Perception, action and the cortical visual streams

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PERCEPTION, ACTION AND THE CORTICAL VISUAL STREAMS

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Schenk, T., Ellison, A., Rice, N.J., Milner, A.D. (2005). The role of V5/MT+ in the control of catching movements: an rTMS study. *Neuropsychologia, 43,* 189-198.

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In loving memory of

Christopher Bain Dickinson

DECLARATION

The author declares that the material presented within this thesis has not been previously submitted for a degree in this or any other university.

The work presented within this thesis is the author's own work. The experiments have been carried out in collaboration with researchers at the University of Durham, University of Birmingham, Lyon INSERM and University of Western Ontario. The contributions of other researchers have been restricted to patient recruitment and scientific and technical advice.

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PERCEPTION, ACTION AND THE CORTICAL VISUAL STREAMS

Nichola J. Rice

Over a decade ago Milner and Goodale suggested that perception and action are subserved by two distinct cortical visual streams. The ventral stream projecting from striate cortex to inferotemporal cortex is involved in the perceptual identification of objects. The dorsal stream projecting from striate cortex to posterior parietal cortex is involved in visually guided actions. A series of experiments have been carried out and are presented within this thesis to investigate how various aspects of visuomotor behaviour fit into such a model. A range of techniques were employed, including: (1) behavioural studies with patients with optic ataxia (dorsal stream damage) and visual form agnosia (ventral stream damage); (2) transcranial magnetic stimulation (TMS) in healthy subjects; (3) functional magnetic resonance imaging (fMRI) in healthy subjects. The following conclusions were made: (1) obstacle avoidance behaviour is impaired in patients with optic ataxia due to damage to the dorsal stream; (2) obstacle avoidance is intact in patients with visual form agnosia as damage is restricted to the ventral stream; (3) obstacle avoidance is mediated by the dorsal stream when an immediate response is required, whereas under delayed conditions the ventral stream comes into play; (4) visual form agnosic patients can use looming information to catch moving objects and they are capable of responding to online perturbations due to an intact dorsal stream; (5) V5 / MT+ is involved in motion processing for perception and action and does not belong exclusively to the dorsal or ventral stream; (6) the dorsal stream is only sensitive to orientation changes if the stimuli are graspable. While some modifications of the original distinction are necessary, the experiments presented within this thesis suggest that this model has, for the most part, withstood the test of time and provides a useful framework for understanding various aspects of perception and action.

CHAPTER ONE: GENERAL INTRODUCTION

1.1 The Dorsal and Ventral Steams: Theory

Flechsig (1896) noted that projecting from the occipital cortex are two fibre bundles projecting rostrally in the brain, the superior longitudinal fasciculus and the inferior longitudinal fasciculus. Since the anatomical identification of these areas, various theories have been presented which have attempted to explain their function. Below is an overview of two such theories, which have had a great impact on cognitive neuroscience and in the understanding of perception and action. It is these theories that have inspired the work of this thesis, and as such they will be the focus of this general introduction. An overview of additional theories and modifications of these theories will be presented in the general discussion.

1.1.1 What and Where pathways:

Ungerleider and Mishkin (1982) proposed that these fibre bundles form two separate cortical streams of visual processing, the superior a dorsal pathway, traversing the posterior parietal area towards the frontal lobe while the latter forms a ventral pathway to the temporal lobe. They hypothesised "the ventral or occipitotemporal pathway is specialised for object perception (identifying what an object is) whereas the dorsal or occipitoparietal pathway is specialised for spatial perception (locating where an object is)". They based this hypothesis on data from the rhesus monkey, tested on object and pattern discrimination tasks and a landmark task. The discrimination task involved presenting the monkeys with two objects and requiring them to retrieve the rewarded object. The landmark task involved requiring monkeys to choose the food well located closest to a cylinder. Thus, the first task involves the knowledge of *what* an object is while the second involves information regarding *where* an object is. Results showed that normal monkeys and those with an ablated posterior parietal cortex were able to perform the object discrimination task, yet monkeys with an ablated inferior temporal cortex were unable to do so (Gross, 1973). On the landmark task, on the other hand, normal monkeys and those with an ablated temporal lobe were able to perform the task successfully, however monkeys with an ablated parietal lobe failed (Pohl, 1973). These experiments were taken to support the hypothesis that the ventral pathway is responsible for identifying what an object is while the dorsal pathway is responsible for identifying where an object is. While Ungerleider and Mishkin (1982) acknowledge the common finding that lesions to the posterior parietal cortex of the monkey lead to deficits in reaching, they attribute such deficits to a broader spatial disorder. They suggested that the ventral stream projects from V1 through to V2, V3, V4 and TEO (posterior portion of the inferior temporal area) to inferior temporal cortex; this stream processes information regarding size, shape, orientation and colour. The dorsal stream projects from V1 through V2, V3, middle temporal area (MT), medial superior temporal area (MST) to the posterior parietal cortex; this stream processes the location of a stimulus. The anatomical separation of these two cortical streams is depicted in figure 1.1.

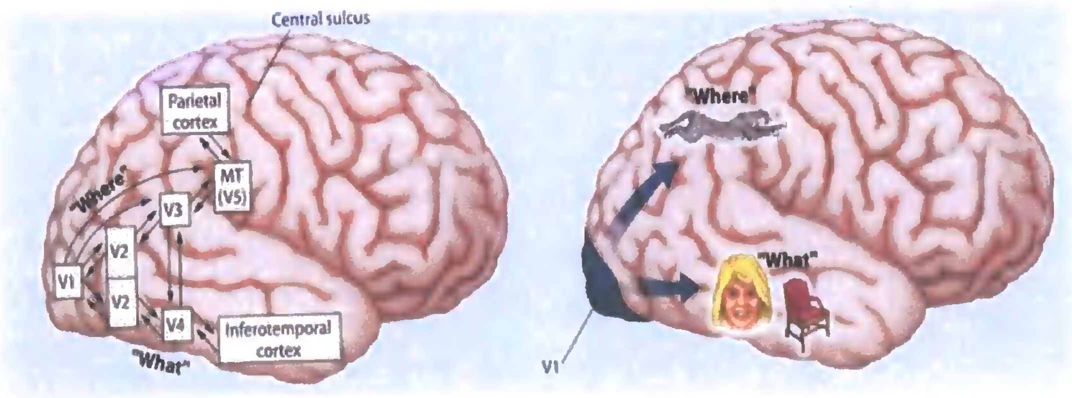

Figure 1.1: From Mishkin and Ungerleider (1982). Figure depicts the anatomical separation of the ventral 'what' pathway, and the dorsal 'where' pathway.

1.1.2 What and How pathways:

Goodale and Milner (1992, 1995, 2004) proposed that this what / where distinction could more appropriately be identified as what / how. This proposal focused on the *output* processing associated with the two cortical streams (i.e. transformations the streams perform upon information), whereas the previous proposal was concerned with input processing (i.e. the processing of incoming visual information). They hypothesised "the ventral stream of projections from the striate cortex to the inferotemporal cortex plays a major role in the perceptual identification of objects, while the dorsal stream projecting from the striate cortex to the posterior parietal region mediates the required sensorimotor transformations for visually guided actions directed at such objects". They argued that the data on monkey landmark performance could be accounted for by the fact that parietal-lesioned monkeys fail to orient towards the landmark and therefore fail to learn its significance.

It was suggested that the proposed distinction arises because perception needs object-centred representations, while action needs viewer-centred visual coding. Milner and Goodale (1995) suggest that the two separate streams of processing evolved to deal with different processing of incoming information required for perception and action. They stated "both cortical streams process information about the intrinsic properties of objects and their spatial locations, but the transformations they carry out reflect the different purposes for which the two streams evolved. The transformations carried out in the ventral stream permit the formation of perceptual and cognitive representations which embody the enduring characteristics of objects and their significance, those carried out in the dorsal stream, which need to capture instead the instantaneous and egocentric features of objects, mediate the control of goal-directed actions". An allocentric (scene-based) frame of reference makes sense for perception as it allows the brain to use different sources of information to identify objects and their relationships, and piece together the meaning of the scene in relative metrics. An egocentric (viewer-based) frame of reference, on the other hand, makes sense for action as the brain needs to compute attributes of the object (e.g. size and distance) in relation to the hand, and as such does so in absolute metrics (Goodale and Milner, 2004).

Milner and Goodale (1995) suggest that the two streams can be differentiated on the basis of time, as well as reference frame. The major goal of the ventral stream is to represent an object over time, visually and / or spatially (i.e. the perceptual system is likely to have a long memory) requiring the enduring characteristics of an object to be maintained across different viewing conditions. If the goal is to act on the object immediately the dorsal stream will be recruited, due to the fact that the co-ordinates are likely to change and as such must be recomputed on each occasion that the action occurs (i.e. the visuomotor system is likely to have a very short memory). In other words, the dorsal stream works in real time and stores the required visuomotor co-ordinates for a brief period, the ventral stream on the other hand is designed to work over a much longer time scale; this difference in time scale is a reflection on the different jobs the two streams are designed to do (Goodale and Milner, 2004). Figure 1.2 illustrates the major projections to the dorsal and ventral stream.

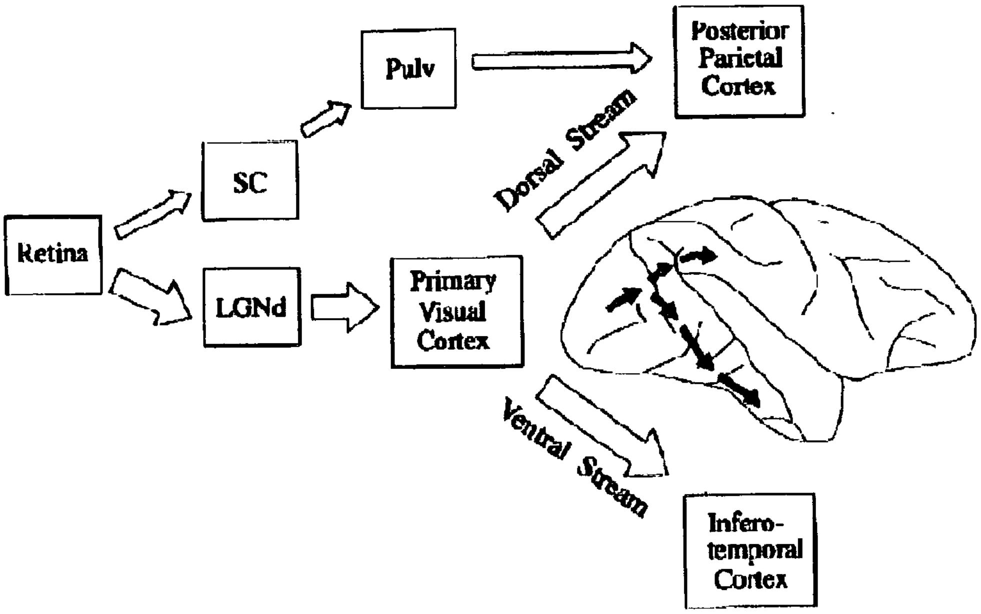

Figure 1.2: From Milner and Goodale (1995). Figure depicts the major visual inputs into the dorsal and ventral stream in the macaque brain and the route of projections from the primary visual cortex to the posterior parietal cortex and inferotemporal cortex.

1.2 The Dorsal and Ventral Streams: Anatomy

The anatomical division of the dorsal and ventral streams has been well established. A range of techniques have been used to identify the major inputs to the dorsal and ventral stream as well as the functional areas which define them; these reveal the modular nature of visual processing within the primate brain. These techniques include single unit recording studies of the monkey brain, lesion studies of the monkey and human brain, reversible disruptive techniques and neuroimaging of the human brain. Below is brief description of the areas in the occipital lobe, which have been shown to provide input into the dorsal and ventral stream. A description is also provided of the major functional brain areas within the parietal and temporal lobe, which define these two streams of processing. It is important to note that the areas discussed are those relevant to this thesis; this is not intended to be a comprehensive overview of human brain areas.

The discussion is restricted to the geniculostriate pathway, which projects from the retina, to the lateral geniculate nucleus to primary visual cortex. The lateral geniculate nucleus has six layers; layers one and two are known as magnocellular layers, layers three to six are known as parvocellular layers. There are many differences between the properties of cells in the magnocellular and parvocellular pathways. For example, magnocellular cells detect low contrast stimuli and are sensitive to motion, whereas parvocellular cells are sensitive to colour and contrast discrimination (Levine, 2000). When the lateral geniculate nucleus projects to the primary visual cortex these layers remain segregated. This segregation continues somewhat into higher cortical areas, with the dorsal stream being magnocellular dominated (Maunsell *et al.*, 1990) and the ventral stream receiving strong inputs from both the magnocellular and parvocellular subdivisions of the lateral geniculate nucleus (Ferrera *et al.*, 1994); this is reflected in the different kinds of processing carried out within each of these processing streams, which will be considered in more detail below.

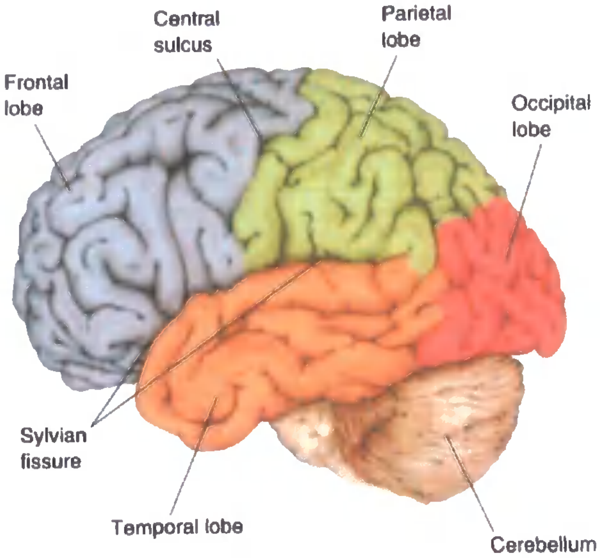

Figure 1.3: Location of the occipital lobe (red), parietal lobe (green), temporal lobe (orange) and frontal lobe (blue) in the human brain

1.2.1 Occipital lobe:

The occipital lobes form the posterior pole of the cerebral hemisphere, lying under the occipital bone; it is distinguished from the parietal lobe by the parieto-occipital sulcus. Figure 1.3 illustrates the position of the occipital lobe in the human brain. There are at least six regions making up the occipital cortex, known as V1, V2, V3, V3A, V4 and V5 / MT+. The organisation of the visual cortex is a hierarchical one. As one moves into higher visual areas neurons are coded for more complex features. It is important to note that this hierarchical organisation is a distributed one, with multiple parallel pathways connected at each level (Kolb and Whishaw, 1999). A brief description of the main areas comprising the occipital lobe will now be provided. It should be noted however that this is a highly simplified version, which is provided mainly to demonstrate the hierarchical organisation of the visual system and to provide an overview of the major inputs into the dorsal and ventral stream. An illustration of the anatomical location of the visual areas within the occipital lobe is provided in figure 1.4.

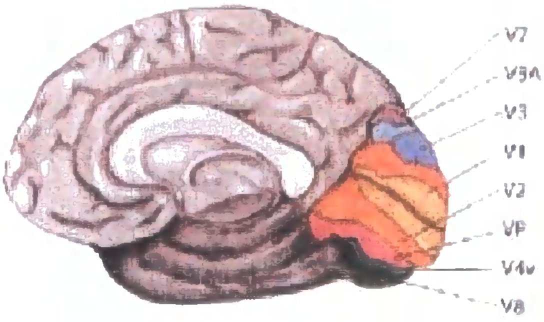

Figure 1.4: From Logothetis (1999). Figure illustrating the anatomical areas within the occipital lobe.

The surface of the visual cortex is organised to create a topographic map of the visual world (a retinotopic map), this map is repeated several times so different visual areas of the visual cortex all have separate maps of the visual world mapped onto it (Levine, 2000). For example, adjacent points on the retina project to adjacent points in V1, and so do projections from V1 to V2 (Zeki, 1969). V1, also known as primary visual cortex, receives its input from the lateral geniculate nucleus and as such it is the first level of the hierarchy. V1 is made up of six layers and several sublayers. Cytochrome oxidase staining has revealed cytochrome-rich areas known as blobs, separated by interblob regions (see figure 1.5). These blobs are commonly associated with colour perception, and the interblobs in form / orientation and motion (Kolb and Whishaw, 1999). Hubel and Wiesel (1958, 1963) used single unit recording of the cat and monkey to show that neurons in V1 code the orientation and position of particular edges in the visual scene, different neurons being tuned to different orientations and being clustered in columns according to their properties. V2 is also heterogeneous, cytochrome oxidase staining reveals (instead of blobs) thin stripes (involved in colour perception), thick stripes (involved in form / orientation perception) and pale stripes (involved in motion perception) (Kolb and Whishaw, 1999). V1 and V2 project to all other occipital regions.

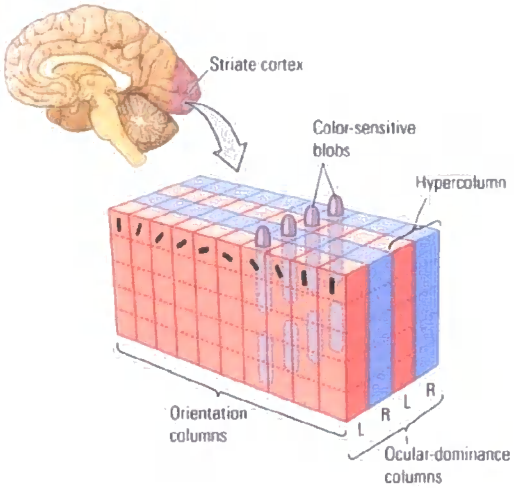

Figure 1.5: From Kolb and Whishaw (2005). Model of striate cortex showing the orientation columns, ocular-dominance columns, and colour sensitive blobs is composed of two hypercolumns. Each hypercolumn consists of a full set (shown in red and blue) of orientation columns spanning 180 degrees of preferred angle as well as a pair of blobs. All other areas are called inter-blobs.

As has already been pointed out, as one progresses through the hierarchy the neurons are coded for more complex features. V3 receives its input from layer 4B of V1 as well as the thick stripes of V2 (Levine, 2000). Cells in V3 have been shown to be selective for stimulus motion direction (Galletti *et al.*, 1990) and edge orientation (Zeki, 1978). V4 receives its input from the thin and pale stripes of V2, as well as V3 (Levine, 2000). V4 is commonly associated with colour perception; due to a large number of colour-selective cells, intermingled with clusters of orientation-selective cells (Zeki, 1983). Desimone *et al.* (1985) demonstrated that V4 was also involved in pattern discrimination. Sacks and Wasserman (1987) have provided evidence to show that damage to V4 results in cortical colour blindness, also known as achromatopsia.

Area V5 was first identified by Zeki (1991) and is believed to be the human homologue of monkey area MT+. V5 mainly receives inputs from V3, the thick stripes of V2, and layer 4B of V1, although there is also some input from the thin stripes in V2 and from V4 (Levine, 2000). This area has been extensively examined and has been shown to make a contribution to a number of aspects of motion perception. It has been found that the preferred speed range of cells in V5 / MT+ (Lagae *et al.* 1993; Maunsell and Van Essen 1983; Mikami *et al.* 1986; Rodman and Albright, 1987) correlates closely with psychophysical performance in speed discrimination tasks (McKee, 1981, Orban *et al.*, 1984, 1985), suggesting that V5 / MT+ is the essential mechanism underlying performance on speed discrimination tasks. This suggestion is confirmed by studies showing degradation in speed discrimination following damage to V5 / MT+, commonly known as akinetopsia or motion blindness (Hess *et al.* 1989; Orban *et al.* 1995; Plant and Nakayama, 1993; Zihl *et al.* 1983, 1991). This will be discussed in more detail in chapter 6. It has also been found that activity in V5 / MT+ is closely related to performance in the perception of global motion stimuli. Saltzman *et al.* (1990) found that stimulation of direction specific cells in monkey V5 / MT+ induced a bias in the perceived direction of global motion stimuli. Several studies have also shown that damage to monkey or human V5 / MT+ impairs performance in tasks involving the identification of direction of global motion stimuli (Baker *et al.*, 1991; Newsome and Pare, 1988; Plant *et al.*, 1993; Plant and Nakayama, 1993; Schenk and Zihl, 1997; Vaina *et al.*, 2001).

1.2.2 Parietal lobe:

The parietal lobe is demarcated by the central fissure (anteriorly), the sylvian fissue (ventrally), the cingulate gyrus (dorsally) and the parieto-occipital sulcus (posteriorly). Figure 1.3 illustrates the position of the parietal lobe in the human brain. The principal regions include the postcentral gyrus (Brodmann's areas 1, 2 and 3), the superior parietal lobule (BA 5 and 7), the parietal operculum (BA 43), the supramarginal gyrus (BA 40), and the angular gyrus (BA 39). The parietal lobe can be divided into two functional zones: (1) the somatosensory cortex (the anterior zone); (2) the posterior parietal cortex (the posterior zone). It is the posterior parietal cortex which will be the focus of this thesis. Figure 1.6 illustrates the location of the some of the functional areas within the posterior parietal cortex in the human brain. A brief description of these areas will be presented below; the areas discussed are those of particular importance within the context of this thesis.

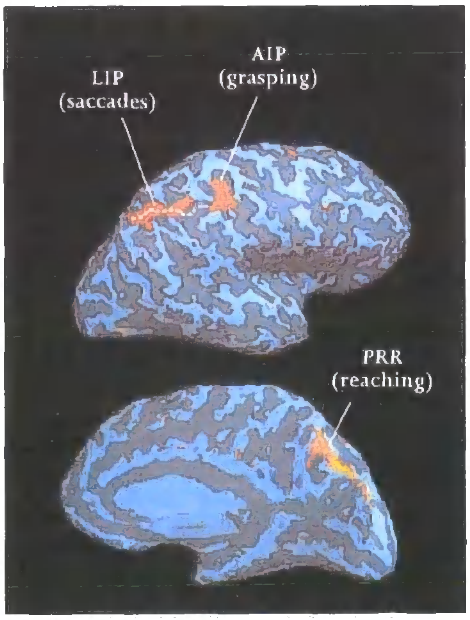

Figure 1.6: From Goodale and Milner (2004). Figure illustrates some of the functional areas within the dorsal stream, which show selective activation for visually-guided saccades (LIP), grasping (AIP), and reaching (PRR). Diagram illustrates an inflated view of the human brain, with the gyri coloured in light blue and the sulci in grey.

Monkey neurophysiology has shown the lateral intraparietal area (LIP) to have visual, attentional, memory and saccade related activation (Colby *et al.*, 1996). Colby (1998) suggested that neurons in LIP of the macaque are activated when a monkey plans to make a saccade to a location in the receptive field and also when the monkey attends to that location without making a saccade. Duhamel *et al.* (1992) have shown that the receptive fields of LIP neurons in the monkey brain change in anticipation of an upcoming eye movement. Muri *et al.* (1996) identified a region in the human brain which becomes active during saccadic eye movements (parietal eye fields), an area which responds strongly even during predictive saccades. This area is also shown to become active during smooth pursuit eye movements (Petit and Haxby, 1999). This may be the human homologue of LIP and is located midway along the anterior-posterior axis of the intraparietal sulcus; activation may be slightly medial to the intraparietal sulcus in the superior parietal lobule (Sereno *et al.*, 2001; Medendorp *et al.*, 2003).

Mountcastle *et al.* (1975) found neurons in the parietal cortex which were active when the monkey manipulated an object but not when the hand or arm was passively stimulated. Taira *et al.* (1990) found a region in the anterior portion of the intraparietal (AIP) cortex where such neurons related to grasping were concentrated in the monkey. This area has been shown to contain neurons which respond to visual and motor components of a grasp and that are tuned to specific shapes to be grasped (Sakata and Taira, 1994). Functional inactivation studies confirmed these findings, showing that inactivation of AIP disrupts the monkey's ability to use vision for pre-shaping the hand (Gallese *et al.*, 1994). Several studies have identified a region of human parietal cortex involved in grasping (Faillenot *et al.*, 1997; Binkofski *et al.*, 1998). For example, Binkofski *et al.* (1998) showed that patients with lesions to AIP were more impaired at grasping than reaching. This region has also been shown to be active during the tactile manipulation of objects (Binkofski *et al.*, 1999), the observation of others' hand movements (Iacoboni *et al.*, 1999) and by passive viewing of tools (Chao and Martin, 2000). The human homologue of monkey AIP has thus now been well established and is located at the junction between the anterior portion of the intraparietal sulcus and the inferior postcentral sulcus (Faillenot *et al.*, 1997; Binkofski *et al.*, 1998; Culham *et al.*, 2003; Frey *et al.*, 2005). Culham *et al.* (in press) suggest that human AIP shares many of the characteristics of monkey AIP, since it is activated by: (1) visually-guided grasping and pantomimed grasping; (2) the act of hand manipulation when vision is unavailable; (3) the visual presentation of objects without an action. The authors further suggest that AIP is not activated by perceptual tasks, for example AIP does not show activation for 2-dimensional images of objects (Culham *et al.*, 2003). However when the images are associated with hand actions, for example tools, a region in the anterior intraparietal cortex, overlapping with AIP, shows activity (Chao and Martin, 2000).

Several monkey neurophysiology studies have identified regions that are selective for reaching movements (which includes both V6A, MIP, areas 7a and 7m, and area 5) (Johnson *et al.*, 1996; Galletti *et al.*, 1997; Snyder *et al.*, 1997; Battaglia-Mayer *et al.*, 2001). A parietal reach region (PRR) has been observed to contain neurons that fire when monkeys reach to targets in the periphery, in an area overlapping MIP, area 5 and V6a (Andersen and Buneo, 2002, Buneo *et al.*, 2002). Kertzman *et al.* (1997) reported activation in the intraparietal cortex during reaching movements in humans, although it was not clear if this area is distinct from other parietal areas such as saccade related areas (Culham and Kanwisher, 2001). Connolly *et al.* (2000) found that although saccade-related and reach-related activity overlapped, pointing related activation was more medial. More recent fMRI work has identified a region in the precuneus, anterior to the parieto-occipital sulcus, which may be the human homologue on monkey PRR, an area which is activated during the intention to reach, although activation is stronger when the reach is executed (Connolly *et al.*, 2003; Astafiev *et al.*, 2003).

1.2.3 Temporal lobe:

The temporal lobe is made up of all the tissue below the Sylvian fissure and anterior to the occipital cortex. Figure 1.3 illustrates the location of the temporal lobe in the human brain. The temporal lobe can be divided into: (1) auditory areas (BA 41, 42 and 22); (2) and those that form the ventral stream on the lateral and ventral surfaces of the temporal lobe (BA 20, 21, 37 and 38), often referred to as inferotemporal cortex which will be focused on below. There are three major gyri visible on the lateral surface of the temporal lobe: (1) superior temporal gyrus; (2) middle temporal gyrus; (3) inferior temporal gyrus. A brief overview of the major functional areas within the inferotemporal cortex will now be presented below. Once again this is not intended to be a comprehensive overview of the temporal lobes, but a description of the major functional areas within the inferotemporal cortex, which will be relevant to this thesis; these areas are illustrated in figure 1.7.

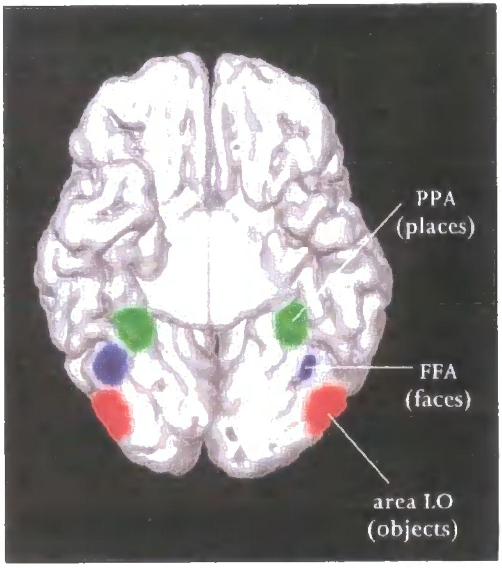

Figure 1.7: From Goodale and Milner (2004). Figure illustrating the functional areas within the ventral stream, which show selective activation for presentation of places (PPA), faces (FFA), and objects (LO). Illustration represents an reconstruction of an anatomical MRI of the human brain.

Kanwisher *et al.* (1997) found a region in the fusiform gyrus in humans that responds twice as strongly for faces as for control stimuli and named it the fusiform face area (FFA). The finding of a face selective area in the temporal lobe has been repeatedly confirmed and includes a wide selection of face stimuli, such as photographs of faces, line drawings of faces (Halgren *et al.*, 1999; Ishai *et al.*, 1999), cartoon faces, inverted faces (Kanwisher *et al.*, 1998; Aguirre *et al.*, 1999; Haxby *et al.*, 1999) when compared to categories such as houses (Haxby *et al.*, 1999; Kanwisher *et al.*, 1997), hands (Kanwisher, 1997), animals (without heads) (Kanwisher *et al.*, 1999), flowers (McCarthy *et al.*, 1997) and cars (Halgren *et al.*, 1999). Kanwisher (2003) suggests that the FFA is not involved in extracting information about gaze direction or emotional expression, and is not involved in representing semantic information about individual people; it is involved primarily in face detection.

Epstein and Kanwisher (1998) identified a region in the temporal cortex which appears to play a role in determining one's location in the environment; this has become known as the parahippocampal place area (PPA). This area responds whenever participants view images of places, including indoor and outdoor scenes, as well as abstract spatial environments (Aguirre *et al.*, 1996; Maguire *et al.*, 1998). Kanwisher (2003) suggests that the visual complexity and number of objects in the scene is unimportant, the response is just as high to an empty room as to a furnished one. Epstein *et al.* (2001) tested a patient without a PPA who had largely preserved place perception but a deficit in learning new place information, suggesting that PPA is important for encoding scenes into memory. Epstein *et al.* (1999) presented participants with images of familiar and unfamiliar places and found no difference in activation in PPA between the two conditions (yet a higher response was observed when familiar buildings were cut out from their backgrounds).

The lateral occipital complex (LOC) has been identified as having a role in object recognition (Bar *et al.*, 2001; Grill-Spector *et al.*, 2000; James *et al.*, 2000; Lerner *et al.*, 2002). Grill-Spector *et al.* (2000) showed that LOC is invariant to size and position of an object, but not viewpoint or direction of illumination. Kourtzi and Kanwisher (2001) provided evidence to suggest that neuronal populations within LOC represent the perceived shape of an object invariant to changes in size and position but not viewpoint. Amedi *et al.* (2001) found that an area within LOC responds to objects compared to textures in both visual and haptic modalities, although most of LOC responds preferentially to visually presented objects. Kanwisher (2003) suggests that LOC sometimes partly overlaps with FFA (on the ventral surface). James *et al.* (2003) provided evidence to show that the location of LOC in healthy participants corresponded to location of the lesion in visual form agnosic patient DF, therefore arguing that it is essential for normal shape perception. This will be considered in more detail in the following section.

1.3 The Dorsal and Ventral Stream: Evidence

The section above provided an overview of the functional areas which define the dorsal and ventral stream, this evidence was largely derived from monkey neurophysiology and neuroimaging work in human participants. This overview provided clear evidence for the functional distinction between the ventral and dorsal stream. The ventral stream comprising areas such as FFA, PPA and LOC have been shown to be involved in perception. The dorsal stream, comprising areas such as LIP, AIP and PRR have been shown to be heavily involved in action. Most of the evidence cited by Milner and Goodale (1995, 2004) in support of their theory has come from research on patients with neurological disorders, in particular, visual form agnosia and optic ataxia. This thesis shall, for the most part, focus on these disorders. As such a description of visual form agnosia and optic ataxia shall now be presented, including an overview of the contributions these patients have made to the understanding of the dorsal and ventral streams of processing.

1.3.1 Optic Ataxia:

Optic ataxia is associated with damage to the dorsal stream of processing. Balint (1909) (reprinted in 1995) first identified the disorder when he was presented with a patient who showed a failure to accurately point or reach towards visually presented stimuli. This patient only displayed problems when using his right hand, and therefore his misreaching could not be accounted for by a visuospatial deficit. In addition, the patient could accurately point to his own body parts, and therefore his misreaching could not be accounted for by a general motor disorder. Perenin and Vighetto (1988) and Jeannerod (1986) have shown that, when asked to reach towards a target, optic ataxic patients have difficulty reaching in the correct direction, positioning their fingers correctly and adjusting the orientation of their hand and grasp size with respect to the orientation and size of the target. Perenin and Vighetto (1988) also suggest that errors in unilateral patients are most commonly observed in the contralesional field with the contralesional hand. Rizzolatti and Matelli (2003) define optic ataxia as "a disorder of visually guided movements of the arm towards a goal. The arm gropes for the target making errors in the frontal or in the sagittal plane, until it runs almost by chance into the object. Typically this deficit is severe when the target is located in the peripheral part of the field of vision, decreases when the target is in parafoveal vision and disappears when the patient fixates the target". Karnath and Perenin (2005) suggest that the majority of ataxic reaches remain uncorrected, however occasionally visually corrected errors are observed and patients are often able to correct on the basis of tactile information.

Clinical diagnosis of optic ataxia is usually made by asking patients to point or grasp targets in the peripheral and central visual field. For example, Karnath and Perenin (2005) clinically diagnosed optic ataxic patients by asking patients to perform reaching movements under two conditions: (1) Patients were asked to fixate on a central camera and grasp a pencil positioned at various locations in the ipsilesional and contralesional visual field with the ipsilesional and contralesional hand; (2) Patients carried out the same task but were told to visually fixate on the target they were required to grasp. Optic ataxic patients typically display gross misreaching in peripheral vision yet show fairly intact reaching in central vision (typically with the contralesional hand in the contralesional space). Figure 1.8 illustrates an example of a clinical diagnosis of optic ataxia.

Figure 1.8: Figure illustrates the clinical diagnosis of optic ataxia. The photograph on the left shows that the patient makes spatial errors and calibrates his grip incorrectly when required to grasp a target in his peripheral visual field. The photograph on the right shows an improvement in performance when the patient is allowed to fixate on the target.

Recently a series of studies have provided evidence that optic ataxia includes a deficit in the online control of actions. Pisella *et al.* (2000) investigated the tendency of an optic ataxic patient to respond online to target perturbations. They asked a patient to point to a target, which remained stationary on 80% of the trials and jumped on 20% of trials. Results showed that motor corrections could only be slow and deliberate, and the authors propose that optic ataxic deficits can be accounted for by an inability to control actions online. In a later study by Grea *et al.* (2002), an optic ataxic patient was instructed to reach and grasp a target presented in different locations; however, on some trials the target position was shifted shortly after movement onset. Results showed that when a target perturbation occurred the patient was unable to adjust her ongoing movement. Two distinct movements were observed, the first towards the initial location and the second (offline) to the final target location. Taken together, the results of these two studies have led some authors to redefine optic ataxia as a deficit in the online control of actions (Glover, 2003). However, it has also been shown that optic ataxic patients direct their reaches inaccurately right from the onset of the movement (Milner *et al.*, 2003), suggesting that faulty online corrections are only part of the deficit.

Optic ataxic patients have difficulty in visuomotor control, yet they have preserved perceptual abilities, and have as such provided evidence in support of the Milner and Goodale model. Perenin and Vighetto (1988) have shown that when asked to pass their hand through a slot optic ataxic patients make both orientation and spatial errors. Yet patients typically perform above chance on perceptual judgements of spatial location and on perceptual judgements of the orientation of a line. Several studies have also shown that optic ataxic patients have deficits in grasping objects, and this can be dissociated from perceptual judgements (Tzavaras and Masure, 1976; Jeannerod, 1986; Jakobson *et al.*, 1991; Goodale *et al.*, 1994a; Milner *et al.*, 2001; Grea *et al.* 2002). For example, Goodale *et al.* (1994a) showed that when an optic ataxic patient was instructed to grasp 'Blake shapes' (irregularly shaped objects) she did not place her index finger and thumb across the centre of mass in the same way as control participants, yet she could accurately distinguish between the shapes. Optic ataxic patients, of course, also by definition have deficits in pointing to targets, particularly in the peripheral visual field (Balint, 1909; Perenin and Vighetto, 1988; Milner *et al.*, 1999; Pisella *et al.*, 2000).

While optic ataxic patients have clear deficits in visuomotor tasks, evidence has suggested that their performance improves when a delay is required before response. A detailed description of the delay literature is provided in chapter 4; however a brief summary of findings shall be presented here. Milner *et al.* (1999) showed that on a pointing task optic ataxic patients respond more promptly and accurately when a delay is required before response. In another study, Milner *et al.* (2001), optic ataxic patients showed an improvement in the calibration of their grip when grasping under delayed conditions. This has been taken as evidence for the time scale in which the ventral and dorsal stream operate. In other words, under delayed conditions the action code created by the dorsal stream decays and a more flexible visuospatial representation comes into play from the ventral stream, which is intact in optic ataxic patients.

In an early study of optic ataxia patients, following missile wound injuries, Ratcliff and Davies-Jones (1972) reported that the patients had lesions located in the superior part of the parietal area. A series of single case studies of patients with optic ataxia using CT scans revealed that the lesion site was the superior parietal lobule (Auerbach and Alexander, 1981; Ferro, 1984; Buxbaum and Coslett, 1998). Perenin and Vighetto (1988) carried out a lesion analysis of ten patients with optic ataxia and determined that the lesions were mostly localised in the medial or ventral part of the superior parietal lobule or sometimes the superior part of the inferior parietal lobule, and always included the intraparietal sulcus.

Karnath and Perenin (2005) recently re-evaluated the view that optic ataxia is ascribed to lesions of the superior parietal lobule and / or intraparietal sulcus, by assessing the lesion site of 16 patients with optic ataxia following a unilateral stroke using a lesion subtraction method. The optic ataxic patients were compared to two control groups, control group one were matched to the patients with respect to age and other impairments (e.g. paresis, visual field defects), control group two were matched to the patients with respect to lesion site (predominantly in the parietal lobe); both control groups were stroke patients without optic ataxia. A comparison of optic ataxic patients with control group one revealed that in both hemispheres the lesion site of optic ataxia patients is laterally centred on the intraparietal sulcus, and in the left hemisphere also included the posterior occipito-parietal junction. In addition, via the underlying parietal white matter the lesion overlap extended medially to the precuneus in both hemispheres, close to the occipito-parietal junction (see figure 1.9, left). A comparison was also made with optic ataxic patients compared to control group 2. Lesion overlay plots revealed that in the right hemisphere the overlap centred laterally on the intraparietal sulcus and extended medially (via underlying parietal white matter) to the precuneus on the medial aspect of the hemisphere close to the parieto-occipital junction. On the left hemisphere the overlap included the precuneus on the medial aspect of the hemisphere, and laterally the lesion included the posterior occipito-parietal junction (see figure 1.9, right).

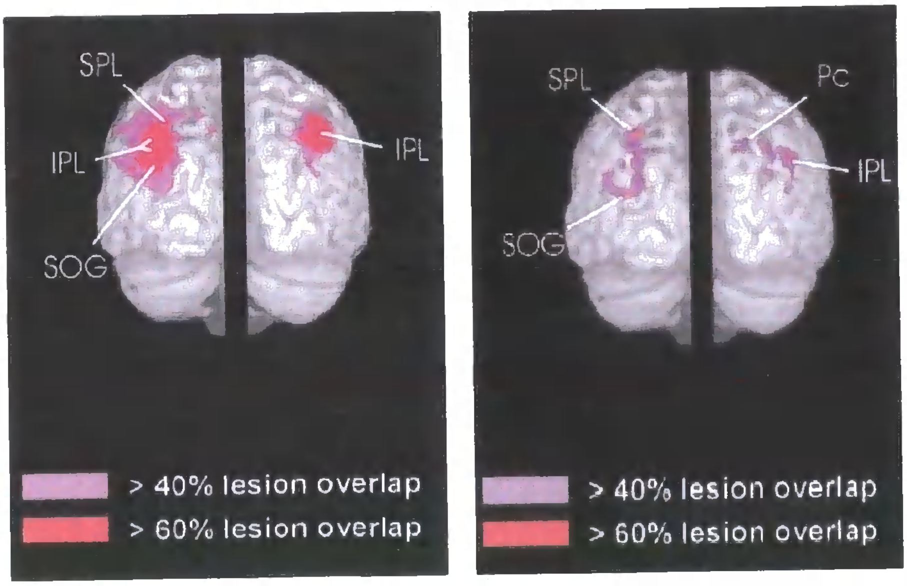

Figure 1.9: From Karnath and Perenin (2005). Figure on the left illustrates the lesion overlay plots of optic ataxic patients compared to control group one. Figure on the right illustrates the lesion overlay plots of optic ataxic patients compared to control group two.

1.3.2 Visual Form Agnosia:

Visual form agnosia is associated with damage to the ventral stream of processing. Benson and Greenberg (1969) first introduced the term 'visual form agnosia' when describing a patient whose recognition deficits they believed could be attributed to a primary defect in form discrimination. They suggested that the disorder was associated with an intact ability to deal with the simple features of an object, but a specific inability to put such features together to permit form discrimination and perception. This loss resulted in the patient having a severe inability to recognize everyday objects, particularly drawings of objects, by virtue of their shape. In a more recent review of four patients with visual form agnosia, Heider (2000) suggests that the basic deficit found in all the patients is a failure to group single elements of a composite visual scene into a Gestalt, and to segregate figure from ground in a static visual display.

Visual form agnosia can be clinically diagnosed using The Efron Shape Discrimination Task (Efron, 1969). This involves presenting patients with pairs of rectangles of differing dimensions, but with the same surface area (see figure 1.10) and asking them whether the two shapes are the same or different. Visual form agnosia patients typically perform at chance on such a task, especially with the least elongated rectangles. This test allows one to assess the degree of disability of a patient, with highly disabled patients being unable to distinguish between a square and even the most elongated rectangle.

