neglect. Behrmann and Meegan (1998) required six patients with left visual neglect to reach for a target LED, presented alone or simultaneous with a distractor LED, with target and distractor distinguished by color. Like normal subjects, neglect patients were slower to initiate a response to any target that was accompanied by a distractor but, compared to controls, they had an increased RT cost for a distractor on the right and a reduced cost for a distractor on the left. Behrmann and Meegan concluded that information from the neglected side must be processed minimally, if at all, in the visuomotor domain. However, we suggest that it is misleading to portray this effect as visuomotor, since conscious perceptual discrimination of the target from any distractor would be a necessary prerequisite for selecting which stimulus to respond to in the task. Thus, the asymmetrical influence of left and right-sided distractors is most likely to reflect a difficulty in choosing the left stimulus in the presence of the irrelevant stimulus on the right, irrespective of what response has to be made to the target. An accentuated influence of right-sided distractors has also been reported for a recovered left neglect patient performing a grasping task (Chieffi et al., 1993). Again, however, it is unclear whether this reflects unbalanced visuomotor processing, or interference with the perceptual discrimination of the target from the distractor object.

A more direct strategy to assess the normality of visuomotor processing in neglect is to compare performance between tasks where the stimuli are matched as closely as possible, but the mode of response differs. Several studies have already employed this general strategy to investigate reaching and grasping in neglect. Robertson et al. (1995, 1997) found that neglect patients showed significantly less bisection error when asked to pick up a rod at its midpoint than when asked only to point to the rod's midpoint. They argued that the pointing task reflected disordered perception in their patients, but that reaching to grasp was an action driven more directly by the dorsal than the ventral stream, thus enabling an improvement in bisection accuracy. In a similar vein, Pritchard et al. (1997) found that a neglect patient (E.C.) was able to calibrate her finger-thumb grip aperture accurately when reaching to grasp different sized cylinders, with no asymmetry in grip size between target locations on the two sides of visual space. Yet when asked to indicate her perceived size of the cylinders, she consistently underestimated them when they were located on her left as compared with her right side. Later studies with groups of neglect patients have replicated this symmetrical grasping behavior (Harvey et al., 2002; McIntosh et al., 2002), though there was no direct demonstration in those papers that the cylinders were perceived as having different sizes on the two sides of space.

In the present paper we report a series of studies aimed at assessing the visuomotor processing underlying simple reaching movements in neglect. In the first study, we asked neglect patients to perform two tasks, both involving the presentation of two upright cylindrical stimuli, whose locations varied from trial to trial. In the 'bisection' task, the patient was asked to judge the midpoint between the two cylinders and to place their finger at that location. In the 'reaching' task, the patient was asked to move the hand rapidly from a start point to touch a 'target zone' located beyond the two objects. This second task was designed to be a simple act of reaching under direct visual control, with an implicit requirement that the reach needs to be executed so as to minimize the risk of collision with either cylinder. The conceptual similarity between these two tasks is that they both require the subject to take account of the location of the cylinders on the left and right simultaneously. In one situation, this demand is part of the explicit spatial analysis underlying a bisection response. In the other, it arises implicitly in computing the optimal spatial path for a visually guided reaching movement. Preliminary data on these tasks have been presented already (Milner and McIntosh, 2002). We found good evidence in this experiment for a dissociation between the two tasks: most of the patients behaved like healthy controls in the reaching task, though they showed asymmetrical behavior when attempting to make explicit bisection responses.

In other words, we found that most neglect patients were able to take a potential obstacle on the left as fully into account as one located on the right when reaching between them. However these results do not of course demonstrate that such obstacle avoidance can take place even when there is no conscious perception of the left obstacle. After all, there was no restriction of viewing time, and no independent evidence that the patients were unaware of the presence of the left-side object. We therefore conducted a single-case study in which we attempted to address this question. We tested a patient (V.E.) with persistent visual extinction who, under appropriate conditions, would often report seeing only the right stimulus when in fact a left stimulus was present as well. Again using a reaching task, we assessed whether his awareness or unawareness of the left object, when two objects were present, affected the trajectories taken by his hand. Normal subjects vary their reaches systematically according to the presence of a left-alone, right-alone, or bilateral pair of objects. Our question was whether V.E. would show these same phenomena, even when he did not ‘see’ the obstacle on the left — or would his reaches on such ‘unaware’ trials be more similar to those he made when there literally was only one object, located on the right? Our data indicate that a failure to ‘see’ an obstacle, due to visual extinction, does not necessarily compromise the ability to process the location of that obstacle in order to avoid it when reaching.

Experiment 1: Reaching and bisection in neglect

Twelve patients with left visual neglect following unilateral right hemisphere stroke, and ten age-matched controls, took part in this experiment. All patients displayed neglect on three or more of five standard diagnostic tests. Full details of the patients can be found in McIntosh et al. (submitted, a). Subjects were seated in front of a 60 cm square white stimulus board depicted in Fig. 1, with the right index finger placed at the start position. Two dark gray cylinders (24.5 cm tall and 3.5 cm in diameter) could be fixed into the board, one to either side of the midline, at a depth of 25 cm with respect to the start position, and 20 cm in front of a 5 cm deep gray strip that spanned the far edge of the board. Each cylinder could occupy one of two possible locations, with its inside edge either 8 cm or 12 cm away from the midline. The factorial combination of these four locations thus created four stimulus configurations. Each patient performed two different tasks on this stimulus board, with the order of tasks alternating between subjects within each group. All responses were recorded by sampling the position of a magnetic marker attached to the nail of the right index finger,

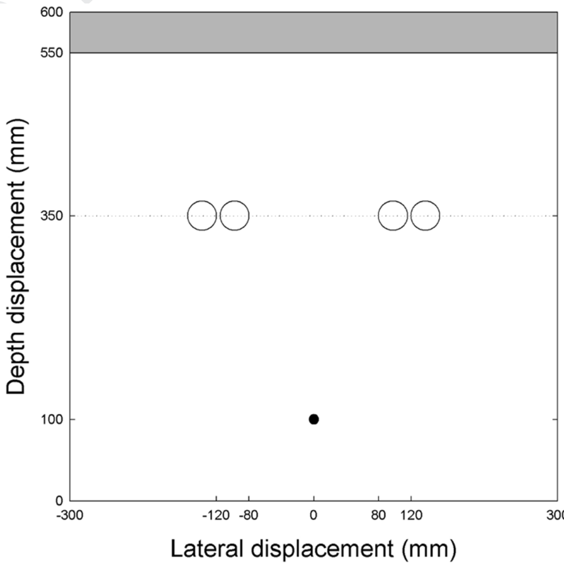

Fig. 1. Plan view of the apparatus used in Experiment 1. Cylinders were always presented in pairs, one on the left and one on the right of the midline. The open circles show their possible locations, with inside edges 8 and 12 cm from the midline. Each trial began with the subject’s right index finger resting on the start position (black dot). In the bisection task, the subject was requested to place their finger midway between the two cylinders, and the dependent measure was the lateral position of the response with respect to middle of the stimulus board. In the reaching task, the subject was instructed to reach out and touch the gray strip as fast as possible. The dependent measure was the lateral position of the right index finger as it crossed the virtual line joining the two cylinder locations (dotted line).

at a frequency of 86.1 Hz (Minibird, Ascension Technology Ltd.). Full methodological details can be found elsewhere (McIntosh et al., submitted, a).

In the *bisection* task, the subject was asked to place their right index finger midway between the two cylinders. The subject was told that this was a test of 'accuracy of judgment', and that an unlimited time was available for each response. On each trial, the subject was allowed to adjust their finger position until satisfied that it was exactly midway between the cylinders. The position of the marker attached to the index finger was then sampled for 1 s. The dependent measure was the average lateral position (P) of the finger marker, with respect to the midline of the stimulus board, during this 1-s period. Each subject made 48 bisection responses, with each of the four stimulus configurations presented 12 times in a fixed pseudo-random order.

In the *reaching* task, the subject received the instruction 'On the *go* signal, reach out and touch the gray strip as quickly as you can', and was told that this was a test of 'speed of movement'. Prior to the task, they were informed that, whenever a cylinder was present, there would be one on the left and one on the right, and that they should pass their hand between the two cylinders, rather than around the outside edge of the board. The presence of the cylinders was not otherwise mentioned. Each reaching response was recorded in full, and the dependent measure was the lateral position (P) of the index finger marker as it crossed the virtual line joining the two cylinder locations (the exact value of P was estimated by linear interpolation). Each subject made 60 reaches, 12 for each of the four cylinder configurations, and 12 in which no cylinder was present on the board, in a fixed pseudo-random order. The 12 trials with no cylinder in place were included to check for any systematic reaching biases when the response was not constrained by potential obstacles. An independent *t*-test (corrected for unequal variances) performed on these responses alone found no difference between the groups [$t(13) = 0.59$, $P = 0.57$], with both groups passing on average slightly to the left of the board midline. This constant bias is unsurprising, since the marker from which responses were recorded was attached to the right index finger and was thus on the left side of the hand in its palm-down reaching posture. These no-cylinder trials were excluded from all further analyses.

Figure 2 shows the group mean responses for each stimulus configuration in each task. A repeated measures ANOVA was performed with the within-subjects factors of task (bisection, reaching), left cylinder location (near, far) and right cylinder location (near, far), and the between-subjects factor of group (control, neglect). Overall, the neglect group responded slightly further rightwards than the controls in the bisection task, and slightly further leftwards than controls in the reaching task, as reflected in a significant interaction of task by group [$F(1, 20) = 6.67$, $P = 0.02$]. Due to the presence of this interaction, and a significant three-way interaction of

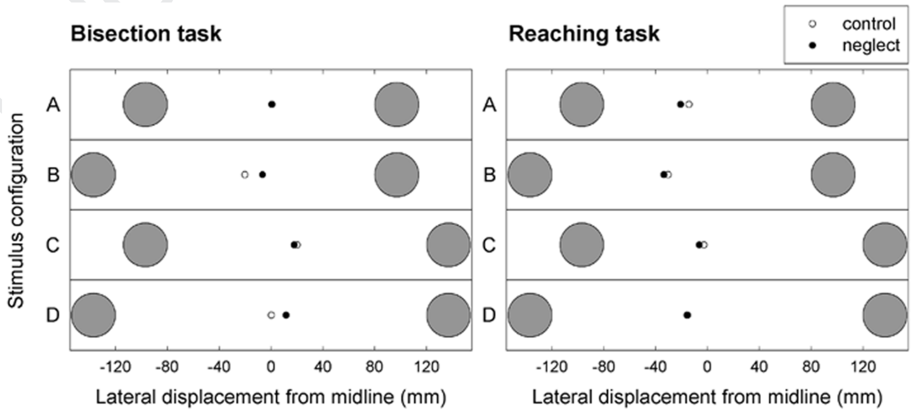

Fig. 2. Experiment 1: Mean responses in the bisection task (left) and the reaching task (right). The dark gray circles depict the stimulus cylinders.

task by group by left cylinder location [$F(1,20) = 20.03$, $P < 0.001$], subsequent ANOVAs were conducted for each task separately.

For the bisection task, the factor of subject group was not significant [$F(1,20) = 1.39$, $P = 0.25$]. Thus, although the neglect group bisected slightly further rightwards than controls, this tendency was not reliable at the group level. This was to be expected from previous evidence that the typical rightward line bisection errors of neglect patients tend to be reduced or eliminated when gaps are presented instead of lines (e.g. Bisiach et al., 1996; McIntosh et al., in press). However, the mere lack of an overall rightward bias amongst neglect patients does not imply that their bisection behavior was normal in terms of its dependence of the locations of the left and the right cylinders. Although the main effects of the left cylinder location [$F(1,20) = 224.42, < 0.001$] and the right cylinder location [$F(1,20) = 351.63, < 0.001$] were robust, a significant interaction of left cylinder location by subject group [$F(1,20) = 55.82, < 0.001$] indicated that the responses of neglect patients were far less influenced by the location of the left cylinder than were the responses of the control subjects. In Fig. 2, this effect is reflected in the conspicuous differences between the groups for stimulus configurations B and D of the bisection task. The control subjects moved their bisection point appropriately (by about 20 mm) when the left cylinder was moved from the near to the far location, but the neglect patients were less affected by this change. In the reaching task, by contrast, both the neglect patients and the controls shifted their reaching trajectories symmetrically when either cylinder moved between near and far locations (Fig. 2, right). Accordingly, the analysis of the reaching data found robust main effects of left cylinder location [$F(1,20) = 78.68, < 0.001$] and right cylinder location [$F(1,20) = 131.36, < 0.001$], and these effects did not interact with the factor of subject group.