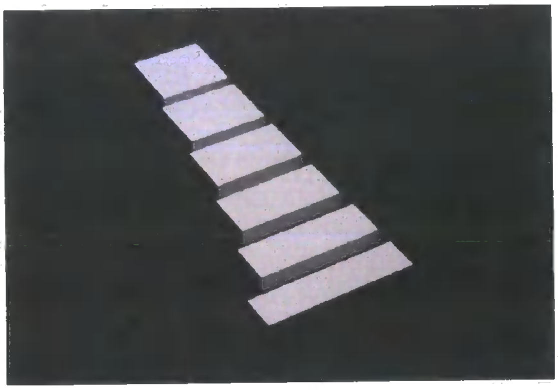

Figure 1.10: Photograph illustrates examples of shapes similar to those designed by Efron (1969). Each rectangle is of differing dimension, but they all have the same surface area. It should be noted that the actual shapes used in diagnosis are actually 2- dimensional shapes presented on sheets of paper.

The most extensively studied patient with visual form agnosia is DF, who was first described by Milner and Heywood (1989). Milner *et al.* (1991) reported that her deficits include a failure to visually recognise objects, difficulty in discriminating shape, reflectance, orientation, symmetry and texture differences. She is unable to recognize the faces of friends and relatives, nor drawings or photographs of everyday objects. She is also unable to copy drawings or letters, has impoverished reading abilities and experiences difficulty estimating the speed of objects. She performs at chance on the Efron shape discrimination task (Goodale and Milner, 2004). Despite these deficits she had largely-preserved visual acuity, colour vision, tactile recognition and intelligence. She can partially describe objects and can make reasonable guesses from this as to what they are. When asked to describe her vision she describes objects as "blurred", elements making up the object "tend to run into each other". However, DF's difficulty cannot be explained by poor visual acuity, for example she can clearly see the hairs on the back of a hand, yet is unable to make out the shape of the hand (Goodale and Milner, 2004). Figure 1.11 illustrates DF's inability to copy form, and demonstrates that this cannot be attributed to problems with visual imagery.

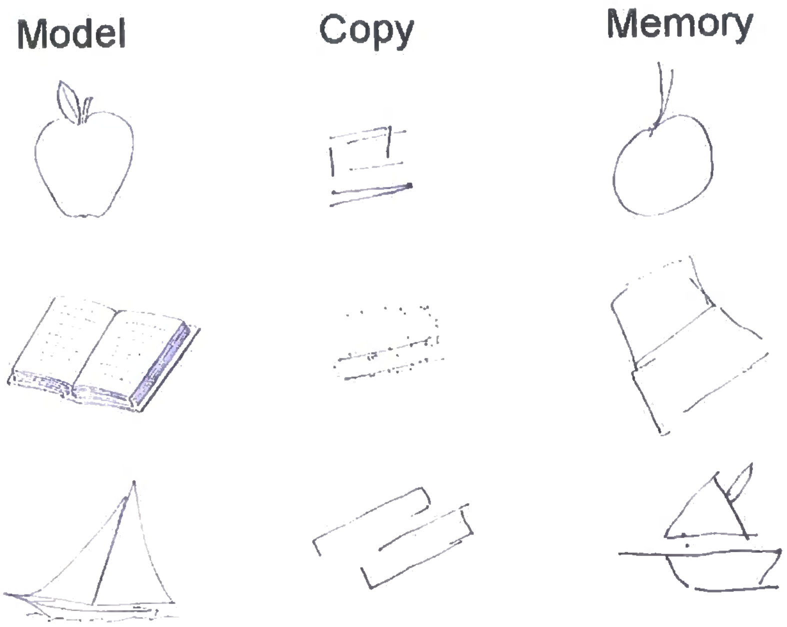

Figure 1.11: From Milner and Goodale (1995). When asked to copy simple line drawings DF is unable to do so, however she does copy some of the elements of the drawing. Yet when asked to draw such images from memory she is able to do so, illustrating that she has intact visual imagery.

Despite these clear perceptual deficits DF has been shown to have relatively preserved visuomotor control, and it is this dissociation which has provided such strong evidence in support of the Milner and Goodale model. This dissociation between perception and action became clear following the observation that she was unable to identify or discriminate the orientation of a pencil held in front of her, yet she was capable of reaching out and grasping the pencil to examine it further (Goodale and Milner, 2004). Milner *et al.* (1991) tested such reports by asking DF to perform a posting and a matching task. In the posting task DF was required to post a hand held card through an open slot positioned in various orientations. In the matching task DF was required to turn the card so it matched the orientation of the slot. Results showed that DF could accurately post the card through the slot, yet was at chance when asked to match the orientation.

Goodale *et al.* (1991) showed that DF was unable to distinguish between rectangular blocks of the same or different dimensions, or to indicate the width of the block manually, however when asked to reach out and pick up a block, the aperture between her index finger and thumb was systematically related to the width of the block, as it is for normal participants, well in advance of reaching the target. In addition, Goodale *et al.* (1994a) have shown that when required to grasp 'Blake shapes' her grasp points were indistinguishable from controls, always placing her thumb and index finger through the centre of mass. However when asked to report whether two shapes were the same or different, she was unable to do so.

Carey *et al.* (1996) presented DF with a variety of everyday objects and asked her to pick them up and mime their use. Results showed that DF did not differ from controls in terms of reaching or grasping or in the miming of the objects' use, however there were large differences in terms of the point at which the objects were grasped (particularly when they were presented in unusual views), and in the amount of tactile exploration. In a second task she was shown to be able to adjust her grip aperture and the orientation of her hand when reaching to grasp blocks of different dimensions presented in different orientations. In a third task she was shown to be insensitive to the orientation of a cross shaped object when required to grasp it in different orientations. Similar difficulties were observed in DF by Goodale *et al.* (1994b), when DF was asked to post a T shaped object through a T shaped hole, she was successful only on about half the trials. Milner and Goodale (1995) suggest that such findings may be accounted for by the fact that DF cannot combine two components of visual 'shape' to guide her actions.

Despite her relatively intact visuomotor skills, DF has been shown to experience difficulty in some visuomotor tasks. In particular when a delay is required before response (Goodale *et al.*, 1994c; Milner *et al.*, 1999), and also when vision is restricted to monocular conditions (Marotta *et al.*, 1997; Dijkerman *et al.*, 1999). These two aspects of DF's impaired visuomotor control will be described in more detail in chapters 3 and 4, respectively. In summary, under delayed conditions DF has been shown to have difficulty in the calibration of her grasp (Goodale *et al.*, 1994c), and also disruption in saccadic eye movements and pointing (Milner *et al.*, 1999). This provides evidence of the time scale in which the two streams operate, suggesting that under delayed conditions the ventral stream is responsible for visuomotor control. In addition, DF shows visuomotor deficits when viewing is restricted to monocular conditions, including a disruption in the calibration of her grasp (Marotta *et al.*, 1997) and also in adjusting the orientation of her hand to the orientation of the target (Dijkerman *et al.*, 1999). This provides evidence to suggest that the ventral stream is responsible for the processing of monocular information, and that DF's successful visuomotor control is highly dependent of the processing of binocular information in the dorsal stream.

Milner *et al.* (1991) suggested that EEG showed bilateral abnormalities, most prominent posteriorly and in temporal regions. Later MRI studies showed abnormalities in the occipital poles bilaterally, with the damage extending laterally in the ventral part of the occipital lobe and dorsally in the posterior parasagittal occipito-parietal region, her primary visual cortex unimpaired. Recently James *et al.* (2003) have shown, with a high resolution anatomical MRI, that DF's lesion is mainly concentrated bilaterally in the ventral lateral occipital cortex (larger in the right hemisphere). Primary visual cortex and fusiform gyrus were spared. In addition, they found a previously undetected region of damage in the left posterior parietal cortex. James *et al.* (2003) went on to demonstrate that DF's ventral stream lesions are almost perfectly coincident with the lateral occipital area in healthy individuals (see above for further information regarding area LO). When functional MRI was used to examine her brain activation in response to complete versus fragmented line drawings of objects, the subtraction of which defines area LO in healthy subjects, no net activation was found (see figure 1.12). It was deduced from these results that it was DF's bilateral damage to area LO that was the direct cause of her visual form agnosia, and by extension that similar damage is the cause of this impairment in other patients.

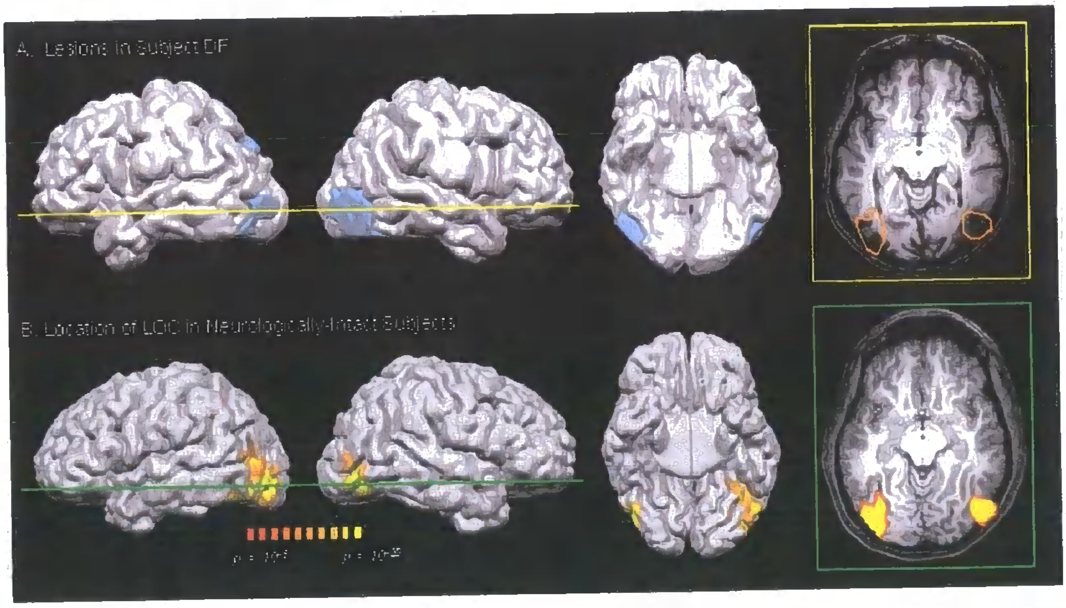

Figure 1.12: From James *et al.* (2003). Figure illustrating that the lesion location in DF overlaps with area LO in the healthy brain.

1.4 Other methods used in cognitive neuroscience

While working with neuropsychological patients has provided important insights into cognitive neuroscience and in the understanding of perception and action, technological advancements provide alternative ways of addressing empirical questions. Below is an overview of two such methods which will be employed in this thesis: Transcranial Magnetic Stimulation (TMS) and Functional Magnetic Resonance Imaging (fMRI). These two methods are complementary in terms of what they do; TMS causing transient disruptions in localised areas of the brain, whereas fMRI is used to map functional areas of the brain by recording neural activity. They both have different advantages and disadvantages in terms of temporal and spatial resolution (see figure 1.13) and they both raise different but important concerns regarding safety. All these issues shall be addressed in a brief overview of these two techniques, which is presented in the following section.

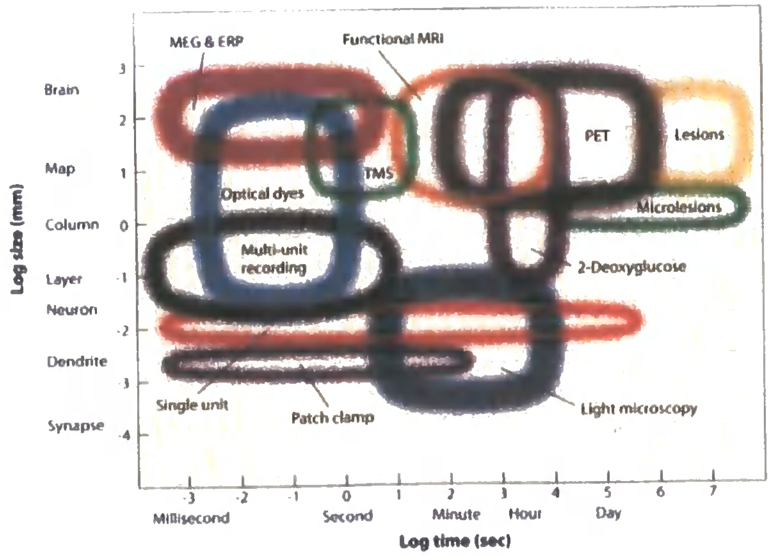

Figure 1.13: From Walsh and Pascual-Leone (2003). Figure illustrates the temporal and spatial resolution of various techniques which can be employed in cognitive neuroscience. As can be seen, TMS and fMRI are comparable in spatial resolution but TMS has a superior temporal resolution.

1.4.1 Transcranial Magnetic Stimulation (TMS):

TMS is based on Faraday's (1832) principle of electromagnetic induction (i.e. electric current passed through one coil produces a magnetic field that in turn induces a current in a nearby coil) (Walsh and Pascual-Leone, 2003). With TMS the second coil is replaced by brain tissue and the induced electric field elicits neuronal activity (Walsh and Cowey, 2000). Walsh and Pascual-Leone (2003) state: "a brief, intense magnetic field is applied to the scalp. This field induces electrical activity in the cortex, effectively disorganising neural processing in that region of the cortex and thus disrupting normal functioning for a few milliseconds". TMS has become a popular method of research in cognitive neuroscience, by creating 'virtual lesions' (Pascual-Leone *et al.*, 1999) in a safe and reversible way in selected brain regions. As such it is used as an investigative tool for clinical conditions such as multiple sclerosis and motor neuron disease (Barker *et al.*, 1986), for clinical purposes to alleviate symptoms of disorders such as depression (George *et al.*, 1996) and to map functions of the motor and sensory cortices (Becker and Zeki, 1995; Hotson *et al.*, 1994).

There are several types of coils available, including a figure-of-eight coil, a circular coil and a cone coil. The most popular of type of coil to use in cognitive neuroscience is a figure-of-eight coil, as this coil increases the focality of stimulation (Ueno *et al.*, 1988). The figure-of-eight coil is designed in such a way that two circular coils carry current in opposite directions, and where the coils meet there is a summation of the electric field (Walsh and Pascual-Leone, 2003). As such the centre of the figure-of-eight coil is placed over the region of interest. Brasil-Neto *et al.* (1992) suggest that the spatial resolution of TMS is about 5 mm. The temporal resolution depends on the type of TMS, which can be applied in single pulses or repetitive pulses (rTMS). A single pulse is delivered in 1 ms (Walsh and Pascual-Leone, 2003), repetitive pulses are delivered in trains ranging from 1-25 Hz (i.e. 1-25 times per second), with functional effects ranging from 30-50 ms.

The identification of the area one wishes to stimulate can be based on functional localisation. For example, the position of V5 / MT+ can be determined by locating the area of the brain in which TMS stimulation induces the perception of moving phosphenes (Stewart *et al.*, 1999). Localisation can also now be based on anatomical landmarks due to the development of Brainsight Frameless Stereotaxy™ (Rogue Research). This system works by utilising an anatomical MRI of a participant's brain, which is linked to the participant's head based on the identification of anatomical landmarks (bridge of the nose, tip of the nose and intracranial notch of the ears). Using trackers, attached to the participant and the TMS coil, the position of the coil can be observed in relation to the position on the participant's brain, and as such can be adjusted until the coil is in the appropriate location based on gyri or sulci in the brain.

While the safety of single pulse TMS has been well established, the consequences of rTMS are less well understood (Wasserman, 1998). One concern is that TMS produces a noise which results in temporary elevations in auditory thresholds (Pascual-Leone, 1993); as such ear plugs should be worn in all experiments. Walsh and Pascual-Leone (2003) also suggest that participants occasionally report headaches, nausea and facial twitching during TMS. Of greater concern, Pascual-Leone *et al.* (1993) showed that seizures could be induced in participants who had no identifiable risk. Wasserman (1998) identified the following as known side effects of TMS: (1) seizures; (2) effects on cognition; (3) effects on mood; (4) increases in auditory thresholds; (6) transient effects on hormones; (7) transient effects on lymphocytes; (5) pain and headache; (6)

burns from scalp electrodes; (7) psychological consequences of induced seizure. The most serious issue is the seizure risk associated with TMS, the report stated that as of June 1996 there were seven reported seizures as a result of high frequency TMS, as such guidelines were put in place for the administration of TMS.

A more recent paper (Machii *et al.*, submitted), attempted to assess the safety of rTMS to non-motor areas by reviewing articles and experiments taking place from 1997 to 2003. This was deemed necessary due to the fact that current safety guidelines were based on a determination of rTMS intensity as a percentage of motor threshold. Stewart *et al.* (2001) found there to be no relationship between motor cortex excitability and that of other cortical regions. The adverse effects reported were infrequent and mild, headache and neck pain were the most common. Other rare complaints were reported including nausea, tinnitus, mood alteration and mild, transient cognitive impairments. More serious effects were also rare and consisted of seizures (two reports of seizures and two cases of seizure-like episodes several hours after TMS) and inducement of psychotic symptoms (four cases reported following rTMS to dorsolateral prefrontal cortex in depression patients). Machii *et al.* (submitted) concluded that the present guidelines are safe when applied to non-motor areas but go on to recommend that safety guidelines independent of motor threshold must be developed for stimulating non-motor areas. It is important to note that these studies have provided little information regarding the long-term consequences of TMS (due to the fact that TMS is a relatively new technique); this is an area of investigation that requires further study.

1.4.2 Functional Magnetic Resonance Imaging:

Formica and Silvestra (2004) suggest that there are three different types of electromagnetic fields utilised in generating an MRI image: (1) the static magnetic field;

(2) the pulsed field gradient magnetic field; (3) the radio frequency electromagnetic waves. The static magnetic field allows protons (hydrogen atoms) in the body to become aligned and produces a nuclear magnetic resonance signal (NMR). The gradient magnetic field allows one to encode spatial information (and thus build an anatomical MRI image), by eliciting distinguishable NMR signals from various positions in the 3-dimensional space of the body (or brain). The radio-frequency electromagnetic wave emits a radio-frequency pulse that knocks the protons over, and as they realign with the field they emit energy which the coil receives, which indicates the haemodynamic changes associated with neural activation. Haemodynamic changes refer to changes in blood flow and venous oxygenation level that follow neural activity (Savoy, 2001). Savoy (2001) suggests that there are two techniques for studying the haemodynamics associated with neural activation: (1) looking at blood flow directly; (2) blood oxygen level dependent response (BOLD); the latter of which is most commonly used in cognitive neuroscience. The BOLD signal arises from an increase in neural activity (due to the brain's involvement in a particular task), which causes an increase in blood flow in that area, and this leads to a decrease in the concentration of deoxygenated haemoglobin in the venous blood, which in turn leads to an increase in the MR signal.

Huettel *et al.* (2004) outlines the basics of an fMRI experiment. For each experimental session an anatomical image is collected with a number of runs of functional images. Within each run the functional data are acquired as a time series of volumes. Each volume is composed of a number of slices (the number depending on how much of the brain one wishes to cover). Each slice consists of thousands of voxels which make up the image of the brain. There are two main types of fMRI studies: (1) blocked designs – consisting of two or more conditions presented in an alternating pattern; (2) event-related design – where stimuli are presented as individual events or trials (in slow event related designs the haemodynamic response decays to baseline after each stimulus, in a fast sequence the response does not have time to decay). With regard to analysis, data can be analysed using: (1) a voxel-wise approach – where statistical tests are conducted on each voxel to evaluate its significance on the experimental hypothesis; (2) a region of interest approach – where a specific region of the brain is selected and analysed individually for its significance.

Huettel *et al.* (2004) points out that the spatial resolution of fMRI is determined by voxel size, which is typically 3-5 mm for full brain studies, but can be less than 1 mm for studies targeted at a single brain region. The temporal resolution is determined by repetition time (TR), which is usually 1-3 s (one image of the brain is collected per TR). While the absolute timing is difficult to determine, the relative timing of activity between different stimuli or different brain regions can be determined within a few hundred milliseconds. Savoy (2001) points out that the spatial resolution of fMRI is dependent on the strength of the magnet (measured in Tesla). In a 1.5 T magnet 1/100,000 hydrogen nuclei aligns itself with the magnetic field, the higher the strength of the magnetic field the more nuclei that align, thus improving the spatial and sometimes the temporal resolution. However, the disadvantage of a higher magnetic field is increased noise and susceptibility to artefacts (Savoy, 2001). Limitations of fMRI are mainly caused by artefacts due to head movements (although these can be corrected using motion correction algorithms). In addition, participants talking during an experiment can create air pockets in the head which leads to a distortion of the magnetic field (Savoy, 2001).

Formica and Silvestri (2004) estimate that since the introduction of MRI as a clinical tool in the 1980's there have been more than 100,000,000 procedures completed worldwide with relatively few major incidents. Most incidents are related to misinformation related to MR safety aspects of metallic objects, implants or biomedical devices (due to movement, dislodgement, heating and induction of electrical currents). In addition some cases of MRI induced thermal or electrical burns associated with currents in conductors in contact with the patient's body. Savoy (2001) suggests that the dangers of fMRI are mainly caused by bringing a metallic object into the room. However dangers are also related to auditory noise, radiofrequency magnetic field oscillations generating internal body heat, and the possibility of inducing direct electrical stimulation (cardiac interference being the main concern). Overall the dangers of fMRI are avoidable given that the correct procedures are employed and participants are screened appropriately.

1.5 Thesis Aims

The work presented within this thesis was sponsored by the Leverhulme Trust. It was an interchange grant which was set up to allow collaborative work between institutions based in three countries (United Kingdom, France and Canada). The endeavour was to bring the methodologies and expertise provided by the specific institutions in these countries together through collaborations. Therefore research has been carried out, and is presented within this thesis using the following methodologies: (1) Behavioural testing of patients with optic ataxia and visual form agnosia; (2) Transcranial Magnetic Stimulation in healthy individuals; (3) Functional Magnetic Resonance Imaging in healthy individuals. The general aim was to gain further insights into the functioning of the dorsal and ventral stream of visual processing, by investigating the way in which various aspects of visuomotor behaviour fit into such a model. The specific aims of each of the experimental chapters will be presented below.

It has been well established that patients with optic ataxia have deficits in visuomotor tasks such as reaching and grasping, and this is attributed to damage to the dorsal stream of processing. The aim of chapter two was to determine if such deficits would be observed in optic ataxic patients when required to automatically avoid non-target obstacles in the work space.

Patients with visual form agnosia have intact visuomotor behaviour, lesions being restricted to the ventral stream. The aim of chapter three was to determine if visual form agnosia patients would be capable of avoiding obstacles in the work space by virtue of an intact dorsal stream of processing.

The Milner and Goodale model has also suggested that the two streams of processing can be differentiated on the basis of time, the dorsal stream with a 'short term memory', the ventral stream with a 'long term memory'. The aim of chapter four was to determine if automatic obstacle avoidance operates within such a time frame.

Research has shown that when visual form agnosic patients are required to carry out visuomotor tasks under monocular conditions these patients show impairment, due to the fact that pictorial cues are processed within the ventral stream. The aim of chapter five was to determine if visual form agnosic patient DF would show intact behaviour when required to catch a moving object under monocular and binocular viewing conditions.

It has been well established that V5 / MT+ is involved in motion processing within the perceptual domain (for example, damage to V5 / MT+ has been shown to cause impairments in motion discrimination tasks). The aim of chapter six was to determine if V5 / MT+ is involved in motion processing within the visuomotor domain, by applying rTMS to V5 / MT+ when participants were required to catch a moving object.

Recent fMRI research has shown that the dorsal stream shows selectivity for changes in object orientation, while the ventral stream shows selectivity for object identity. The aim of chapter seven was to determine if dorsal stream selectivity for object orientation is restricted to graspable objects, or whether it extends to non-graspable objects also.

CHAPTER TWO: TAKING ACCOUNT OF PERIPHERAL VISUAL STIMULI IN BILATERAL OPTIC ATAXIA

2.1 Introduction

In everyday life we are required to avoid obstacles in our workspace to prevent collisions; we may do this by shifting our movement trajectories and / or slowing down our movements. Similar behaviour is observed in the laboratory. Jackson *et al.* (1995) found that the placement of non-target objects in the workspace caused changes in both the transport (modified peak velocity and deceleration time) and grasp components (increased peak grip aperture and later time of peak grip aperture when not normalised as a function of movement time) when subjects were required to reach and grasp a target object, especially when it was performed in open loop (i.e. no visual feedback available). In other studies, it was reported that even a non-target object in the form of an LED would cause reaching movements to veer away from it (Tipper *et al*, 1997; Howard and Tipper, 1997). Although the authors conceptualized this effect as a kind of attentional repulsion, in functional terms it may reflect a failsafe mechanism to minimize the likelihood of colliding with non-targets, which is automatically recruited even when there is no actual physical risk of collision.

Tresilian (1998) carried out a study in which participants were required to reach and grasp a target in the presence of a flanker positioned behind, beside or in front of the target in either a wrist-flexed or wrist-extended posture (the type of posture required determining how the flanker would obstruct the target). The results suggest that both the grasp and transport components of prehension movements are adjusted to avoid potential obstacles. In addition he proposed that people move so as to avoid the hand coming within a minimum preferred distance from non-target objects within the workspace. He suggested that what constitutes the preferred distance depends on speed of movement and psychological factors related to the cost attached to a collision. More recently, Mon-Williams and McIntosh (2000) have shown that as the distance between two flanking obstacles gets smaller, movement time to grasp a target object increases, according to a quasi-Fitts' Law function (i.e. movement time is a function of distance to and size of the target) (Fitts, 1954). In a further investigation, Mon-Williams *et al.* (2001) found that the presence of obstacles during a reach to grasp task causes both an increase in movement time and decrease in maximum grip aperture, but in varying proportions depending on the layout of the workspace. They suggest that their findings indicate a flexible control strategy in which movements are adjusted to avoid collision with obstacles in a subtle and precise manner.

Until recently, there have been no investigations directed at understanding the neural underpinnings of non-target processing during movements. In contrast, a host of neurobehavioural and neurophysiological studies are in agreement that the visual control of *target-directed* reaching and grasping depends upon systems in the dorsal stream of cortical processing (Milner and Goodale, 1995; Jeannerod, 1997; Goodale and Milner, 2004) (see general introduction for an overview of the dorsal stream of processing). Yet non-target processing clearly plays an important role in determining the parameters of reaching and grasping movements. One of the first studies of non-target processing following brain damage was performed by McIntosh *et al.* (2004a) with neglect patients. Neglect has been defined as "the failure to report, respond or orient to novel or meaningful stimuli presented to the side opposite a brain lesion, when this failure cannot be attributed to either elemental sensory or motor deficits" (Heilman, 1979). The area that is most heavily implicated in the causation of neglect is the temporo-parietal region of the right hemisphere and it has been proposed that this region functions as a high-level representational system that is fed principally by visual inputs arising from the ventral stream, and may be regarded as the end-point of the perceptual processing pathway (Milner and McIntosh, 2003). They tested 12 neglect patients and 12 normal control subjects on a bisection task and a reaching task, in both cases using the same spatial layout. Subjects were presented with two cylinders, each of which could be located in one of two positions either to the left or right of the midline. In the bisection task participants were required to judge the midpoint between the two cylinders by making a pointing response, while in the reaching task they where required to touch a wide target zone located beyond the two cylinders by reaching between them. The former can thus be regarded as an explicit bisection task, the latter as an implicit one. The results showed that 10 out of the 12 neglect patients performed similarly to controls on the reaching task, taking full account of both cylinder locations as they carried out the movements. However, as would be expected, in the bisection task the neglect patients failed to take full account of the varying locations of the left cylinder in making their spatial judgements. McIntosh *et al.* (2004a) argued that this preservation of non-target processing in their patients might be due to the sparing of dorsal-stream cortex in and around the intraparietal cortex (Culham and Kanwisher, 2001).

While subjects failed to take account of shifts in the leftward cylinder during their bisection response, they took account of such shifts during the reaching task. It remains unclear however if subjects were visually *aware* of the left cylinder during this task, as participants were not required to verbally report which cylinders they saw. Therefore in a separate study (McIntosh *et al.*, 2004b) a patient with visual extinction was tested in a comparable reaching task. Extinction is a condition in which patients with unilateral brain damage fail to report stimuli on the contralesional side of space when stimuli are presented bilaterally, yet can accurately report the presence of a single stimulus presented on either side of space (Bender, 1952; Driver *et al.*, 1997). In this experiment thin poles were presented for a brief stimulus duration, in order to induce extinction of the left pole on about half of the test trials. There were four trial types in which the poles could be presented with either the left pole alone, the right pole alone, both, or neither of the poles. Participants were required to reach to a target zone located beyond the two poles and verbally report which poles they had seen. The results showed that the patient shifted his reach trajectory according to whether the left, right, or both poles were present, much as healthy control subjects did, and these shifts occurred to the same degree regardless of whether he reported the presence of the left-side pole (i.e. he took account of the presence and location of both poles in his reach despite a failure to verbally report the presence of the two poles).

Unlike neglect or extinction, which are associated with damage to the parieto-temporal region, optic ataxia is associated with damage to the dorsal stream of processing, in the superior parietal region (see general introduction for more details of optic ataxia). The aim of the present experiment was to determine if bilateral optic ataxic patients have difficultly in reaching between objects and to examine if this can be dissociated from the bisection of space between two objects. It would be predicted that optic ataxic patients would show the opposite pattern of results to the neglect patients in the previous study (McIntosh *et al.*, 2004a), in that they would show impaired obstacle avoidance behaviour due to their damaged dorsal stream, yet would behave like normal participants when asked to bisect the space between the same two obstacles, given their intact ventral stream. The demands of these two tasks differ in that in the bisection task participants are required to make a deliberate perceptual judgement, whereas in the reaching task participants are required to automatically and unconsciously modify their reaching movements in a way which will minimize the risk of collision with the potential obstacles. It is automatic in the sense of being quite unintentional; the separations used would pose very little risk of collision in healthy subjects.

2.2 Method

2.2.1 Participants:

Two patients with bilateral parietal damage resulting in optic ataxia (AT and IG) took part in this experiment along with eight healthy female controls, between 32-50 years old. All control participants were right-handed by self-report, had no history of neurological disorder and had normal or corrected to normal vision.

Patient AT was aged 48 at the time of testing. Her optic ataxia resulted from an eclamptic attack 14 years prior to testing, which provoked a haemorrhagic softening in the territory of both parieto-occipital arteries (branches of the posterior cerebral arteries). Her lesion is depicted in figure 2.1. She now continues to show the symptoms of Bálint's syndrome, including visual disorientation, simultanagnosia and severe optic ataxia for objects in the peripheral visual field. She shows no symptoms of occipito-temporal damage (i.e. alexia, object agnosia, achromatopsia, or prosopagnosia) and she is able to leave a relatively normal life despite her lesion.

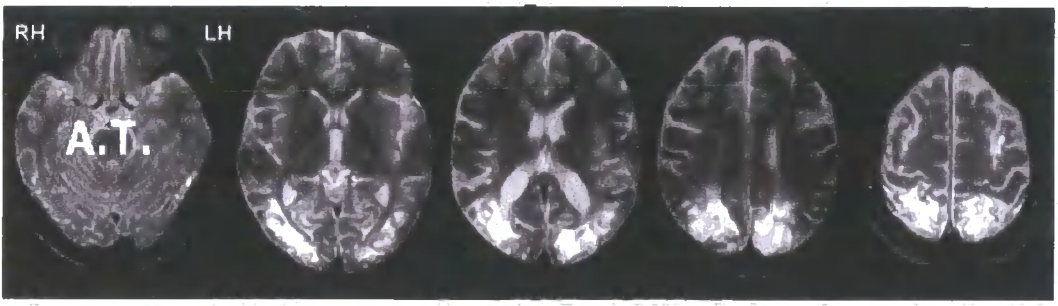

Figure 2.1: An early MRI scan revealed that AT's lesion involved bilateral parietal damage extending to the upper part of the occipital lobes and slightly into the medial part of the right premotor cortex. The calcarine area remained intact except for the upper lip on the left hand side.

Patient IG was aged 33 at the time of testing. Her optic ataxia resulted from a bilateral parieto-occipital infarction 3 years prior to present testing. She initially presented with severe headache, dysarthia and bilateral blindness, which lasted for 3 days. Subsequently bilateral optic ataxia and simultanagnosia became apparent (Pisella *et al.*, 1999). Her simultanagnosia has now subsided at least for presentations of two or three objects (Pisella *et al.*, 2000). She received a diagnosis of ischemic stroke, related to acute vasospastic angiopathy in the posterior cerebral arteries. Her lesion is depicted in figure 2.2.

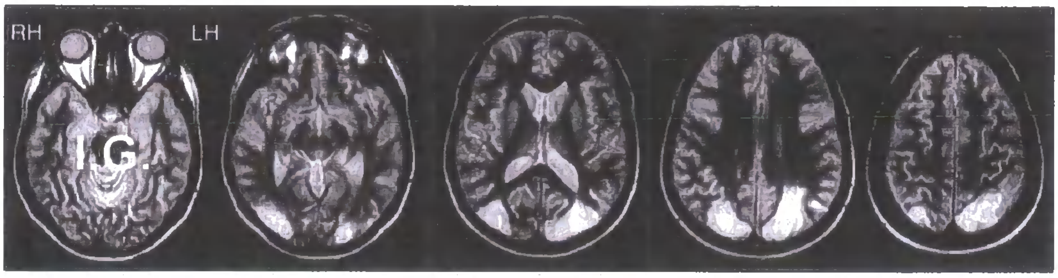

Figure 2.2: A structural MRI scan revealed that IG's damage is in the posterior parietal and upper and lateral occipital cortico-subcortical regions. Reconstruction of her lesion indicated that it involved mainly Brodmann's areas 7, 18, 19, the intraparietal sulcus, and part of area 39.

2.2.2 Experimental equipment:

The experimental setup used in the present experiment is depicted in figure 2.3.

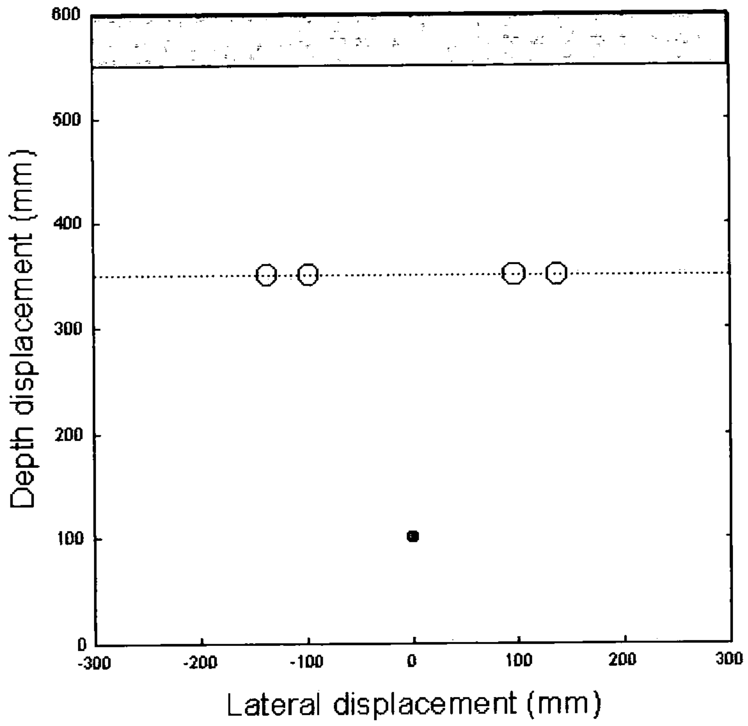

Figure 2.3: Figure depicts the experimental set-up used. Participants were presented with a 60cm^2 white stimulus board. This board consisted of a start button (filled black circle) located 10cm away from the edge of the board and a 5cm grey target zone, which spanned the far edge of the board. Two grey cylinders (24.5cm tall and 3.5cm in diameter) could be fixed to the board one on either side of the mid-line at a distance of 25cm from the start position and 20cm in front of the grey target zone. Each of the cylinders could occupy one of two locations (open circles), with its inside edge either 8cm or 12cm away from the midline. The factorial combination of these locations thus created four possible stimulus configurations. A strip of white card was placed between the two cylinders in every trial to prevent participants using the visible holes to guide them.

Liquid crystal shutter glasses (Plato System, Translucent Technologies, Toronto, CA) were used which opened when the start button was pressed and closed on movement onset, signalled by release of the hand button. Hand movements were recorded using an electro-magnetic motion analysis system (Minibird, Ascension Technology Inc.). Responses were recorded by sampling the position of a marker attached to the nail of the right index finger, at a sampling frequency of 86.1 Hz. Responses were recorded for

3 seconds (allowing the entire movement to be captured); both start position and end position were defined as that recorded on the frame at which hand velocity fell below a threshold of 50 mm/s.

2.2.3 Procedure:

Participants were required to perform both a reaching task and a bisection task in separate blocks, with the order of blocks balanced across participants within each group. Participants were requested to place their right index finger on the start button when they were ready to begin each trial. This signalled the shutter glasses to open and participants were required to fixate on a central cross, located at the back of the stimulus board 16 cm above the surface. On a verbal 'Go' signal, which was given as soon as participants indicated that they were ready, participants were required to perform each trial. In the reaching task subjects were required to reach out and touch a target zone located beyond the two cylinders and were instructed that the emphasis in this task was speed of movement. Participants were instructed that when a cylinder was present there would be one on the left and one on the right of the midline and they should pass their hand between the two cylinders rather than around the outside edge of the board. Each participant made 60 reaches in a fixed pseudo-random order, with 12 trials for each of the four cylinder configurations and 12 in which no cylinders were present (these types of trials were included as a control condition to check for any systematic bias when the reaching response was not constrained by any potential obstacles and were not included in the main analysis). In the bisection task participants were informed that the position of the cylinders would vary from trial to trial, but there would always be one on the left and one on the right. They were instructed to indicate where they estimated the midpoint was between the two cylinders, and were instructed that the emphasis on this task was on accuracy of judgement. Each participant made 48 bisection responses, which involved 12 trials for each of the stimulus configurations, presented in a fixed pseudo-random order.

2.2.4 Analysis:

The dependent measure taken for each trial in the reaching task was the lateral position (P) of the marker, with respect to the midline of the stimulus board, as it crossed the virtual line joining the two cylinder locations. The dependent measure for the bisection task was the lateral position (P) of the marker on the index finger at the end of the movement.

A two-way ANOVA of response positions P was computed, with two factors (left / right cylinder) each with two levels (near / far). A separate ANOVA was carried out on the data of each individual participant.

The main analyses were weighting indices dP_L and dP_R (McIntosh *et al.*, 2004a). These indices measure the mean change in P that is associated with a shift of each cylinder between its two locations (i.e. how much the response shifts in relation to a 40 mm shift of one or the other cylinder). These were calculated according to the following equations (see figures 2.4 and 2.7 for stimulus configurations):

dP_L = (mean P in configurations A and C) – (mean P in configurations B and D)
dP_R = (mean P in configurations C and D) – (mean P in configurations A and B)

This measure provides a weighting indices of dP_L and dP_R, where a positive value indicates a shift in response in the appropriate direction (with a 2 mm shift being a perfect response), a negative response indicates a shift in the wrong direction, and a zero value indicates that participants failed to shift their response at all relative to changes in cylinder location.

The modified t-test (one-tailed) recommended by Crawford and Garthwaite (2002) was used to make a separate statistical comparison between each patient and the control group on each of the two indices in each test condition.

In a third set of analyses, the variability of reaches was assessed by calculating the variance of P for each of the four test configurations, and averaging these to give a mean variability score for each participant. The modified t-test (one-tailed) was used to make a statistical comparison between each patient and the control group.

Finally, each subject's kinematics were analysed by computing movement time, peak velocity and time of peak velocity. Again the modified t-test (one-tailed) was used to make a statistical comparison between each patient and the control group.

2.3 Results

2.3.1 Reaching task:

Figure 2.4 shows the mean position of each response with respect to the midline of the stimulus board at the point of intersection with an imaginary line joining the object locations for AT, IG and the healthy controls. This shows that for the control subjects the four cylinder configurations elicited lawful shifts in the reaching trajectories, in that configuration B shows a leftward shift and C a rightward shift, each relative to the symmetrical configurations of A and D. In contrast the two patients AT and IG showed no such changes in their reaches as a function of the location of the cylinders. Individual two-way ANOVAs were conducted on the data, with two factors (left cylinder location and right cylinder location) each with two levels (near and far). For AT there was no effect of left cylinder ($F_{(1, 44)} = 0.97$, $p = 0.33$), or right cylinder ($F_{(1, 44)} = 0.11$, $p = 0.74$). This pattern of results was also revealed in IG who showed no effect of either the left cylinder ($F_{(1, 44)} = 0.07$, $p = 0.79$) or right cylinder ($F_{(1, 44)} = 2.39$, $p = 0.13$). It is thus clear from the pattern of results that neither patient took account of the cylinder locations when executing their reaching responses. In contrast, all control participants showed a significant effect of both left and right cylinder (in every case $p < 0.005$, except for one participant (N4) for whom the left object was significant only at $p < 0.021$). Individual significant levels are reported in appendix 1.1.