In summary, the reaching responses of both groups were sensitive to the locations of the cylinders on either side of space, but the bisection responses of the neglect group were specifically insensitive to the location of the left cylinder. This pattern can be most clearly appreciated if we visualize the data in terms of the 'weights' given to the left and right cylinders in determining the responses. As we have described elsewhere (McIntosh et al., in preparation), it is possible to analyze bisection data in a way that emphasizes the dependence of the response position (P) on the locations of the left endpoint (L) and the right endpoint (R), provided that these endpoint locations have been manipulated independently. Whenever L or R changes by some amount (40 mm in this experiment), P will also change by some amount: dP_L and dP_R, respectively. The values of dP_L and dP_R can be considered to reflect the 'weight' given to either endpoint in determining the response. In a series of line bisection experiments, we have found that neglect patients invariably accord a lower weight to the left endpoint (dP_L) than to the right endpoint (dP_R); this may be true even for patients who do not produce mean rightward bisection errors.

Figure 3 represents the data from Fig. 2 in terms of the mean weights, dP_L and dP_R, given to the left and right cylinders (i.e. how much the response shifts as a function of 40 mm shift of one or the other cylinder). As the left half of the figure illustrates, the control subjects were equally attentive to the location of the left and the right cylinders in making their bisection responses, producing similar values of dP_R and dP_L (approximately 20 mm). In other words, the controls adjusted their bisection responses by approximately half of the distance by which the cylinders shifted. The neglect patients, however, had values of dP_L that were dramatically lower than those of $\mathrm{dP_R}$, just as we have found in comparable analyses of line bisection data (McIntosh et al., in preparation). This effect was present in all twelve patients (see Fig. 4), despite the fact that five patients had mean bisection errors that were leftward or zero. A very different picture is apparent from the right half of Fig. 3, where the results for the reaching task are presented. The values of dP_R and dP_L are more similar across the neglect group as a whole (with two notable exceptions: see Fig. 4), indicating that the point of transection was more evenly determined by the locations of the cylinders on the left and right. It thus appears that task demands may greatly modulate the expression of neglect: the patients take normal account of the location of the left cylinder when making a speeded reaching movement, but fail to do so when making an explicit bisection response.

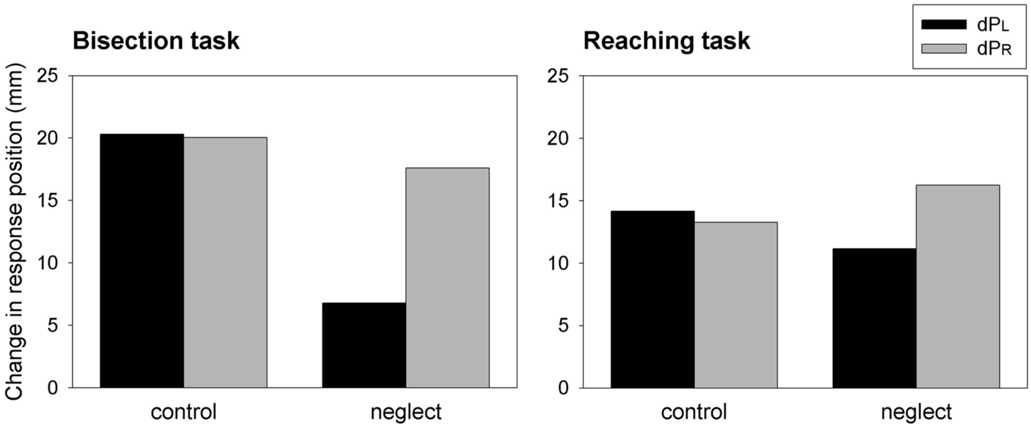

Fig. 3. Experiment 1: The mean change in response induced by a 40 mm shift in the location of the left cylinder (dP_L) and right cylinder (dP_R) in each task.

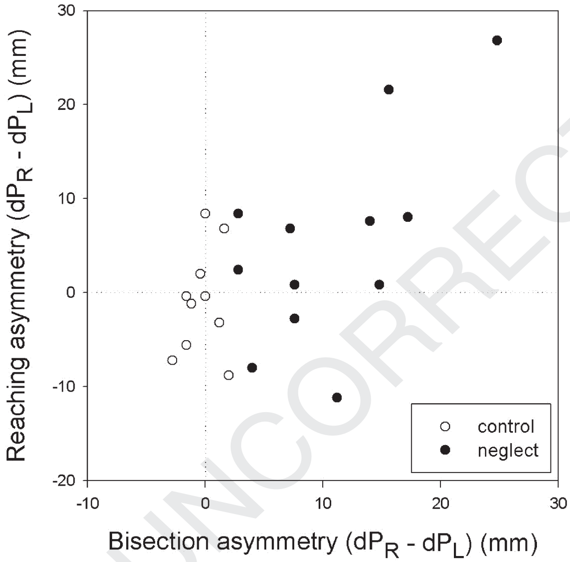

Fig. 4. Experiment 1: A plot comparing the asymmetries found for each subject in the influence (weighting) of the two cylinders ($dP_R - dP_L$), between the reaching task and the bisection task.

Discussion of Experiment 1

In this experiment, the *reaching* responses of both groups were similarly sensitive to the locations of the cylinders on either side of space, but the bisection responses of the neglect group were peculiarly insensitive to the location of the left cylinder. We have concluded that neglect patients make normal use of spatial information from the left side in programming a fast reaching response, information that they fail to take into account when making a more explicit bisection judgment. However, this broad conclusion is subject to a caveat. Figure 3 shows that even in the reaching task there is a qualitative (though nonsignificant) trend toward a reduced influence of the left cylinder relative the right cylinder. This seems to result from the fact that while most patients show the group dissociation between the two tasks, some do not.