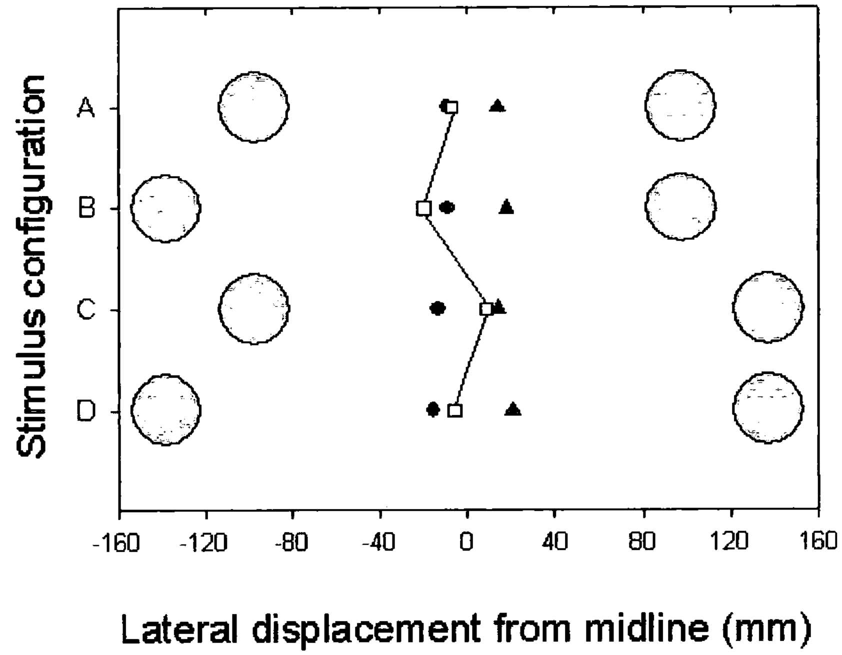

Figure 2.4: Data for the two patients AT (filled triangles) and IG (filled circles) and control subjects (open squares) in the reaching task. The responses plotted are P values (i.e. the point where each response intersects the imaginary line joining the four possible cylinder locations. The dark grey circles depict the four possible stimulus configurations (A, B, C, D)

Figure 2.5 shows the two indices of sensitivity of the varying locations of the left and right cylinder, dP_L and dP_R, respectively, for the reaching task for the two patients and the healthy controls (i.e. the weightings attached to the left and the right cylinder in determining the trajectories). This shows that there is a qualitative difference between the two patients and the controls, in that the two patients both have weightings which lie around the zero point, which is well outside the range of the control participants. Modified t-tests were conducted on these data. This confirmed that AT differed significantly from controls on both dP_L ($t = -3.13$, $p = 0.008$) and dP_R ($t = -3.11$, $p = 0.009$), this pattern of results was also observed in IG who significantly differed from controls in both dP_L ($t = -2.13$, $p = 0.036$) and dP_R ($t = -4.72$, $p < 0.001$).

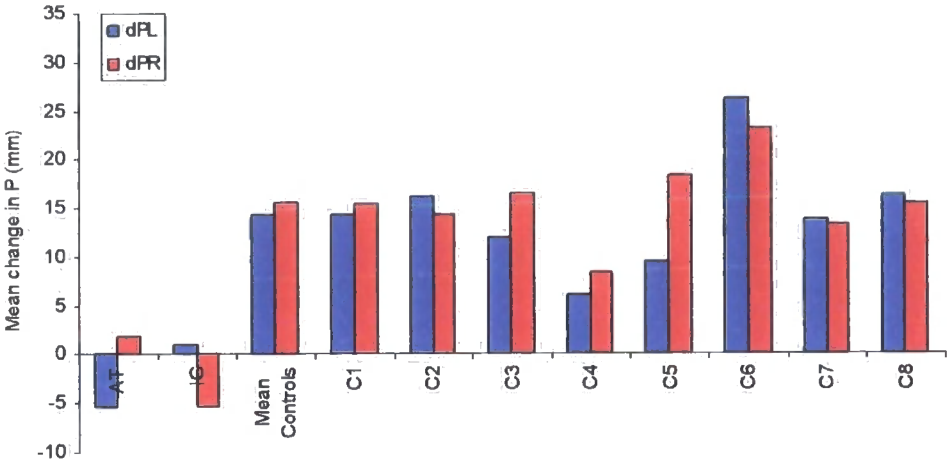

Figure 2.5: Figure depicting the weightings attached to the left and right cylinder in the reaching task for the two patients and controls (both individually and as a group mean). This represents the mean change in response induced by a 40mm shift in location of the left (dPl) and right (dPr) cylinder.

The variability of each participant's trajectory (as measured by the mean variance of P) for the reaching task was computed (AT = 356.87; IG = 140.96) (Mean controls = 74.80). It is clear that the variability of movement trajectories is higher for both the patients than for the controls. A modified t-test conducted on these data showed that this difference reaches significance for patient AT ($t = 6.99$, $p < 0.001$) but not in patient IG ($t = 1.64$, $p = 0.073$). It should be noted that although this higher variability would have militated strongly against finding significant effects of left or right cylinder locations in the patients, it would not affect the dP_L or dP_R values as these are based on mean trajectories only and not their variability.

Table 2.1 shows several kinematic parameters from the reaching task. A modified t-test shows that mean movement time was significantly longer in AT than controls ($t = 2.633$, $p = 0.017$), and mean time of peak velocity was significantly longer in AT than controls (t = 1.981, p = 0.013), reflecting her generally slowed movements. No other significant differences were observed, and in fact the kinematics of IG's movements appear to be remarkably normal.

Table 2.1: Table showing mean movement time (ms), mean peak velocity (mm/s) and mean time to peak velocity (ms) for the reaching task, averaged across the four stimulus configurations.

	MT (sd)	**PV (sd)**	**TPV (sd)**
AT	830.7 (168.39)	1033.55 (98.08)	324.7 (32.50)
IG	561.36 (30.34)	1598.24 (99.96)	171.55 (27.66)
Mean Controls	570.63 (93.13)	1592.87 (289.02)	204.83 (39.92)

2.3.2 Bisection task:

Analysis of the bisection data reveal a quite different pattern of results than those observed in the reaching task. Figure 2.6 shows the mean position of each response with respect to the midline of the stimulus board at the point of intersection with an imaginary line joining the object locations for AT, IG and the healthy controls. This shows that for the control subjects and the two patients, the four cylinder configurations elicited lawful shifts in the reaching trajectories, in that configuration B shows a leftward shift and C a rightward shift, each relative to the symmetrical configurations of A and D. As before, individual two-way ANOVAs were conducted on the data, with two factors (left cylinder location and right cylinder location) each with two levels (near and far); this showed that for both patients and controls there was a highly significant effect ($p < 0.001$) of both left and right cylinder location. For AT there was a significant effect of left cylinder ($F_{(1, 44)} = 46.37$, $p < 0.001$) and right cylinder ($F_{(1, 44)} = 64.52$, $p < 0.001$). This pattern of results was also shown in IG who also showed a significant effect of both the left cylinder ($F_{(1, 44)} = 40.85$, $p < 0.001$) and right cylinder ($F_{(1, 44)} = 45.55$, $p < 0.001$). In other words both patients and controls took full account of the locations of both cylinders in executing their bisection responses. Individual significance levels are reported in appendix 1.2.

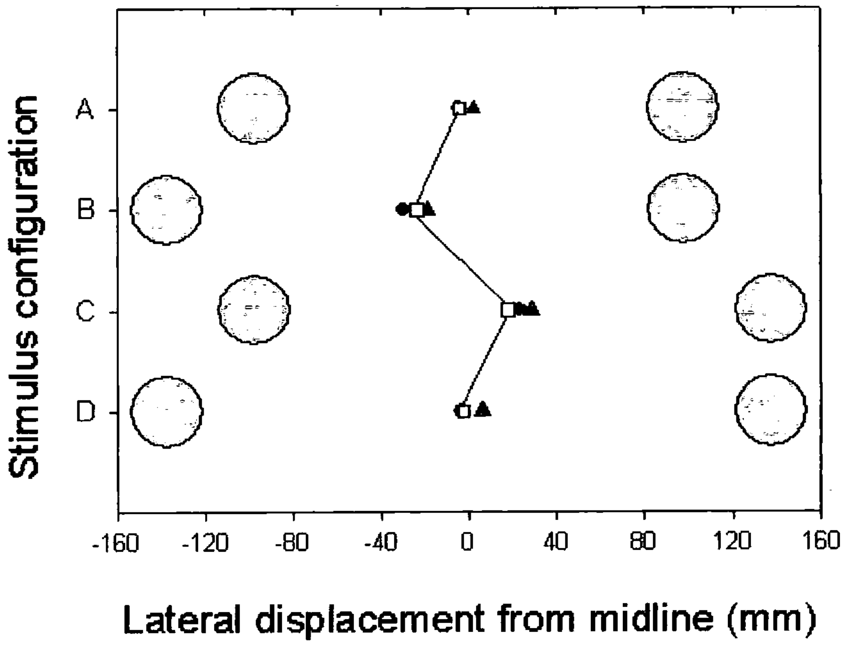

Figure 2.6: Data for the two patients AT (filled triangles) and IG (filled circles) and control subjects (open squares) in the bisection task. The responses plotted are P values (i.e. which in this case is the bisection point between the cylinders. The dark grey circles depict the four possible stimulus configurations (A, B, C, D)

Figure 2.7 shows the two indices of sensitivity of the varying locations of the left and right cylinder, dP_L and dP_R, respectively for the reaching task for the two patients and the healthy controls (i.e. the weightings attached to the left and the right cylinder in determining the trajectories). This shows the normality of the patients bisection response, in that both patients lie within (at the high end of) the normal range. Modified t-tests were conducted on these data and confirmed that there was no significant differences between AT and controls on dP_L ($t = 0.385$, $p = 0.356$) or dP_R ($t = 0.803$, $p = 0.224$) or between IG and controls on either dP_L ($t = 1.249$, $p = 0.126$) or dP_R ($t = 1.166$, $p = 0.141$).

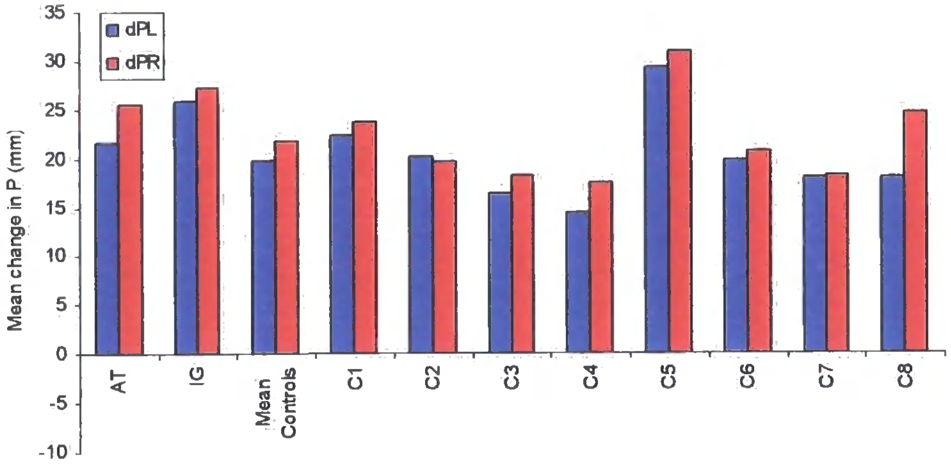

Figure 2.7: Figure depicting the weightings attached to the left and right cylinder in the bisection task for the two patients and controls. The data represent the mean changes in response induced by a 40mm shift in location of the left (dP_L) and right (dP_R) cylinder.

The variability of each participant's trajectory (as measured by the mean variance of P) for the bisection task was computed (AT = 120.89; IG = 195.30) (Mean controls = 48.18). It is clear that the variability of movement trajectories is higher for both the patients than for the controls. A modified t-test conducted on the data showed that this difference reaches significance for both AT ($t = 2.54$, $p = 0.019$) and IG ($t = 5.14$, $p < 0.001$). It should be noted that this increased variability still did not prevent the highly significant effects of cylinder location as reported above.

Table 2.2 below shows several kinematic parameters from the bisection task. A modified t-test shows that AT had a significantly longer movement time than control subjects (t = 3.11, p = 0.025) and a significantly later time to peak velocity (t = 2.702, p = 0.015). IG had a significantly *higher* peak velocity than control subjects (t = 4.307, p = 0.002). No other significant differences were observed.

Table 2.2: Table showing mean movement time (ms), mean peak velocity (mm/s) and mean time to peak velocity (ms) for the bisection task averaged across the four stimulus configurations.

	MT (sd)	**PV (sd)**	**TPV (sd)**
AT	809.38 (81.61)	721.97 (63.79)	323.03 (46.74)
IG	563.60 (32.85)	1595.70 (96.27)	165.26 (22.89)
Mean Controls	551.32 (102.28)	900.15 (152.24)	225.79 (33.93)

2.4 Discussion

The aim of the present experiment was to test whether damage to the dorsal stream of processing, causing the visuomotor symptoms of optic ataxia, would lead to impaired obstacle avoidance behaviour. The results show that optic ataxic patients made reaches between the two objects that took no account at all of the varying locations of the objects. The variance of their reaches was also considerably higher than healthy controls. In the bisection task, however, the patients were completely unimpaired in taking account of the object shifts, even though they showed more variance in their bisections than the controls, presumably reflecting the aiming impairment that is characteristic of optic ataxia.

There are other differences between the two tasks that could potentially explain the pattern of results observed. In particular, it could be argued that the reaching task, being carried out with an emphasis on speed and not accuracy, would inevitably cause the patients to take little account of the left and right objects. This idea gains no support, however, from the present data or from previous data. First, the healthy controls almost all showed highly significant dP_L and dP_R indices in the reaching as well as in the bisection task, although the mean magnitudes were slightly smaller. And second, a group of neglect patients (McIntosh *et al.*, 2004a), showed the opposite pattern of results (i.e. they took normal account of the two objects during the reaching task, despite showing reduced weightings of the left object in the bisection task).

It could also be argued that simultanagnosia was present in these patients, and that, like many patients with Bálint's syndrome, they would have difficulty holding more than one object within their span of attention at once. There are, however, three reasons to reject this suggestion. First, I.G. shows very little sign of simultanagnosia, having no difficulty in perceiving up to 3 objects together (Pisella *et al.*, 2000). Patient A.T. does retain a degree of simultanagnosia, despite the passage of many years since her brain lesion, but she only experiences it when viewing time is restricted to 500 ms or less (which was not the case in this experiment). Second, even if the patients had difficulty in seeing both objects simultaneously, they should at least have been able to see one or other of them on every trial. If they had no intrinsic problem with obstacle avoidance, this ability to see at least one object would have raised their values of dP_L and dP_R above zero, to at least half of the normal values. However, this was not the case, and dP_L and dP_R remained steadfastly around zero. Third, and most convincingly, both patients performed in a comparable way to healthy controls on the bisection task, despite the fact that the same objects were presented in identical configurations. This strongly suggests that simultanagnosia played no part in determining the results of the present study.

A third argument is that the patients have no problem with obstacle avoidance *per se*, but that they are simply impaired at target-directed reaching. It is unlikely that this is the case, as it has been shown that AT and IG, like most patients with optic ataxia, show little or no impairment for reaching to fixated targets (Pisella *et al.*, 2000; Grea *et al.*, 2002) and in this study the grey target strip was in line with fixation. However, the fact that both patients showed abnormally high variance in their reach trajectories could be seen as support for this argument. This increased variance may explain the failure to find a significant effect of either object on P (by leading to a lower F-value in the statistical comparison of their trajectories). The analysis of the data in terms of the indices dP_L and dP_R, however, explicitly does *not* depend in any way on trial-to-trial variability. These indices are based only on the mean values of the variable P, and therefore are unaffected by the variance of P. It is therefore these indices that give the most unambiguous evidence of a loss of obstacle avoidance skill in A.T. and I.G. Furthermore, despite even higher response variability in the bisection task, both patients nonetheless still show highly significant effects of the left and right cylinder locations on their responses.

There has been much debate in the literature between the respective merits of 'distractor' and 'obstacle avoidance' accounts of the effects of non-target objects on motor behaviour (Tresilian, 1999; Castiello, 1999). It has been argued that effects in normal participants such as those observed in the present experiment cannot be explained by obstacle avoidance alone and may be due to the fact that the non-target objects serve as distractors and cause competition for attention (Castiello, 1999). However, if the cylinders used in the present experiment were treated as distractors rather than obstacles, it is difficult to explain why participants moved their hand trajectories consistently away from them, differentially according to the location of the cylinders. Given this pattern of findings, it seems more appropriate to discuss the results of the present experiment within the framework of obstacle avoidance (i.e. that participants move away from the cylinders in order to minimize the risk of collision).

Taken with previous results (McIntosh *et al.*, 2004a), this study fits well within the framework of the current functional understanding of the ventral and dorsal processing streams (see general introduction for more details). That is, like target-directed reaching and grasping movements, it can be proposed that automatic obstacle avoidance is a dorsal stream function (abolished when superior parietal cortex is destroyed as in optic ataxia, but typically preserved in neglect, where the damage is predominantly temporo-parietal). Bisection, on the other hand, depends on a conscious strategy which optic ataxic patients can implement using perceptual information processed within their ventral stream and its right temporo-parietal elaboration; both of which may remain largely intact. A prediction from this interpretation, of course, is that while damage to the ventral stream itself would be expected to impair gap bisection to some degree, it should entirely spare obstacle avoidance. There are some conditions under which the ventral stream may be involved in obstacle avoidance, for example if the obstacle is fragile or noxious. Under such conditions one would assume that the ventral stream would be required to determine the perceptual attributes of the obstacles; this requires further testing.

CHAPTER THREE: TAKING ACCOUNT OF PERIPHERAL VISUAL STIMULI IN VISUAL FORM AGNOSIA

3.1 Introduction

Chapter 2 gave an overview of the literature on obstacle avoidance behaviour and provided evidence that such behaviour is mediated by the same dorsal stream systems as those involved in target directed reaching and grasping movements. It was argued that automatic obstacle avoidance is a dorsal stream function, abolished when superior parietal cortex is destroyed as in optic ataxia (Chapter 2) but typically preserved in neglect, where the damage is predominantly temporo-parietal (McIntosh *et al.*, 2004a). Bisection, on the other hand, was argued to depend on a conscious perceptual strategy which optic ataxic patients can implement using perceptual information processed within the ventral stream (Chapter 2), and its right temporo-parietal elaboration (McIntosh *et al.*, 2004a). As outlined in Chapter 2, a prediction from this interpretation is that damage to the ventral stream would be expected to impair gap bisection to some degree; however it should entirely spare obstacle avoidance behaviour. This chapter shall attempt to provide evidence in support of this prediction by testing two visual form agnosic patients (with bilateral damage to the ventral stream of processing) in a similar set-up to that described in Chapter 2. An overview of visual form agnosia in provided in Chapter 1.

Patient DF who suffers from visual form agnosia as a result of bilateral damage to the ventral stream of processing (Milner *et al.*, 1991; James *et al.*, 2003) has been shown to have preserved visuomotor behaviour, which is attributed to the fact that she has an intact dorsal stream of processing (see general introduction for more details). Little is known about DF's performance in obstacle avoidance tasks. Recently, however, (Rice *et al.*, submitted) a study was carried out to address this issue. DF was asked to reach out and grasp an object in the presence of secondary objects, placed either to the left or right of the target. It was shown that DF took account of the obstacle's location relative to the target, by systematically shifting her reach trajectories and adjusting her grip aperture in a similar manner as controls. It was inferred that she may be using her intact dorsal stream to allow her to take account of these obstacles, suggesting that both target related processing and obstacle related processing might share a common parietal substrate. A problem with this experiment was that no control task was used to enable a dissociation to be illustrated between DF's intact visuomotor behaviour and impaired perceptual processing; such a task would enable stronger claims regarding DF's intact obstacle avoidance behaviour (i.e. a task which is similar to the visuomotor task but demands an element of perceptual processing). In addition the experimental design of this study was not tightly controlled in terms of viewing time, and no constraints were placed on the subjects regarding speed of movement (DF's movement time was approximately twice as slow as controls on all conditions which makes kinematic parameters difficult to compare). Finally, it would enable stronger claims to be made if more than one visual form agnosic patient was tested.

The aim of the present experiment was to examine obstacle avoidance behaviour in two visual form agnosic patients and thereby to assess the relative contributions of the dorsal and ventral streams to this type of visuomotor behaviour. If automatic obstacle avoidance is subserved by the dorsal stream of processing it would be predicted that both patients would show somewhat impaired performance on the bisection task due to their damaged ventral streams, but that they would perform in a similar way to normals when required to reach between the two cylinders, due to their intact dorsal streams. In other words, a double dissociation between optic ataxic and visual form agnosic patients was predicted on these respective perceptual and visuomotor tasks.

3.2 Method

3.2.1 Participants:

Two patients with visual form agnosia (DF and SB) and sixteen age-matched controls took part in the study. Eight of the controls were females aged between 38-58 years old, while the others were males aged between 28-39 years old. All participants were right-handed by self-report, had normal or corrected to normal vision and no history of neurological disorders.

DF was 48 years old at the time of testing; she developed visual form agnosia after carbon monoxide poisoning 14 years prior to testing (see general introduction for more details of DF and visual form agnosia). EEG showed bilateral abnormalities, most prominent posteriorly and in temporal regions. Later MRI studies showed abnormalities in occipital poles bilaterally, with the damage extending laterally in the ventral part of the occipital lobe (area 18) and dorsally in the posterior parasagittal occipitoparietal region, her primary visual cortex remaining largely intact (Milner *et al.*, 1991). Figure 3.1 illustrates a recent MRI depicting the lesion in DF.

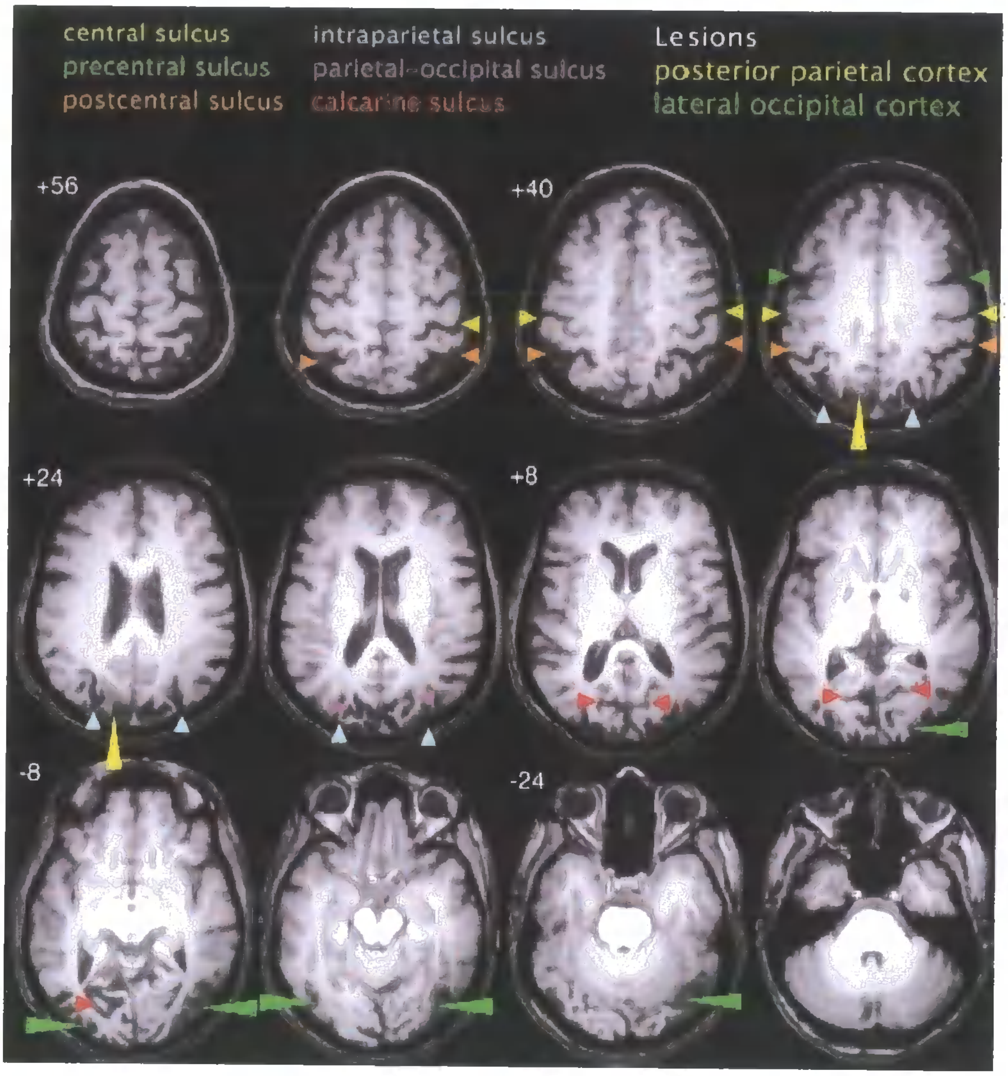

Figure 3.1: MRI scan (neurological convention) for DF. Small arrows indicate areas of atrophy, yellow = central sulcus, orange = postcentral sulcus, green = precentral sulcus, blue = intraparietal sulcus, magenta = parietal occipital sulcus, red = calcarine sulcus. Long arrows indicate lesion areas, yellow = posterior parietal cortex, green = lateral occipital cortex. From James *et al.* (2003).

Patient SB was 34 years old at the time of testing; he developed visual form agnosia following meningoencephalitis at 3 years old. As shown in the extensive studies of Lê *et al.* (2002), his deficits include achromatopsia (cortical colour blindness), prosopagnosia (inability to recognise faces), alexia (inability to read) and object agnosia. Like DF, he typically focuses on parts of objects rather than the objects themselves, and can process local aspects of shapes while failing to link and integrate them as a global whole. Yet also like her, he is able to generate and manipulate visual images. He performs better than DF in matching meaningful and meaningless objects, as well as in copying drawings (relying on feature by feature analysis of the objects), and in being able to confidently navigate his way in both familiar and non-familiar environments. He also has a striking ability to use motion information to help him identify objects. MRI scans show lesions of the occipitoparietal and occipitotemporal regions in the right hemisphere and the occipitotemporal junction of the left hemisphere. The right hemisphere lesion includes complete or partial damage to areas V2, V3, V4, V5 and LO, and there is limited damage to the right inferior parietal lobule in the region of the supramarginal gyrus. There is a spared region in the right occipital pole including the calcarine fissure (primary visual cortex), in its rostral and superior aspects. In the left hemisphere the lesion involves mainly the ventrolateral visual cortex, including the fusiform gyrus and area LO. Figures 3.2a and 3.2b illustrate the lesion in patient SB.

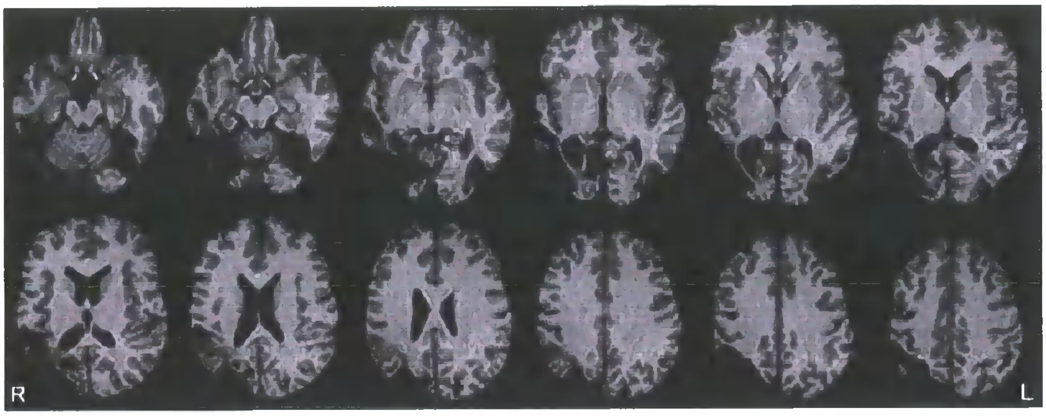

Figure 3.2a: From Lê *et al.* (2003). Figure depicts 12 MRI axial slices (every 4mm; thickness = 1mm) parallel to the bi-commissural plane showing the main lesions in SB.

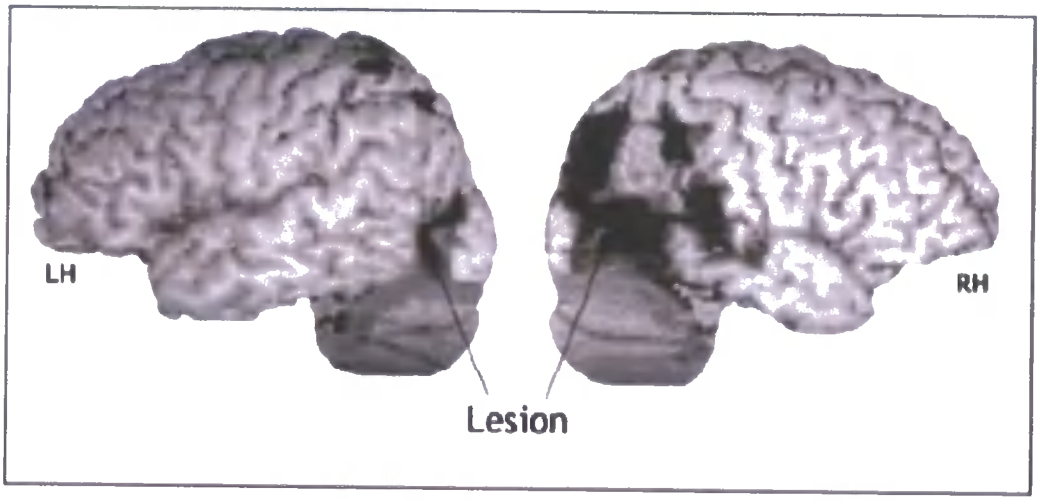

Figure 3.3b: From Lê *et al.* (2002). Figure depicts a three-dimensional rendering of the cortical surface from SB's MRI. The lesion area is visualized in black, illustrating areas of damage in the occipitotemporal and occipitoparietal area of the right hemisphere and at the occipitotemporal junction of the left hemisphere.

3.2.2 Experimental equipment:

The experimental set-up used in the present experiment is depicted in figure 2.3 (chapter 2). Liquid crystal shutter glasses (*Plato* System, Translucent Technologies, Toronto, Canada) were used which were programmed to open for 2 seconds at the beginning of each trial. A tone was used to indicate that participants should initiate their response; this occurred immediately as the shutter glasses closed. Hand movements were recorded using Optotrak (Northern Digital Inc., Waterloo, Ontario); responses were recorded by sampling the position of a marker attached to the nail of the right index finger, at a sampling frequency of 100 Hz. For both the reaching and bisection task recording was made for 5 seconds, allowing the movement to be recorded in full (i.e. from the initial start position to movement offset). Both start position and end position were defined as that recorded on the frame at which hand velocity fell below a threshold of 50 mm/s.

3.2.3 Procedure:

Participants were required to perform both a reaching task and a bisection task, in separate blocks. They were instructed to place their right index finger on the start button when they were ready to begin each trial, and to initiate their response when they heard a tone, which was presented immediately on the closure of the shutter glasses. In the reaching task participants were instructed to reach out and touch a target zone located beyond the two cylinders, and they were told that the emphasis in this task was speed of movement. They were instructed that whenever a cylinder was present there would be one on the left and one on the right and they should pass their hand between the two cylinders rather than around the outside edge of the board. Each participant made 60 reaches in a fixed pseudo-random order, with 12 trials for each of the four cylinder configurations and 12 in which no cylinders were present (these trials were included to check for any systematic bias when the reaching response was not constrained by any potential obstacles; they were not included in the main analysis). In the bisection task participants were informed that the position of the cylinders would vary from trial to trial, and that there would always be one on the left and one on the right. They were instructed to point to the midpoint between the two cylinders, and were told that the emphasis in this task was on accuracy of judgement. Each participant made 48 bisection responses, including 12 trials for each of the stimulus configurations, presented in a fixed pseudo-random order.

3.2.4 Analysis:

The dependent measure taken for each trial in the bisection task was the final lateral position (P) of the marker on the index finger with respect to the midline of the stimulus board. The dependent measure for the reaching task was the lateral position of the marker as it crossed the virtual line joining the two cylinder locations (here the exact value of P was estimated by linear interpolation).

The main analyses were weighting indices dP_L and dP_R (McIntosh *et al.*, 2004a; Chapter 2). These indices measure the mean change in P that is associated with a shift of each cylinder between its two locations (i.e. how much the response shifts in relation to a 40mm shift of one or the other cylinder). They were calculated according to the following equations (see Chapter 2, figure 2.4 for the four stimulus configurations):

dP_L = (mean P in configurations A and C) – (mean P in configurations B and D)
dP_R = (mean P in configurations C and D) – (mean P in configurations A and B)

The modified t-test (one-tailed) recommended by Crawford and Garthwaite (2002) was used to make a separate statistical comparison between each patient and the control group on each of the two indices in each test condition. An independent-samples t-test was also used to compare the group of patients ($n = 2$) to controls ($n = 16$).

In another set of analyses, the variability of reaches was assessed by calculating the variance of P for each of the four test configurations, and averaging these to give a mean variability score for each participant. The modified t-test (one-tailed) was used to make a statistical comparison between each patient and the control group.

Finally the kinematics of the movements were analysed, including reaction time, movement time, peak velocity, time to peak velocity and percentage time to peak velocity normalised as a function of movement time. The kinematic data of 11 of the 16 controls were included in the analysis. For 5 of the control subjects the kinematic data had to be excluded due to technical problems with the trigger sent from the shutter glasses to the Optotrak at the time of testing, which caused the timing of the start of the recording to be unreliable. The modified t-test (one-tailed) was again used to make statistical comparisons between each patient and the control group.

3.3 Results

3.3.1 Reaching task:

Figure 3.3 shows the mean changes in reach trajectory (measured as P) that were associated with a 40 mm shift of either the left or right cylinder (i.e. the 'weightings' given to the left and the right cylinder, dP_L and dP_R). It is clear that while a great deal of behavioural variability exists between the control subjects, both DF and SB perform within the normal range, taking account of both the left and the right cylinder when making their reaches. Modified t-test comparisons revealed no significant differences between DF and the controls on either dP_L (t = 1.389, p = 0.092) or dP_R (t = 0.589, p = 0.282). Likewise there were no significant differences between SB and the controls on either dP_L (t = 0.581, p = 0.285) or dP_R (t = 1.052, p = 0.155). In addition, a conventional independent-samples t-test carried out on the data also failed to reveal any significant difference between the patients (n = 2) and the controls (n = 16) on either dP_L (t = 1.383, p = 0.186) or dP_R (t = 1.160, p = 0.263).

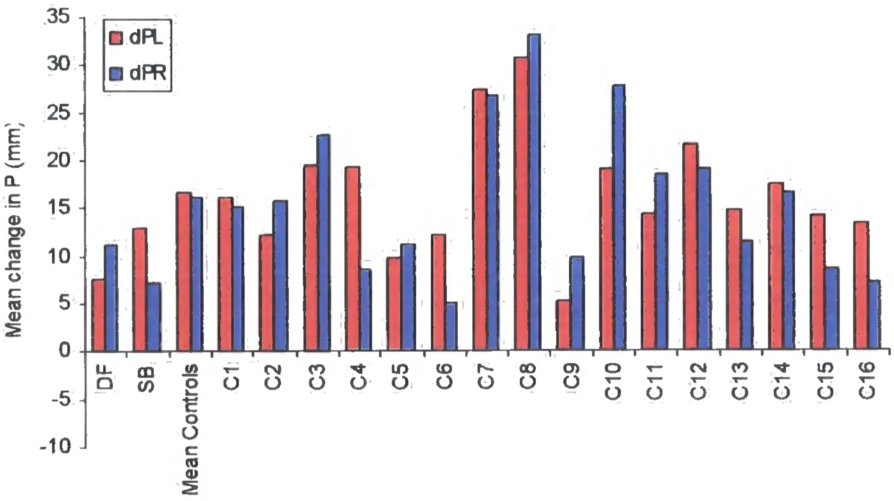

Figure 3.3: The 'weightings' (dP_L and dP_R) given to each cylinder by DF and SB and the controls in the reaching task.

The variance of both patient's P values was higher (DF = 165.75; SB = 544.03) than the controls (Mean Controls = 131.7). Modified t-tests showed that this was significant for SB (t = 3.349, p = 0.004), but not for DF (t = 0.277, p = 0.393).

Table 3.1 shows the kinematic data for DF and SB compared with those of controls. Modified t-tests reveal that there was no difference between DF (t = 1.381, p = 0.094) or SB (t = 0.592, p = 0.281) and controls in terms of reaction time. DF was significantly slower than controls in movement time (t = 2.024, p = 0.031), however there was no difference between SB and controls (t = -0.954, p = 0.178). There was no difference between DF (t = -0.819, p = 0.213) or SB (t = 1.499, p = 0.077) and controls in terms of peak velocity. Similarly there was no difference between DF (t = 1.474, p = 0.081) or SB (t = 2.392, p = 0.015) and controls for time of peak velocity. SB differed from controls in the % time to peak velocity (t = 2.392, p = 0.015), no such difference occurred for DF (t = -0.421, p = 0.340).

	RT (ms)	MT (ms)	PV (mm/s)	TPV (ms)	%TPV
DF	448.75	932.46	1203.43	351.46	37.56
SB	351.25	439.17	2926.58	220.74	50.26
Mean Controls	206.85	603.45	1742.98	238.56	39.46

Table 3.1: The kinematic data for DF and SB comparing them to 11 of the healthy control subjects in the reaching task.

3.3.2 Bisection task:

Figure 3.4 shows the mean change in bisection response (P) that was associated with a 40 mm shift of either the left or right cylinder in the bisection task. It can be seen that

DF lies outside the normal range for dP_L and dP_R, and that SB lies outside the normal range for dP_R. While he remains just within the range of controls on dP_L, his score falls right at the lower end. Modified t-tests reveal a significant difference between DF and controls on both dP_L (t = 2.507, p = 0.012) and dP_R (t = 2.286, p = 0.019) and a significant difference between SB and controls on dP_R (t = 1.778, p = 0.048). The difference between SB and controls on dP_L failed to reach significance (t = 1.245, p = 0.116). Independent t-tests revealed significantly lower values in the patients as a group (n = 2) than in the controls (n = 16) on both dP_L (t = 2.590, p = 0.02) and dP_R (t = 2.867, p = 0.011).

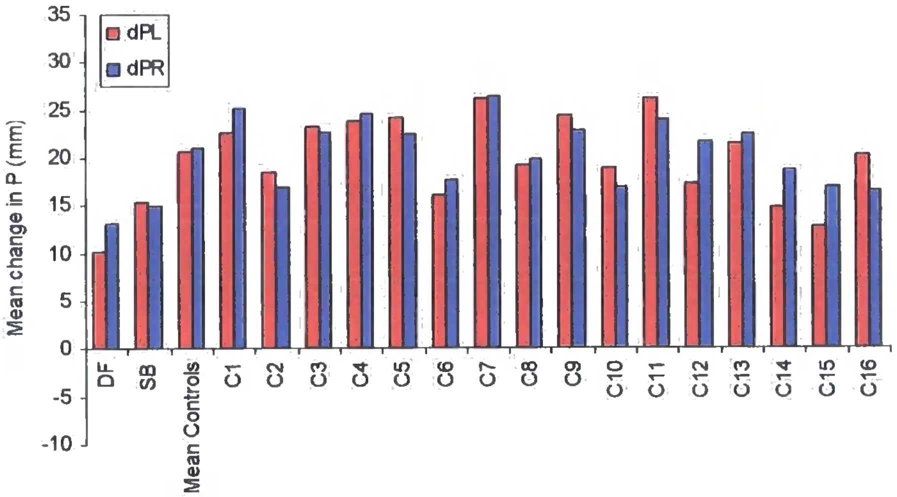

Figure 3.4: The 'weightings' given to each cylinder by DF and SB and the controls in the bisection task.

The variance of the both patients' P values (DF = 133.53; SB = 63.67) was higher than controls (Mean Controls = 61.39). A modified t-test shows that this was significant for DF (t = 3.551, p = 0.001), though not for SB (t = 0.112, p = 0.456).

Table 3.2 shows DF and SB's kinematic data compared to controls for the bisection task. Modified t-tests revealed that there was no difference between DF (t = 0.612, p = 0.275) or SB (t = 1.720, p = 0.053) and controls in terms of reaction time. Both DF (t = 2.207, p = 0.022) and SB (t = 2.093, p = 0.027) differed significantly from controls in movement time. There were no differences between controls and DF (t = -1.315, p = 0.104) or SB (t = -0.860, p = 0.202) for peak velocity. However, DF (t = 1.967, p = 0.034) and SB (t = 3.379, p = 0.002) differed from the controls in time to peak velocity. This was due to the longer movement durations as these differences disappear when time to peak velocity is computed as a % of movement time for both DF (t = -0.042, p = 0.483) and SB (t = 0.848, p = 0.205).

	RT (ms)	**MT (ms)**	**PV (mm/s)**	**TPV (ms)**	**%TPV**
DF	431.46	948.44	564.1	425.42	44.85
SB	580.21	930.63	682.86	538.57	57.87
Mean C	349.2636	602.71	907.6009	267.7645	45.47

Table 3.2: The kinematic data for DF and SB and 11 of the healthy control subjects in the bisection task.

3.4 Discussion

The aim of the present experiment was to examine automatic obstacle avoidance behaviour in two patients with bilateral ventral stream damage resulting in visual form agnosia, when they were asked to reach between or bisect the space between two cylinders varying in location from trial to trial. The results clearly show that both patients shifted their reaching trajectories in response to shifts in cylinder position to an extent that fell within the normal range, despite failing to shift their bisections of the space between the same two cylinders to an appropriate extent. The results provide a clear double dissociation in combination with those of Chapter 2, with optic ataxic patients (see figures 3.5 and 3.6). This double dissociation provides strong evidence to support the role of the dorsal stream in automatic obstacle avoidance. It should be noted however that there are differences in the way the two groups of patients were tested, in that the optic ataxia patients were required to maintain central fixation during the tasks whereas the visual form agnosic patients were allowed free vision. This difference in testing conditions was due to the fact that SB suffers from hemianopia in his left visual field, and this ensured that he could see both of the obstacles.