This individual variation within the neglect group is illustrated in Fig. 4, in which the magnitude of asymmetry between the weightings of the left and right cylinders ($dP_R - dP_L$) for the reaching and bisection tasks are co-plotted as a scattergram. All neglect patients have a positive asymmetry in the bisection task, giving a higher weight to the right cylinder than to the left, and there is no overlap with the control group. In the reaching task, there is considerable overlap between groups, but there are nonetheless two clear instances of an abnormally positive asymmetry within the neglect group. Indeed, the group trend toward a reduced influence for the left cylinder in the reaching task (Fig. 3) is driven very substantially by the behavior of the two patients in the upper right-hand corner of Fig. 4. These two patients show a comparably strongly positive asymmetry, reflecting a reduced influence of the left cylinder, in both tasks. In these two patients at least, there is no dissociation between neglect for the reaching and bisection tasks. It may be that their similar values of (dP_R–dP_L) on the two tasks reflect the same underlying deficit, causing a reduced sensitivity to the left cylinder location in both tasks. However it is also possible that the lesions were simply more extensive in these two patients, causing a disruption of mechanisms of visuomotor attention as well as those of perceptual integration (see General Discussion). Certainly these were two of the most severe cases of neglect in our group, as indicated by screening tasks.

Excluding these two patients, Experiment 1 provides a clear example of a dissociation between perception and action, in that all of our other patients took good account of the location of the left-sided cylinder during a reaching task, but failed to do so when making a bisection judgment. Of course the bisection judgment in itself required the patient to make an action, but this was a very different kind of action from reaching between the cylinders to a location beyond them. The bisection response was an act of communication: a form of ostensive behavior, whereby the patient was telling us what he or she perceived to be the midpoint of the space between the two cylinders on each trial. In contrast, the reaching task required the patient only to avoid colliding with the cylinders while moving the hand between and beyond them. Such successful obstacle avoidance clearly required taking into account the location of both cylinders, and this was almost universally achieved by the patients, as shown by their high dP_L values in the reaching task. Yet, of course, our data do not allow us to claim that our neglect patients were necessarily unaware of the left-sided cylinder during the reaching and bisection tasks. In fact it is clear that even during the bisection task, most of them did pay some attention to it, as shown by the fact that their values of dP_L were generally greater than zero (though always smaller than their dP_R values). This is not too surprising, since there was no restriction of the time available for subjects to view the stimulus array, and no attempt to restrict their eye movements. We sought clearer evidence on this specific question of the role of visual awareness in obstacle avoidance by studying a patient with visual extinction to double simultaneous stimulation.

Experiment 2: Obstacle avoidance in visual extinction

We have now undertaken a series of studies of a 75-year-old patient, V.E., who experiences left-sided visual extinction, due to a predominantly parieto-temporal infarct in the right hemisphere (based on CT and MRI scans). He shows no visual field defect on Tübingen perimetry, and no hemispatial neglect (though neglect had been apparent acutely following his stroke, some 12 months prior to our study). To assess the influence of extinguished stimuli on V.E.'s visually guided actions, we have taken advantage of the normal tendency for reaching movements to veer away from potential obstacles in the workspace (Tresilian, 1998). Normal reaches tend to swerve leftwards away from an obstacle on the right, rightwards away from an obstacle on the left, and the bilateral presence of obstacles induces intermediate reaching trajectories. Our question was whether V.E. would also produce such intermediate reaching trajectories when obstacles were present bilaterally, and whether this ability would depend on an explicit awareness of both obstacles. To address this question, we recorded V.E.'s reaching responses in the presence of obstacles, whilst collecting a verbal report of his awareness of the obstacles on each trial. By time-limiting V.E.'s view of the stimulus array, we were able to ensure that he correctly reported a single object located on either side of space, but failed to report the left object (i.e. showed extinction) on about half the trials in which both objects were present. We reasoned that if extinguished stimuli are able to influence his reaches, then he should make intermediate reaches irrespective of whether he reports seeing the left obstacle. If, however, extinguished stimuli do *not* influence his reaches then, whenever he fails to report an obstacle on the left, his trajectories should show a typical leftward swerve as if there was only an obstacle present on the right.

Experiment 2.1 employed a simple stimulus setup in which V.E. had to reach and touch a target zone in the presence of potential obstacles, which in this case were thin poles, 15 cm high. There were two obstacle locations, one on either side of the midline, allowing room for the hand to pass through, but making it necessary to pay full regard to any poles present in order to make a smooth and uninterrupted reach (see Fig. 5). V.E. was required to fixate centrally at the beginning of each trial and, following stimulus exposure, to reach out and touch the target zone as rapidly as possible and then to report verbally any poles that he had seen. A pair of liquid crystal glasses limited stimulus exposure to 500 ms. Poles were presented bilaterally or unilaterally, with bilateral trials twice as frequent as left-unilateral or right-unilateral trials. Trials cycled through a pseudo-random schedule until at least 20 bilateral trials had been collected in which V.E. reported both poles, and at least 20 in which he reported only the right pole. Since V.E. never initiated his reaching movements less than 835 ms after stimulus onset, he executed all reaches without visual feedback (visually 'open-loop'). Reaches were recorded by sampling the position of a marker attached to the right index finger at a frequency of 86.1 Hz, again using the Minibird motion analysis system. Full methodological

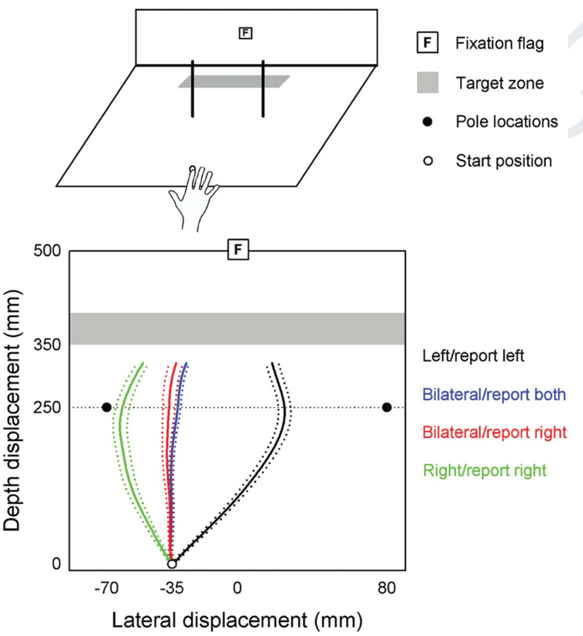

Fig. 5. Experiment 2.1: The upper panel shows a schematic diagram of the experimental set-up. V.E. fixated the flag (F) at the start of each trial. Following stimulus exposure, he reached out rapidly to touch the target zone and then reported any poles that he had seen. The lower panel shows spatially averaged trajectories in each condition (dotted lines indicate standard errors), where the zero lateral coordinate is aligned with V.E.'s mid-sagittal axis.

details can be found elsewhere (McIntosh et al., submitted, b).