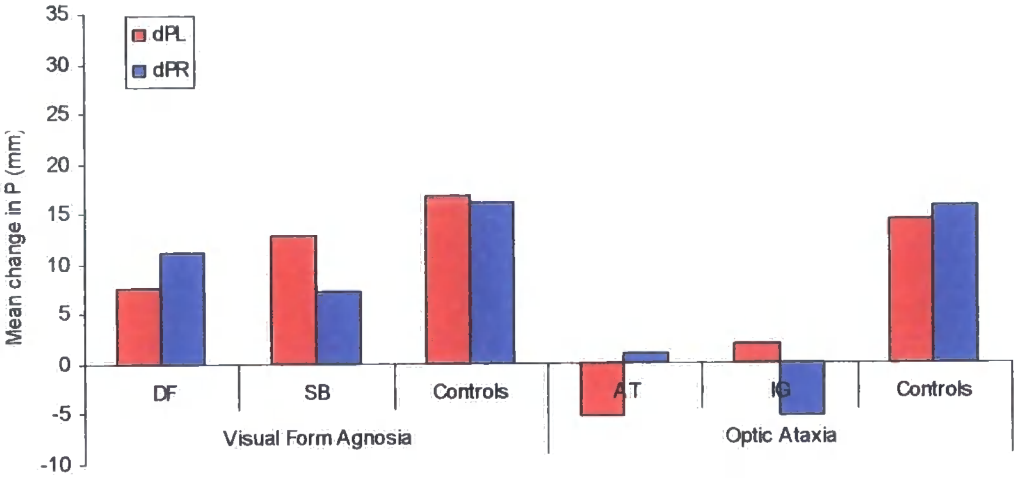

Figure 3.5: The 'weightings' given to the two cylinders by our two visual form agnosic patients (DF and SB) and their control group, and by two optic ataxic patients (AT and IG) and their control group in the reaching task. Graph illustrates that both optic ataxic patients perform worse than visual form agnosic patients and control groups.

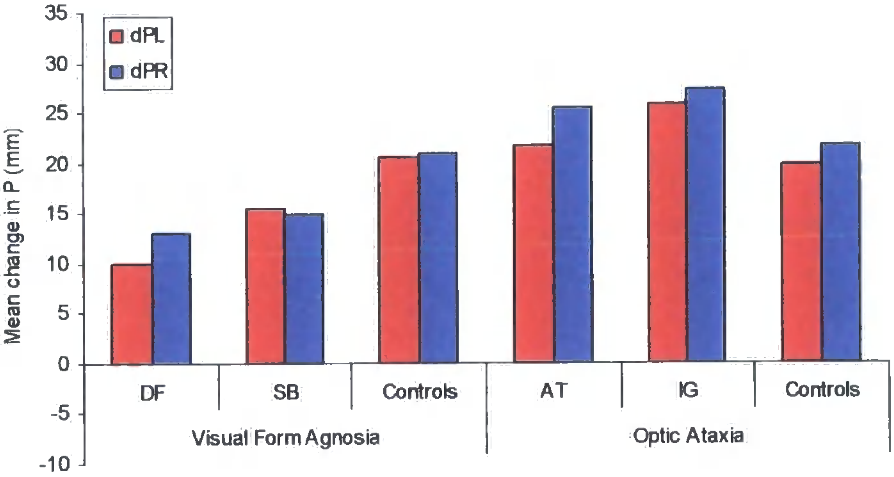

Figure 3.6: The 'weightings' given to the two cylinders by our two visual form agnosic patients (DF and SB) and their control group, and by two optic ataxic patients (AT and IG) and their control group in the bisection task. Graph illustrates that both visual form agnosic patients perform worse than optic ataxic patients and control groups.

The major prediction of this study was that their functionally-intact dorsal streams should allow both DF and SB to perform normally in the reaching task, where no perceptual judgements were required. The prediction as to how they would perform in the bisection task, however, was always less strong, since neither has a totally destroyed ventral stream. James *et al.* (2003) demonstrate that the ventral stream lesion in DF is largely restricted to area LO in healthy individuals. The damage is larger in the right hemisphere than the left, and primary visual cortex as well as lingual and fusiform gyrus are spared. Studies have shown that there is sparing of face selective cortex in the fusiform gyrus (Steeves *et al.*, 2002) as well as the parahippocampal place area (Steeves *et al.*, 2004). These spared ventral stream areas could be implicated in spatial perception in healthy individuals, and this could explain some of DF's preserved abilities in the bisection task. A close look at SB's lesion reveals a similar sparing of some ventral stream areas, particularly in the left hemisphere, which may account for some of his preserved abilities in the bisection task. In sum, it is clear that neither patient has a completely destroyed ventral stream and as such it would be unlikely that either patient would be totally unable to perform the bisection task; indeed both of them did perform at above-chance levels.

It is also important to note that in the bisection task there was no significant difference between SB and controls in the weightings attached to the left pole. This asymmetry may perhaps be explained by the fact that SB has a left hemianopia, and has acquired a compensatory strategy of habitually paying more attention to the left than the right side of space. He could have done this easily in the present task through overt scanning, since there was no requirement to fixate centrally while initially viewing the array. Indirect evidence for this possibility is that SB tended to take long reaction times prior to lifting his finger from the start switch (at which point the shutter glasses closed). Also, it is notable that despite his left visual hemifield being 'blind', SB's responses are more heavily influenced by the left cylinder than the right in both the reaching and bisection tasks. In contrast, in a separate reaching experiment, in which SB was required to fixate on a central target during the viewing period, his responses showed little influence of shifts in the left cylinder, his dP_L value dropping from the present 12.86 mm to a non-significant 3.83 mm, as might be expected.

While the variability of the patients' responses was higher than that of controls in both tasks, this cannot explain the absence of a statistically significant deficit in the reaching task for several reasons. Firstly, the calculation of the weightings attached to the change in position of the left and the right cylinder was based on the mean intercept of the reaches as they crossed an imaginary line joining the cylinders, and as such would not have been affected by the variability of responses. Secondly, while both patients tended to have higher variability of responses than controls in both tasks, the difference was small and non-significant for DF in the reaching task (and for SB in the bisection task). Finally, if variability of responses could explain the data it is unlikely that a dissociation between the two tasks would have emerged, since it was present in both tasks.

The results of the kinematic analyses are consistent with these conclusions, in that overall the patients showed greater deficits relative to the controls on the bisection task than on the reaching task. Although DF moved significantly more slowly than the controls in both tasks, SB did so only in the bisection task. Of course the slower movement times in the bisection task cannot themselves explain the deficits seen in the same task; if anything one would expect a speed-accuracy trade-off. In general the control subjects showed greater dP_L and dP_R values in the bisection than the reaching task, in agreement with previous work (McIntosh *et al.*, 2004a; Chapter 2). In the reaching task, observers shift their reaches less from one object configuration to another than might be expected (i.e. they do not behave like 'ideal observers'). The objects do exert an effect on reaching in all participants, indicating that they act as potential obstacles, but these effects are not so great as to force shifts equal to 50% of the object shifts. In the case of the bisection task, the need for accuracy was reflected in longer reaction times and movement times, and lower peak velocities, than in the reaching task. Presumably the two patients were also themselves reflecting these different task demands in their kinematic behaviour. For these various reasons the weighting indices on the two tasks could not be compared directly with each other. The only appropriate comparisons were between patients and controls on each task separately and not directly between tasks.

It is important to note that while both DF and SB show visual form agnosia, that there are distinct differences between them in their pathology and associated deficits. For example, DF detects high spatial frequencies well, whereas SB performs better at low spatial frequencies; and DF has relatively preserved colour vision, whereas SB is achromatopsic (Lê *et al.*, 2002). SB's right ventral stream damage is more extensive than DF's, and his right parietal lesion is more extensive than DF's left parietal lesion. On the other hand DF has associated sulcal widening that is less apparent in SB, and she sustained her brain damage in adulthood rather than childhood. Finally, SB's extensive right hemisphere (including white matter) damage has resulted in a hemianopia in his left visual field, whereas DF has a smaller lower visual-field scotoma. The remarkable thing is that despite all of these differences, the two patients behaved in a comparable fashion in the two tasks. Such an observation is consistent with the findings of Dijkerman *et al.* (2004) who illustrate similar behaviour in DF and SB on a number of visuo-motor tasks, for example both patients show deficits in monocular grasping and in anticipating a comfortable wrist posture when grasping an object.

In conclusion, both DF and SB shifted their trajectories with respect to shifts in cylinder location when asked to reach between two cylinders in the same manner as controls, while showing a reduced influence of the same two objects when required to make an explicit bisection judgement between them. This pattern of data can be interpreted in terms of automatic obstacle avoidance being an implicit skill, whereby movement programming is modified as a function of non-target objects. In line with previous findings with neglect patients (McIntosh *et al.*, 2004a) and optic ataxic patients (Chapter 2), it is suggested that the present data provide further convergent support for the view that automatic obstacle avoidance is a function of the dorsal stream of visual processing. When this system is damaged, the automatic motor adjustments are absent; whereas when either the ventral stream or the largely temporo-parietal systems associated with spatial neglect are damaged, these adjustments remain intact. The results extend the functional description of the ventral and dorsal streams that has been developing over recent years (Milner and Goodale, 1995; Goodale and Milner, 2004). Just as the dorsal stream is intimately involved in the transformation of target properties such as size and location into motor coordinates for programming and controlling reaching and grasping movements, so also it appears to take into account the location of non-target stimuli when programming such movements.

CHAPTER FOUR: DELAY IMPROVES VISUOMOTOR DEFICITS IN UNILATERAL OPTIC ATAXIA

4.1 Introduction

When one considers vision for action and vision for perception it is clear that these two systems must operate on different time scales. In vision for action the target is likely to change co-ordinates on a moment-to-moment basis and therefore it could lead to imprecise actions if the system held this information over a long time scale. Vision for perception on the other hand would not require such a constraint. Bridgeman *et al.* (1997; 2000) suggest that there are two functionally distinct representations of the visual world in humans, one which holds information used in perception (a cognitive map) and the other which drives visually guided behaviour (a motor map) (figure 4.1). This model shows that after a common input from early visual areas, spatial information is mapped separately into a cognitive and a motor representation. Extraretinal information is supplied to these maps separately (as it will affect them differently). If the motor map has no spatial information, it can receive information from the cognitive map. If a subject is asked to carry out a perceptual task, the information in the cognitive map is assessed; this map has sensitivity to small motions or translations of objects in the visual scene however it is insensitive to the absolute egocentric calibration of visual space. On the other hand the motor map, whose contents are not necessarily available to the perceptual system, is not as sensitive as the cognitive map, however it is robust; it is not subject to visual illusions, it has only an extremely short-term memory in that it uses currently available visual information to guide action. If a delay in response is required, the system takes its spatial information from the cognitive map.

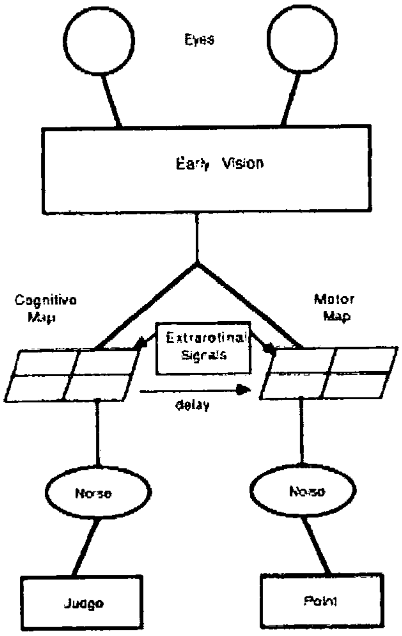

Figure 4.1: Diagram showing the proposed information flow scheme for perceptual judgements and visually guided behaviour. From Bridgeman (1997).

Hu *et al.* (1999) carried out a study to investigate the effects of delay on the kinematics of grasping in normal subjects. They had four conditions: (1) Open loop delayed grasping;(2) Open loop immediate grasping; (3) Closed loop immediate grasping; (4) Delayed perceptual matching. The results showed that there were no kinematic differences between the open and closed loop immediate grasping conditions. When subjects carried out the task in open loop delay however reaches took significantly longer, they achieved peak velocity earlier and grip aperture was significantly larger. They conclude that motor actions performed after a delay use different transformations than those used in immediate action and that the visual information used to drive delayed actions arises from perceptual rather than visuomotor analysis of the target. Hu and Goodale (2000) suggest that the computations of required coordinates for action are computed immediately in egocentric coordinates before movements are initiated and it makes little sense to store these coordinates. Evidence has suggested that this begins to decay in less than 800 ms for saccades (Gnadt *et al.*, 1991) and in less than 2 seconds for manual aiming movements (Goodale *et al.*, 1994c). Vision for perception on the other hand is computed in an allocentric frame of reference. Hu and Goodale (2000) asked participants to either grasp or estimate the size of objects, either under immediate conditions or when a five second delay was required before responding. The results showed that in the delayed grasping condition subjects showed evidence of a size-contrast effect, whereas in the immediate condition they did not. For size estimation the size-contrast effect was found under both immediate and delayed conditions. They conclude that immediate visuomotor control relies on absolute metrics, whereas delayed grasping uses the same relative metrics as that used by conscious perception. Evidence in support of this interpretation comes from Wong and Mack (1981) who provided evidence that immediate visuomotor responses depend on egocentrically coded spatial information, while perceptual judgements and delayed visuomotor responses tend to be driven by allocentric information. They showed participants a small target surrounded in a frame, which disappeared for 500 ms and then reappeared with the frame displaced and the target in the original position. Participants reported that they thought the target had moved (not the frame) however they consistently directed their eye-movements to the true location of the target. When a delay was required before making the eye movements, however, responses were made to the perceived target location not the true one.

Taken together, the evidence suggests that when normals are required to carry out a visuomotor task under immediate conditions an egocentric representation of the spatial location is computed by the dorsal stream of processing, whereas when a delay is required this representation quickly decays and the subject will rely on the perceptual representation (computed in an allocentric framework) created by the ventral stream to carry out the task. For a perceptual task, normals will use the perceptual representation created by the ventral stream, and when a delay is required they will still be able to rely on this representation as it is long lasting.

Evidence to support this theory has been provided from testing patients with visual form agnosia. Goodale *et al.* (1994c) showed that when DF was required to carry out immediate grasping tasks she could accurately calibrate her grip, but when a delay of two seconds was imposed her performance fell to chance. It was shown that this could not be accounted for by problems with imagery or understanding as she could accurately pantomime actions to objects. Milner *et al.* (1999a) carried out a study looking at manual reaching and saccadic eye movements to peripheral visual targets in DF in real time and following a delay. In the immediate saccade task DF performed similarly to controls, however in the delayed task DF showed a significantly reduced performance compared to controls. A similar pattern of results was observed for the manual reaching movements, in that DF performed similarly to controls in the immediate condition, however, a decrease in accuracy was observed in the delayed condition. The authors argue that these results suggest that the visuomotor system DF uses is highly time limited (i.e. the dorsal stream is responsible for controlling movements in the 'here and now' and thus her performance falls when a delay is introduced). They also discuss these findings, along with others, in terms of the ego- / allo-centric coding of space, in that visuomotor tasks require egocentric coding whereas perceptual tasks require allocentric coding; DF is not capable of this allocentric coding. One other possible explanation for this is that frontal damage interferes with DF's spatial working memory. Early reports on DF (Milner *et al.*, 1991) have shown that she has some bilateral prefrontal damage. Evidence has shown that short-term working memory for spatial location depends on prefrontal mechanisms (Funahashi *et al.*, 1989, 1993). However the authors suggest that this explanation is unlikely, due to the fact that DF has difficulty with many perceptual tasks not requiring a memory component and also that when asked to perform an anti-saccade task DF would never move her eyes in the wrong direction (which would be expected if prefrontal damage were severe enough to cause a profound disruption of spatial coding). They conclude that although DF is unable to code spatial locations in allocentric co-ordinates, she copes in the spatial world well as by using egocentric coordinates to code location.

Evidence from patients with optic ataxia has also been taken as support for this theory. Milner *et al.* (1999b) tested patient AT (see chapter 2) and normals on an immediate and delayed pointing task. Results showed that AT responded more promptly and accurately in the delayed task than the immediate whereas normals were more accurate at the immediate task. Milner *et al.* (2001) carried out two further studies to address this issue. In experiment one, they measured maximum grip aperture while patient IG (see chapter 2) carried out a perceptual matching task, delayed real grasping, and delayed pantomimed grasping. Results showed that in the perceptual task maximum grip aperture was in proportion to size of object. In the delayed pantomimed grasping task reliable grip scaling was observed. In the delayed real grasping weak evidence of grip scaling was observed, but when compared to immediate conditions, significant scaling was observed. There was also a notable reduction in exaggerated grip size from first to second testing block. In experiment two they attempted to determine if IG's improvement in real grasping from first to second testing block is due to use of pantomiming strategy. They measured maximum grip aperture while IG and normals reached to grasp blocks in a delayed real grasping task where the width of the objects is changed during the delay. Results showed that while normals reached maximum grip apertures consistent with width of the object, IG always had wide grip aperture when target was initially wide even when the object had been changed to narrow during the delay. These studies were taken as evidence of the time scale in which the two visuomotor control systems operate in superior parietal lobe. For immediate tasks a visuomotor system (damaged in optic ataxia) comes into play, when delay is required and this system is not acted upon this decays and a more flexible visuospatial system comes into play. In a recent study, Himmelbach and Karnath (2005) asked two optic ataxic patients to point to targets with delays ranging from 0 to 10 seconds. This showed that pointing errors decreased as the delay period increased, the authors interpret this finding as suggesting that there is a gradual change between the dorsal and ventral control of reaching rather than a sudden switch. This contradicts earlier findings (Westwood and Goodale, 2003) which have suggested that the change from dorsal to ventral control, in the case of grasping at least, takes place immediately after the target disappears.

In Balint's (1909) (reprinted in 1995) original report on optic ataxia it was noted that the inaccuracies of manual control seen in optic ataxia are frequently restricted to one hand. Perenin and Vighetto (1988) showed that optic ataxia patients with damage to the right hemisphere generally show deficits related to the contralateral visual field, whereas patients with damage to the left hemisphere in addition to a visual field effect often show deficits related to the contralateral hand. Revol *et al.* (2003) recently attempted to address the pointing deficits associated with unilateral optic ataxia using detailed error analysis. They tested a unilateral optic ataxic patient (OK), with damage to the right hemisphere on immediate and delayed pointing tasks with both the contralateral and ipsilateral hand to targets in both the contralateral and ipsilateral visual field. They found a combination of errors related to the visual field (i.e. errors occurred in the left visual field, independent of hand used) and the hand (i.e. errors with the left hand, independent of visual field). (It should be noted however that the errors related to the visual field were expressed in terms of accuracy and variability, whereas errors related to hand were expressed only by variable errors). In addition they found that a five second delay improved the variability of the pointing errors due to the visual field effect. They conclude that optic ataxia is not a general deficit of action or visuomotor transformation but a specific deficit in real time action, and further suggest that optic ataxia may in fact be a temporal rather than a spatial disorder.

The aim of the present experiment is to determine if a unilateral optic ataxic patient (MH), with damage to the left hemisphere, has difficulty in reaching between two obstacles, and to examine if this can be dissociated from the bisection of space between the objects, as demonstrated in our recent study with bilateral patients (Chapter 2); the hand-field combinations of any deficits shall also be examined. In addition this experiment will examine if a 5 second delay will improve the accuracy of reaching between two obstacles by allowing ventral stream involvement. It is predicted, based on the results of a previous study with MH (M.G. Edwards *et al.*, unpublished data) and previous work with bilateral optic ataxia patients (Chapter 2) that MH will show impaired performance on an obstacle avoidance task. However, since MH is only impaired at pointing with his right hand to targets in his right visual field, it was also predicted that this impairment will be restricted to a reduced weighting attached to the right obstacle when using his right hand. Finally, it was predicted that a delay will result in an increase in the weighting attached to the right obstacle when using his right hand.

4.2 Method

4.2.1 Participants:

One patient with unilateral parietal damage resulting in optic ataxia (MH) took part in this experiment along with eight healthy age-matched controls between 44 and 60 years old. All subjects were right-handed by self-report, had normal or corrected to normal vision and no history of neurological disorder. Patient MH was aged 50 at the time of testing, his optic ataxia resulted from an anoxic incident 8 years prior to testing (figure 4.2). No clinical signs of neglect were observed. Edwards *et al.* (unpublished data) recently tested MH on a pointing task with both the left and right hand to targets in the left and right visual field. Results showed that MH only exhibited abnormal pointing errors when he used his right hand and when targets are in his right visual field. In addition, Edwards *et al.* (unpublished data) investigated MH's ability to predict movement, while control subjects showed a correlation between speed of the hand and speed of the ball, MH showed no such correlation when the ball was in the right side of space or when he uses his right hand.

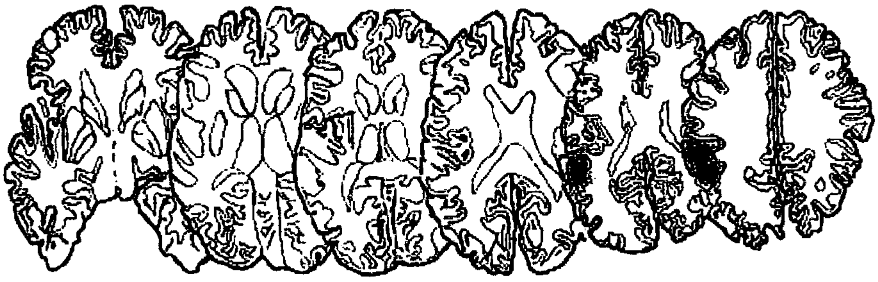

Figure 4.2: CT scan of patient MH reveals unilateral damage of the left angular and supermarginal gyrus and bilateral damage of the lentiform and caudate nucleus

4.2.2 Experimental equipment:

The experimental set-up used in the present experiment is depicted in Chapter 2 (see figure 2.3). Liquid crystal shutter glasses (Plato System, Translucent Technologies, Toronto, CA) were used which were programmed to open for 2 seconds at the beginning of each trial. A tone was used to indicate that participants should initiate their response, this occurred immediately after the shutter glasses closed (immediate condition) or 5 seconds after the shutter glasses closed (delayed condition). Hand movements of patient MH were recorded using a ProReflex System. Responses were recorded by sampling the position of a marker attached to the nail of the right index finger, at a sampling frequency of 200 frames per second (5ms/frame), accuracy was set to 0.1mm. For control participants hand movements were recorded using Optotrak (Northern Digital Inc., Waterloo, Ontario); responses were recorded by sampling the position of a marker attached to the nail of the right index finger, at a sampling frequency of 100 Hz. For both the reaching and the bisection task the movements were recorded in full (i.e. from the initial start position to movement offset); for the immediate condition movements were recorded for a total of ten seconds and for the bisection task they were recorded for five seconds. Both start position and end position were defined as that recorded on the frame at which hand velocity fell below a threshold of 50 mm/s.

4.2.3 Procedure:

Participants were required to perform the reaching task with both hands under immediate and delayed conditions and the bisection task with both hands under immediate conditions (this was due to time constraints and the fact that the hypothesis predicted improved performance following a delay in the reaching task only). As such there were six separate blocks, performed in the following order: (1) Immediate reach, Right hand; (2) Delayed reach, Right hand; (3) Bisection, Right hand; (4) Immediate reach, Left hand; (5) Delayed reach, Left hand; (6) Bisection, Left hand. Participants were informed to place their right or left index finger (depending on condition) on the start button when they were ready to begin each trial. The shutter glasses then opened for 2 seconds during which time participants were instructed to fixate on a central cross, located at the back of the stimulus board, 16 cm above the surface. They were instructed to make their response when they heard the tone, in the immediate condition this occurred immediately as the shutter glasses closed and in the delayed condition it occurred 5 seconds after the shutter glasses closed. In the reaching task subjects were required to reach out and touch a target zone located beyond the two cylinders, they were instructed that the emphasis on this task is speed of movement. Participants were instructed that when a cylinder was present there would be one on the left and one on the right and they should pass their hand between the two cylinders rather than around the outside edge of the board. Each participant made 60 reaches in a fixed pseudo-random order, with 12 trials for each of the four cylinder configurations and one in which no cylinders were present (these types of trials were included as a control condition to check for any systematic bias when the reaching response was not constrained by any potential obstacles, and were not included in the main analysis). In the bisection task participants were informed that the position of the cylinders would vary from trial to trial, but there would always be one on the left and one on the right. They were instructed to indicate where they estimated the midpoint was between the two cylinders, they were instructed that the emphasis on this task was on accuracy of judgement. Each participant made 48 bisection responses, which involved 12 trials for each of the stimulus configurations, presented in a fixed pseudo-random order.

4.2.4 Analysis:

Values of the dependent variable P were computed as described in Chapter 3 on each trial. The analyses carried out were also the same as outlined in Chapter 3.

4.3 Results

4.3.1 Immediate Reaching task:

Figure 4.3 illustrates the weightings attached to the left and right pole in the immediate reaching task with both the left and the right hand for MH and controls. Modified t-tests were conducted on these data, which revealed that for the left hand there was no significant difference between MH and controls for dP_L (t = -1.114, p = 0.151) or dP_R (t = -0.426, p = 0.342). For the right hand there was no significant difference between MH and controls for dP_L (t = -0.927, p = 0.192), however a significant difference exists for dP_R (t = -2.954, p = 0.011).

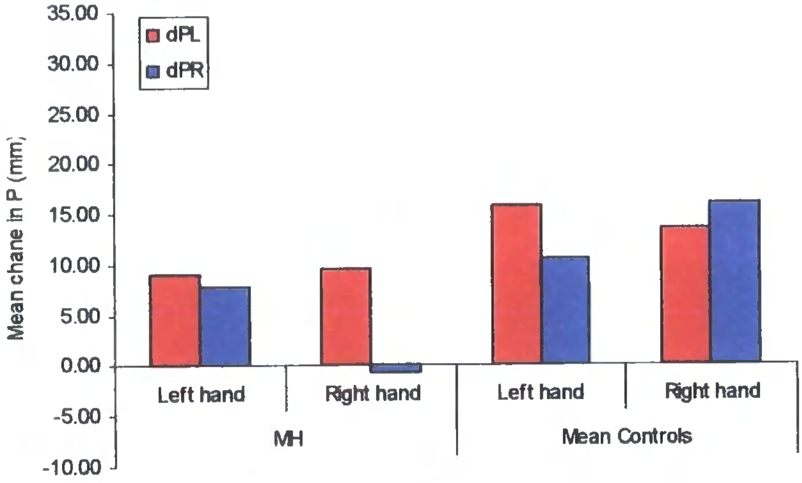

Figure 4.3: Graph illustrating the weightings attached to shifts in the left and the right pole in the immediate reaching task with the left and right hand. The left side of the graph depicts results for MH the right side depicts mean controls (n = 8).

The variability of each participant's trajectory, as measured by the mean variance of P, was computed. The pattern of results shows that MH's variability is higher than controls with both the left hand (MH = 130.69) (Mean controls = 96.72) and the right hand (MH

= 283.81) (Mean controls = 112.30). A modified t-test conducted on this data showed that this difference reaches significance with the right hand (t = 2.22, p = 0.031), but not the left (t = 0.944, p = 0.188).

Table 4.1 illustrates the kinematic data for MH and controls. Modified t-tests were conducted on this data, which revealed, for reaction time there was a significant difference between MH and controls with the right (t = 4.417, p = 0.002) and the left hand (t = 4.922, p = 0.001). For movement time, there was a non-significant difference between MH and controls for the right (t = 1.276, p = 0.121) and the left hand (t = 1.279, p = 0.121). For peak velocity there was a non-significant difference between MH and controls for both the right (t = -0.870, p = 0.206) and the left hand (t = -0.842, p = 0.214). There was a significant difference between MH and controls in time of peak velocity for the right (t = 2.041, p = 0.040) and the left hand (t = 2.776, p = 0.014). This difference however disappears when time to peak velocity is computed as a function of movement time for both the right (t = 0.615, p = 0.279) and the left hand (t = 0.380, p = 0.358).

Table 4.1: Table of kinematic data for MH and controls participants for the right and the left hand. Including reaction time (RT), movement time (MT), peak velocity (PVEL), time of peak velocity (TPV) and percentage time of peak velocity (%TPV)

	MH		Mean controls	
	Right hand	Left hand	Right hand	Left hand
RT (ms)	591.43	562.5	338.65	285.55
MT (ms)	789.6	826.88	592.6	627.08
PVEL (mm/s)	1321.8	1300.71	1685.7	1555.56
TPV (ms)	314.29	334.09	211.15	227.24
%TPV (%)	39.8	40.4	36.27	37.34

4.3.2 Delayed reaching task:

Figure 4.4 illustrates the weightings attached to the left and right pole in the delayed reaching task with both the left and the right hand for MH and controls. A modified t-test was conducted on this data, which revealed that for the left hand there was no significant difference between MH and controls for dP_L (t = 0.829, p = 0.217) or dP_R (t = 0.251, p = 0.404). In addition, for the right hand there was now no significant difference between MH and controls for dP_L (t = 0.042, p = 0.484) or dP_R (t = -1.142, p = 0.145).

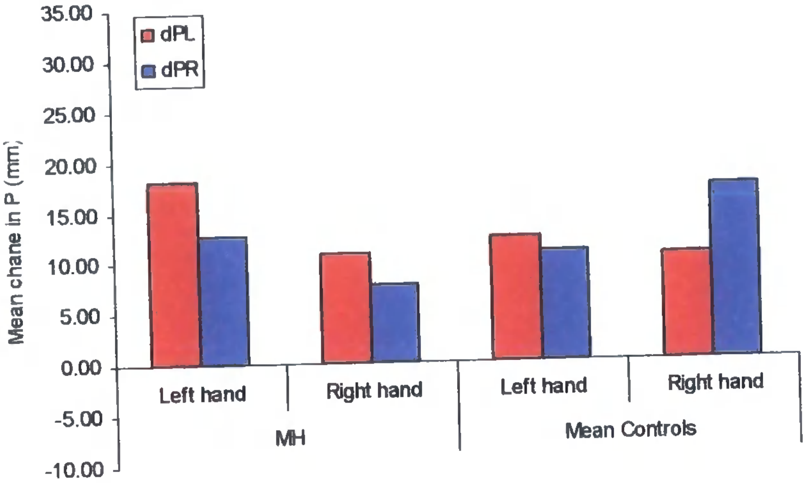

Figure 4.4: Graph illustrating the weightings attached to shifts in the left and the right pole in the delayed reaching task with the left and right hand. The left side of the graph depicts results for MH the right side depicts mean controls (n = 8).

The variability of each participant's trajectory, as measured by the mean variance of P, was computed. The pattern of results shows that MH's variability is lower than controls with both the left hand (MH = 98.11) (Mean controls = 155.93) and the right hand (MH = 75.50) (Mean controls = 180.96). A modified t-test conducted on this data showed that this difference is not significant for either the right hand (t = -1.244, p = 0.127), or the left (t = -0.76, p = 0.236).

Table 4.2 illustrates the kinematic data for MH and controls. A modified t-test was conducted on this data, which revealed, for the variable reaction time there was a non-significant difference between MH and controls for the right (t = 1.136, p = 0.147) but a significant one for the left hand (t = 4.169, p = 0.002). For the variable movement time, there was a non-significant difference between MH and controls for the right (t = 1.817, p = 0.056) and the left hand (t = 1.440, p = 0.096). For peak velocity there was a non-significant difference between MH and controls for both the right (t = -1.231, p = 0.129) and the left hand (t = -1.182, p = 0.138). There was a significant difference between MH and controls in time of peak velocity for the right (t = 2.406, p = 0.024) and the left hand (t = 1.964, p = 0.045). This difference however disappears when time to peak velocity is computed as a function of movement time for both the right (t = 0.198, p = 0.424) and the left hand (t = 0.517, p = 0.310).

Table 4.2: Table of kinematic data for MH and controls participants for the right and the left hand. Including reaction time (RT), movement time (MT), peak velocity (PVEL), time of peak velocity (TPV) and percentage time of peak velocity (%TPV)

	MH		Mean controls	
	Right hand	Left hand	Right hand	Left hand
RT (ms)	447.44	531.90	358.66	300.89
MT (ms)	844.51	859.51	554.32	597.99
PVEL (mm/s)	1104.46	1035.66	1693.76	1502.33
TPV (ms)	312.33	338.10	195.91	202.37
%TPV (%)	36.98	39.34	36.01	34.10

4.3.3 Bisection task:

Figure 4.5 illustrates the weightings attached to the left and right pole by MH and controls in the bisection task with the left and the right hand. For the left hand no significant difference exists between MH and controls for dP_L (t = -1.468, p = 0.093) however a significant difference exists for dP_R (t = -2.281, p = 0.028). For the right hand there was no significant difference between MH and controls in dP_L (t = -1.801, p = 0.057) but a significant difference exists in dP_R (t = -2.198, p = 0.032).

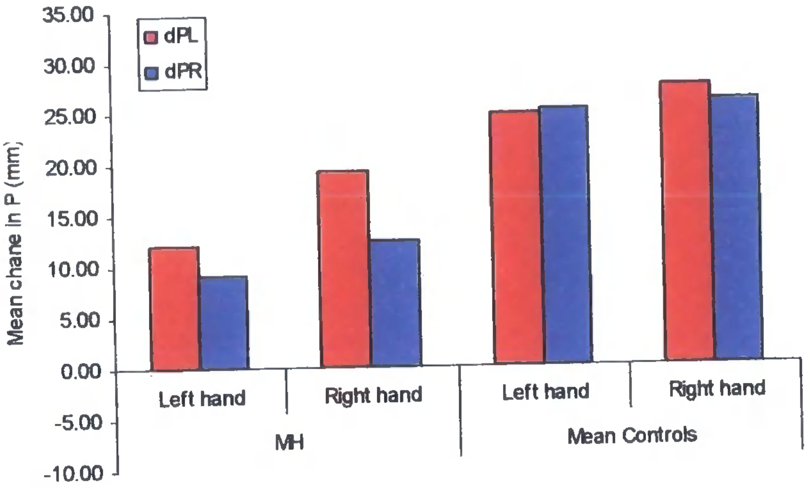

Figure 4.5: Graph illustrating the weightings attached to shifts in the left and the right pole in the bisection task with the left and right hand. The left side of the graph depicts results for MH the right side depicts mean controls (n = 8).

The variability of each participant's trajectory, as measured by the mean variance of P, was computed. The pattern of results shows that MH's variability is higher than controls for both the left hand (MH = 107.42) (Mean controls = 72.37) and the right hand (MH = 203.21) (Mean controls = 108.13). A modified t-test conducted on this data showed that this difference does not reach significance for either the left hand ($t = 1.474$, $p = 0.092$) or for the right hand ($t = 1.431$, $p = 0.098$).

Table 4.3 illustrates the kinematic data for MH and controls in the bisection task. A modified t-test was conducted on these data and revealed that for the variable reaction time MH was significantly slower than controls with both the right ($t = 5.559$, $p < 0.001$) and the left hand ($t = 4.699$, $p = 0.001$). MH's movement time was significantly slower than controls with the right ($t = 5.456$, $p < 0.001$) but not the left hand ($t = 1.387$, $p = 0.104$). In addition, MH's peak velocity was slower than controls with the right (t =

-2.884, p = 0.012) but not the left hand (t = -1.462, p = 0.094). While MH's time of peak velocity was significantly later with the right (t = 5.531, p < 0.001) and the left hand (t = 3.046, p = 0.009), this can be accounted for by increased movement times as when time of peak velocity is computed as a function of movement time there is no significant difference between MH and controls with either the right (t = 0.038, p = 0.486) or the left hand (t = 0.444, p = 0.335).

Table 4.3: Table of kinematic data for MH and controls participants for the right and the left hand. Including reaction time (RT), movement time (MT), peak velocity (PVEL), time of peak velocity (TPV) and percentage time of peak velocity (%TPV).

	MH		Mean controls	
	Right hand	Left hand	Right hand	Left hand
RT (ms)	764.89	730.63	352.58	354.84
MT (ms)	962.80	784.97	541.72	591.48
PVEL (mm/s)	591.82	664.06	957.72	886.44
TPV (ms)	384.19	338.13	213.41	233.88
%TPV (%)	39.90	43.07	39.70	40.35

4.4 Discussion

The aim of the present experiment was to determine if a unilateral optic ataxic patient (MH), with damage to the left hemisphere would have difficulty in reaching between two obstacles and to examine if a five second delay would improve the accuracy of reaching between the two obstacles by allowing ventral stream involvement. It was predicted, based on the results of a previous study with MH (M.G. Edwards *et al.*, unpublished data) and previous work with bilateral optic ataxia patients (Chapter 2) that MH would show impaired performance on an obstacle avoidance task, and this impairment would be restricted to a reduced weighting attached to the right obstacle when using his right hand; also that a delay would result in improved performance. The results confirm all the predictions made, that is MH attached a reduced weighting to shifts in the right obstacle when using his right hand under immediate reaching conditions, however when a delay was required before response this deficit disappeared.

These results support the conclusions of chapters 2 and 3, that obstacle avoidance behaviour is a function of the dorsal stream, damaged in patients with optic ataxia and preserved in patients with visual form agnosia. It also provides evidence to suggest that this behaviour is lateralised, in that the left dorsal stream subserves the avoidance of obstacles in the contralateral visual field with the contralateral hand. This confirms previous observations with patient MH (M.G. Edwards *et al.*, unpublished data), who shows visuomotor deficits when using his right hand to catch or point to targets in his right visual field. It builds upon previous data which suggest an asymmetry in hand / field effects depending on side of the lesion. Perenin and Vighetto (1988) showed that optic ataxia patients with damage to the right hemisphere show deficits related to a visual field effect, patients with damage to the left hemisphere in addition to a visual field effect show deficits related to a hand effect. As a partial exception to this rule, Revol *et al.* (2003) showed that an optic ataxic patient (OK) with damage to the right hemisphere exhibited a combination of errors related to visual field effect (i.e. errors occurred in the left visual field, independent of hand used) and hand effect (i.e. errors with the left hand, independent of visual field). However OK's errors related to the visual field effect were expressed in terms of both absolute accuracy and variable error, whereas errors related to hand effect were expressed only by variable errors. Thus patient MH, while exhibiting asymmetry in hand / field effects, does not display a traditional pattern of optic ataxic errors. We would expect based on our findings that he would show obstacle avoidance deficits in his right visual field with both hands and deficits when using his right hand in both visual fields. However it is important to note that the method of analysing the results of the present experiment are somewhat different to previous methods of analysing optic ataxia errors, in that in the present experiment an analysis of weightings were taken, whereas previous experiments have used errors as the dependent variable. To gain further insights into the lateralisation of obstacle avoidance behaviour, it will be necessary to obtain data using the tasks employed in the present experiment with a patient with damage to the right hemisphere.

The results of the present experiment further confirm previous work with optic ataxic patients (Milner *et al.*, 1999b, 2001; Revol *et al.*, 2003) showing that a delay before response improves visuomotor deficits, extending these previous findings to the domain of obstacle avoidance behaviour. This can be interpreted as providing further evidence for the time scale in which the dorsal and ventral stream operate. That is, under immediate conditions obstacle avoidance requires recruitment of the dorsal stream (damaged unilaterally in patient MH), whereas under delayed conditions this representation decays and the ventral stream is required to carry out the task (presumed intact in patient MH). This time scale for which obstacle avoidance behaviour operates on makes sense as it is likely that the position of obstacles in the workspace could change on a moment to moment basis and as such if the representation created is long lasting it is likely to increase the chances of collision should the representation be acted upon under delayed conditions.

The present experiment also provides some evidence of the time scale for the change from a dorsal to ventral representation. Westwood and Goodale (2003) suggested that such a change occurs immediately after the target disappears; the present study provides evidence directly against this finding. In the immediate reaching condition participants are required to perform their movement on the onset of the close of the shutter glasses. If the dorsal representation decays immediately after the target disappears it would be expected that MH would show no deficit in this reaching task, as the ventral stream would be recruited immediately after the glasses close. This is however not the case, MH fails to take account of the right pole when using his right hand when required to respond immediately after the glasses close. A delay of 5 seconds however improves his performance suggesting that the ventral representation cannot be accessed immediately after the target disappears. This could be taken as evidence to support recent work by Himmelbach and Karnath (2005) who have shown that there is a gradual change between a dorsal and ventral representation (i.e. the longer the delay the more optic ataxic errors improve). To gain further insights into this it would be necessary to vary the delay in the obstacle avoidance task to assess if there is an increase in weighting attached to the poles as the delay increases.

One surprising result arose in the bisection task it was shown that MH shifts his response in a similar way to control participants for shifts in the left cylinder but not the right. One argument may be that the observed deficits in obstacle avoidance behaviour may be due to the fact that MH has difficulty with objects in his right visual field. This however cannot explain the results of the present experiment for several reasons, first in the immediate reaching task MH did not show deficits with the right pole when using his left hand. Second, when a delay was required before response the deficits with the right pole show a recovery. Finally previous studies with MH have shown that he shows deficits in visuomotor behaviour in his right visual field only when using his right hand (M.G. Edwards *et al.*, unpublished data). Taken together, these results provide evidence to suggest that MH's obstacle avoidance deficits cannot be explained by the fact that he has problems with objects in his right visual field. The kinematic results of the bisection task also fail to account for his preserved performance with the left pole but not the right pole on the bisection task. Based on observations with immediate and delayed reaching it would be expected that if MH slows down his responses on the bisection task he may perform better. The opposite pattern of results is, however, observed as MH has a significantly slower movement time and peak velocity (when compared to control participants) when using his right but not his left hand. In addition, MH's lesion includes inferior parts of the left parietal lobe, which may cause some impairment in localizing objects in the right half of his perceptual representation of space, thus leading to reduced weighting attached to the right pole during the bisection task.

Another argument that may be raised to explain the results of the present experiment is that the deficits in the immediate reaching task can be explained by the fact that the variability of MH's reaches was higher than control participants. This cannot be the case for several reasons. Firstly in the immediate reaching task the deficits in obstacle avoidance occurred only for the right hand, yet the variability was higher for reaches with both the right and the left hand. In addition in the bisection task, MH performed significantly different from controls on the weighting he attached to the right pole with both hands, yet in both cases the variability of his responses was not significantly different from controls. Finally, the calculation of the weightings attached to the change in position of the left and the right cylinder was based on the mean intercept (P) of the reaches as they crossed an imaginary line joining the cylinders, and as such would not have been affected by the variability of responses. As such while the variability of MH's reaches may be significantly different from controls in the immediate reaching task, this cannot explain the observed deficits in obstacle avoidance behaviour.

Kinematic variables are also unable to explain the pattern of results of this study. The kinematic results of the immediate reaching task reveal that MH's reaction time is significantly slower than controls for both hands, in the delayed condition on the other hand he only shows significantly longer reaction times with the left hand. The longer reaction times cannot explain the results of the immediate reaching task as reaction times are longer with both the right (591.43 ms) and the left hand (562.5 ms), yet the observed deficit occurs only with the right hand and only affects the obstacle on the right side of space. The improved performance in the delayed reaching task can also not be explained by reaction time patterns. If normal reaction time with the right hand under delayed conditions can explain the improved performance it would be expected that in the immediate condition he would show deficits using both hands as he is significantly different from normals with both hands. The fact that MH shows longer reaction times than control participants could be due to the fact that he has gained some awareness that if he delays his response his performance improves, though as a general rule neurological patients almost always show slowed reaction times (one notable exception being patient IG – see Chapter 3). In both the immediate and delayed reaching task MH was shown to have a later time to peak velocity than control participants, this difference disappears however when time to peak velocity is computed as a function of movement time, and as such any differences observed can be accounted for by the fact that MH has longer movement times than controls (although these are non-significant for all conditions).

In conclusion, the results of the present experiment show that a unilateral optic ataxic patient, following a left hemisphere lesion, shows impaired obstacle avoidance behaviour for obstacles in his right visual field when using his right hand. Such a deficit shows recovery however, when a 5 second delay is required before response. These results can be taken as further evidence to show that automatic obstacle avoidance is a function of the dorsal stream of processing (Chapters 2 and 3). However, when either reaching is delayed or a conscious bisection judgement is required a more flexible visuospatial coding system comes into play mediated by the ventral stream of processing. This change from a dorsal to a ventral representation may not occur immediately after a target disappears, instead these data suggest that a gradual change from dorsal to ventral representation takes place.

CHAPTER FIVE: CATCHING UNDER MONOCULAR AND BINOCULAR CONDITIONS IN VISUAL FORM AGNOSIA

5.1 Introduction

Visual form agnosia patients typically have difficulty recognising and discriminating form, due to damage in their ventral visual pathway (see general introduction for further details of visual form agnosia). Despite these perceptual problems, such patients display intact visuomotor behaviour. For example, patient DF (Milner *et al.*, 1991) has been shown to be able to grasp objects appropriately (Goodale *et al.*, 1994a; Carey *et al.*, 1996), to orient her wrist appropriately when attempting to post her hand through a slot placed in various orientations (Milner *et al.*, 1991) and to automatically avoid obstacles in her workspace (chapter 3). These preserved perceptual abilities, and deficits in visuomotor behaviour have been taken as evidence to support the Milner and Goodale model (1995) (see general introduction for further details). That is, DF has preserved visuomotor behaviour as a function of her intact dorsal stream of processing, and her perceptual deficits can be accounted for by bilateral damage to the ventral stream.

To date DF's intact visuomotor behaviour has been investigated by using relatively simple spatial tasks. The present experiment attempted to expand upon this literature by investigating how DF performs in more complex visuomotor tasks such as catching and how she responds to online perturbations. Catching is a particularly interesting behaviour as it requires the processing of motion information. It has been shown that DF has difficulty in estimating the speed of objects but can accurately detect direction of movement (Milner *et al.*, 1991). Observations such as these raise the issue as to whether these previously described perceptual deficits will affect DF's ability at a visuomotor task requiring the processing of the same information. While informal observations (Carey *et al.*, 1996) of DF catching a ball or stick have been reported as being normal, to date this has not been formally tested.

While it has been established that DF is able to perform simple visuomotor tasks in a similar way to normals, it has become clear that there are limitations on these abilities (Milner *et al.*, 1999). In particular it has become evident that DF's intact visuomotor behaviour becomes impaired under at least two conditions (1) when a delay is required before response (see chapter 4 for overview of delay literature) and, (2) when binocular viewing is prevented. Marotta *et al.* (1997) showed that the removal of binocular cues disrupted the calibration of grip aperture in two visual form agnosia patients (including DF). They concluded that binocular information plays a critical role in prehension, but that when such information is denied to normals they use pictorial (monocular) cues to calibrate their grasp, whereas visual form agnosia patients cannot. This suggests that although pictorial information reaches the visuomotor control system via ventral networks in normals, it cannot do so in visual form agnosia patients as such networks are damaged. Dijkerman *et al.* (1999) confirmed this pattern of results by showing that DF is impaired at adjusting her hand orientation to the orientation of a target in depth when reaching under monocular conditions, however when allowed to move her head (i.e. had access to motion parallax information) her performance at such tasks is restored. Milner *et al.* (1999) suggest that this evidence that the ventral stream is responsible for the processing of pictorial cues and that the dorsal stream is highly dependent on binocular depth cues fits well with single unit recording studies. For example, Sakata *et al.* (1997) demonstrated that many visually driven neurons in the posterior parietal cortex that are selectively sensitive to orientation of surfaces in depth lose this sensitivity under monocular viewing conditions. As such, the present experiment also aimed to determine whether DF relies on binocular information when carrying out complex visuomotor tasks such as catching or whether monocular information is sufficient.

When subjects are required to catch a moving object they must compute when they will contact the target and in what direction it is moving. This time to contact information can be obtained from the ratio of the image size to the rate of changing size, also known as *tau* (Lee, 1976; Lee *et al.*, 1983). This can be computed on the basis of monocular or binocular information (Servos and Goodale, 1998). Servos and Goodale (1998) investigated the use of monocular and binocular information in the control of catching in normals. They found that there was no difference between monocular and binocular viewing conditions and concluded that moving targets provide adequate depth and direction information from monocular cues (i.e. looming information). They suggest however that the predictability of the flight path in this study may have reduced the need to use binocular cues (i.e. stereomotion) as previous studies (Judge and Bradford, 1988; Regan, 1992) have shown that stereomotion cues are more critical when the flight dynamics of a target are erratic. They state "there have been no studies that have specifically investigated the effects of non-constant 3D target direction and velocity on the monocular and binocular mechanisms that compute motion in depth".

Evidence to suggest that DF may be able to compute time to contact on the basis of such information comes from a recent fMRI study (Field and Wann, 2005), which was designed to determine the neural correlates of time to contact judgements. The experiment involved three tasks: (1) Time to contact judgement - in which two balls approached the observer with velocities calculated so as one ball would arrive 200 ms earlier. Participants were required to estimate (based on optical size and expansion rate) which ball would arrive first; (2) Inflation judgment – in which two balls were presented that inflated in size (yet did not move) at different rates, the slow one inflating at 75% of the fast one. Participants were required to indicate which ball was inflating faster; (3) Gap closure judgement – in which two balls, presented either side of a central cross, approached the cross at velocities calculated so as one would arrive 200 ms earlier. Participants were required to indicate (based on speed and distance) which would arrive first. The results revealed that activation in area MT+ / V5 occurred in all tasks, and the authors suggest that this is most likely to reflect the role of generating a signal related to the rate of optical expansion. Specific activation was however observed for the time to contact task in sensorimotor areas that are the target of the dorsal stream of processing; these activations correspond closely to networks previously identified for reaching and grasping. These areas remain largely intact in DF, whose lesion involves bilateral ventral stream damage (James *et al.*, 2003).

The purpose of this experiment was to attempt to answer several questions regarding DF's visuomotor behaviour: (1) Does DF perform in a similar way to normals when required to carry out a complex visuomotor task such as catching? (2) In what way do DF's previously described deficits in motion perception affect her ability to catch moving objects? (3) If DF can successfully catch moving objects will she depend on binocular cues such as vergence or will she be able to use monocular cues such as looming? (4) How will DF and normals respond to on-line perturbations when catching a moving object under monocular and binocular conditions (i.e. will binocular information from stereomotion be crucial to be able to make online responses to changes in speed and direction)?

5.2 Method

5.2.1 Participants:

The experiment involved testing DF and five female age matched controls (age range 40 - 58). DF was 48 years old at the time of testing; she had developed visual form agnosia 14 years prior to testing (see chapter 3 for further details). All controls were right-handed by self report, had normal or corrected to normal vision, and no history of neurological disorder.

5.2.2 Experimental equipment:

The experiment involved the use of an electromechanical setup which comprises two motor-driven linear axes to produce object motion on a horizontal plane (SOC, Schenk *et al.*, 2000a) (figure 5.1). The system is controlled by a PC, which also allows the triggering of other events used in this experiment including liquid crystal shutter glasses (Plato System, Translucent Technologies, Toronto, CA), which were used to manipulate viewing time. The system contains a start switch, which signals the beginning of the manual response. The target object also contains a switch, which is released when the object is picked up, signalling the end of the manual response. Both the signals from the start switch and the target object switch were emitted to the PC.

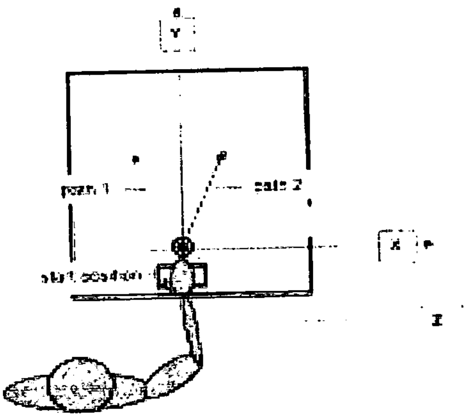

Figure 5.1: Figure depicts the experimental set-up used (Schenk *et al.*, 2000a). This involved the use of a Servo-object-controller (SOC) table, which is used to generate two-dimensional motion of objects. This system uses two motor driven linear axes to move an object within a horizontal area of 1 m^2. The linear axes are covered by a metal plate. Magnets transfer the movement of the linear axis to an object carrier that sits on the surface of the metal plate. The target object is a small cylinder weighing 15 g with a height of 6 cm and a diameter of 4 cm. This object contains a magnet that is strong enough to allow it to sit firmly on the object carrier but weak enough to allow a participant to lift the object off the carrier without requiring too much force.

To prevent head movements a head and chin rest was used, as a recent study (Dijkerman *et al.*, 1999) has shown that when DF is allowed to move her head, performance on tasks under monocular conditions is restored due to access to motion parallax information. A CD player was used to play music in the laboratory throughout the experiment; this was to dampen the acoustic cues that are produced from the table, which could have assisted participants' judgments of the speed and direction of the moving object.

A three-dimensional movement registration device (CMS 70, Fa. Zebris, Germany) was used to record the trajectory of the arm and fingers during the participants' manual response. This registration device employs ultrasonic loudspeakers as markers and a panel with embedded microphones as receivers for the ultrasonic signals. The system has a spatial resolution of 0.1 mm and achieves a sampling frequency of 50 Hz when three markers are used. Three markers were used to record the manual response; one was placed on the wrist above the styloid process of the ulna, one was placed on the nail of the index finger and the final one on the nail of the thumb.

5.2.3 Procedure:

The experiment consisted of two tasks, in both tasks participants were seated in front of the SOC table in a central position and asked to place their head in the chin rest provided. The participants were told to place their hand on the start button when they were ready to start each trial. Pressing the start button sent a signal to the PC which enabled the opening of the shutter glasses. The shutter glasses remained open 100 ms before the object began to move to allow participants to orientate themselves with the starting position of the target. They were instructed that they should catch the object with their right hand as soon a possible after the object began to move; trials in which participants attempted to catch the object before the onset of movement were discarded and repeated. The experiment was performed under both monocular and binocular conditions, which were controlled through the use of liquid crystal shutter glasses. Under binocular conditions both the left and the right lens opened and under monocular conditions the lens for each participant's dominant eye was opened (this was determined by asking participants to look through a cylinder with whichever eye they felt most comfortable using). The shutter glasses remained open for 100ms after the start of the object movement in task one. Viewing time was not restricted in task two (i.e. the shutter glasses remained open until the participants returned to the start button). After each trial, the object was returned to the carrier and participants returned to the start button when they were ready to begin the next trial.

The first task was designed to investigate catching performance as an object moved away from the participant at different speeds and directions. The object moved to the left or the right at different speeds (0.25, 0.5 and 0.75 m/s) (figure 5.2). These speeds were chosen as piloting had revealed that most healthy participants could successfully catch objects moving at these speeds. The angle at which the object moved to the left or the right was 25 degrees, this was chosen to ensure that the object remained in the participants' field of view while the shutter glasses were open under monocular conditions. In task one there were a total of six trial types (0.25 m/s right; 0.5 m/s right; 0.75 m/s right; 0.25 m/s left; 0.5 m/s left; 0.75 m/s left). These trial types were presented a total of 20 times each in a randomised order resulting in a total of 120 trials for each condition (monocular / binocular), meaning a total of 240 trials were carried out for task one. These were presented in 8 blocks of 30 trials, 4 of which were monocular and 4 of which were binocular.

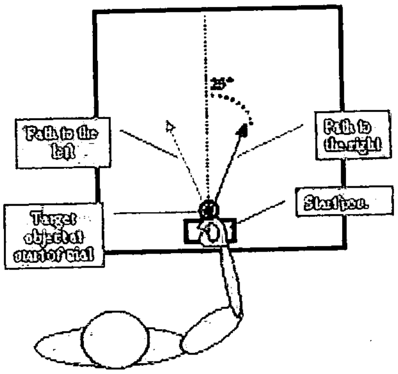

Figure 5.2: Experimental set-up for task one. The target object moves 25 degrees to the left or the right of the participants midline at various speeds (0.25, 0.5, 0.75 m/s)

The second task looked at responses to on-line perturbations (figure 5.3). The target object would move away from the participants in one of four paths: (1) the object would travel in a straight path away from the participant at a velocity of 0.5m/s; (2) the object would move in a straight path and then, 150 ms after movement onset, would have a sudden increase in velocity (increase in velocity from 0.5 to 0.75m/s); (3) the object would move in a straight path and then, 150 ms after movement onset, would have a sudden decrease in velocity (increase in velocity from 0.5 to 0.25m/s); (4) the object would move in a straight path and would perturb 10 degrees to the left 150ms after movement onset, the velocity remaining at 0.5m/s; (5) the object would move in a straight path and would perturb 10 degrees to the right, the velocity remaining at 0.5m/s. Again pilot studies were performed on this task to determine the best baseline velocity. All perturbations occurred 150 ms after the hand button was released. For task two there were a total of five different trial types, which were carried out a total of 20 times each. This results in a total of 100 trials for each condition (monocular and binocular), and thus a total of 200 trials were carried out for task two. These were again carried out in 8 blocks of 25 trials, 4 of which were monocular and 4 of which were binocular.

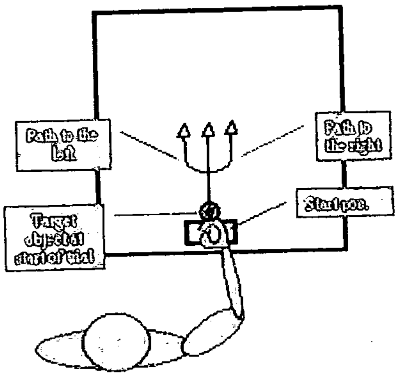

Figure 5.3: Experimental set-up for task two. The target object moved at a velocity of 0.5 m/s, and could perturb to the left, the right, increase in velocity or decrease in velocity

All participants carried out task 1 first and then task 2. For both tasks the conditions were presented in a block-by-block basis (i.e. binocular / monocular / binocular / monocular). A short break was given in between each block to control for fatigue effects.

5.2.4 Analysis:

Measures of timing and accuracy were chosen that produced consistent effects in control subjects during piloting. While the variables of reaction time and movement time are typical performance measures in tasks such as these they were not included for two reasons, first preliminary analysis revealed that consistent effects could not be found in these variables for control subjects and therefore it would have been difficult to determine if DF performs normally on these variables, and secondly it is not clear what these measures tell us about catching behaviour. For completeness the data for these variables in task 1 and task 2 are included in appendix 2.1 and 2.2, respectively. For task one, data were averaged across direction (left / right) to increase the power of the analysis; pilot studies revealed that there was no effect of direction on any variables for DF or control subjects. In addition DF's lesion is bilateral and as such it would be unlikely that any directional effects would be observed, these trials were included mainly to make the task less predictable.

Accuracy was measured by computing the percentage of trials in which the participant successfully caught or grasped the target object, for the computation of this variable all trials were included. A grasp was considered successful if the participant lifted the object from the carrier and did not drop it. Trials were considered unsuccessful if the participant dropped the target object after picking it up, if they knocked it off the carrier before grasping it or if they missed the object entirely. Chi-square analysis was conducted on these data to test for effects of speed and viewing condition. Modified t-tests (two-tailed) were conducted to compare the performance of DF and controls on each condition.

For timing measures peak velocity was used, only trials in which the participant successfully caught the target were included in the analysis. For task 1 this included 64% of trials for DF and 79.6% of trials for controls. For task 2 this included 78.1% of trials for DF and 80.1% of trials for controls. Previous experiments have shown that peak velocity of reaching movements increases with the velocity of a moving target (Schenk *et al.*, 2000b; Smeets and Brenner, 1995; Carnahan and McFadyen, 1996). As such this variable was used to determine if subjects adjusted the speed of the reach to the speed of the object. Peak velocity is defined as maximum tangential velocity of the marker attached to the wrist. Individual ANOVAs were conducted for each subject to test for effects of perturbation and viewing condition. Planned comparisons were also carried out to look for significant differences between the no perturbation condition and each perturbation. Finally, modified t-tested (two-tailed) were conducted to compare the performance of DF to controls on each condition. It may be considered that the inclusion of unsuccessful trials in the analysis of peak velocity may give a better performance measure than only the analysis of successful trials (as participants may have failed to catch the target as they did not adjust their peak velocity to an appropriate extent). Such trials could not be included in the analysis however as the kinematic profiles of unsuccessful trials was extremely variable (e.g. some participants stopped their movement immediately after releasing the start button). Any differences between the patient and control group in terms of unsuccessful trials should be apparent in the analysis of accuracy and therefore it is not necessary for such trials to be included in peak velocity measures.

5.3 Results

5.3.1 Task One:

Figure 5.4 illustrates the accuracy of DF and controls for each of the conditions, averaged across left and right. A chi-square analysis was conducted on these data and revealed for DF there was a significant effect of stimulus speed on accuracy (χ^2 = 99.186, $p < 0.001$), this was also true for all the control participants ($p < 0.005$ for all controls). This is due to the fact that there was a decrease in accuracy as the speed of objects increased. Chi square analysis revealed that for DF ($\chi^2 = 1.737$, $p = 0.187$) and all the controls there was no significant effect of viewing condition on performance ($p > 0.159$ for all controls) (individual p values are illustrated in appendix 2.3). Modified t-tests revealed that there is no significant difference between DF and controls for any of the conditions ($p > 0.210$ for all comparisons) (significance levels for all comparisons are reported in appendix 2.4).

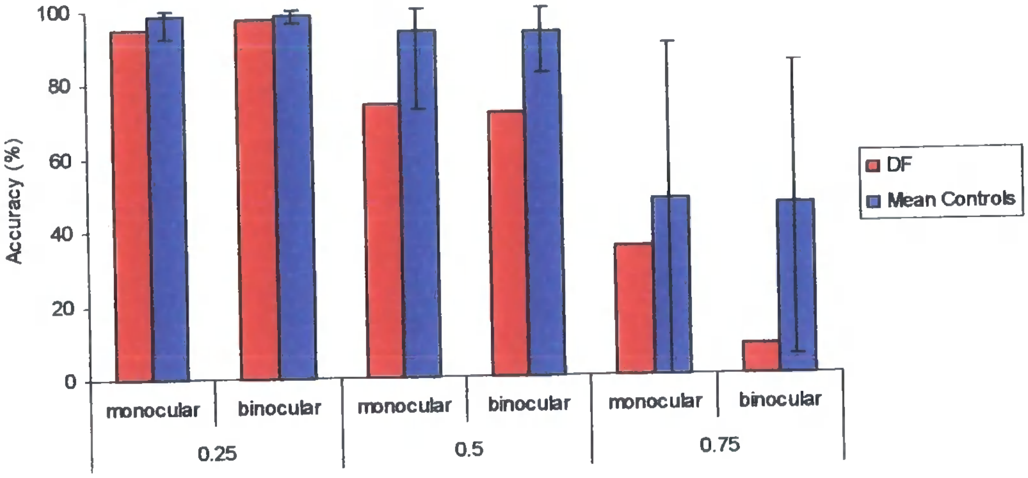

Figure 5.4: Graph illustrating the accuracy (%) of DF (red bar) and mean controls (blue bar). Error bars indicate the range of accuracy for the control participants

Figure 5.5 illustrates the peak velocity for DF and controls for each speed under monocular and binocular viewing conditions. Only trials where the participant successfully caught the object were included in the analysis. A two-way ANOVA was conducted, with factors speed (0.25 / 0.5 / 0.75) and viewing condition (Monocular / Binocular). For DF there was a significant effect of speed ($F_{(2, 145)} = 60.145$, $p < 0.001$); this was true for all controls ($p < 0.001$ in all controls). For DF there was no significant effect of viewing condition ($F_{(1, 145)} = 0.173$, $p = 0.678$); this was true in all controls ($p > 0.07$ for all controls). Finally, for DF there was a non significant interaction between speed and viewing condition ($F_{(2, 145)} = 0.767$, $p = 0.466$); this was also true for all controls ($p > 0.184$ for all controls) (individual p values are reported in appendix 2.5). Modified t-test revealed that there are no significant differences between DF and controls in any of the conditions ($p > 0.164$ for all comparisons) (p values of all comparisons are reported in appendix 2.6).

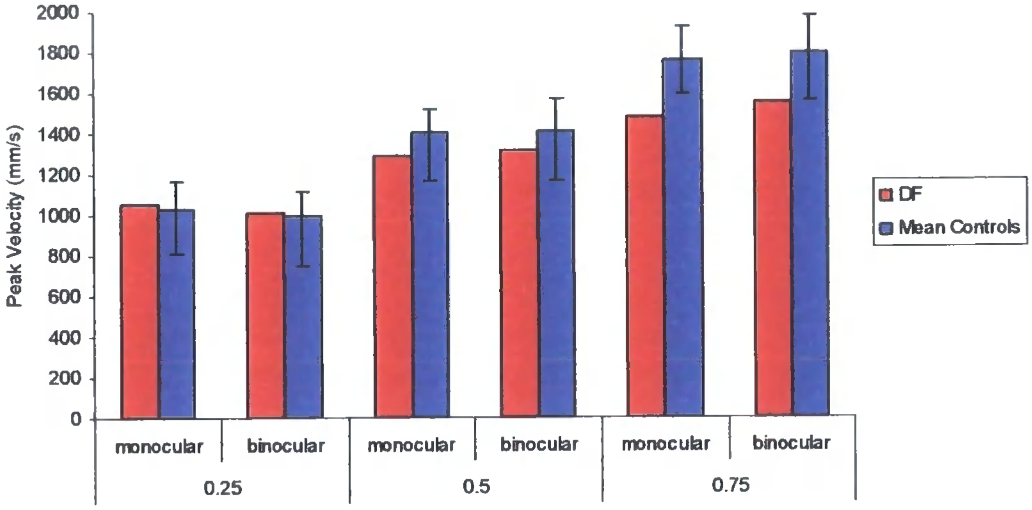

Figure 5.5: Graph illustrating the peak velocity (mm/s) of DF (red bar) and mean controls (blue bar). Error bars indicate the range of accuracy for the control participants

5.3.2 Task Two:

Figure 5.6 illustrates the accuracy of DF and controls for task two. Chi square analysis was conducted on this data, for DF there was a significant effect of perturbation condition on accuracy ($\chi^2 = 57.649$, $p < 0.001$); this was true for all the control participants ($p > 0.001$ for all control participants). The graph below illustrates that this effect can be accounted for mainly by the decrease in accuracy for the condition in which the target increased in speed. There was no significant effect of viewing condition on accuracy for DF ($\chi^2 = 0.004$, $p = 0.949$); this was also true for all the control participants ($p > 0.062$ for all control participants) (individual p values are reported in appendix 2.7). Modified t-tests revealed that there is no significant difference between DF and controls for all conditions ($p > 0.072$ for all comparisons) (significance levels for all comparisons are reported in appendix 2.8)

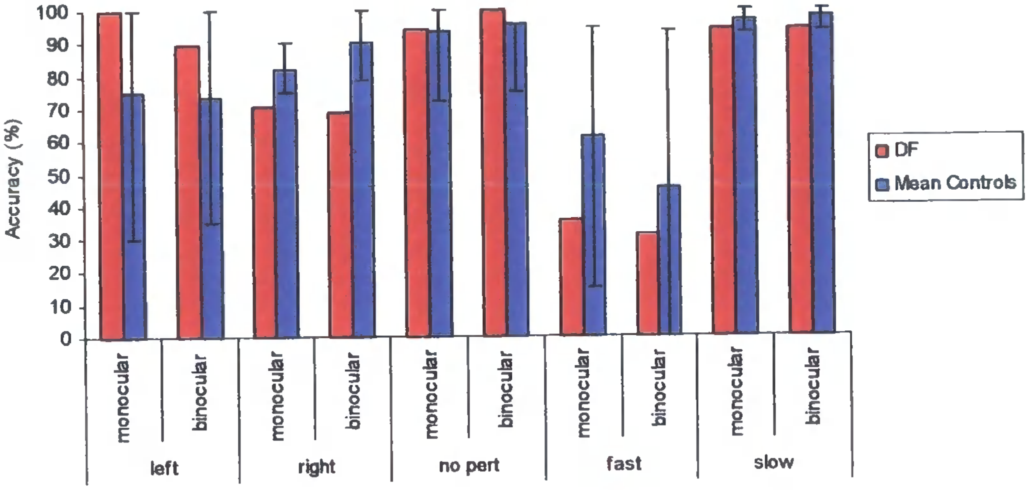

Figure 5.6: Graph illustrating the accuracy (%) for DF (red bar) and controls (blue bar) for (1) perturbation to the left, (2) perturbation to the right, (3) no perturbation, (4) increase in velocity and (5) decrease in velocity. Error bars illustrate the range of control subjects

Figure 5.7 illustrates the peak velocity for DF and controls for task two. A two-way ANOVA revealed for DF there was a significant effect of perturbation condition ($F_{(4, 122)} = 12.945$, $p < 0.001$); this was also true in 2 of the controls ($p < 0.008$). Post hoc comparisons revealed that this can mainly be accounted for by an increase in peak velocity when the velocity of the target increased and a decrease in peak velocity when the velocity of the target decreased. No significant effect of viewing condition was observed in DF ($F_{(1, 122)} = 0.220$, $p = 0.640$) or in any of the controls ($p > 0.208$ for all control participants). A significant interaction exists between perturbation and viewing condition for DF ($F_{(4, 122)} = 5.569$, $p < 0.001$) and in one of the control subjects ($p > 0.009$). The graph below illustrates that this interaction is due to the fact that the effect of perturbations in speed (increase and decrease in velocity), is stronger under binocular than monocular conditions, this is the case for both DF and the one control subject who demonstrated a similar pattern of results. Individual significance levels are reported in appendix 2.9. Modified t-tests revealed no significant difference between DF and controls for any of the conditions ($p > 0.05$ for all comparisons) (significance levels for all comparisons are reported in appendix 2.10)

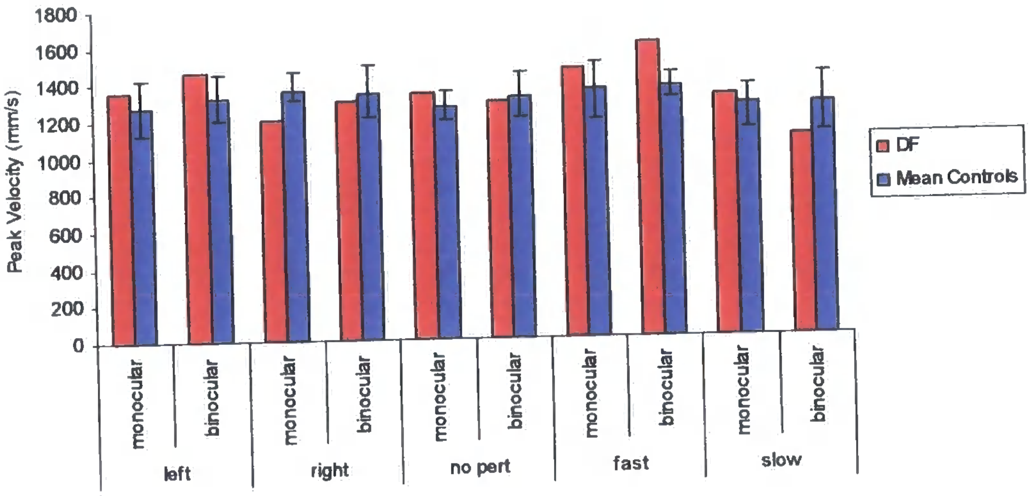

Figure 5.7: Graph illustrating the peak velocity (mm/s) for DF (red bar) and controls (blue bar) for (1) perturbation to the left, (2) perturbation to the right, (3) no perturbation, (4) increase in velocity and (5) decrease in velocity. Error bars illustrate the range of control subjects

5.4 Discussion

The results of the present experiment can be summarised as follows. In task 1, participants were required to catch a target as it moved to the left or right at various speeds under monocular and binocular conditions. Results revealed that both DF and controls showed a decrease in accuracy and increase in peak velocity as the speed of the target increased. In task 2, participants were required to respond to perturbations in direction and speed under monocular and binocular conditions. The results revealed that both DF and controls showed a decrease in accuracy in the condition where the velocity of the target increased. In addition both DF and controls adjusted their peak velocity appropriately according to changes in the velocity of the target. There was no effect of viewing condition on accuracy or timing in either task one or task two.

Overall these results suggest that DF performs in a similar manner to controls on complex visuomotor tasks such as catching and DF's previously described deficits in motion perception (Milner *et al.*, 1991) have no effect on her ability to catch moving objects. This is consistent with previous observations with DF that have shown that she has intact visuomotor behaviour yet deficits in perceptual tasks (Milner *et al.*, 1991; Goodale *et al.*, 1994a; Milner, 1998; Milner *et al.*, 1999). There could, however, be other reasons why DF does not show deficits in processing the speed of the moving target in the present task. Formal testing revealed that DF could accurately identify direction of motion when dots presented moved at 100% coherence, her success rate fell to chance at 50% coherence and below (Milner *et al.*, 1991). In the present experiment there is no incoherence in the moving target and therefore it would be anticipated based on this previous observation that DF would be able to accurately process the direction of motion. Previous studies assessing DF's ability to perceive motion accurately have failed to formally test her ability to detect the speed of moving objects; previous observations are restricted to the fact that DF reports difficulty in estimating the speed of vehicles. The results of the present experiment could in fact be taken as evidence to suggest that DF can accurately process speed of motion.

It is clear in task 1 that DF can accurately detect the speed of the moving target. So, what cues is DF using to enable her to carry out this task? It is important to note that DF performs in a similar manner to controls under both monocular and binocular viewing conditions. This may seem to contradict previous observations with DF that have shown that DF has preserved visuomotor behaviour when allowed binocular viewing, yet her performance falls to chance under monocular conditions (Marotta *et al.*, 1997; Dijkerman *et al.*, 1999). One cue that is available in this task under both monocular and binocular conditions, however, is looming information. It is possible that DF uses such information to compute time to contact based on *tau* (i.e. the ratio of the image size to the rate of changing size) (Lee, 1976; Lee *et al.*, 1983). Evidence to suggest that DF is using looming information in task 1 is supported by recent observations with DF showing that she is able to use such information to make time-to-contact judgements when only looming information is provided (M. Mon-Williams, personal communication). In addition the recent fMRI study by Field and Wann (2005) suggest that such information is processed by the dorsal stream of processing, which is functionally intact in DF.

While it is possible that DF is using looming information in task one to make her time-to-contact judgements, it is unlikely that she is doing so in task two as she can accurately respond to perturbations in velocity. Tresilian (1999) suggests that *tau* is a limited source of time to contact information for several reasons, one of which is that it neglects accelerations. It is possible in the perturbation task that DF is using looming information to make time-to-contact judgements, and then when the perturbation in velocity occurs she computes the distance between her hand and the target and adjusts her movement appropriately. This would be supported by Carey *et al.* (1998) who contrasted the use of distance information for perceptual report to visuomotor control and to examine to what extent distance cues are dependent on binocular vision. In their first experiment DF and controls carried out a visuomotor and perceptual task under monocular and binocular conditions. The results indicated that DF showed distance scaling (increased peak velocity for objects further away) in a visuomotor task although her perceptual report was impaired, under binocular conditions; these spared visuomotor abilities were unaffected by monocular viewing. In their second experiment DF and controls were asked to point to a target LED under monocular and binocular conditions. Results showed that DF's endpoint accuracy was higher when allowed binocular viewing, however the correlation between peak velocity and distance was within the normal range under monocular conditions. Thus while binocular vision may be essential for DF to achieve high accuracy, monocular vision is sufficient to get in a close proximity to the target. This explanation of DF's ability to respond to online perturbations is one which requires further investigation.

The present experiment provides clear evidence to suggest that DF has intact online visuomotor control. Schenk *et al.* (in press) suggest "Online visuomotor control is required whenever a change in the target or an error in the ongoing motor response is visually detected" and provide evidence to suggest that such behaviour is independent of visual awareness. They tested a visual extinction patient on a pointing task in which vision of the hand was available or when it was denied and found that the patient showed a benefit of visual feedback regardless of whether such information was available for verbal report. Desmurget *et al.* (1999) used TMS over the left posterior parietal cortex to show that online visuomotor control is a function of the dorsal stream of processing. Such observations have been supported by experiments showing that optic ataxic patients (with damage to the dorsal stream of processing) are unable to make online corrections (Pisella *et al.*, 2000). The present experiment provides evidence to support these conclusions, suggesting that DF is capable of responding to perturbations in velocity and speed of a moving target as a function of her intact dorsal stream of processing.

It is important to note one clear difference between this catching study and traditional catching studies, which is that in the present experiment the participants were required to catch a target that is moving away from them. The experiment could in fact be viewed as a reach-to-grasp task involving a moving target, rather than a catching task. One potential cue that may be available in such a task is an aperture closing gauging system (i.e. participants monitor the aperture of the hand as it closes to grasp the target and base time to contact judgements on this). This is unlikely to be the case as viewing time was restricted, so that participants received no visual feedback of the hand as it grasped the target. The direction that the target moves (towards or away from the participant) should not affect the results of the present experiment as the same looming information is available to subjects whether the target is moving towards or away from subjects and therefore participants should be able to use *tau* to make time-to-contact judgements. The design of the present experiment should in fact remove some potential limitations of traditional catching studies. If subjects are required to catch an object that is approaching them it is possible for them to judge the position in space the target will arrive and simply wait for the target to reach that point. The present study on the other hand requires that participants adjust the speed of their reach to the speed of the target in order to successfully catch the target, and thus can accurately determine if participants are judging time to contact information correctly.

In conclusion, the results of the present experiment suggest that DF has preserved visuomotor behaviour when required to carry out complex tasks such as catching. She can accurately detect the direction and speed of targets and there is no difference in her performance under monocular and binocular viewing conditions. While DF may be using looming information in task one, she would be unable to use such information in task two as she can accurately respond to perturbations in velocity. It is possible that she responds to such perturbations by computing the distance between her hand and the target and adjusting her response appropriately (this explanation requires further testing). The fact that DF is capable of responding to online perturbations in speed and direction in a similar way as healthy participants, provides further evidence to suggest that the ability to respond to such perturbations is a function of the dorsal stream (intact in DF).

CHAPTER SIX: THE ROLE OF V5 IN CATCHING – AN rTMS STUDY

6.1 Introduction

The Milner and Goodale (1995) model has been well supported with empirical evidence (see general introduction for further details). It has been suggested however that most of the support for this model comes from experiments investigating visuospatial attributes such as form, size and orientation perception (Norman, 2002). Goodale (1993) suggests that it remains unclear as to whether the model applies to visual attributes such as motion and depth perception as these have not been extensively examined in this context. The aim of the present study is to determine if the model applies to motion perception.

Motion perception is important for object recognition given that motion is an important cue for figure-ground segregation (Anstis, 1978; Sekuler *et al.* 1990). Motion perception is also important for visuomotor control; this is supported by the findings of Paillard (1996) who suggested that manual movements towards stationary objects require visual monitoring of the moving hand. Our visuomotor control skills also include the ability to catch non-stationary target objects; it is reasonable to assume that successful catching behaviour is impossible without knowledge of the motion of the moving object. Considerations such as these raise the question as to whether there are distinct brain areas processing visual motion information for either perceptual (object recognition) or action (visuomotor) tasks.

Braddick *et al.* (2000) carried out an fMRI study which showed that five distinct regions were activated by motion stimuli, including V5, V3A, the posterior ventral surface, the

IPS and STS. Culham *et al.* (2001) found that area V5 is the most easily and consistently activated region in the human cortex responding to a whole range of dynamic stimuli in almost all observers (see general introduction for further details of area V5/MT+). Evidence clearly shows that V5/MT+ plays an essential role in motion processing in a variety of perceptual tasks (see general introduction), however it remains unclear as to the role of motion perception in visuomotor tasks such as catching.

Schenk *et al.* (2000b) attempted to address the issue of the role of V5/MT+ in visuomotor tasks by studying the motor behaviour of a patient with akinetopsia. Akinetopsia involves a specific deficit in motion perception; the most famous case of such a disorder is patient LM (Zihl *et al.* 1983; Hess *et al.* 1989) who developed akinetopsia after bilateral extrastriate damage to areas that include the human homologue of V5. Her perceptual deficits have been extensively documented (Zihl *et al.* 1991), however little was known about how her deficits affect her motor performance. Schenk *et al.* (2000b) carried out a study consisting of three experiments in which LM and age matched controls were required to reach and grasp an object as it moved away from them. In their first experiment, they attempted to examine the effect of target speed on performance. Participants were asked to reach and grasp an object as it moved away from them in one of two paths at different speeds. Results showed that LM could only catch objects that moved less than 0.5 m/s, whereas controls could accurately catch objects moving at 1.0 m/s. In their second experiment they attempted to determine the effect of observation time on performance, by manipulating viewing time using liquid crystal shutter glasses. Participants were required to reach and grasp an object as it moved away from them, and were allowed either full vision or vision restricted to the first 400 or 200 ms. Results showed that LM required a longer observation time than controls, particularly for rapidly moving objects, catching significantly more objects with a longer exposure period. In their third experiment they attempted to examine the effects of visual feedback on performance. The experiment was the same as experiment one except that the task was carried out with or without vision of the reaching hand; this was manipulated by the use of a luminescent glove and object. Results showed that controls performed accurately with and without vision of the reaching hand; however, LM required vision of the reaching hand to perform the task accurately. Schenk *et al.* (2000b) concluded that LM's visual motion deficit affected her performance in both the perceptual and visuomotor domain and that this indicates that V5/MT+ is located at an early stage of the extrastriate hierarchy, providing input to both the dorsal and ventral streams of processing. This is supported by the fact that V5/MT+ receives direct inputs from area V1 (Felleman & Van Essen, 1991).

A problem with this conclusion however is that LM's lesion extends beyond V5/MT+ into surrounding areas (Shipp *et al.*, 1994). In particular, her lesions have been shown to extend dorsally to the intraparietal sulcus, infringing on area 39 at least in her right hemisphere (figure 6.1). Her lesions may therefore include motion-responsive areas in the intraparietal sulcus; these regions have been found to selectively respond to visual motion stimuli (Culham *et al.*, 2001). Given the extent of LM's lesion it is therefore possible that areas other than V5/MT+ are responsible for her visuomotor deficits.

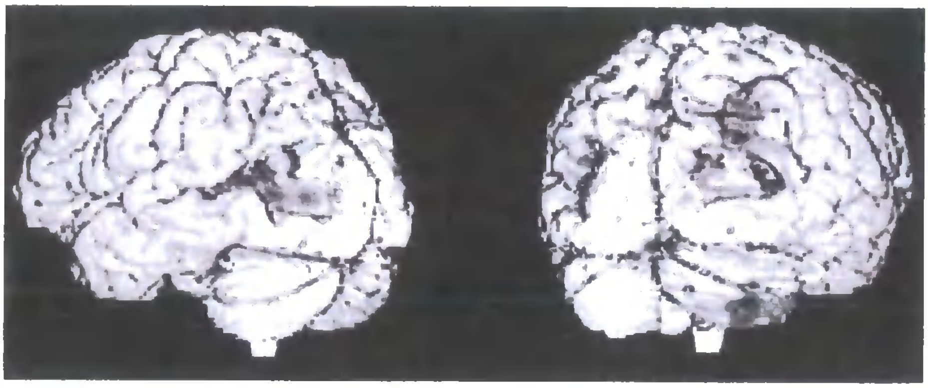

Figure 6.1: Figure depicting the lesion of patient LM, illustrating damage to V5/MT+ bilaterally (Zihl *et al.*, 1991).

As a way of avoiding such problems, a number of TMS studies have induced transient disruptions in V5/MT+ to investigate the role of this area in visual motion processing. Beckers and Homberg (1992) showed that selective disruption of V5/MT+ produces deficits in the perception of visual motion direction in the corresponding contralateral hemifield and that this degradation in performance was more pronounced when stimulation was applied to the left hemisphere. Beckers and Zeki (1995) showed that magnetic stimulation of V5/MT+ at intervals of –20 to +10 ms after onset of visual stimuli were effective in impairing the perception of direction of motion. Walsh *et al.* (1998) attempted to recreate the deficits of patient LM to assess the specificity of the deficits when TMS was applied to V5/MT+; they confirmed that TMS applied over V5/MT+ impairs performance on visual search tasks which require attention to motion. However TMS studies using visuomotor tasks have not been conducted, therefore it still remains to be questioned whether a selective disruption of V5/MT+ would produce a visuomotor deficit.