As Fig. 5 illustrates, the spatial path of the hand shifted according to the poles that were present, reflecting a strategic minimization of the risk of collision. The overall influence of the right pole was more pronounced than that of the left pole. This pattern is common in normal subjects (McIntosh et al., submitted, b) and presumably reflects the fact that, when responding with the right arm, objects on the right are more obstructive than those on the left. More interestingly, however, V.E.'s performance on the bilateral-pole trials was totally independent of his verbal report: there was no significant difference between the 'extinction' and 'non-extinction' reaching trajectories at the point where they crossed the line joining the two poles. A one-way ANOVA performed on the lateral displacement of the index finger at the point crossing the virtual line joining the two pole locations was highly significant [$F(3, 85) = 140.79$, $P < 0.001$]. Scheffé post hoc tests found reliable differences ($P < 0.001$) between all conditions except between the two sets of bilateral-pole trials ($P = 0.73$). In other words, V.E. avoided the obstacle on the left regardless of whether or not he reported its presence verbally. His reaching trajectories when he failed to report the left pole on bilateral-pole trials were not at all like those he made when there really was only an obstacle on the right present. This suggests that V.E. was implicitly processing the left obstacle's presence and location: he denied awareness of the left pole on many trials, and yet his reaching behavior on those same trials showed that the presence and location of the left pole had been fully taken into account.

Nonetheless, a lingering doubt remained. After all, V.E. did not give us his verbal report until after he had completed his reach on each trial. A skeptic might suggest that he somehow 'forgot' that he had seen the left obstacle, having first processed it for motor guidance. We therefore ran a second experiment (Experiment 2.2), in which we asked V.E. again to report what he saw on a trial-by-trial basis, but this time under two different conditions. In the 'motor–verbal' (MV) condition, he was asked (as before) to 'touch the gray strip as quickly as possible, then report which poles you saw'. In the 'verbal–motor' (VM) condition, however, he was asked to

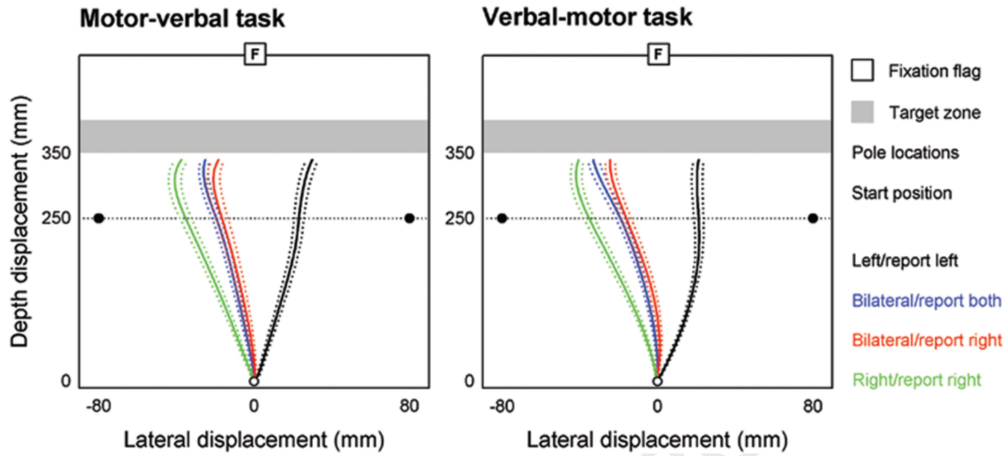

Fig. 6. Experiment 2.2: V.E.'s spatially averaged trajectories in the motor–verbal (MV) and verbal–motor (VM) tasks (dotted lines indicate standard errors).

'shout out which poles you see as quickly as possible, then touch the gray strip'. Identical results were obtained in the two temporal order conditions: V.E.'s reaches took full account of any pole on the left, regardless of whether or not that pole was reported (Fig. 6). For the MV task, a one-way ANOVA performed on the lateral displacement of the index finger at the point crossing the virtual line joining the two pole locations was highly significant [$F(3, 109) = 68.14$, $P < 0.001$]. Scheffé post-hoc tests found reliable differences ($P < 0.001$) between all conditions except between the two sets of bilateral trials ($P = 0.90$). A similar main effect was found for the VM task [$F(3, 113) = 75.28$, $P < 0.001$]. Scheffé post-hoc tests again found reliable differences ($P < 0.002$) between all conditions bar the two sets of bilateral trials ($P = 0.89$). The MV result thus replicated Experiment 2.1, whilst the VM result confirms that the dissociation between verbal awareness and reaching behavior depends on the two different response modes, and not on their order of occurrence. It is notable that there was now no tendency for V.E.'s trajectories on bilateral trials where he reported only the right pole to be shifted slightly toward those when there really was only the right pole present. In fact the reverse was the case, suggesting that the trend in Experiment 2.2 (Fig. 5) was not a real one. In our view, this series of experiments establishes beyond reasonable doubt that V.E. was able to use unconscious visual information just as effectively as conscious information in the guidance of his actions.