Culham *et al.* (2001) state that V5 is usually placed in the dorsal stream and motion processing is therefore considered a 'dorsal function' as functions of the dorsal stream include spatial localization, spatial attention, and visuomotor control which depend on stimulus location and movement. Braddick *et al.* (2000)'s fMRI study suggested that the areas activated by form and motion stimuli do not divide anatomically between the dorsal and ventral streams, as both the parietal lobe (target of the dorsal stream) and the temporal lobe (target of the ventral stream) show responses for both form and motion stimuli, these responses occurring in distinct but nearby foci. Grill-Spector *et al.* (1998) also provided evidence to suggest that motion input reaches the ventral stream when they demonstrated that area LO in the ventral stream responds to objects defined by luminance, texture or motion. It therefore remains to be determined to which stream of processing V5/MT+ belongs, or whether it belongs to both (or indeed neither).

The aim of the present study was to determine the role of V5/MT+ in the visuomotor domain by comparing the effects of TMS to V5/MT+ with the effects obtained over two control sites, namely vertex and a site 2 cm dorsal to V5/MT+, when participants were required to carry out an appropriate task. Two visuomotor tasks were used, a catching task (involving the use of a moving object) and a standard reach-to-grasp task (involving the use of a stationary object). It is expected that if V5/MT+ is involved in visuomotor processing, stimulation of V5/MT+ will interfere with participants' ability to predict the course of the target's movement and thereby impair catching performance. This experiment is designed to improve upon the study with patient LM as it will investigate the role of a more localised region (i.e. V5/MT+) in catching in a cohort of participants, and will also enable a contrast to be carried out between the effects of TMS to V5/MT+ and to parietal areas, allowing it to be determined which part of LM's lesion was responsible for her deficit in catching. The present experiment will expand upon previous findings using TMS, which have shown that V5/MT+ plays a role in visual motion processing in the perceptual domain (Beckers and Homberg, 1992; Beckers and Zeki, 1995; Walsh *et al.*, 1998) by addressing this question in the visuomotor domain.

6.2 Method

6.2.1 Participants:

Six participants took part in the study (three female, three male), with an age range of 21-38 years. All participants were right-handed by self-report and had normal or corrected to normal vision. All participants consented to take part in the study after receiving detailed information regarding TMS and the safety issues surrounding it. They were screened for TMS exclusion criteria, including the absence of epilepsy in their family medical history. Local ethical committee approval was granted for all procedures.

6.2.2 Experimental equipment:

To prevent head movements during the experiment a head and chin rest were used. To confirm that head movements were negligible, they were recorded in three participants as they carried out both catching and reach-to-grasp trials. Three markers were used; one marker was placed at the centre of the coil (coil-marker), the other marker (reference marker) was placed on the centre of the dorsal surface of the skull (i.e. vertex). 10 trials per participant per task were recorded. To assess the extent of coil-displacement during the period of TMS stimulation, the maximum value of change in the distance between the coil and reference marker was determined during the 500 ms stimulation period. The average value of maximal displacement was less than 0.7 mm (standard deviation = 0.16) during the catching task, and less than 0.8 mm (standard deviation = 0.29) during the reach-to-grasp task.

A MagStim 200 Super Rapid Stimulator was used with a 90 mm figure-of-eight coil (Magstim, Whitland, Dyffed, Wales, UK). The coil was placed tangential to the surface of the skull with the coil handle pointing backwards at approximately 45 degrees to the spinal cord. The coil was held to the skull manually by the experimenter using the right hand to hold the coil and the left hand to stabilize the coil to the head. Repetitive pulse TMS (rTMS) was delivered at 10 Hz for 500ms at 65% of stimulator output (corresponding to 1.3 Tesla or 110% of the average TMS motor thresholds of participants). TMS was delivered at trial onset, which was indicated by the opening of the liquid crystal shutter glasses.

The experimental set-up is depicted in chapter five (figure 5.1). The system was controlled by a PC, which also allowed the triggering of other events used in this experiment including the shutter glasses and the triggering of the TMS pulses. The system contained a start switch, which signalled the beginning of the manual response. The target object also contained a switch, which was released when the object was picked up, and signalled the end of the manual response. Both the signals from the start switch and the target object switch were transmitted to the PC. Liquid crystal shutter glasses (Plato System, Translucent Technologies, Toronto, CA) were used to manipulate viewing time and earplugs were used to ensure that participants were not using acoustic cues to judge the speed and direction of the moving object and to dampen the noise of the TMS stimulation.

A three-dimensional movement registration device (CMS 70, Fa. Zebris, Germany) was used to record the trajectory of the arm and fingers during the participants' manual response. This registration device employs ultrasonic loudspeakers as markers and a panel with embedded microphones as receivers for the ultrasonic signals. The system has a spatial resolution of 0.1 mm and achieves a sampling frequency of 50 Hz when three markers are used. Three markers were used to record the manual response, one was placed on the wrist above the styloid process of the ulna, one was placed on the nail of the index finger and the final one on the nail of the thumb.

6.2.3 Procedure:

TMS was used to stimulate three sites: (1) V5/MT+ (the experimental condition) (2) Vertex and (3) Dorsal site, located 2cm above V5/MT+. Previous studies have shown that the location of V5/MT+ varies between individuals (Watson *et al.*, 1993). Therefore before the experiment began V5/MT+ was located functionally using TMS, by locating the area of the brain in which TMS stimulation induced the presence of moving phosphenes (Stewart *et al.*, 1999). The co-ordinates were selected on the basis of previously successful studies with TMS (Walsh *et al.*, 1998). This was approximately 3 cm above the mastoid-inion and 5 cm lateral to the midline on the sagittal plane, however deviations of up to 1.5 cm in either direction were found for the participants in this experiment. In addition, V5/MT+ was located anatomically for five out of the six participants, using a frameless stereotaxic system (Brainsight, Rogue Research, Montreal, CA) in conjunction with each participant's structural MRI scan. It was confirmed that the chosen stimulation site was in acceptable proximity to the anatomical landmark for V5/MT+, which is the intersection of the ascending limb and the posterior continuation of the inferior temporal sulcus (Dumoulin *et al.*, 2000). Stimulation was always applied unilaterally to the left hemisphere as previous studies have found there to be more reliable and pronounced effects with stimulation over the left than the right hemisphere (Stewart *et al.*, 2001). In addition, Walsh *et al.* (1998) found that stimulation of left V5/MT+ produced perceptual deficits similar to those observed in LM.

The second stimulation site was vertex; this is the point of intersection of the mid-sagittal plane (defined by the nasion to inion line) and the mid-coronal plane (defined by the line between the intertrachial notches of the ears). This location corresponds to the position Cz of the 10-20 International EEG system. This stimulation site was chosen as a control condition as it is known that it evokes the unspecific effects of TMS (i.e. noise and tapping sensations), without inducing activity in specific relevant brain areas. The second control site chosen was an area near to V5/MT+ but outside its border. The purpose of this site as a control condition was to determine the spatial specificity of any effects. The site was located by first determining the site of V5/MT+ and then moving the coil dorsally along the surface of the skull in 1 cm intervals until stimulation no longer induced moving phosphenes. The position of this site was on average 1.8 cm (standard deviation = 0.4) dorsal to the position of V5/MT+.

Two visuomotor tasks were used: (1) Catching task (2) Reach-to-grasp task (figure 6.2 a and b, respectively). These tasks are similar with respect to the demands on the motor system in that participants are required to produce rapid grasping movements, but produce different demands with respect to the visual system (i.e. in the catching task participants are required to take account of the motion information). In the catching task participants were required to catch an object moving away from them, the object moved in one of two trajectories (left or rightward movement) at a fast and slow speed (0.25 m/s or 0.50 m/s respectively). The parameters of the task were the same as those of the previous catching experiment carried out by Schenk *et al.* (2000b) with akinetopsic patient LM. In the reach-to-grasp task participants were required to reach and grasp a stationary object. In both tasks liquid crystal shutter glasses were used to manipulate exposure time to 100 ms (non-visually guided movement, in which participants saw the start of the trial but not the movement of their hand) or 800 ms (visually guided movement, in which participants were able to view the entire movement of both the object and the hand). In other words, the 100 ms condition required open-loop responding, whereas the 800 ms condition permitted full closed-loop control of the movement. Exposure time was manipulated, as the previous study with patient LM (Schenk *et al.*, 2000b) revealed that she caught significantly more objects when allowed to view the object for longer and if she could see her hand. Participants were allowed free viewing. In both tasks participants were instructed to use their right hand and carry out the movement as fast as possible. At the start of each trial participants placed their right hand on the start switch which was located in a central position directly in front of them. When the start switch was pressed, this signalled the shutter glasses to open and at the same time the rTMS was triggered, and in the case of the catching task the object began to move.

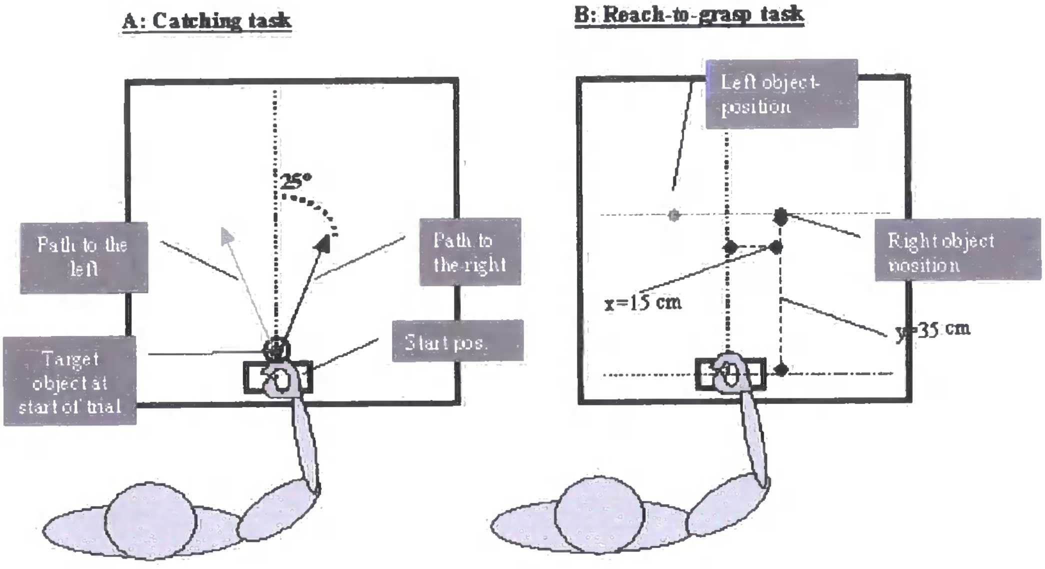

Figure 6.2: Figure depicting the experimental setup used for the catching task (a) and reach-to-grasp task (b). In the catching task the object moved to the left or right at an angle of 25 degrees at either 0.25 m/s or 0.50 m/s. In the reach-to-grasp task the object was placed 15cm to the left or right of the midline, 35cm away from the start button.

There were three TMS conditions (V5/MT+, Dorsal site and Vertex) and two visual conditions (100 ms and 800 ms), for each condition 40 trials were presented in separate blocks, which were presented twice in an interleaved order. The order of blocks and thus the order of TMS and visual conditions were counterbalanced across participants. Within each block trial types were randomly mixed, for the catching task in terms of direction and speed of target, and for the reach-to-grasp task with respect to the position of the object. The two tasks were carried out in two separate sessions occurring on different days to control for fatigue effects. For each of the sessions the TMS site was established using functional localisation. The sites used during the second session correlated well with the first session for all participants. Participants had 40 practice trials at the beginning of each session. Each session lasted approximately 90 minutes and a short break of 10 minutes was allowed mid-session.

6.2.4 Analysis:

The performance measures used were based on previous studies carried out with TMS (e.g. Walsh *et al.*, 1998) and the previous catching experiment carried out with patient LM (Schenk *et al.*, 2000b). Measures of accuracy were used for the catching task, and timing measures were used for both the catching and reach-to-grasp task.

Accuracy was measured by computing the percentage of trials in which the participant successfully caught or grasped the target object. For the computation of this variable all trials were included. A grasp was considered successful if the participant lifted the object from the carrier and did not drop it. Trials were considered unsuccessful if the participant dropped the target object after picking it up, if they knocked it off the carrier before grasping it, or if they missed the object entirely.

Several measures of timing were used, including average reaching speed; this was based on the results of the previous study by Schenk *et al.* (2000b), which showed that LM's reaching speed was lower than that of normals. Reaction time was also used as a measure of timing; this measure was chosen based on the results of previous TMS studies (Walsh *et al.*, 1998), which have shown that reaction time measures are a sensitive indication of TMS induced processing delays. For measures of timing, trials had to be discarded in which the participant did not successfully catch or grasp the object and trials in which recording artefacts were present. After such trials were discarded, 94% of trials remained. For the computation of reaching speed the recording traces had to be filtered using a non-parametric regression method (Marquardt and Mai, 1994); this effectively 'smoothes' the kinematic data.

A final measurement was used which expresses the amplitude of the TMS effect for variables in which TMS was shown to have a significant effect in one or more conditions (i.e. reaching speed). This measure expresses the TMS effect (of V5/MT+ or dorsal site stimulation) relative to performance in the control condition (vertex) as a normalized percentage difference. To calculate this % TMS effect the following formula was used:

$$\%\ \text{TMS effect (for condition x)} = ((\text{TMS} - \text{Vertex TMS}) / \text{Vertex TMS}) * 100$$

This index expresses the TMS effect relative to the performance in the control condition (i.e. vertex) as a normalised percentage difference.

The results from the catching task and the reach-to-grasp task were analysed separately. For the catching task a three-way within-subjects ANOVA was conducted, where the within-subjects factors were TMS condition (with three levels - V5, DS and vertex), observation time (with two levels - 100 and 800 ms) and motion direction, (with two levels - leftward and rightward motion). For the reach-to-grasp task a three-way within-subjects ANOVA was also conducted, where the within-subjects factors were TMS condition (with three levels – V5, DS and vertex), observation time (with two levels – 100 and 800 ms) and object position (with two levels – left and right). Bonferroni corrections were used for post-hoc analysis. A 5% significance threshold was adopted.

6.3 Results

6.3.1 Catching Task:

For the variable of percentage error, a three-way within-subjects ANOVA revealed no significant effect of TMS stimulation site ($F_{(2,\ 10)} = 0.341$, $p = 0.719$) or motion direction ($F_{(1,\ 5)} = 0.493$, $p = 0.514$), however the factor observation time had a significant effect on % error ($F_{(1,\ 5)} = 7.987$, $p = 0.037$). Post-hoc comparisons revealed that a shorter observation time (100 ms) leads to higher error rates than longer observation times (800 ms) (figure 6.3). No significant interactions were found between TMS stimulation site, observation time or motion direction.

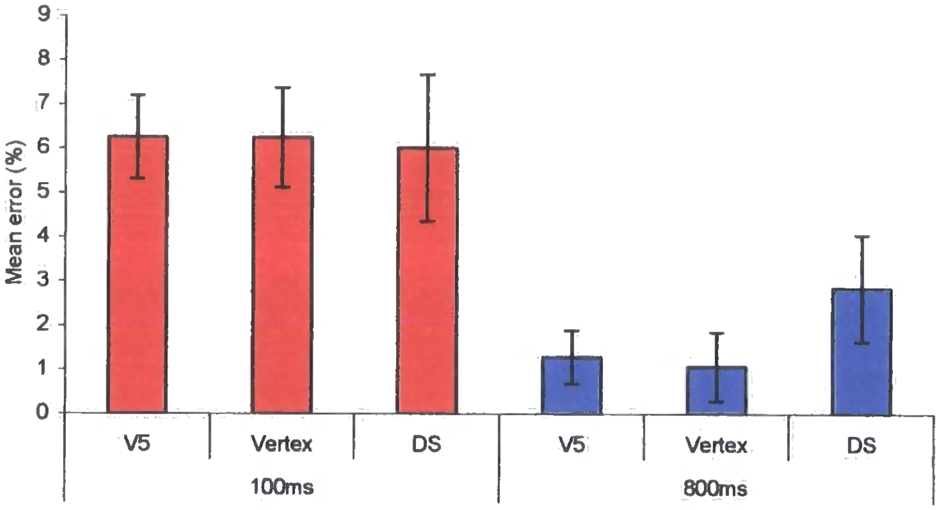

Figure 6.3: Graph illustrating mean error (%) and standard errors for observation time (100 or 800ms) and TMS site (V5/MT+, Vertex or Dorsal site) averaged across participants

For the variable of reaction time, a three-way within-subjects ANOVA revealed no significant effect of stimulation site ($F_{(2,\ 10)} = 1.243$, $p = 0.330$) or motion direction ($F_{(1,\ 5)} = 0.174$, $p = 0.694$), however a significant effect of observation time was again observed ($F_{(1,\ 5)} = 18.18$, $p = 0.008$). Post-hoc comparisons revealed that shorter observation times (100 ms) led to shorter reaction times (reaction time = 188.30 ms) than longer observation times (800 ms) (reaction time = 193.01 ms) (figure 6.4). No significant interactions were found between TMS stimulation site, observation time or motion direction.

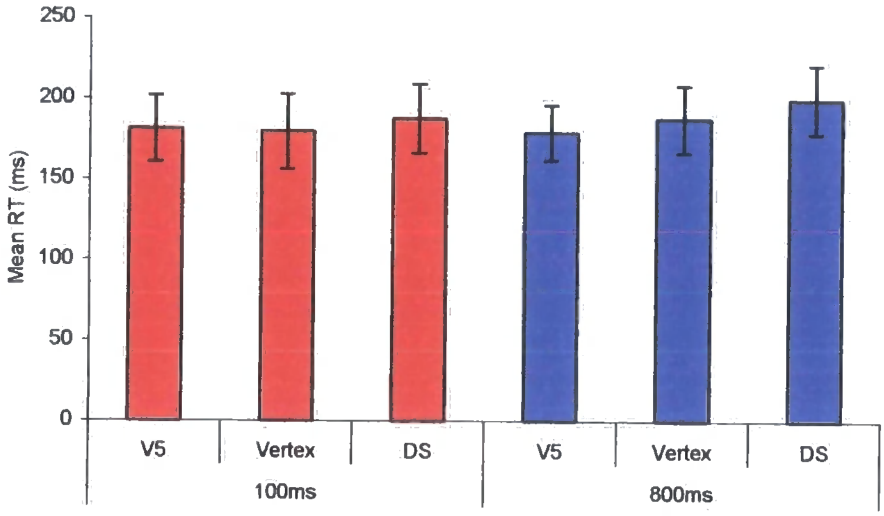

Figure 6.4: Graph illustrating mean reaction time (ms) and standard errors for observation time (100 or 800ms) and TMS site (V5/MT+, Vertex or Dorsal site) averaged across participants

For the variable of reaching speed, a three-way within-subjects ANOVA revealed a significant effect of TMS stimulation site ($F_{(2, 10)} = 9.98$, $p = 0.004$), however no significant effects of observation time ($F_{(1, 5)} = 4.469$, $p = 0.088$) or motion direction ($F_{(1, 5)} = 0.126$, $p = 0.738$) were observed. Post-hoc comparisons revealed that a significant reduction in reaching speed occurred for V5/MT+ stimulation compared to both dorsal site and vertex across both observation times (figure 6.5). No significant interactions were found between TMS stimulation site, observation time or motion direction.

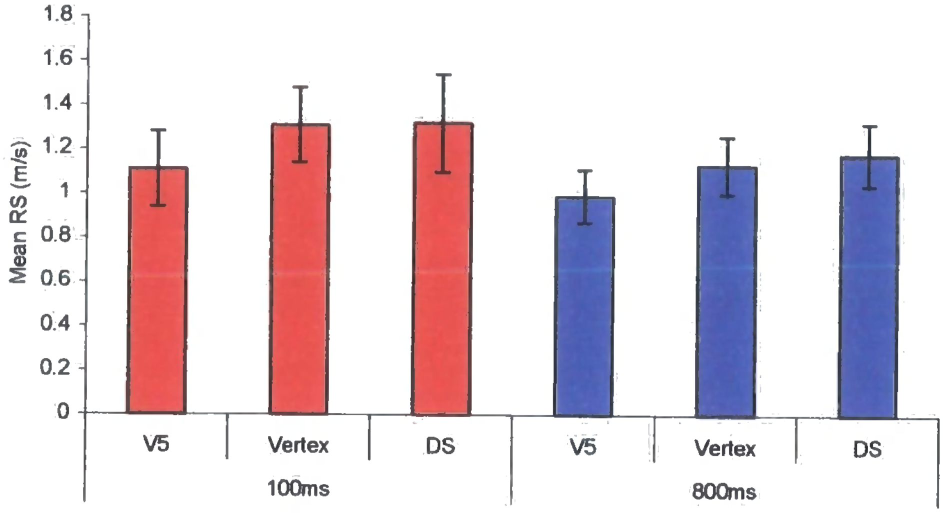

Figure 6.5: Graph illustrating mean reaching speed (m/s) and standard errors for observation time (100 or 800ms) and TMS site (V5/MT+, Vertex or Dorsal site) averaged across participants

As significant effects of TMS stimulation site on reaching speed were observed, the percentage TMS effect was computed for this variable. Figure 6.6 shows the percentage TMS effect on reaching speed for V5/MT+ and dorsal site stimulation for the 100 and 800 ms observation times. A repeated measures ANOVA, with the factors TMS site (V5/MT+ versus Dorsal site) and observation time (100 versus 800ms), was conducted. A significant effect of TMS site ($F_{(1, 5)} = 10.46$, $p = 0.023$) was revealed; this confirms that the reduction in reaching speed was more pronounced after V5/MT+ stimulation than dorsal site stimulation. No significant effect of observation time ($F_{(1, 5)} = 1.142$, $p = 0.334$) or interactions were found. In addition one-sample t-tests showed that the %TMS effect was significantly different from zero for V5/MT+ stimulation for both the 100 ms ($t = 3.053$, $p = 0.028$) and 800 ms ($t = 3.052$, $p = 0.028$) viewing time but not for the dorsal site stimulation for either the 100 ms ($t = -0.010$, $p = 0.992$) or 800 ms ($t = 1.210$, $p = 0.280$) viewing condition.

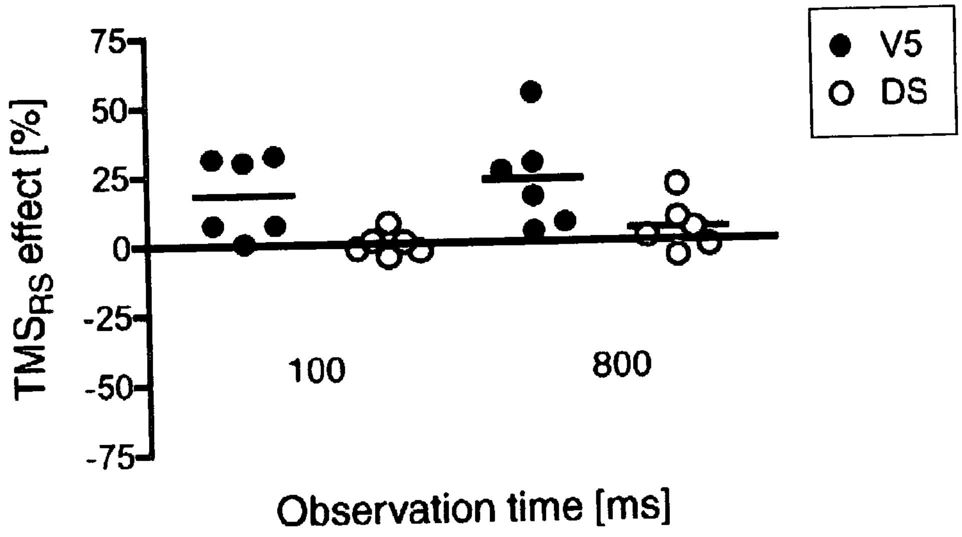

Figure 6.6: Graph illustrating the % TMS effect on reaching speed of V5/MT+ stimulation and Dorsal Site stimulation for 100 and 800ms observation time, for each individual participant and averaged across participants (horizontal lines).

6.3.2 Reach-to-grasp task:

For the variable reaction time, a three-way within-subjects ANOVA revealed that no significant effects were found for the factors TMS site ($F_{(2, 10)} = 0.411$, $p = 0.674$) or observation time ($F_{(1, 5)} = 0.497$, $p = 0.512$), however a significant effect was found for object position ($F_{(1, 5)} = 10.165$, $p = 0.024$). Post hoc analysis revealed that participants responded earlier for objects on their right (ipsilateral to the responding hand) than their left (figure 6.7). A significant interaction was found for object position and observation time for reaction time ($F_{(1, 5} = 7.977$, $p = 0.037$). Post hoc analysis revealed that the reaction time for movements towards the left are significantly more prolonged for the 100 ms observation time (mean reaction time = 208.41 ms) than the 800 ms (mean reaction time = 189.26 ms). On the other hand, there is little difference between the 100 ms (mean reaction time = 182.91 ms) and 800 ms (mean reaction time = 178.63 ms) observation time for movements towards the right (figure 10).

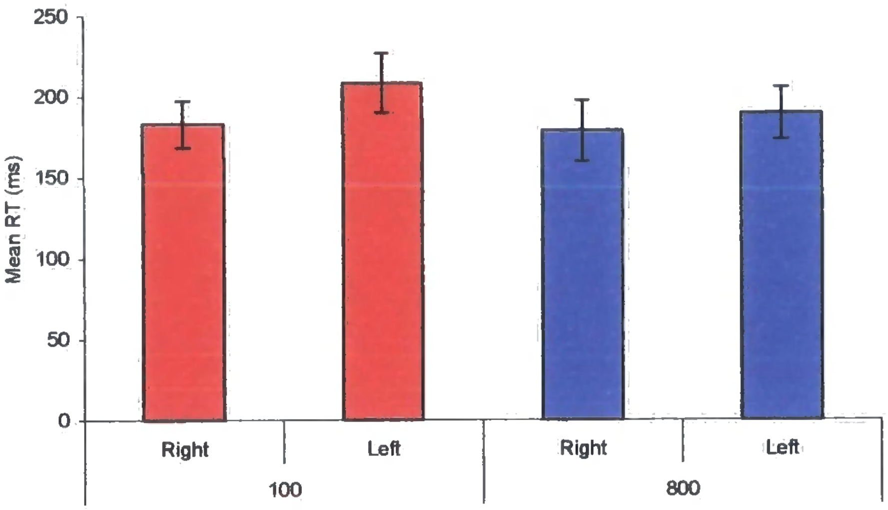

Figure 6.7: Graph illustrating mean reaction time (ms) and standard errors for observation time (100 and 800ms) and object position (left and right) averaged across participants

For the variable reaching speed, a three-way within-subjects ANOVA revealed no significant effects for the factors TMS site ($F_{(2, 10)} = 1.611$, $p = 0.247$) or observation time ($F_{(1, 5)} = 5.946$, $p = 0.059$), however a significant effect was again found for object position ($F_{(1, 5)} = 44.19$, $p = 0.001$). Post hoc analysis revealed that participants responded faster for objects on the right (mean reaching speed = 1.33 mm/s) than the left (mean reaching speed = 0.97 mm/s) (figure 6.8).

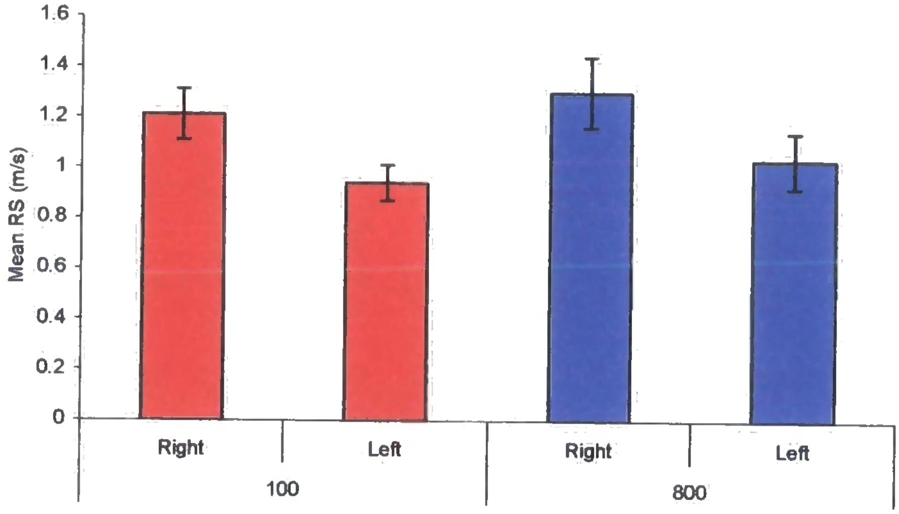

Figure 6.8: Graph illustrating mean reaching speed (m/s) and standard errors for observation time (100 and 800ms) and object position (Right and Left) averaged across participants

As % TMS effect on reaching speed was computed for the catching task, this variable was also computed for the reach-to-grasp task. Figure 6.9 shows the % TMS effect on reaching speed for V5/MT+ and dorsal site stimulation for each observation time. A repeated measures ANOVA, with the factors TMS site (V5/MT+ versus Dorsal site) and observation time (100 versus 800 ms) was conducted and revealed no significant effect of either TMS site ($F_{(1, 5)} = 2.225$, $p = 0.196$) or observation time ($F_{(1, 5)} = 0.666$, $p = 0.451$), and no significant interactions. In addition, one-sample t-tests revealed that % TMS effect did not differ significantly from zero in the case of V5/MT+ stimulation for either the 100 ms ($t = 0.205$, $p = 0.846$) or 800 ms ($t = 1.571$, $p = 0.177$) viewing condition or dorsal site stimulation for either the 100 ms ($t = -0.910$, $p = 0.404$) or 800 ms ($t = -1.402$, $p = 0.220$) viewing condition

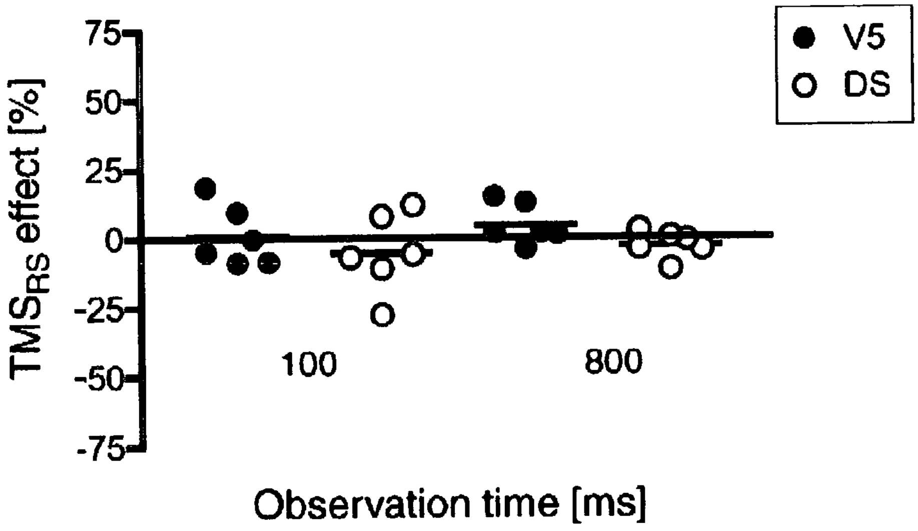

Figure 6.9: Graph illustrating the % TMS effect on reaching speed of V5/MT+ stimulation and Dorsal Site stimulation for 100 and 800ms observation time, for each individual participant and averaged across participants.

6.4 Discussion

The results of this study show that rTMS causing selective disturbance to V5/MT+ affects catching performance by causing a reduction in reaching speed, whereas stimulation of nearby dorsal regions does not affect performance. These results broadly confirm the findings of Schenk *et al.* (2000b) with patient LM, suggesting that it is the disruption of processing in V5/MT+ and not other more dorsal areas which are responsible for LM's catching deficits. The results further show that V5/MT+ is involved in both perceptual (Beckers and Homberg, 1992; Beckers and Zeki, 1995; Walsh *et al.*, 1998) and visuomotor tasks (the present data), therefore it can be argued that V5/MT+ provides visual motion input to both the ventral and dorsal streams of processing.

It was observed in the present study that in the catching task shorter observation times lead to higher error rates and shorter reaction times. This can be explained by the fact that participants produce better performance if they are able to view the target for 100 ms or more. When deprived of vision the accuracy of their movements suffer (leading to higher error rates), as they have to initiate their responses earlier as the closing of the shutter glasses cue their movement. TMS over area V5/MT+ did not influence this effect. The results of the reach-to-grasp task also revealed that reaction time for movements to the left was prolonged in the short observation time condition (but not in the long observation time condition). This may be because participants are more hesitant to begin their movement as they feel there is a greater risk of collision with the headrest or object as they are unable to see their response.

There are some differences in the results obtained in the present study and those obtained with LM. LM's performance was significantly affected by the observation time in that her performance dropped to subnormal levels if the duration interval was less than 400 ms (Schenk *et al.*, 2000b). This was not the case in the present study, which revealed no significant interaction between stimulation site and observation time in the catching task. It is possible that LM's improved performance with longer observation times can be attributed to a compensatory strategy, which she has acquired to use her intact spatial vision to compensate for her loss of motion vision. A long observation time may allow her to use the length of the path travelled by the object throughout the period to estimate velocity. Such strategies are probably only developed over time and only in the response to the experience of behavioural problems, whereas due to the transient nature of TMS such strategies could not be developed in the present study. Another difference in the two studies is that LM's deficits reflected a decrease in reaching speed and an increase in errors, whereas in the present study TMS deficits were only reflected in a decrease in reaching speed. This suggests that TMS-induced deficits to V5/MT+ are more subtle than a lesion to the same area. This is not surprising as rTMS only induces a transient increase of noise in the affected area (Walsh and Rushworth, 1999), and therefore does not replicate the total disruption of information flow that results from structural brain damage.

It is important to note that LM's lesion is bilateral whereas TMS was only applied unilaterally in the present study; this may account for some of the differences between the two studies. It would be expected that disruption in one hemisphere is likely to produce a smaller effect in performance than disruption in two hemispheres, or that disruption in performance would only occur in the contralateral hemispace. Results from this study, however, have shown that deficits in catching occurred for objects travelling to both the left and right hemispace. Previous studies have provided electrophysiological evidence in the monkey (Maunsell and Van Essen, 1987; Van Essen, 1985; Zeki, 1974, 1980), and lesion-based evidence in both humans and monkeys (Newsome and Pare, 1988; Plant *et al.*, 1993; Plant and Nakayama, 1993; Schenk and Zihl, 1997; Vaina *et al.*, 2001), that V5/MT+ in each hemisphere contains only a representation of the contralateral visual field. Several TMS studies have provided evidence to suggest that unilateral TMS over V5/MT+ can lead to contralateral deficits only (Beckers and Homberg, 1992; Beckers and Zeki, 1995; Stewart *et al.*, 1999) whereas other studies have found that unilateral TMS results in deficits in both the contra- and ipsilateral hemispace (Hotson *et al.*, 1994; Walsh *et al.*, 1998). These discrepancies may be resolved by noting that Dukelow *et al.* (2001) have identified subregions within V5/MT+ complex; a posterior one which responds only to stimuli within the contralateral hemifield, and an anterior one which responds to stimuli in both the contra- and ipsilateral hemifields.

It is also possible however that the unilateral stimulation of left V5/MT+ could lead to contralateral responses in the right hemisphere. The first study to measure contralateral responses to TMS was carried out by Cracco (1989) using EEG. Since then a number of studies, using various methodologies, have confirmed that unilateral TMS does indeed cause activation in the contralateral hemisphere (Paus *et al.*, 1997; Illmoniemi *et al.*, 1997; Komssi *et al.*, 2002). Paus *et al.* (1997) used TMS to stimulate left frontal eye field (FEF) while simultaneously measuring changes in cerebral blood flow using PET. The results showed a significant positive correlation between cerebral blood flow and number of pulse trains in the target region (i.e. left FEF) as well as several other areas of visual cortex including left medial parieto-occipital cortex and left and right superior parietal cortex. In addition a positive correlation was found in right supplementary eye field located on the medial wall of the frontal lobe. Ilmoniemi *et al.* (1997) used high resolution EEG to locate the changing pattern of neuronal activity evoked by TMS applied to the left motor and visual cortices. When TMS was applied to the left motor cortex, EEG revealed a strong response 3 ms post-stimulus in the ipsilateral stimulation site, activation at the adjacent ipsilateral motor and pre-motor areas was observed during the next few milliseconds. A clear activation was observed in contralateral homologous cortical areas 20 ms post-stimulus, and activation was also observed in parietal areas. Similar results were also observed for stimulation over left occipital cortex (i.e. immediate ipsilateral activation with contralateral response occurring at around 20 ms post-stimulation). Ilmoniemi *et al.* (1997) propose that contralateral activation probably occurs by transmission through transcallosal connections. In another study, Komssi *et al.* (2002) applied TMS to left sensorimotor cortex (area M1) while EEG recordings were made. The results showed that ipsilateral activation occurred in the precentral gyrus, supermarginal gyrus and superior parietal lobule. Activation also occurred over the contralateral cortex in all participants at 22 ms (+/- 2 ms), with the maximal activation located in the precentral gyrus, superior frontal gyrus and inferior parietal lobule. They propose that the contralateral activation occurs due to a physiologically effective interhemispheric conduction pathway between the hand representation area in M1. The contralateral activation of premotor and posterior parietal association cortices in addition to the M1 hand area may reflect either heterotopic interhemispheric connections or intercortical transmission through association fibres to adjacent fields. It is also possible that subcortical pathways are mediators of the contralateral response (Komssi *et al.*, 2002).

While studies such as these provide strong evidence that unilateral TMS produces contralateral activation in homotopic and adjacent cortical areas, it is unclear if this observed activation would be strong enough to impair performance on tasks such as catching. The above studies do not investigate the strength of the activation in either the ipsi- or contralateral site; in addition the studies do not use any cognitive tasks to determine if the activation would be functionally significant enough to impair task performance. Nikulin *et al.* (2003) recently aimed to demonstrate, using EEG, increased cortical excitability preceding voluntary movement on the basis of changes in ERP response to TMS applied over the left motor cortex. They investigated the N100 component of the response in 10 electrodes over the stimulated sensorimotor areas in the ipsi- and contralateral hemisphere, which they propose represents an inhibitory response following TMS at approximately 100 ms post-stimulus. They note that while the N100 response occurred in both the ipsi- and contralateral hemisphere, the responses were much smaller in the contralateral electrodes. This provides evidence to suggest that while contralateral activation as a result of TMS does occur, this activation is unlikely to be enough to impair task performance on tasks requiring the area and as such cannot account for the observed pattern of results in the present study. Another explanation for the observed pattern of results in this study would be that participants were free to move their eyes and as such the target object always started in a central position and it is therefore likely that participants followed the object with their eyes, thus causing the image to always be near the centre of the visual field.

There are two possible sources of visual motion processing during the catching task, which may have been affected by interference with V5/MT+: (1) movement of target object (2) movement of the hand. There are three arguments suggesting that it is not the interference with perception of the moving hand (i.e. on-line visual feedback) causing the deficits. Firstly, if this were the case we would expect to observe similar deficits in the reach-to-grasp task. Secondly, we would only expect to see deficits when visual feedback is provided (whereas in the present study TMS induced catching deficits were observed equally for both the 100 ms and 800 ms viewing conditions). Thirdly, interference with on-line visual feedback could only explain induced catching deficits if one assumes that such feedback is used during catching. A recent study by Schenk *et al.* (2004) has shown however that on-line visual feedback is used in grasping but not in catching tasks. Taken together these findings indicate that it is not interference with on-line visual feedback that accounts for the V5/MT+ TMS catching deficits, it is interference with the processing of the target's movement.

This study suggests that it is the degradation of information about target speed and not its movement direction that results in the TMS-induced catching deficits (i.e. deficits in catching speed). This observed reduction in catching speed probably reflects an underestimation of the speed of the target object that results from interference with V5/MT+. Previous studies with patient LM (Hess *et al.*, 1989; Zihl *et al.*, 1991) and patients with unilateral damage to V5/MT+ (Plant and Nakayama, 1993) have shown that such damage results in a perceptual underestimation in speed of moving objects. Moreover, evidence from neurophysiological and behavioural studies suggest that V5/MT+ plays a unique role in velocity perception, but that its contribution to the identification of unambiguous motion direction is much less essential. The range of velocities represented in V5/MT+ (Lagae *et al.*, 1993; Maunsell and Van Essen, 1983; Mikami *et al.*, 1986; Rodman and Albright, 1987; Van Essen, 1985) extends to much higher values than that for cells in either V1 (Newsome et al, 1986; Orban et al, 1986) or V3 (Felleman and Van Essen, 1987). This means that interference with V5/MT+ affects cell populations that code higher velocities, so that such velocities have then to be coded in lower velocity cells in V1 and V3, leading to an underestimation in velocity of the moving target. In contrast direction discrimination can be found reliably in

V5/MT+ as well as V1 and V3 (Van Essen, 1985), suggesting that disruption of V5/MT+ would not lead to a significant deficit in the identification of the direction of moving objects. This suggestion is supported by lesion studies (Baker *et al.*, 1991; Hess *et al.* 1989; Shipp *et al.*, 1994). However, single unit studies (Movshon *et al.*, 1985; Salztman *et al.*, 1990; Snowden *et al.*, 1992), lesion studies (Baker *et al.*, 1991; Marcar *et al.*, 1997) and TMS studies (Beckers and Homberg, 1992; Beckers and Zeki, 1995) have all provided evidence to suggest that other types of motion discrimination tasks, involving ambiguous stimuli (e.g. random kinematograms or moving plaid patterns) involve a unique contribution from V5/MT+.