General discussion

The results of our first study, documenting a dissociation between perception and action in neglect, agree nicely with those of Robertson et al. (1995), who contrasted picking up a rod at its midpoint with pointing to the rod's midpoint. In effect we have provided evidence for the generality of this phenomenon by replacing the rod with an empty gap. At a general level, these dissociations between perception and action in neglect are reminiscent of the examples of preserved visuomotor control observed in the visual-form agnosic patient D.F., in the face of dramatically impaired perceptual experience (Milner et al., 1991; Goodale et al., 1991). Indeed, we have long been aware at an informal level that D.F. has no difficulty in negotiating her way through a cluttered room. More recently we have observed this preserved ability in a formal test situation in which D.F. was asked to reach out to grasp an object which was flanked by an irrelevant object on the left or right (McIntosh et al., 2000). She was consistently found to adjust her trajectories appropriately to take account of the obstacles.

This parallel with D.F. encourages us to construct a hypothesis for explaining our neglect data in terms similar to those we have used to understand D.F.'s pattern of visual abilities and disabilities. On the basis of the known neural properties of the ventral and dorsal visual processing streams in the primate cortex, Milner and Goodale (1995) proposed that D.F. had lost her ability to process form for perception through damage to the ventral stream, but was still able to use her residual dorsal stream structures to process form for the purpose of visuomotor control. This hypothesis has now been dramatically confirmed by recent functional and structural MRI studies (Culham, 2003, in press) and James et al., submitted). These studies have revealed that the lateral occipital complex (LOC), generally believed to be equivalent to the inferotemporal area in the monkey's ventral stream, has been destroyed bilaterally in D.F. The posterior parietal region has also suffered some degeneration, but an area lying anteriorly in D.F.'s intraparietal sulcus, believed to correspond to area AIP in the monkey's dorsal stream, is still active during visual grasping, just as it is in healthy subjects.

Of course the lesions that cause hemispatial neglect are different from those that are present in D.F., but they are also very different from those that cause visuomotor problems such as optic ataxia (Perenin 1997; Karnath et al., 2001). As we mentioned in the Introduction, the lesions in neglect are typically located inferiorly, in the right parieto-temporal region, rather than in the superior parts of the parietal lobe. In contrast, it is in superior parietal regions, in and around the intraparietal sulcus, where lesions cause optic ataxia. This superior region thus, by analogy with the monkey data, appears to form a central part of the human homolog of the dorsal visual stream, a conclusion further supported by fMRI evidence (Culham and Kanwisher, 2001; Culham, 2003 (in press)).

Since neglect is almost by definition a disorder of perceptual awareness, we have therefore argued that the inferior parts of the right parietal lobe (and superior parts of the right temporal lobe) probably relate more closely to the ventral than to the dorsal stream (Milner and Goodale, 1995). [Of course, it is not claimed that activity in the ventral stream circuits is sufficient for visual awareness; indeed there is evidence that even in patients with extinction unconscious stimuli can still elicit activation — at low levels — within the ventral stream (Driver and Vuilleumier, 2001). Presumably it is through such sub-optimal ventral activation that aspects of object perception and identification can still occur in the absence of conscious awareness (see review by Merikle et al., 2001).] Our present data are consistent with this broad idea: we may assume that most of our neglect patients will have a relatively intact dorsal stream enabling them to avoid obstacles normally, just as D.F. appears to do. However, most of them have suffered damage to areas in the right inferior parietal lobule and/or superior temporal gyrus, which we believe embody a system concerned with constructing and manipulating mental representations of the spatial array (Milner, 1997; Driver and Mattingley, 1998; Driver and Vuilleumier, 2001). This damage evidently unbalances that system, causing the patients to attach reduced weightings to items on the contralesional side of the array when making perceptual judgments.

Our related studies of patient V.E. have taken us further, by establishing a novel form of unconscious processing of extinguished visual stimuli. Although V.E. was unaware of the presence of the left object on many of the bilateral-object trials, his reaches on those trials were influenced by the extinguished object to just the same extent as on 'aware' bilateral trials. It is important to note that V.E.'s brain damage lies in the right inferior parietal lobe and right temporal lobe. This damage is consistent with our view that these areas play an important role in determining the contents of our perceptual awareness. The lesion does not encroach on the superior parietal region around the intraparietal sulcus, so we may assume that the human homologue of the dorsal visual stream is unscathed. Indeed it seems likely that V.E.'s implicit processing of obstacle location reflects the sparing of this superior region.

But, of course, the superior parietal region is not only implicated in the visual guidance of movement. It also plays an important role in the control of visuospatial attention. This function seems to be most closely associated with systems that provide visual guidance for saccadic eye movements, particularly area LIP (Rizzolatti et al., 1994; Goldberg et al., 2002). This attentional control appears to operate 'top-down' by modulating activity in the inferior parietal region and occipito-temporal visual areas (Corbetta et al., 2000; Hopfinger et al., 2000; Kastner and Ungerleider, 2001; Yantis et al., 2002).

Such a multiplicity of areas involved in visual attention makes it unsurprising that visual extinction can result from a range of different lesion sites. For example, although an early report by Posner et al. (1984) reported a stronger 'extinction-like effect' in the standard Posner spatial cuing paradigm at short inter-stimulus intervals in patients with superior rather than inferior parietal lesions, more recent evidence from Friedrich et al. (1998) indicates that lesions around the parieto-temporal junction are more crucial. These results make sense in the context of a modulatory pathway or pathways passing down from the intraparietal sulcal region to the inferior parietal and occipito-temporal regions. It is reasonable to suppose that the pathological imbalance of perceptual attention that constitutes extinction could result from damage at any point in these pathways.

In the present context, where we have been at pains to distinguish between visual processing for perception and visual processing for action, it is important to note that the attentional imbalance that constitutes extinction is by definition one of attention for perception, whereby the ipsilesional stimulus of a pair consistently out-competes the contralesional stimulus for entry into awareness. As V.E.'s case shows, however, this can happen without a similar imbalance in visuomotor attention (Rizzolatti et al., 1994; Milner and Goodale, 1995), presumably by virtue of V.E.'s bilaterally intact superior parietal areas, including LIP. In contrast, if an extinction patient's lesion were to include such superior parietal damage, then we would not expect visuomotor attention to escape unscathed. In other words, we would predict that the patient would not show the spared obstacle avoidance that V.E. shows so beautifully: instead, reaching trajectories on extinguished trials should look more like trials with only a unilateral right obstacle present, and not at all like unextinguished bilateral trials.

Our evidence for a neurological dissociation between 'visuomotor attention' and 'perceptual attention' provides direct support for a distinction between these two concepts (e.g. Milner and Goodale, 1995: p. 190). Milner and Goodale suggested specifically that these two varieties of visuospatial attention might take the form of modulations of neural activity within the dorsal and ventral visual streams, respectively. It is important to emphasize that there has never been any suggestion that these two kinds of attention would operate independently in most normal circumstances. Both functional MRI (Corbetta et al., 2000; Hopfinger et al., 2000; Kastner and Ungerleider, 2001; Yantis et al., 2002) and behavioral evidence (e.g. Schneider and Deubel, 2002) now support the idea that the two kinds of attention are normally closely coupled, and agree with Milner (1995) proposal that the dorsal stream takes the lead in co-ordinating the two. This would make good sense for most everyday situations. Our present findings indicate however that a ventrally located lesion can have a direct unbalancing effect on perceptual attention, without involving visuomotor attention at all. Interestingly, if our speculations are correct, the reverse should never occur: that is, it should not be possible to find a case of 'visuomotor extinction' in the absence of perceptual extinction.

Acknowledgments

We thank all of our test subjects for their patience and co-operation, and also several colleagues whose collaboration has been central to the work described here, especially Chris Dijkerman, Kevin McClements, Tim Cassidy and Igor Schindler. We also gratefully acknowledge the financial support of the Wellcome Trust (grant no. 052443), the Leverhulme Trust (grant no. F00128C), and the UK Medical Research Council (grant no. G0000680).

References

Behrmann, M. and Meegan, D.V. (1998) Visuomotor processing in unilateral neglect. Consc. Cognit., 7: 381–409.

Bisiach, E., Pizzamiglio, L., Nico, D. and Antonucci, G. (1996) Beyond unilateral neglect. Brain, 119: 851–857.

Chieffi, S.M., Gentilucci, M., Allport, A., Sasso, E. and Rizzolatti, G (1993) Study of selective reaching and grasping in a patient with unilateral parietal lesion. Brain, 116: 1119–1137.

Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P. and Shulman, G.L. (2000) Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nature Neurosci., 3: 292–297.

Culham, J.C. and Kanwisher, N.G. (2001) Neuroimaging of cognitive functions in human parietal cortex. Curr. Opin. Neurobiol., 11: 157–163.

Culham, J.C. (2003) Neuroimaging investigations of visually-guided grasping. In: Kanwisher, N. and Duncan, J. (Eds.), Attention and Performance XX: Functional Brain Imaging of Human Cognition. Oxford University Press, Oxford, in press.

Driver, J., Mattingley, J.B., Rorden, C. and Davis, G. (1997) Extinction as a paradigm measure of attentional bias and restricted capacity following brain injury. In: Thier, P. and Karnath, H.-O. (Eds.), Parietal Lobe Contributions to Orientation in 3D Space. Springer-Verlag, Heidelberg, pp. 401–429.

Driver, J. and Mattingley, J.B. (1998) Parietal neglect and visual awareness. Nature Neurosci., 1: 17–22.

Driver, J. and Vuilleumier, P. (2001) Perceptual awareness and its loss in unilateral neglect and extinction. Cognition, 79: 39–88.

Friedrich, F.J., Egly, R., Rafal, R.D. and Beck, D. (1998) Spatial attention deficits in humans: a comparison of superior parietal and temporal-parietal junction lesions. Neuropsychology, 12: 193–207.

Glickstein, M. and May, J.G. (1982) Visual control of movement: the circuits which link visual to motor areas of the brain with special reference to the visual input to the pons and cerebellum. In: Neff, W.D. (Ed.), Contributions to Sensory Physiology, Vol. 7. Academic Press, New York, pp. 103–145.

Goldberg, M.E., Bisley, J., Powell, K.D., Gottlieb, J. and Kusunoki, M. (2002) The role of the lateral intraparietal area of the monkey in the generation of saccades and visuospatial attention. Ann. N.Y. Acad. Sci., 956: 205–215.

Goodale, M.A., Milner, A.D., Jakobson, L.S. and Carey, D.P. (1990) Kinematic analysis of limb movements in neuropsychological research: Subtle deficits and recovery of function. Canad. J. Psychol., 44: 180–195.

Goodale, M.A., Milner, A.D., Jakobson, L.S. and Carey, D.P. (1991) A neurological dissociation between perceiving objects and grasping them. Nature, 349: 154–156.

Harvey, M., Milner, A.D. and Roberts, R.C. (1994) Spatial bias in visually-guided reaching and bisection following right cerebral stroke. Cortex, 30: 343–350.

Harvey, M., Jackson, S.R., Newport, R., Krämer, T., Morris, D.L. and Dow, L. (2002) Is grasping impaired in hemispatial neglect? Behav. Neurol., 13: 17–28.

Heilman, K.M., Watson, R.T. and Valenstein, E. (2002) Spatial neglect. In: Karnath, H.-O., Milner, A.D. and Vallar, G. (Eds.), Cognitive and Neural Bases of Spatial Neglect. Oxford University Press, Oxford, pp. 3–30.

Hopfinger, J.B., Buonocore, M.H. and Mangun, G.R. (2000) The neural mechanisms of top-down attentional control. Nature Neurosci., 3: 284–291.

Hornak, J. (1992) Ocular exploration in the dark by patients with visual neglect. Neuropsychologia, 30: 547–552.

Jackson, S.R., Newport, R., Husain, M., Harvey, M. and Hindle, J.V. (2000) Reaching movements may reveal the distorted topography of spatial representations after neglect. Neuropsychologia, 38: 500–507.

James, T.W., Culham, J., Humphrey, G.K., Milner, A.D., and Goodale, M.A. (submitted manuscript) Ventral occipital lesions impair object recognition but not object-directed grasping: an fMRI study.

Karnath, H.-O., Niemeier, M. and Dichgans, J. (1998) Space exploration in neglect. Brain, 121: 2357–2367.

Karnath, H.-O., Dick, H. and Konczak, J. (1997) Kinematics of goal-directed arm movements in neglect: control of hand in space. Neuropsychologia, 35: 435–444.

Karnath, H.-O., Ferber, S. and Himmelbach, M. (2001) Spatial awareness is a function of the temporal not the posterior parietal lobe. Nature, 411: 950–953.