In conclusion the results of the present study confirm that left V5/MT+ is important for visuomotor as well as perceptual tasks that require visual motion processing. This suggests that V5/MT+ does not belong exclusively to either the dorsal or ventral stream but provides a common input to both streams. This is consistent with the well established anatomical fact that V5/MT+ projects to areas in both the dorsal and ventral streams, and that it receives direct inputs from V1 (Felleman and Van Essen, 1991). The results confirm the conclusions of the study with motion blind patient LM (Schenk *et al.*, 2000b); however there are differences between the two studies that must be noted. Firstly, the dependence on extended observation times found with LM, were not observed in the present TMS study. Secondly, LM showed impairments in terms of error and reaching speed, whereas TMS produced deficits in reaching speed only. These differences can be explained by the transient nature of TMS, which does not induce a total disruption in information flow that occurs following structural brain damage.

CHAPTER SEVEN: ORIENTAION SENSITIVITY TO GRASPABLE OBJECTS: AN fMR ADAPTATION STUDY

7.1 Introduction

Functional magnetic resonance-adaptation (fMR-A) was introduced to enable one to tag specific neuronal populations within an area of interest and investigate the functional properties of this area (Grill-Spector and Malach, 2001). Conventional brain mapping typically involves measuring the overall activation within an area during the acquisition time; this makes it impossible to assess whether the source of activity is a mixture of neuronal populations, each tuned to a different property, or if it is the outcome of the activity of a homogeneous group of neurons sharing a common property (Grill-Spector and Malach, 2001). The principles behind fMR-A are as follows: (1) the neuronal population is adapted by repeatedly presenting the same stimulus (the repeated presentation of a stimulus will result in reduced activation within the voxels tuned to this particular stimulus); (2) a property of this stimulus is varied and the recovery from the adaptation is assessed, if the signal remains adapted it indicates that the neurons are invariant to the property which has been changed, whereas if the signal recovers from the adapted state it indicates that the neurons are sensitive to the property which has been changed (Grill-Spector and Malach, 2001). fMR-A is now a popular method of conducting imaging studies, for example Grill-Spector *et al.* (1999) used it to demonstrate that area LOC is less sensitive to changes in object size and position compared to changes in illumination and viewpoint.

A recent experiment (Valyear *et al.*, 2005) used an event-related fMR-adaptation paradigm to investigate changes in BOLD activity in the dorsal and ventral streams as a function of object identity and object orientation. Results of this study revealed that a region in the parieto-occipital cortex (within the dorsal stream) showed selective increase in activity with changes in object orientation, but was insensitive to changes in object identity (figure 7.1). In contrast, a region in the temporo-occipital cortex (within the ventral stream) showed selective increases in activity with changes in identity but was insensitive to changes in orientation. It is important to note, however, that all of the stimuli used in this experiment were real-world graspable objects. The Milner and Goodale (1995) model identifies the dorsal stream of processing as being involved in action (see general introduction). Changes in orientation of a tool or a graspable object would alter the way in which an action is performed upon it (i.e. the way it is grasped). It remains unclear, however, whether the dorsal stream responds selectively to the orientation of these objects specifically because they are graspable (i.e. the 'graspability' of these objects caused action-related information to be automatically represented in the dorsal stream of processing).

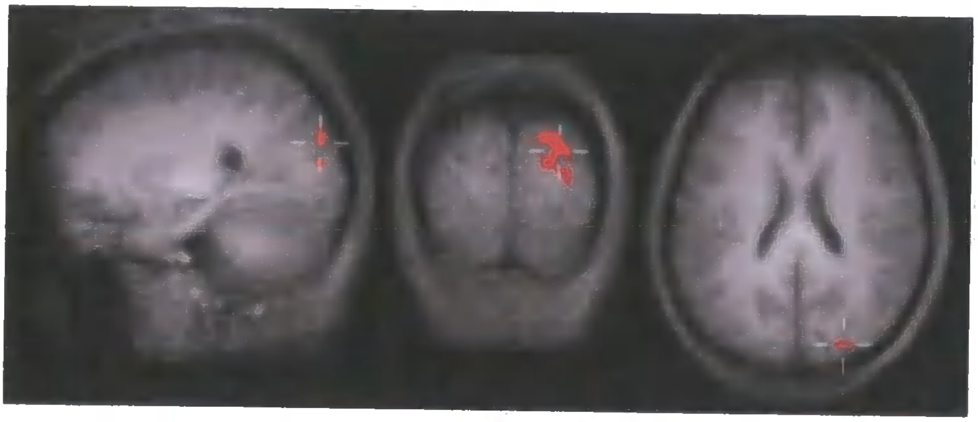

Figure 7.1: From Valyear et al. (2005). Figure depicts area in the occipito-parietal junction of the right hemisphere activated by orientation change versus no change conditions.

To grasp an object successfully requires the extraction of various properties of the object, such as shape, size and orientation. Some understanding of the neural correlates of grasping comes from single unit recording studies in the monkey, for example Gallese *et al.*, (1994) demonstrated the importance of neurons in AIP in pre-shaping the hand for grasping. In addition, work with patients with optic ataxia has suggested that the intraparietal sulcus is important for grasping (Perenin and Vighetto, 1988). Recent fMRI studies have attempted to gain further understanding of the brain regions involved in grasping. Culham *et al.* (2003) found an area in the anterior part of the intraparietal sulcus (AIP) activated more for grasping compared to reaching (the difference in the two tasks is that grasping required pre-shaping of the hand). In a review article, Culham *et al.* (in press), suggest that AIP is activated by the following: (1) visually guided grasping (Binkofski *et al.*, 1998; Culham *et al.*, 2003; Grezes *et al.*, 2003; Frey *et al.*, 2005) and pantomimed grasping (Simon *et al.*, 2002; Grezes *et al.*, 2003); (2) the act of object manipulation even when vision is unavailable (Binkofski *et al.*, 1999; Jancke *et al.*, 2001; Stoeckel *et al.* 2003); (3) the visual presentation of 3 dimensional objects without an action (Shikata *et al.*, 2001; Shikata *et al.*, 2003; Grezes *et al.*, 2003). The last of these is particularly relevant to the present experiment as it suggests that grasp related areas become activated automatically by the visual presentation of graspable objects.

Behavioural evidence has suggested that when a tool is viewed action related information is automatically represented. For example, Tucker and Ellis (1998) showed that the position of an object's handle had a significant effect on speed of key press response (i.e. handle orientation towards the right facilitated key presses with the right hand), despite the fact that the position of the handle was irrelevant to the task. In addition single unit recording studies with monkeys have shown that 'grasp' related neurons discharge when the monkey views images of a graspable object (when no action is required) (Sakata *et al.*, 1995; Murata *et al.*, 1997). Studies such as these suggest that simply viewing a graspable object causes action-related information to be automatically represented.

Recent fMRI work has attempted to investigate such claims within the human brain. Chao *et al.*, (1999) revealed that when participants were shown pictures and names of tools this elicited bilateral activation in the medial aspect of the fusiform gyrus and middle temporal gyrus. In a follow-up study, Chao and Martin (2000), attempted to examine the neural responses in frontal and parietal cortices associated with viewing and naming pictures of tools relative to other categories of animate and inanimate objects (animals, faces, houses). They found that viewing and naming tools selectively activates the left ventral premotor cortex (BA 6), an area which has shown activity in PET studies of imagined hand movements (Decety *et al.*, 1994; Stephan *et al.*, 1995; Grafton *et al.*, 1996). The authors suggest that this area may be related to retrieval of information about hand movements associated with the use of graspable man-made objects and may be the human homologue of monkey premotor area F5. In addition, Chao and Martin (2000) found activity in the left posterior parietal cortex (BA 40) for viewing and naming tools, an area close to human AIP as been identified in fMRI grasping studies (Binkofski *et al.*, 1999; Culham *et al.*, 2003) and the intraparietal areas commonly associated with optic ataxia deficits (Perenin and Vighetto, 1988). The authors suggest that this area may be related to retrieval of information about hand and finger movements associated with the use of graspable man-made objects. They conclude based on these results and previous findings (Chao *et al.*, 1999) that there is a network of ventral and dorsal sites active when we recognise and identify graspable man-made objects.

Creem-Regehr and Lee (2005) suggest that tools are different from other types of graspable objects because they have a semantic identity tied to an action representation. They carried out an fMRI experiment in which participants were presented with images of 3-dimensional tools (with familiar functional identity) or 3-dimensional shapes (graspable objects with no known function) and were asked to either passively view or imagine grasping them. Results showed activation in posterior middle temporal gyrus, ventral premotor areas, and posterior parietal cortex during the passive viewing task for tools compared to shapes. During imagined grasping a network of activation (frontal-parietal-temporal) was observed for both tools and shapes. Differences were observed however in the extent and location of the premotor and parietal activation for tools compared to shapes and there was also an area in the middle temporal gyrus and fusiform gyrus for tools compared to shapes. They conclude that an object's functional identity influences its perceived potential for action (i.e. the extent of the motor representation associated with it). A problem with this study is, however, that it is unclear if the 'graspable shapes' were actually perceived by participants as being graspable.

In another (unpublished) study, Creem-Regehr *et al.* (2004), gave participants experience holding and manipulating a series of novel graspable objects, attaching specific functions to half of the objects (making them 'tools'). Participants were then scanned while viewing images of these novel objects (either tools or non-tools), and were required to passively view, imagine grasping or imagine using them. During passive viewing they found ventral premotor cortex activation for tools but not non-tools (suggesting a representation for action with functional tools even when action is not required). In addition they found activation in posterior parietal cortex for viewing both tools and non-tools (suggesting that both non-tools and tools are represented for their graspability due to motor experience before the scan). In the imagined grasping task activation was found in the posterior parietal cortex, dorsal and ventral premotor cortex, and ventral temporal cortex for both types of objects. Finally in the imagined using task greater activation was seen in dorsal and ventral premotor cortex, SMA, insula, cerebellum and posterior parietal cortex, including more inferior region of the supermarginal gyrus for tools compared to non-tools (suggesting that representation for action differs based on known motor patterns associated with the object use).

The aim of the present experiment was to determine whether dorsal stream selectivity to orientation changes, identified by Valyear *et al.* (2005), is specific to graspable objects. The experiment involved presenting participants with graspable real world objects (i.e. tools and kitchen utensils), and non-graspable real world objects (i.e. furniture and vehicles); the orientation of which may or may not change. The orientation change was such that the object was flipped 180 degrees on its horizontal axis; the purpose of looking at such changes in orientation is that such a change would alter the way in which one would be required to pick the object up. If the dorsal stream is sensitive to orientation changes *per se* it would be predicted that there would be an increase in neuronal activity in dorsal stream regions when an orientation change occurs for both graspable and non-graspable objects. If, on the other hand, the dorsal stream is only sensitive to orientation changes for graspable objects it would be predicted that there would be an increase in neuronal activity in dorsal stream regions when an orientation change occurs for *graspable objects* only.

7.2 Method

7.2.1 Participants:

10 neurologically healthy participants took part in the study, 6 male and 4 female, age range 23 - 40. All subjects were right-handed by self-report and had normal or corrected to normal vision. Each participant provided informed consent according to procedures approved by the University of Western Ontario Review Board for Health Sciences Research Involving Human Subjects.

7.2.2 Stimuli:

The visual stimuli were presented to the participants using a video projector which was connected to a PC laptop. The images were projected onto a rear-projection screen which straddled the participants' waist while they lay supine in the scanner. A small mirror was attached to the head coil which was tilted to allow participants to view the stimuli on the screen.

Stimuli were selected from the Hemera Photo-Objects image database. Stimuli were two-dimensional photographs of either graspable (i.e. tools or household utensils) or non-graspable (i.e. vehicles or furniture) objects. All images selected had a horizontal principal axis. Images were then rendered in greyscale and resized (320 × 320 pixels) using Adobe Photoshop. Each of the images was flipped 180 degrees along the horizontal axis for use in the orientation change condition. A total of 100 images were used, 50 of which were graspable objects (tools or kitchen utensils) and the remaining 50 were non-graspable (vehicles or furniture). A mask stimulus was created using Matlab to divide an image into a 320 × 320 pixel grid then randomly reorder the cells (each comprising 32 × 32 pixels) of the grid. A fixation cross was generated using Adobe Photoshop. The stimulus program was created using Super Lab.

7.2.3 Procedure:

Each event-related experimental scan was 6 minutes 43.5 seconds in length (269 volumes), and participants underwent between 5 and 10 experimental scans (depending on time constraints). Each scan comprised 20 stimulus events, each separated by a fixation period presented for a duration of 12, 13.5 or 15 seconds (chosen at random). This was long enough to allow the BOLD signal to return to baseline levels before the next stimulus was presented (Valyear *et al.*, 2005). Each stimulus event consisted of a prime stimulus (1.5 s), followed by a mask (1.5 s), followed by a target stimulus (1.5 s), ending with a mask (1.5 s); each stimulus event lasted a total of 6 seconds. The prime stimulus was a graspable or non-graspable image, the target stimulus was always the same object as the prime, however the orientation of the target stimulus would either be the same or different (flipped along the horizontal axis). As such there were a total of four event types: (1) Graspable object, orientation same (G-OS); (2) Graspable object, orientation different (G-OD); (3) Non-graspable object, orientation same (NG-OS); (4) Non-graspable object, orientation different (NG-OD), (figure 7.2). Each event type occurred randomly five times during each scan, as such a total of 20 different object identities were used during each scan, and images were not repeated across scans. In half of the events the 'business end' (i.e. handle or front) of the prime stimulus was presented to the right of fixation while in the other half it was presented to the left. Participants were instructed to fixate centrally throughout each event. They were told that a prime image would appear followed by a mask, followed by a second target image, followed by a mask. The task was to decide if the orientation of the target image was the same or different than that of the prime; using their right hand they pressed key

1 on the response box if the orientation had changed and key 2 if no change had occurred. A perceptual task was used in the present study as Murray and Wojciulik (2003) have shown that attention to a dimension of interest increases the neural responses and sharpens the population level response to the attended dimension of interest, thus increasing the efficiency of the population code.

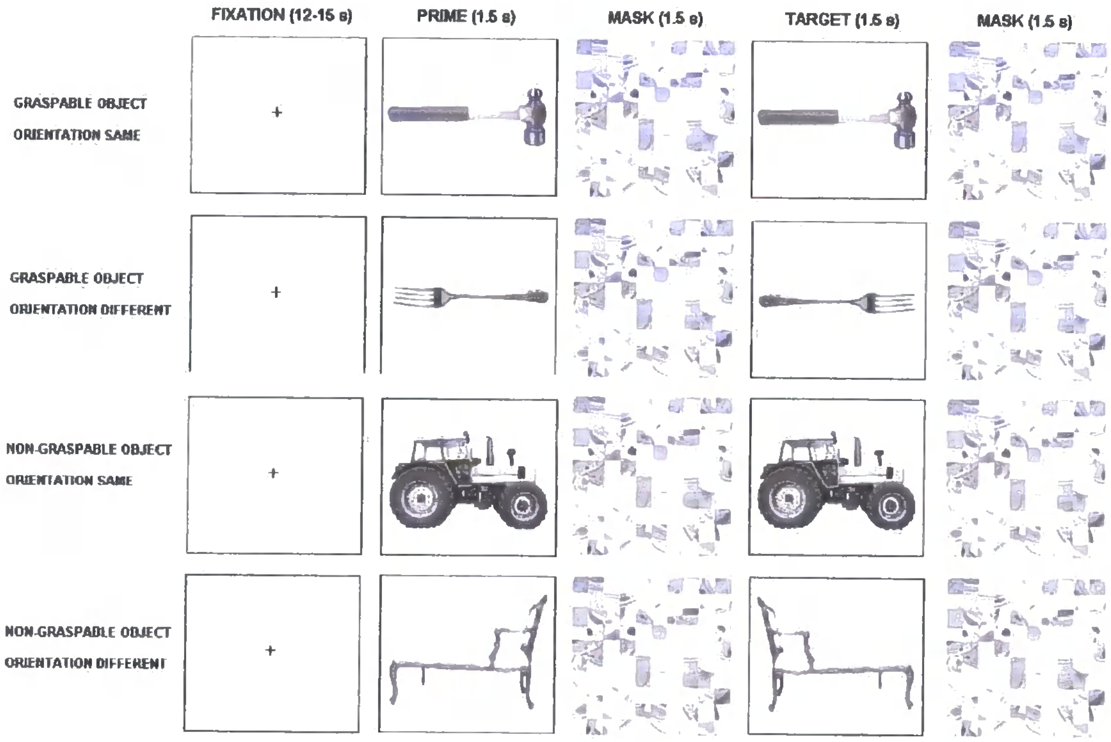

Figure 7.2: Figure illustrating the stimuli and timing for each of the four event types.

7.2.4 Imaging parameters:

A 4 Tesla, whole-body MRI system (Varian, Siemens) and a quadrature radiofrequency head coil were used; these were located at the Robarts Research Institute (London, ON, Canada). Each imaging session consisted of both functional scans and a high resolution anatomical scan. Functional volumes were collected every 1.5 seconds using a T2*-weighted, segmented (navigator corrected), interleaved spiral acquisition (TE = 15 ms, TR = 750 ms, FA = 45 degrees, 2 segments / plane) for BOLD-based imaging (Ogawa *et al.*, 1992). A single volume acquisition covered 14 continuous, 6 mm, pseudo-axial slices, ranging from the most superior point of the cortex down through the ventral fusiform, encompassing approximately ¼ of the cerebellum. The imaging field of view was set at 22 cm × 22 cm, providing a resultant voxel resolution of 3.4 mm × 3.4 mm × 6 mm. High resolution T1-weighted anatomical volumes were acquired using 3D magnetization-prepared FLASH acquisition (T1 = 1300 ms, TE = 3 ms, TR = 50 ms, FA = 20 degrees).

7.2.5 Analysis:

The imaging data were pre-processed and analyzed using Brain Voyager QX (Brain Innovation, Maastricht, The Netherlands). Anatomical volumes were transformed into a brain space that was common for all participants (Talairach and Tournoux, 1988). Each functional run was screened for head movements using Brain Voyager 3D motion correction parameter plots and those that were found to be significantly corrupted (i.e. containing movements that were 2 mm / degrees or larger for abrupt movements) were removed from the analysis. Each run underwent temporal high-pass frequency filtering (2 cycles per scan) to remove low frequency trends in the signal. Functional volumes were then aligned to the transformed anatomical volumes, and as such all functional data were transformed into a standard stereotaxic space (Talairach and Tournoux, 1988).

The data was analysed using a general linear model (GLM) in Brain Voyager QX. Random effects analyses was performed, which included separate subject predictor functions for each participant to ensure that effects could not have been driven by only a small number of participants and that the results were applicable to the general population. Two main statistical contrasts were performed by contrasting the orientation different from the orientation same trials for: (1) graspable objects (G-OD versus G-OS); (2) non-graspable objects (NG-OD versus NG-OS). Thus orientation sensitivity was assessed independently for each of the two stimulus categories. Resultant activation maps were set to a minimum cluster size threshold of 110 mm^3 and a minimum significance threshold of $t = 3.9$. To determine these statistical settings, the events were first pseudo-randomised such that each condition had an equivalent number of events from each of the four conditions within it. In other words, stimulus events were divided into four 'arbitrary' conditions. Thus, in principle contrasting any two of these conditions should yield no significantly active voxels. In this way it was possible to evaluate the reliability of data and determine the appropriate statistical setting for use in the subsequent analysis. To do this contrasts were made between two of the conditions versus the remaining two conditions and the statistical thresholds for which no significant voxels were identified was determined. Using this data driven approach, it was revealed that at the above thresholds ($k = 110$ voxels, $t = 3.9$) no voxels were found to be significantly active.

Once the orientation sensitive areas were identified for each of the stimulus categories, averaged time courses were extracted from the regions and converted into percent signal change. Various planned comparisons were then conducted on the data. These included, determining main effects of orientation (G-OD and NG-OD versus G-OS and NG-OS) and category (G-OD and G-OS versus NG-OD and NG-OS), and also contrasting orientation different versus orientation same trials for both the graspable (G-OD versus G-OS) and non-graspable (NG-OD versus NG-OS) categories of objects. This was to determine if regions identified in the main contrasts were selective for one of the categories of objects or whether they were selective for orientation *per se*.

7.3 Results

To identify regions that were sensitive to changes in the orientation of graspable objects a contrast was made between the average BOLD response associated with the G-OD condition, against the average BOLD response associated with the G-OS condition. To ensure that this activity would also be greater than baseline a comparison (i.e. conjunction analysis) was added, which contrasted the G-OD condition against fixation. This revealed two significant clusters of activation: one in the right hemisphere in the occipito-parietal junction (see figure 7.3), and the other in the left hemisphere in the middle temporal gyrus (see figure 7.5). To identify regions that were sensitive to changes in the orientation of the non-graspable objects a contrast was made between the averaged BOLD response associated with the NG-OD condition against the averaged BOLD response associated with the NG-OS condition. Again, to ensure that this activity was greater than baseline a conjunction comparison was added contrasting the NG-OD condition against fixation. This second contrast revealed no significant clusters of activation.

The first cluster of activation observed was in the right hemisphere in the occipito-parietal junction (figure 7.3). The Talairach co-ordinates for this cluster are, $x = 24$, $y = -85$, $z = 6$; a total of 132 voxels were included in this cluster. The averaged time course of activation within this cluster is plotted for each of the experimental conditions in figure 7.3. Planned comparisons revealed a non-significant main effect of orientation ($t = 1.905$, $p = 0.086$). A significant effect of category was observed ($t = -3.399$, $p = 0.007$), the graph below shows that this is due to a higher response in the non-graspable object category than the graspable. A significant difference was observed between orientation change and no change for the graspable objects ($t = 4.973$, $p < 0.001$), but not for the non-graspable objects ($t = 0.328$, $p = 0.749$), this is illustrated in figure 7.4.

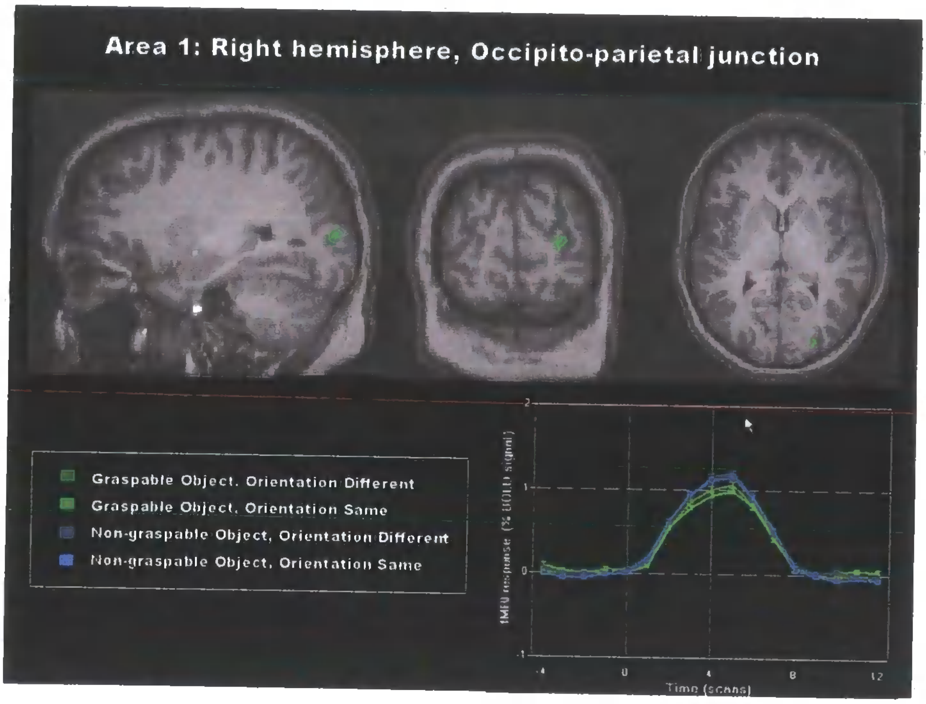

Figure 7.3: Figure illustrating the activation map identified by contrasting orientation different versus orientation same within the graspable object category. The area defined lies at the occipito-parietal junction on the right hemisphere. Talairach coordinates: $x = 24$, $y = -85$, $z = 6$. The graph illustrates the averaged time course for each of the experimental conditions.

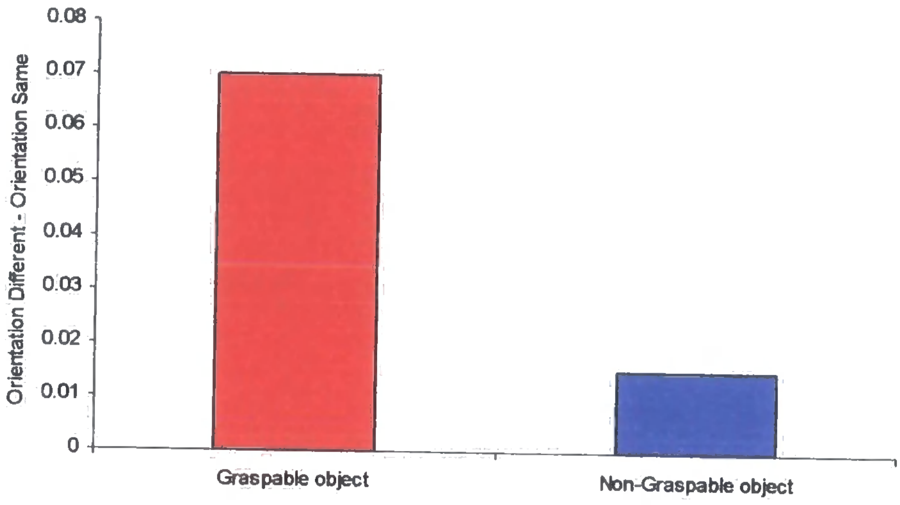

Figure 7.4: Graph illustrating the sensitivity to orientation changes for graspable and non-graspable stimuli for area OPJ in the right hemisphere. The y axis indicates % signal change for orientation different trials minus % signal change for orientation same trials.

The second cluster of activation identified was in the left hemisphere in the middle temporal gyrus. The Talairach co-ordinates for this area are x = -40, y = -66, z = -3, a total of 169 voxels were included within this cluster. The averaged time course of activations for each of the four experimental conditions is plotted in figure 7.5. Planned comparisons revealed a significant effect of orientation (t = 2.859, p = 0.017), this is due to increased activity in the orientation different conditions. There was a non-significant effect of category (t = 1.284, p = 0.228). A significant difference was observed between orientation change and no change within the graspable object category (t = 2.646, p = 0.024) but not the non-graspable object category (t = 1.344, p = 0.209), this is illustrated in figure 7.6.

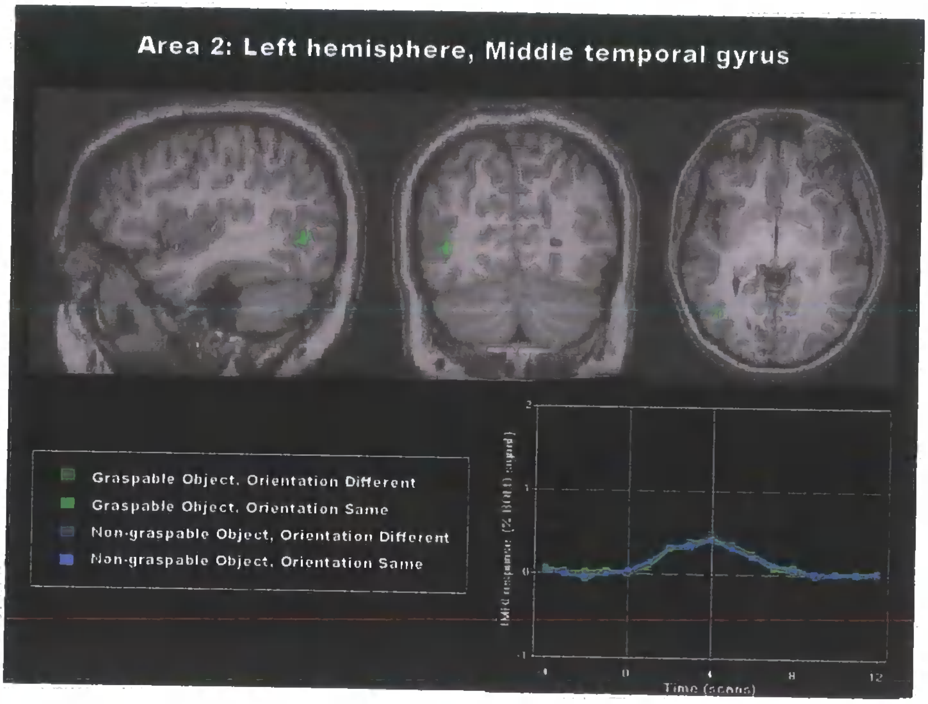

Figure 7.5: Figure illustrating the activation map identified by contrasting orientation different versus orientation same within the graspable object category. The area defined lies in the middle temporal gyrus on the left hemisphere. Talairach coordinates: x = -40, y = -66, z = -3). The graph illustrates the averaged time course for each of the experimental conditions.

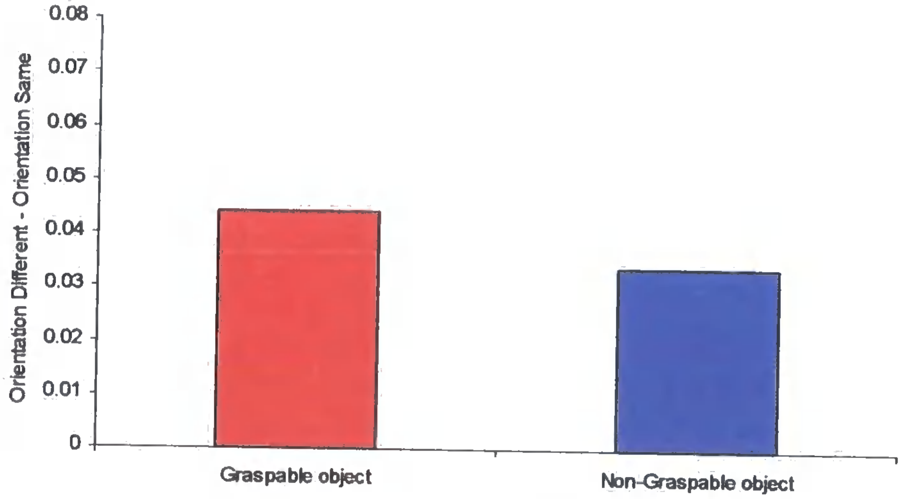

Figure 7.6: Graph illustrating the sensitivity to orientation changes for graspable and non-graspable stimuli for area MTG in the left hemisphere. The y axis indicates % signal change for orientation different trials minus % signal change for orientation same trials.

7.4 Discussion

The aim of the present experiment was to determine if dorsal stream selectivity to orientation changes is restricted to graspable objects. Participants were presented with an image of either a graspable or non-graspable stimulus, which was followed by the same image in either the same or different orientation (i.e. a flip on the horizontal axis). A comparison was made between orientation change and no change conditions within the graspable object category. This revealed two clusters of activation, one in the occipito-parietal junction of the right hemisphere, and the other in the middle temporal gyrus of the left hemisphere. Each of these areas was shown to be sensitive to orientation changes in the graspable object category only. No areas of activation were revealed for a comparison of orientation change versus no change within the non-graspable object category.

The first area identified within this study is at the occipito-parietal junction (OPJ) on the right hemisphere (x = 24, y = -85, z = 6). This corresponds remarkably closely to the area identified by Valyear *et al.* (2005) showing sensitivity to orientation changes (x = 22, y = -81, z = 19). Valyear *et al.* (2005) suggest that the most likely candidate for a functionally similar region to OPJ in the macaque is an area in the lateral bank of the caudal intraparietal sulcus (CIP) and further suggest that human CIP may in fact overlap with the area they identify as OPJ. In the macaque brain, CIP contains neurons that respond selectively to 3 dimensional features of an object, such as shape and orientation (Sakata *et al.*, 1998; Taira *et al.*, 2000; Tsutsui *et al.*, 2002). This area not only contains neurons tuned to object orientation but sends projections to AIP for the visual guidance of hand actions (Sakata *et al.*, 1997; 1999) as AIP has no direct access to spatial properties of objects (Sakata *et al.*, 1998). Faillenot *et al.*, (1997; 1999) suggest there is a region in the caudal part of the intraparietal sulcus in the human brain which becomes active during object matching and grasping and during discriminations of object size and orientation. In an fMRI study Shikata *et al.* (2003) identify a possible human homologue of monkey CIP in the posterior part of the intraparietal sulcus in both the right and the left hemisphere. This region showed activation when a comparison was made between orientation and colour discrimination tasks, and they conclude that human CIP is involved in coding the 3 dimensional features of objects. It is thus possible that the region in the OPJ of the right hemisphere observed in the present study codes the orientation of objects to be grasped, providing an input into AIP.

If the area identified in the present study is in fact the human homologue of monkey CIP, which sends projections to AIP for the visual guidance of hand actions, then it seems surprising that activation is observed in the right but not the left hemisphere given that all participants were right handed and that they used the right hand in making their choice responses. Faillenot *et al.* (1999) revealed activation in the posterior part of the intraparietal sulcus in the right hemisphere in an orientation discrimination task. Taira *et al.* (2001) also suggested that the perception of structure based on shading revealed activation in the caudal part of the intraparietal sulcus on the right hemisphere. In a later study however, Faillenot *et al.* (2001), showed activation in the caudal part of the intraparietal sulcus of the left hemisphere. Finally, Shikata *et al.* (2001, 2003), showed activation bilaterally in the posterior portion of the intraparietal sulcus for orientation discrimination. While the evidence of hemispheric lateralization is contradictory, Shikata *et al.* (2003) state that the right parietal cortex is more involved in visuospatial information processing, whereas the left is more involved in visuomotor integration. While it is difficult to explain why activation was not observed in the left hemisphere in the present study, it is possible that the task employed (i.e. to detect a change in orientation) can account for this, as this is predominantly a visuospatial task.

The second region identified within this study was the middle temporal gyrus (MTG) in the right hemisphere (x = -40, y = -66, z = -3). This area corresponds closely to one of the regions identified by Chao *et al.* (1999) in the middle temporal gyrus most prominent in the left hemisphere (x = -45, y = -57, z = 7) for tools compared to animal stimuli. This area showed greatest activation when participants where required to silently name pictures of tools and also when participants were required to silently read names of tools. The authors suggest that this area may be a site for stored information about non-biological motion given its close proximity to V5 / MT+ (Zeki, 1991) (see general introduction) and selective activation when subjects generate action words (Wise *et al.*, 1991; Martin *et al.*, 1995; Fiez *et al.*, 1996) and name and retrieve information about tools (Mummery et al., 1996, 1998; Cappa et al., 1998; Perani et al., 1999; Moore and Price, 1999). In a more recent study Creem-Regehr and Lee (2005) also suggest that the posterior middle temporal gyrus and middle fusiform gyrus have been associated with perceiving and naming tools.

Beauchamp *et al.* (2002) attempted to determine if different regions of lateral temporal cortex are specialized for processing different types of motion information, in particular human and tool motion. They found that area MT (bilaterally) responded similarly to human and tool motion. In addition they found an area in the superior temporal sulcus (STS) which responds more strongly to human motion, and an area in the middle temporal gyrus (MTG) more strongly activated by tool motion. This latter area (x = -38, y = -63, z = -6) is extremely close to the cluster of activation identified in the MTG in the present experiment as being sensitive to orientation changes in graspable objects. They also showed that MTG prefers static tools to static humans and shows a trend towards preferring unarticulated motion (typical of tools) to articulated (typical of humans). They conclude that within the lateral temporal cortex there are two parallel visual motion processing streams, which begin just anterior to MT: (1) the superior stream, in STS, which is responsive to biological motion; (2) the inferior stream, in MTG, which is responsive to tool motion.

There are two things which are important to note here, the first is that the activation observed within area MTG cannot be accounted for by the fact that the orientation change elicited apparent motion, as if this were the case the effects would not be specific to the graspable object category. In addition, this area is not sensitive to orientation *per se* as we would expect to see activation in both categories of objects. What is observed here is that the region in MTG in the left hemisphere shows sensitivity to orientation changes of graspable objects only. This may be accounted for by the fact that an orientation change affects the way in which one will grasp and manipulate a tool. The manipulation of a tool has a strong motion component, which can account for the fact that this area lies in close proximity to motion sensitive areas. It may also be the case that this area provides an input into the dorsal stream of processing for action. Evidence in support of this suggestion has been provided in chapter 6, where it was shown that area MT / V5+ is involved in motion processing for perception and action and thus belongs exclusively to neither the dorsal or ventral stream of processing but provides a common input into both streams.

In the present experiment two areas were shown to be sensitive to orientation changes of graspable objects, whereas in the original experiment by Valyear *et al.* (2005) there was only one region identified (OPJ of the right hemisphere). There is one important difference between the present study and the original which may account for this, and that is the fact that in the present study the orientation change was a flip on the horizontal axis, allowing the principal axis to remain unchanged. In contrast, Valyear *et al.* (2005) used stimuli which were tilted either 45 degrees to the left or right of the horizontal meridian with respect to the observer. The change used in the present study means that it would have a more clear effect on the way in which the object is grasped and manipulated, and as such is more likely to cause orientation sensitive areas to become active (as the orientation of an object determines the way in which it should be grasped and manipulated). One other difference between the two experiments is that the present study employed a task where participants were required to attend to the orientation of the stimuli, thus making it more likely that orientation sensitive areas would show activation.

It is possible that the effects observed in the present study could be due to spatial attention. In other words, orientation change events caused an increase in spatial attention, which in turn causes an increase in neuronal activity. This is however unlikely to be the case for two reasons, firstly previous imaging studies have identified area LIP (see general introduction for more details) as being responsive to saccadic eye movements and shifts in spatial attention (Corbetta, 1998; Beauchamp *et al.*, 2001), yet no such activation was observed in the present study. Secondly if orientation changes caused an increase in spatial attention one would expect to see an increase in neuronal activity for orientation shifts of both graspable and non-graspable objects.

One other finding from the present experiment, which requires consideration is the fact that area OPJ showed higher levels of activity for non-graspable objects when compared to graspable objects (although critically the area was only sensitive to orientation changes if the stimuli were graspable). Such an observation is difficult to interpret. One possibility is that the non-graspable stimuli are larger and thus in general are more 'visually stimulating' than the graspable stimuli.

In conclusion, the present study provides evidence to suggest that the dorsal stream sensitivity to orientation changes previously observed in area OPJ in the right hemisphere (Valyear *et al.*, 2005) is restricted to graspable objects only, presumably because such changes affect the way in which an object is grasped. This area is possibly a functionally equivalent region to area CIP in the macaque brain which has been shown to be sensitive to the 3 dimensional features of an object and sends projections to AIP for guiding grasping. In addition, another region in the MTG of the left hemisphere was also shown to be sensitive to orientation changes of graspable objects. This area may be the site for stored information regarding tool motion, and may send projections to the dorsal stream for action with tools (hence sensitivity to orientation changes), which requires a strong motion component. In other words, the data can be interpreted as reflecting an initial 'semantic' processing of the stimulus taking place in the MTG, which in turn provides inputs to dorsal areas concerned with visuomotor control (specifically the OPJ).

CHAPTER EIGHT: GENERAL DISCUSSION

8.1 Summary of the work reported in the thesis

A brief summary of the aims, methodology, results and conclusions of each of the experimental chapters will be presented below.

It has been well established that patients with optic ataxia have deficits in visuomotor tasks such as reaching and grasping, and this is attributed to damage to the dorsal stream of processing. The aim of chapter two was to determine if such deficits would be observed in optic ataxic patients when required to automatically avoid non-target obstacles in the work space. If so, this would extend our knowledge of the kinds of visuomotor processing that are controlled by the dorsal stream. Two bilateral optic ataxic patients were tested on two tasks: (1) Reaching task – in which they were required to reach between two poles to a target location located beyond them; (2) Bisection task - in which they were asked to bisect the space between the two poles. Results showed that both optic ataxic patients failed to take account of the varying locations of the poles in the reaching task, but took full account of such information when asked to make a perceptual judgement. Taking these results in conjunction with other recent data using similar tasks with neurological patients, it was concluded that automatic avoidance of obstacles is a function of the dorsal stream of processing, which is damaged in patients with optic ataxia.

Much of the evidence in support of the Milner and Goodale model has been obtained from illustrating double dissociations in perception and action with patients with optic ataxia and visual form agnosia. The aim of chapter three was to determine if such a double dissociation could be observed using the tasks employed in chapter two. Two patients with visual form agnosia (with ventral stream lesions) were tested in a reaching and bisection paradigm. Results showed that such patients performed in a similar way to controls in the reaching task, but performed outside the normal range on the bisection task. In other words, a double dissociation was observed between optic ataxic patients and visual form agnosic patients (i.e. optic ataxic patients were impaired at reaching but not bisection; visual form agnosic patients were impaired at bisection but not reaching). This provides further evidence to support the conclusion of chapter two, that automatic avoidance of obstacles is a function of the dorsal stream of processing, intact in patients with visual form agnosia.

The Milner and Goodale model has also suggested that the two streams of processing can be differentiated on the basis of time, the dorsal stream with effectively no memory, the ventral stream with both a short and a long-term memory. The aim of chapter four was to determine if automatic obstacle avoidance (which has been argued to be a function of the dorsal stream of processing) operates within such a 'dorsal' time frame. One patient with unilateral optic ataxia (left hemisphere damage) was tested on the bisection task, and on the reaching task under immediate conditions and when a five second delay was required before response. The results confirmed the observations of chapter two, that optic ataxic patients perform the bisection task in a manner similar to controls. On the immediate reaching task the patient ignored shifts in the right obstacle when using his right hand. On the delayed reaching task however this deficit showed recovery. It was concluded that automatic obstacle avoidance is a function of the dorsal stream, however when a delay is required before response a more flexible visuospatial coding system comes into play mediated by the ventral stream. These, however, have to be treated as preliminary data, due to unfortunate practical problems in testing two further unilateral patients (in Lyon).