Kastner, S. and Ungerleider, L.G. (2001) The neural basis of biased competition in human visual cortex. Neuropsychologia, 39: 1263–1276.

Mattingley, J.B. and Driver, J. (1997) Distinguishing sensory and motor deficits after parietal damage: an evaluation of response selection biases in unilateral neglect. In: Thier, P. and Karnath, H.-O. (Eds.), Parietal Lobe Contributions to Orientation in 3D Space. Springer-Verlag, Heidelberg, pp. 309–337.

McIntosh, R.D., Dijkerman, H.C., Mon-Williams, M. and Milner, A.D. (2000) Visuomotor processing of spatial layout in visual form agnosia. Presented at Experimental Psychology Society, Cambridge.

McIntosh, R.D., Pritchard, C.L., Dijkerman, H.C., Milner, A.D. and Roberts, R.C. (2002) Prehension and perception of size in left visuospatial neglect. Behav. Neurol., 13: 3–15.

McIntosh, R.D., McClements, K.I., Dijkerman, H.C. and Milner, A.D. (in press) 'Mind the gap': the size-distance dissociation in visual neglect is a cueing effect. Cortex.

McIntosh, R.D., McClements, K.I., Dijkerman, H.C. and Milner, A.D. (submitted, a) Perception and action in bisecting a space: a dissociation in neglect patients.

McIntosh, R.D., McClements, K.I. and Milner, A.D. (in preparation) Weights and measures: a new look at line bisection behaviour in neglect.

McIntosh, R.D., McClements, K.I., Schindler, I., Cassidy, T.P., Birchall, D. and Milner, A.D. (submitted, b) Avoidance of unseen obstacles in visual extinction.

Merikle, P.M., Smilek, D. and Eastwood, J.D. (2001) Perception without awareness: perspectives from cognitive psychology. Cognition, 79: 115–134.

Milner, A.D. (1987) Animal models for the syndrome of spatial neglect. In: Jeannerod, M. (Ed.), Neurophysiological and Neuropsychological Aspects of Spatial Neglect. Elsevier, Amsterdam, pp. 259–288.

Milner, A.D. (1995) Cerebral correlates of visual awareness. Neuropsychologia, 33: 1117–1130.

Milner, A.D. (1997) Neglect, extinction, and the cortical streams of visual processing. In: Thier, P. and Karnath, H.-O. (Eds.), Parietal lobe contributions to orientation in 3D space. Springer-Verlag, Heidelberg, pp. 3–22.

Milner, A.D. and Goodale, M.A. (1995) The Visual Brain in Action. Oxford University Press, Oxford.

Milner, A.D. and McIntosh, R.D. (2002) Perceptual and visuomotor processing in spatial neglect. In: Karnath, H.-O., Milner, A.D. and Vallar, G. (Eds.), Cognitive and Neural bases of Spatial Neglect. Oxford University Press, Oxford, pp. 153–166.

Milner, A.D., Perrett, D.I., Johnston, R.S., Benson, P.J., Jordan, T.R., Heeley, D.W., Bettucci, D., Mortara, F., Mutani, R., Terazzi, E., Davidson, D.L.W. (1991) Perception and action in 'visual form agnosia'. Brain, 114: 405–428.

Perenin, M.-T. (1997) Optic ataxia and unilateral neglect: clinical evidence for dissociable spatial functions in posterior parietal cortex. In: Thier, P. and Karnath, H.-O. (Eds.), Parietal Lobe Contributions to Orientation in 3D Space. Springer-Verlag, Heidelberg, pp. 289–308.

Posner, M.I., Walker, J.A., Friedrich, F.J. and Rafal, R.D. (1984) Effects of parietal lobe injury on covert orienting of attention. J. Neurosci., 4: 1863–1874.

Pritchard, C.L., Milner, A.D., Dijkerman, H.C. and MacWalter, R.S. (1997) Visuospatial neglect: veridical coding of size for grasping but not for perception. Neurocase, 3: 437–443.

Rizzolatti, G., Riggio, L. and Sheliga, B.M. (1994) Space and selective attention. In: Umiltà, C. and Moscovitch, M. (Eds.), Attention and Performance XV: Conscious and Nonconscious Information Processing. MIT Press, Cambridge, MA, pp. 231–265.

Robertson, I.H., Nico, D. and Hood, B. (1995) The intention to act improves unilateral left neglect: two demonstrations. NeuroReport, 7: 246–248.

Robertson, I.H., Nico, D. and Hood, B.M. (1997) Believing what you feel: using proprioceptive feedback to reduce unilateral neglect. Neuropsychology, 11: 53–58.

Schneider, W.X. and Deubel, H. (2002) Selection-for-perception and selection-for-spatial-motor-action are coupled by visual attention: a review of recent findings and new evidence from stimulus-driven saccade control. In: Prinz, W. and Hommel, B. (Eds.), Attention and Performance XIX: Common Mechanisms in Perception and Action. Oxford University Press, Oxford, pp. 609–627.

Tresilian, J.R. (1998) Attention in action or obstruction of movement? A kinematic analysis of avoidance behaviour in prehension. Exp. Brain Res., 120: 352–368.

Ungerleider, L.G. and Mishkin, M. (1982) Two cortical visual systems. In: Ingle, D.J., Goodale, M.A. and Mansfield, R.J.W. (Eds.), Analysis of Visual Behavior. MIT Press, Cambridge, MA, pp. 549–586.

Vallar, G. (1993) The anatomical basis of spatial hemineglect in humans. In: Robertson, I.H. and Marshall, J.C. (Eds.), Unilateral Neglect: Clinical and Experimental Studies. Erlbaum, Hove, UK, pp. 27–59.

Vallar, G., Rusconi, M.L., Bignamini, L., Geminiani, G. and Perani, D. (1994) Anatomical correlates of visual and tactile extinction in humans: a clinical CT scan study. J. Neurol. Neurosurg. Psychiat., 57: 464–470.

Yantis, S., Schwarzbach, J., Serences, J.T., Carlson, R.L., Steinmetz, M.A., Pekar, J.J. and Courtney, S.M. (2002) Transient neural activity in human parietal cortex during spatial attention shifts. Nature Neurosci., 5: 995–1002.