It has been well established that visual form agnosic patients have intact goal-directed visuomotor behaviour as a function of their frequently intact dorsal stream of processing. Research has shown however that when viewing is restricted to monocular conditions these patients show impairment, due to the fact that pictorial depth cues are processed within the ventral stream. The aim of chapter five was to determine if visual form agnosic patient DF would show intact behaviour when required to catch a moving object under monocular and binocular viewing conditions. In task one, participants were required to catch a moving object that moved away from them at different speeds and directions. In task two, participants were required to respond to online perturbations in speed and direction. Results showed that DF was capable of catching objects moving at different speeds and directions under both monocular and binocular viewing conditions, and it was concluded that she was using looming information to enable her to carry out this task. In addition, results showed that DF could accurately respond to online perturbations in speed and direction, providing evidence to suggest that this ability is a function of the dorsal stream of processing.

It has been well established that V5 / MT+ is involved in motion processing within the perceptual domain (for example, damage to V5 / MT+ has been shown to cause impairments in motion discrimination tasks). The aim of chapter six was to determine if V5 / MT+ is also involved in motion processing within the visuomotor domain. While it has been demonstrated that akinetopsic patient LM has deficits in catching a moving object it is impossible to determine if her deficits are due to damage to V5 / MT+ *per se*, as her lesion has been shown to extend into more dorsal regions. Repetitive TMS (rTMS) was used to transiently disrupt V5 / MT+ while healthy participants carried out a catching task and a reach to grasp task. Results showed that rTMS caused deficits in catching performance but not in reaching, by causing a reduction in reaching speed. It was concluded that V5 / MT+ is involved in motion processing for perception and action, and as such it appears not to belong exclusively to either the ventral or the dorsal stream, but provides a common input into both streams of processing.

A recent fMRI study has shown that visual processing in the dorsal stream is sensitive to changes in object orientation. What remains unclear is if such sensitivity is restricted to graspable objects, due to the fact that the dorsal stream is involved in action and orientation affects the way in which one manipulates an object. The aim of chapter seven was to determine if dorsal stream sensitivity to object orientation is restricted to graspable objects. An fMR adaptation study was carried out in which participants viewed both graspable and non-graspable stimuli; the orientation of which either changed or did not change. While no activation was observed for orientation changes in non-graspable stimuli, two clusters of activation were shown to be sensitive to orientation changes in the graspable stimuli. The first region was in the occipito-parietal junction of the right hemisphere. This may be a functionally equivalent region to the caudal intraparietal region in the macaque, an area which is sensitive to orientation and sends projections to the anterior intraparietal area for grasp processing. The second region was in the middle temporal gyrus of the left hemisphere, an area which has been shown to be sensitive to tool motion and possibly sends projections to the dorsal stream for action with tools (which requires a motion component).

8.2 The dorsal and ventral streams revisited

Chapter one gave an overview of two influential theories regarding the functions of the ventral and dorsal streams of processing. Ungerleider and Mishkin (1982) called them the 'what' and 'where' stream, respectively, whereas Milner and Goodale (1995) labelled them the 'what' and 'how' streams. In a recent review, Goodale and Westwood (2004) have argued that the Milner and Goodale model has survived the test of time relatively well. Some authors (see below) would disagree with this, arguing that the model is oversimplified, particularly with regard to the processing of the dorsal stream. Below is a brief overview of some of the criticisms directed at the model in recent years, particularly with respect to the functioning of the dorsal stream.

Creem and Profitt (2001) in a review of the two streams of processing suggest that there is evidence of both a 'where' and a 'how' stream in the posterior parietal cortex. For example, damage to the posterior parietal cortex can result in visuomotor deficits (e.g. optic ataxia) as well as visuospatial deficits (e.g. neglect); they also provide evidence from monkey neurophysiology and human fMRI to support this distinction. They suggest that the problem can be resolved if the posterior parietal cortex is categorized structurally and functionally into distinct subsystems of spatial processing. They suggest that the superior portion of the dorsal stream may process 'how' information involved in visually guided action, whereas the inferior portion may be involved in global spatial 'where' processing.

A similar distinction is made in a more recent paper by Rizzolatti and Matelli (2003) who propose that the dorsal stream and its recipient parietal areas form two distinct functional systems: (1) the dorso-dorsal (d-d) stream; (2) the ventro-dorsal (v-d) stream.

The d-d stream includes area V6 as well as areas V6A and MIP of the superior parietal lobule. The role of this stream is in action organization, damage of which leads to optic ataxia. The v-d stream includes area MT / V5+ and visual areas of the inferior parietal lobule. This stream plays a role in space perception and action recognition, damage to the right inferior parietal lobule results in neglect, and damage to the left inferior parietal lobule results in ideomotor apraxia (in which patients fail to implement the internal representation of a gesture into an appropriate motor action).

While Glover (2004) also acknowledges a distinction between the functions of the superior and inferior parietal lobe, he takes a different line of argument revolving around a dichotomy between the planning of an action and its online control in humans. He suggests that higher level intentional planning of complex action relies on the inferior parietal lobe (along with the frontal lobes and basal ganglia) whereas online automatic control of visually guided actions relies on the superior parietal lobe (along with the cerebellum). He suggests that an example of this distinction can be seen between patients with ideomotor apraxia and optic ataxia. Ideomotor apraxia is associated with damage to the left inferior parietal lobule; these patients display impairments in planning familiar over-learned actions towards tools, yet have no deficits in online control. Optic ataxic patients on the other hand, with damage to the superior parietal lobule, have difficulty in movements towards peripheral targets, the kinematics are impaired late in the reach only and they have difficulty in making online corrections.

While Jeannerod (1997) accepts the bifurcation between vision for perception and vision for action presented by Milner and Goodale, he refers to this distinction as semantic and pragmatic processing, respectively. Semantic representation involves integration of elementary features of an object into higher order properties that allow a percept to exist as a meaningful whole. Pragmatic representation involves rapid sensorimotor transformations when treating the object as a goal for action. Recently, Jeannerod and Jacob (2005) suggest that the Milner and Goodale model "seriously underestimates the complexity of representations for actions produced by pragmatic processing of visual information". While they agree that one of the functions of the parietal lobe is to enable visuomotor transformation, they suggest that there are other functions, namely to allow the perception of spatial relations among objects and to store complex representations of actions (such as schemas for the use of cultural tools). For example apraxic patients, with lesions of the left inferior parietal lobule, have no basic visuomotor impairment, but they are impaired in the recognition of tools and actions involving the use of tools. They suggest that the superior parietal lobe is involved in visuomotor processing, the right inferior parietal lobule contributes to the perception of spatial relationships and the left inferior parietal lobule contributes to a representation related to visually goal-directed actions.

The criticisms directed at the Milner and Goodale model have mainly focused on the fact that disorders such as neglect and apraxia cannot be accounted for within the realms of the two cortical visual streams. So, can the Milner and Goodale model account for such observations? With regards to neglect, they have suggested that the visuospatial representation systems in the right posterior parietal cortex receives inputs from both streams, the input from the ventral stream being especially critical (Milner and Goodale, 1995), rather than constituting a separate stream of processing as suggested by Creem and Profitt (2001) and Rizzolatti and Matelli (2003). This is supported by the findings of McIntosh *et al.* (2004a) who demonstrated that neglect patients, following damage to the right hemisphere, ignore shifts in a leftward cylinder when required to bisect the space between two cylinders, yet took account of shifts in both cylinders when required to reach between them. The authors interpret this behaviour by arguing that the bisection task requires a conscious perceptual strategy mediated by the ventral stream (damaged in neglect patients). The reaching task, on the other hand, requires participants to unconsciously navigate their way around obstacles and is mediated by the dorsal stream (intact in neglect patients). With regards to apraxia, Milner and Goodale (1995) acknowledge the existence of a praxic control system in the left posterior parietal lobe, but suggest that this receives its inputs from the ventral stream of processing, which then 'instructs' the relevant visuomotor system. This is supported by the findings of Sirigu *et al.* (1995) who describe a patient who can accurately recognise and grasp objects (i.e. will calibrate grip appropriately), yet will place their grasp inappropriately for object use. This suggests that the two systems can function adequately in isolation but may be disconnected from each other. Evidence from DF also supports this suggestion; Carey *et al.* (1996) have shown that DF is able to grasp everyday tools and utensils with a well formed hand posture but has difficulty selecting the correct part of the object to be grasped. She is only able to grasp the implement in the appropriate place or demonstrate its function following tactile exploration which allows her to establish its identity.

8.3 Implications of findings

The discussion section within each experimental chapter provides a description of the implications of the findings of each of the experiments. The purpose of this section is to give some consideration to the overall implications of the findings for the understanding of perception and action, and in turn of the cortical visual streams. The section above (8.2) gave an overview of some of the models of brain function in perception and action, including some modifications of the Milner and Goodale model. All of these suggest that the original model may be oversimplified, particularly with regard to the understanding of the function of the dorsal stream of processing. The intention of this thesis was not to directly determine which of these models is the most plausible, and the experiments were not designed in such a way to make any such conclusions. Instead, the experiments presented within this thesis were inspired by the model of visual processing presented by Milner and Goodale, with a view to providing a fuller description of them and gaining a further understanding of how the brain processes visual information to guide actions. So, what are the overall implications of these finding to this model?

The first three experimental chapters presented focused on obstacle avoidance and the way in which such behaviour fits into the model presented by Milner and Goodale. Chapters 2 and 3 have provided strong evidence to show that obstacle avoidance is mediated by the dorsal stream of processing, impaired in optic ataxia yet intact in visual form agnosia. Previous research has relied on tasks such as reaching and grasping of target obstacles within the workspace, such findings have now been extended to the processing of non-target obstacles. Chapter 4 goes on to provide evidence of the time frame in which the streams operate and the way in which they can interact, confirming the idea that the dorsal stream operates within a short time frame and the ventral in a longer one. These studies would appear to provide strong support for the original model proposed by Milner and Goodale. More importantly, however, they provide for the first time good evidence that the dorsal stream does not merely process stimuli as goals for action, but also non-goal stimuli that nonetheless need to be taken into account when programming and executing actions.

Chapters 5 and 6 have looked at how motion processing fits into the model. While it has been well established that V5 / MT+ is involved in the perception of motion there is relatively little evidence as to how this area is involved in motion processing for action. Chapter 5 has shown that a visual form agnosic patient is capable of catching a moving object, concluding that motion processing for action can take place in the absence of a ventral stream. Chapter 6 went on to directly assess the contribution of area V5 / MT+ in catching and has provided evidence to suggest that visual motion can be used in perception and action. This suggests that area V5 / MT+ may provide a common input into both the ventral and dorsal stream for perception and action, respectively. The original model places V5 / MT+ within the dorsal stream, this finding would suggest that the model needs to be modified, placing V5 / MT+ as an input to both streams. Connectionist neuroanatomy would strongly support the idea that this area is "early" in the cortical visual processing hierarchy, for example it has been shown that V1 sends strong projections directly to V5 / MT+ (Felleman and Van Essen, 1991).

The Milner and Goodale model focuses on the output processing associated with the two streams of processing. In other words, if the goal is an action the primary visual processing will be mediated by the dorsal stream of processing, whereas if the goal is perception the ventral stream will come into play. Does chapter 8 provide evidence against this distinction? Chapter 8 delineated evidence which showed dorsal stream sensitivity for the mere presentation of stimuli such as tools, when no action is required. This does not necessarily mean, however, that the distinction provided by Milner and Goodale should be rejected. This merely suggests that the presentation of stimuli such as tools automatically causes an action representation. This action representation leads to increased neural activity in dorsal stream regions associated with the action. This also highlights one of the drawbacks of functional MRI, in that increased neural activity does not necessarily imply that a brain area is functionally involved in the task at hand, only that neurons within that brain area are sensitive to some of the properties of the stimuli. Thus, chapter 8 can also be taken as evidence to elaborate the distinction provided by Milner and Goodale, rather than to contradict it.

8.4 Future directions

The aim of this thesis was to gain further insights into the understanding of perception and action. While several questions have been answered, many questions have also been raised. This section shall give a brief overview of some suggestions for further research, which will attempt to address such questions.

Chapters 2 and 3 provided some understanding of the neural correlates of obstacle avoidance behaviour, suggesting it is governed by the dorsal stream of processing (damaged in optic ataxic but preserved in visual form agnosia). To gain a further understanding of precise areas governing such behaviour an fMRI study could be carried out. Participants could carry out a grasping task, in which they would be required to grasp a target object in the presence and absence of flanker (non-target) objects. While it may also be possible to carry out a reaching task (such as the one employed within this thesis) in the magnet, this could be problematic due to movement artefacts. In addition to an fMRI study a TMS study could also be used to determine which areas of the dorsal stream of processing are *necessary* for obstacle avoidance behaviour. While fMRI is useful in identifying areas responsive to such behaviour it is unclear if areas of activation are actually functionally involved in the task.

Chapter 4 provided some understanding of the time frames in which the dorsal and ventral streams of processing function in the presence of obstacles in the workspace. It was shown that when an immediate response was required obstacle avoidance is subserved by the dorsal stream of processing (impaired in optic ataxia), yet when a delay is required before response a flexible visuospatial coding system comes into play from the ventral stream (intact in optic ataxia). Studies are currently underway at the

University of Western Ontario using fMRI to investigate immediate and delayed grasping in normal participants (Culham *et al.*, personal communication). These are suggesting that although the dorsal stream is involved in both forms of behaviour, there is additional activation in the ventral stream area LOC during delayed grasping which is time-locked to the occurrence of the motor act. It will be interesting to scan optic ataxic patients during performance of the delayed task to see whether they show similar patterns of ventral-stream activation. Another useful way of addressing this issue will be with TMS. Participants could carry out a reach to grasp task under both immediate and delayed conditions, with TMS being applied to area AIP and area LOC. It would be hypothesised that TMS to AIP would disrupt the calibration of grip aperture under immediate but possibly not delayed conditions, and also that TMS to area LOC would disrupt the calibration of grip aperture under delayed but not immediate conditions.

Chapter 5 has provided evidence to show that DF is capable of catching moving objects using looming information and is capable of responding to online perturbations in speed and direction as a function of her intact dorsal stream. Chapter 6 has provided evidence to suggest that V5 / MT+ is involved in motion processing within the visuomotor domain in healthy subjects. It remains to be established at what time such motion information is critical for catching. A TMS study could employed to address this. Single pulse TMS could be applied to V5 / MT+ at varying intervals as participants are required to catch a moving object.

Chapter 7 provided evidence to suggest that dorsal stream sensitivity to orientation changes is specific to graspable objects. One of the areas identified within this experiment was the occipito-parietal junction of the right hemisphere a region which may be functionally equivalent to the caudal part of the intraparietal sulcus (CIP) in the macaque brain. CIP contains neurons tuned to object orientation and sends projections to AIP for the visual guidance of hand actions (Sakata *et al.*, 1997; 1999) as AIP has no direct access to spatial properties of objects (Sakata *et al.*, 1998). To test this hypothesis in the normal human brain a TMS study could be employed to tease apart such an interaction. If such an interaction does exist it would be predicted that TMS to CIP would impair grasping when a change in object orientation occurs, but not when no orientation change occurs.

Studies with optic ataxic patients suggest that visuomotor deficits are restricted to targets in the peripheral visual field, actions directed at objects within the central field remaining relatively intact (e.g. Milner *et al.*, 1999). Rossetti (2003) suggests that actions directed to centrally viewed objects must be processed by visuomotor channels that bypass the dorsal stream. To test this it would be possible to carry out an fMRI study asking subjects to point to targets in the peripheral and central visual field. To test the critical involvement of areas of activation, TMS could be used to determine if stimulation of posterior parietal cortex will interfere with pointing deficits in the peripheral but not the central visual field.

Some studies have shown that bilateral activation occurs in AIP when subjects grasp an object with the right hand (e.g. Culham *et al.*, 2003) whereas others have shown unilateral activation (Frey *et al.*, 2005). Culham *et al.* (2003) carried out an fMRI study looking at grasping with the right and left hand and found bilateral activation in AIP, which was larger in the contralateral hemisphere. It would be possible to address this issue by carrying out a TMS study stimulating AIP on the right, the left and bilaterally when subjects are required to grasp objects with the right and the left hand to determine if the ipsilateral activation is functionally involved in such tasks.

8.5 A final thought

The evidence presented within this thesis suggests that in many ways the Milner and Goodale model has stood the test of time. In other words, projecting from striate cortex to infereotemporal cortex is the ventral stream, which is associated with the perceptual identification of objects. Projecting from striate cortex to posterior parietal cortex is the dorsal stream, which is involved in action. It would be naïve to state that such a model can fully account for all aspects of perception and action as the human brain is a complex organ. Indeed, all models of visual processing should be approached with some degree of caution for this reason. Such a model has however been hugely influential, providing cognitive neuroscientists with a framework to understand how the brain processes visual information for perception and action. There is still a long way to go and many questions remain to be answered, particularly regarding the way in which the two cortical streams interact with one another. No doubt the inevitable future developments of technology for neuroscience research will help us in the quest to understand perception and action and the functions of the cortical visual streams, and ultimately to transcend the rather broad-brush theories that we currently have.

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APPENDIX

Table 1.1

Results of the two-way ANOVA for the reaching task in chapter two.

	Left cylinder		Right cylinder	
	F	p	F	p
AT	0.966	0.331	0.110	0.742
IG	0.073	0.788	2.387	0.129
C1	28.710	0.000	33.064	0.000
C2	18.656	0.000	14.616	0.000
C3	21.438	0.000	40.894	0.000
C4	5.702	0.021	11.183	0.002
C5	20.083	0.000	73.907	0.000
C6	189.519	0.000	146.706	0.000
C7	10.770	0.002	9.908	0.003
C8	41.986	0.000	37.517	0.000

Table 1.2

Results of the two-way ANOVA for the bisection task in chapter two.

	Left cylinder		Right cylinder	
	F	p	F	p
AT	46.368	0.000	64.518	0.000
IG	40.847	0.000	45.545	0.000
C1	113.715	0.000	127.789	0.000
C2	64.734	0.000	61.973	0.000
C3	53.214	0.000	65.78	0.000
C4	46.006	0.000	68.761	0.000
C5	111.149	0.000	123.263	0.000
C6	61.094	0.000	67.541	0.000
C7	96.800	0.000	129.544	0.000
C8	73.022	0.000	136.65	0.000

Table 2.1

Reaction time and movement time data for DF and controls for task one in chapter five.

			DF	C1	C2	C3	C4	C5
monocular	0.25	RT	542.63	578.00	600.00	537.33	617.50	612.00
		MT	304.21	415.50	437.30	268.67	253.00	274.50
	0.5	RT	493.79	594.15	594.48	563.45	627.00	613.33
		MT	337.24	370.24	293.79	252.41	234.00	221.54
	0.75	RT	465.71	584.00		524.44	617.78	611.67
		MT	335.71	376.00		224.44	237.78	235.00
binocular	0.25	RT	495.38	595.38	605.00	481.48	621.71	620.51
		MT	330.77	384.62	443.50	308.89	286.86	275.38
	0.5	RT	500.71	592.00	606.88	515.00	624.00	629.19
		MT	325.71	308.00	261.25	295.71	256.00	231.89
	0.75	RT	520.00	584.71	590.00	467.69	595.24	626.67
		MT	346.67	303.53	210.00	301.54	256.19	233.33

Table 2.2

Reaction time and movement time data for DF and controls for task two in chapter five.

			DF	C1	C2	C3	C4	C5
monocular	no pert	RT	530.67	610.00	571.58	526.67	608.00	636.92
		MT	350.67	303.00	326.32	248.00	297.00	263.08
	right	RT	445.00	605.88	571.11	526.15	621.33	640.00
		MT	288.33	147.06	376.67	261.54	228.00	210.77
	left	RT	474.12	588.00	506.67	524.00	609.47	652.22
		MT	376.47	348.00	346.67	380.00	246.32	238.89
	fast	RT	516.67	590.59	553.33	540.00	605.00	660.00
		MT	370.00	277.65	280.00	242.86	271.67	163.53
	slow	RT	525.33	597.89	567.37	540.00	610.00	629.23
		MT	278.67	225.26	354.74	358.67	238.00	227.69
binocular	no pert	RT	477.78	603.00	560.00	486.67	616.00	646.32
		MT	367.78	267.00	365.33	302.67	269.33	225.26
	right	RT	516.36	613.68	574.44	492.00	623.08	652.00
		MT	338.18	163.16	356.67	237.33	195.38	197.33
	left	RT	496.47	596.00	545.71	476.92	622.67	655.29
		MT	371.76	286.00	208.57	366.15	274.67	248.24
	fast	RT	544.00	572.50		506.67	598.57	603.33
		MT	348.00	287.50		275.56	270.00	173.33
	slow	RT	486.25	607.00	555.00	512.00	614.29	650.59
		MT	346.25	220.00	339.00	361.33	245.71	185.88

Table 2.3

Results of the chi-square analysis of accuracy for task one in chapter five.

Subject	Variable	x^2	p
DF	Speed	99.186	0.000
	Condition	1.737	0.187
C1	Speed	90.356	0.000
	Condition	1.572	0.210
C2	Speed	161.783	0.000
	Condition	1.271	0.260
C3	Speed	83.990	0.000
	Condition	0.499	0.480
C4	Speed	59.384	0.000
	Condition	1.987	0.159
C5	Speed	12.859	0.002
	Condition	0.815	0.367

Table 2.4

Results of the modified t-test of accuracy for task one in chapter five.

		DF	Mean Controls	SD controls	t	p
0.25	monocular	95.00	98.50	46.33	-0.069	0.948
	binocular	97.50	98.73	47.33	-0.024	0.982
0.5	monocular	74.36	93.73	40.46	-0.437	0.685
	binocular	71.79	93.25	41.53	-0.472	0.662
0.75	monocular	35.00	47.76	28.31	-0.411	0.702
	binocular	7.89	46.44	23.59	-1.492	0.210

Table 2.5

Results of the two-way ANOVA of peak velocity for task one in chapter five.

Subject	Effect	F	p
DF	Speed	60.145	0.000
	Condition	0.173	0.678
	Speed X Condition	0.767	0.466
C1	Speed	317.366	0.000
	Condition	3.325	0.070
	Speed X Condition	1.260	0.286
C2	Speed	182.514	0.000
	Condition	2.478	0.118
	Speed X Condition	1.856	0.175
C3	Speed	47.672	0.000
	Condition	1.611	0.207
	Speed X Condition	0.075	0.928
C4	Speed	271.713	0.000
	Condition	0.014	0.907
	Speed X Condition	0.040	0.961
C5	Speed	567.061	0.000
	Condition	1.289	0.257
	Speed X Condition	1.708	0.184

Table 2.6

Results of the modified t-test of peak velocity for task one in chapter five.

		DF	Mean Controls	SD controls	t	p
0.25	monocular	1048.16	1025.13	131.91	0.160	0.881
	binocular	1009.34	993.36	145.55	0.100	0.925
0.5	monocular	1289.36	1402.98	135.64	-0.765	0.487
	binocular	1313.24	1406.74	148.86	-0.573	0.597
0.75	monocular	1478.25	1757.63	136.33	-1.833	0.164
	binocular	1545.95	1792.89	151.68	-1.486	0.212

Table 2.7

Results of the chi-square analysis of accuracy for task two in chapter five.

Subject	Variable	x^2	p
DF	Pert	57.649	0.000
	Condition	0.004	0.949
C1	Pert	49.548	0.000
	Condition	1.476	0.224
C2	Pert	43.939	0.000
	Condition	0.253	0.615
C3	Pert	43.939	0.000
	Condition	0.253	0.615
C4	Pert	20.807	0.000
	Condition	3.488	0.062
C4	Pert	18.953	0.001
	Condition	0.999	0.318

Table 2.8

Results of the modified t-test of accuracy for task two in chapter five.

		DF	Mean Controls	SD controls	t	p
left	monocular	100.00	75.00	32.79	0.696	0.525
	binocular	89.47	73.22	28.93	0.513	0.635
right	monocular	70.59	81.78	7.73	-1.321	0.257
	binocular	68.75	90.12	8.03	-2.429	0.072
no pert	monocular	93.75	93.44	12.06	0.023	0.982
	binocular	100.00	95.79	9.42	0.408	0.704
fast	monocular	35.29	61.12	32.60	-0.723	0.51
	binocular	31.25	45.33	34.45	-0.373	0.728
slow	monocular	93.75	96.57	3.25	-0.792	0.473
	binocular	94.12	97.56	3.37	-0.932	0.404

Table 2.9

Results of the two-way ANOVA of peak velocity for task two in chapter five.

Subject	Effect	F	p
DF	Perturbation	12945	0.000
	Condition	0.220	0.640
	Perturbation X Condition	5569	0.000
C1	Perturbation	2,295	0.062
	Condition	1,599	0.208
	Perturbation X Condition	1,041	0.388
C2	Perturbation	12,892	0.000
	Condition	0.880	0.350
	Perturbation X Condition	1,270	0.288
C3	Perturbation	3,605	0.008
	Condition	0.514	0.475
	Perturbation X Condition	0.263	0.901
C4	Perturbation	1,678	0.158
	Condition	0.044	0.834
	Perturbation X Condition	2,435	0.050
C5	Perturbation	0.935	0.446
	Condition	0.006	0.939
	Perturbation X Condition	3,517	0.009

Table 2.10

Results of the modified t-test of peak velocity for task two in chapter five.

		DF	Mean Controls	SD controls	t	p
left	monocular	1358.89	758.38	692.93	0.731	0.505
	binocular	1459.67	774.07	708.11	1.373	0.242
right	monocular	1195.97	801.60	733.30	-2.339	0.079
	binocular	1295.29	774.90	708.98	-0.340	0.751
no pert	monocular	1332.90	751.36	685.74	1.085	0.339
	binocular	1288.76	778.59	710.89	-0.170	0.873
fast	monocular	1458.14	783.37	718.41	0.955	0.394
	binocular	1598.80	801.67	731.59	3.180	0.050
slow	monocular	1302.63	765.60	698.77	0.400	0.710
	binocular	1079.28	750.32	685.69	-1.400	0.234

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Automatic avoidance of obstacles is a dorsal stream function: evidence from optic ataxia

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When we reach out to pick something up, our arm is directed to the target by visuomotor networks in the cortical dorsal stream. However, our reach trajectories are influenced also by nontarget objects, which might be construed as potential obstacles. We tested two patients with bilateral dorsal-stream (parietal lesions, both of whom were impaired at pointing to visual stimuli (optic ataxia). We asked them to reach between two cylinders, which varied in location from trial to trial. We found that the patients' reaches remained invariant with changes in obstacle location. In a control task when they were asked to point midway between the two objects, however, their responses shifted in an orderly fashion. We conclude that the dorsal stream provides the visual guidance we automatically build into our movements to avoid potential obstacles, as well as that required to ensure arrival at the target.

When we reach out for an object, for example to pick up a cup, we use a set of exquisitely calibrated visuomotor processes in our brains that unthinkingly take into account the location and physical properties of the target object as well as the location and state of the body, arm and hand. Neurophysiological and functional MRI studies show that these brain systems are largely located in superior parts of the posterior parietal cortex in and around the intraparietal sulcus—the so-called 'dorsal stream'[1–4]. As well as being tailored to the properties of the target, however, our actions also need to take into account the location of any potential obstacles near the intended route of the reaching movement. The brain seems to insure against collisions by building into our movements a tendency to veer away from nontarget objects, even when they are actually too far away to pose a serious threat of collision[5]. As yet, no studies have investigated the brain mechanisms that mediate this implicit obstacle avoidance.

Some recent studies of neurological patients, however, have helped to narrow down the search. Our first study was with patient D.F., who has visual-form agnosia[6]. We asked her to reach out and grasp a target block in the presence of a secondary object placed in locations to the left or right of the target (R.D.M., H.C. Dijkerman, M. Mon-Williams & A.D.M., unpublished data). D.F. took good account of the obstacle's location relative to the target, systematically shifting her reach trajectories in the same manner as control subjects. D.F. has bilateral damage to her ventral stream of visual processing (recently confirmed through high-resolution structural and functional MRI[7]), which severely impairs her form perception. We therefore inferred that she might depend on her functionally intact dorsal stream[7] in achieving this skilled navigation. In other words, we suggested that both target-related processing and obstacle-related processing might share a common parietal substrate.

In a subsequent group study, we tested twelve patients suffering from spatial neglect, a condition that generally spares reaching and grasping performance, despite the presence of marked perceptual and attentional biases in other tasks[8–10]. To see whether this visuomotor sparing extends to obstacle avoidance, we compared the trajectories of arm movements on two tasks, both of which required the patient to steer between two objects[11]. In one task the patients had to point to the midpoint between two objects, while in the other they had to reach between them to a more distant target area. In both tasks, the locations of the left and right object varied independently of each other from trial to trial. We found that all but two of our patients retained their ability to take appropriate account of both objects while reaching between them, though they failed to take adequate account of the ones on the left ('neglected') side when trying to bisect the space between them[11]. The brain damage sustained by most of our neglect patients included areas around the temporo-parietal junction, but generally spared the more superior parietal areas where the human dorsal stream is located[12].

A crucial distinction can be drawn between the demands of our two tasks[11]. The bisection task requires a deliberate perceptual judgment, whereas the reaching task merely requires the programming of a route that will minimize the risk of collision as the hand passes between the objects. Accordingly, we recently tested patient D.F. on a closely similar pair of tasks. We found that she makes normal adjustments to her movements while reaching between the potential obstacles, but fails to do so in the bisection task, where she performs clearly below the normal range (N.J.R., I.S. & A.D.M., unpublished data).

These studies have provided indirect evidence for dorsal-stream involvement in obstacle navigation, by showing that the skill survives damage that mainly affects perceptual processing systems while leaving dorsal-stream structures relatively intact. Our objective in the present study was to test the dorsal-stream hypothesis more directly, by testing two patients with well-attested problems in directing reaches toward visual targets (so-called 'optic ataxia'[1,13])

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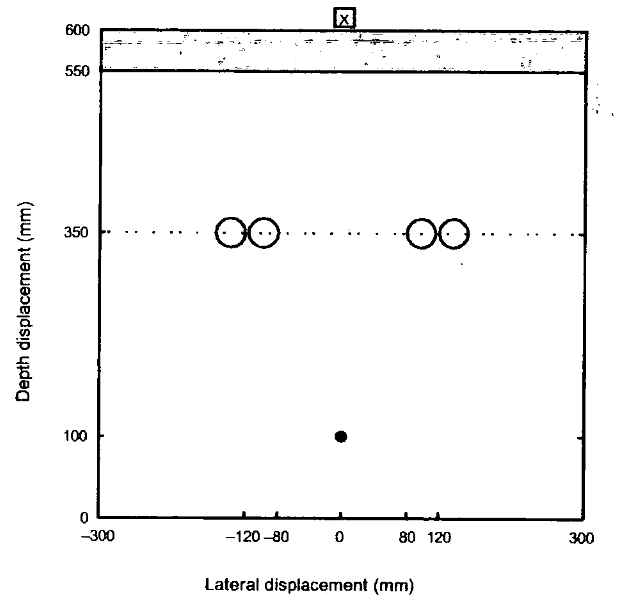

Figure 1 Plan view of the apparatus used in the experiment. Open circles, possible locations of the two cylinders, which were always presented one on the left and one on the right. Black dot, start position. Cross, fixation point.

Table 1 Mean variability of response trajectories in the reaching and bisection tasks

Task	A.T.	I.G.	Controls (mean)	*t* (A.T.)	*t* (I.G.)
Reaching	356.87	140.96	74.80	6.99**	1.64
Bisection	120.89	195.30	48.18	2.54*	5.14**

These figures are mean variance values for p, the point at which reaching movements crossed the imaginary line joining the cylinder locations, averaged across the four cylinder configurations used in each task. $^{*}P < 0.02$; $^{**}P < 0.001$ (one-tailed tests).

following bilateral superior parietal damage. In full confirmation of our prediction, they took no account whatsoever of the obstacle positions during reaching. As before[11], we also tested the same patients on a task of bisecting the space between the two objects, to exclude a purely attentional interpretation of their impairment on the reaching task. In accordance with our hypothesis, the patients took perfectly normal account of the objects in this more explicit 'perceptual' task.

RESULTS

Reaching task

The primary dependent variable was p, the position of each reaching response with respect to the midline of the stimulus board at the point of intersection with an imaginary line joining the object (cylinder) locations (**Fig. 1**). The four different cylinder configurations elicited lawful shifts of reaching trajectory in our control subjects (**Figs. 2a** and **3c**). Thus configuration B shows a leftward shift and configuration C a rightward shift, each relative to the symmetrical configurations A and D. This was true for every control subject. In contrast, the two patients showed no such changes in their reaches as a function of the locations of the left or right cylinder. For both patients, the mean trajectories were near-coincident over the four cylinder configurations (**Fig. 3a,b**).

Individual two-way ANOVAs confirmed these observations. There was no effect of left cylinder or right cylinder in either patient (A.T., F1,44(left) = 0.97, F1,44(right) = 0.11; I.G., F1,44(left) = 0.07, F1,44(right) = 2.39). Although the last of these F-values ($F = 2.39$) approaches significance ($P = 0.129$), it goes in the 'wrong' direction, that is, as if the patient were making reaching adjustments in the direction opposite to the shifts of the right cylinder—presumably the result of random variation. It is clear that neither patient took any account of cylinder location in the execution of their reaching responses. In contrast, every healthy control subject showed a significant effect of both left cylinder and right cylinder. (In every case $P < 0.005$, except for one subject (C4) for whom the left cylinder was significant at only $P = 0.021$.)

A.T. and (to a lesser extent) I.G. each had an idiosyncratic tendency to pass their hand between the cylinders with a rightward or leftward bias (**Fig. 2a**). There was, however, no constraint as to where on the gray strip their reaches should terminate, and in fact I.G.'s mean p score fell within the control range of mean p scores (−10.7 mm – +1.4 mm). Also, while A.T.'s mean p scores fell outside and to the right of the control range, this changed *en route* to the gray strip, so that the actual endpoints of her reaches fell squarely within the normal range (**Fig. 3a,b**).

We also analyzed two indices of sensitivity to the varying locations of the left and right cylinder, dp_{L} and dp_{R} respectively[11,14]. These indices measure the mean change in p that is associated with a shift of each cylinder between its two locations (that is, how much the response shifts in relation to a 40 mm shift of one or the other cylinder). Thus dp_{L} and dp_{R} represent the 'weightings' given to the left and right cylinder location respectively in determining the trajectories. There is a qualitative difference between the patients and the controls (**Fig. 4a**). Both patients have values that hover around zero, lying well outside the normal range. Modified t-test comparisons[15] confirm that A.T. differed significantly from the controls on both dp_{L} ($t = 3.13$, $P = 0.008$) and dp_{R} ($t = 3.11$, $P = 0.009$), as did I.G. (dp_{L}, $t = 2.13$, $P = 0.036$; dp_{R}, $t = 4.72$, $P = 0.001$).

Trial-to-trial reaching variability (as measured by the mean variance of the p scores; **Table 1**) was higher in the patients than in the controls: significantly so in A.T. (modified $t = 6.99$, $P < 0.001$), though not in I.G. ($t = 1.64$, $P < 0.073$; one-tailed tests). Although this higher variability would have militated against finding significant main effects of left or right cylinder locations in the patients, it would not have affected the values of dp_{L} and dp_{R}, which are based on mean trajectories only and take no account of variability.

Bisection task

The individual ANOVAs carried out on the bisection data tell a very different story (**Fig. 2b** and **Fig. 3d–f**). In every subject treated individually, patients as well as controls, there was a highly significant ($P < 0.001$) effect of both left cylinder and right cylinders. For patient A.T., the F values were $F_{1,44}$ (left) = 46.37 and $F_{1,44}$ (right) = 64.52; for I.G. they were $F_{1,44}$ (left) = 40.85 and $F_{1,44}$ (right) = 45.55. Thus both patients took full account of the locations of both cylinders in executing their bisection responses. Furthermore, they both embarked in appropriate heading directions according to the different cylinder configurations, right from the start of the movements (**Fig. 3d,e**).

The values of dp_{L} and dp_{R} in the patients and controls (**Fig. 4b**) confirm the normality of the patients' bisection responses: both patients have values that lie within (indeed at the high end of) the normal range. Modified t-tests[15] confirm this impression: all comparisons between patients and controls were nonsignificant at $P > 0.25$.

The mean variance for each subject's bisection responses (**Table 1**) is again clearly much higher than that of the controls, as confirmed by

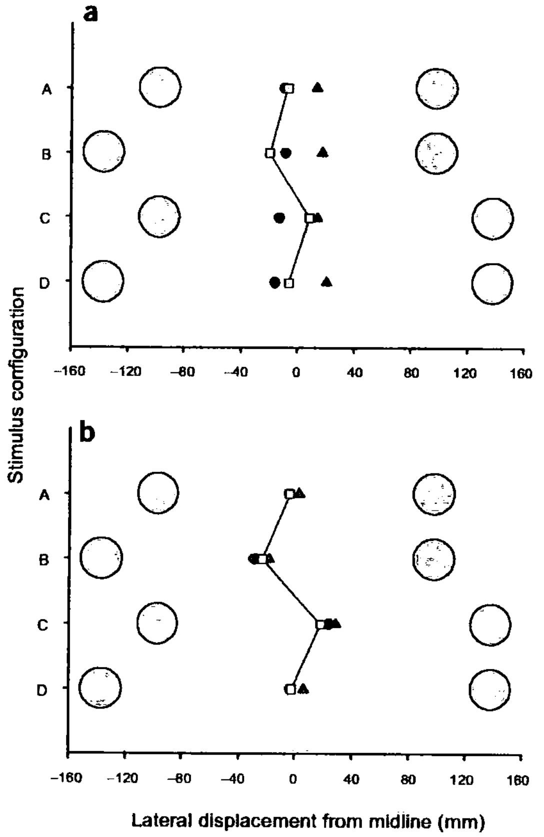

Figure 2 Mean responses in the reaching task (**a**) and bisection task (**b**). Data for the two patients are given as filled triangles (A.T.) and filled circles (I.G.), with the mean data for the eight control subjects given as open squares. The responses plotted are '*p*' scores, that is, the points where each response intersects the imaginary line joining the four possible cylinder locations. The dark gray circles depict the stimulus cylinder locations in the four configurations (A, B, C, D).

Table 2 Kinematic parameters of movements in the reach task

Subject	**MT**	**PV**	**TPV**
A.T.	830.7	1,033.6	3s24.7
I.G.	561.4	1,598.2	171.6
C1	480.3	1,757.8	189.9
C2	590.4	1,671.5	220.7
C3	656.2	1,458.1	207.4
C4	454.4	2,008.9	156.3
C5	711.1	1,295.2	209.8
C6	617.3	1,226.8	260.6
C7	601.3	1,365.3	251.2
C8	454.0	1,959.5	142.8
Mean C	570.6	1,592.9	204.8

MT, mean movement time (ms); PV, mean peak velocity in the horizontal (x-y) plane (mm/s); TPV, time to peak velocity in the x-y plane (ms). The start and end of each movement was defined as a rise or fall below a threshold velocity of 50 mm/s. Data are given individually for patients A.T. and I.G. and for 8 healthy control subjects (C1–C8).

modified t-tests (A.T., $t = 2.54$, $P = 0.019$; I.G., $t = 5.14$, $P < 0.001$, both one-tailed tests). However, although this elevated variability during bisection is even clearer than in the reaching task, it did not prevent the highly significant effects of cylinder location noted above.

DISCUSSION

The aim of the present experiment was to test whether damage to the parietal lobes, as well as causing the pointing errors symptomatic of optic ataxia, would have a specific effect on a task requiring reaching between two obstacles. The results were very clear. Both patients made reaches between the two objects that took no account at all of the varying locations of the objects. Yet in the bisection task, the patients were completely unimpaired in taking account of identical object shifts.

There are, of course, other differences between the two tasks that could potentially explain why our patients behaved so differently on them. For example, it could be argued that the reaching task, being carried out with more speed, and without instructions for accuracy, would inevitably cause the patients to take little account of the left and right objects. This idea gains no support, however, from the present data or from previous data. First, the healthy controls almost all showed highly significant dp_L and dp_R indices in the reaching as well as in the bisection task, although the mean magnitudes were slightly smaller. And second, in our previous study, a group of severely brain-damaged patients with spatial neglect showed an opposite result: they took normal account of the two objects during the reaching task, despite showing reduced weightings of the left object in the bisection task[11].

A converse argument might be that our two patients, due to their severe brain damage, would perform their reaches somewhat more slowly than the controls, and that this might reduce the need for them to give the obstacles a suitably wide berth. However, movement times were slow only in patient A.T.; they were normal in I.G. (Table 2). Furthermore, as mentioned in the Introduction, our visual agnosia patient D.F. has been tested in a similar task. Her movement times in the reaching task were even longer than those of A.T. (mean 932.8 ms). Yet D.F. showed the converse pattern of results to A.T. and I.G., taking good account of the shifts in object location during reaching.

It could alternatively be argued that simultanagnosia, a component of the 'Bálint syndrome' associated with large bilateral parietal lesions, might prevent our patients from attending to more than one object at once. If so, one would expect them to give a reduced weighting to potential obstacles during reaching. There are, however, several reasons to reject this suggestion. First, I.G. shows very little sign of simultanagnosia, having no difficulty in perceiving up to three objects presented together. Patient A.T. does retain a degree of simultanagnosia, but she only experiences it when viewing time is restricted to 500 ms or less. Thus neither patient was likely to have encountered a problem in the present testing conditions. Second, both patients performed absolutely normally on the bisection task, even though the same objects, in identical configurations and for the same duration, were present in that task as well. Third, although neither A.T. nor I.G. reported any difficulty in seeing both of the nontarget stimuli, patient D.F. did report such difficulties. Yet as we mentioned in the Introduction, her data showed the opposite pattern from that described here. And fourth, we have recently tested an optic ataxic patient (M.H.) with left parietal damage, whose pointing impairment is limited to responding with his right hand to targets in his right visual field (I.S., N.J.R., M.G. Edwards, G.W. Humphreys & A.D.M., unpublished data). This patient takes normal account of obstacles when reaching with his left hand, but selectively fails to take account of obstacles on the right side when using his right hand. This highly specific pattern of impairment cannot be accounted for by simultanagnosia.

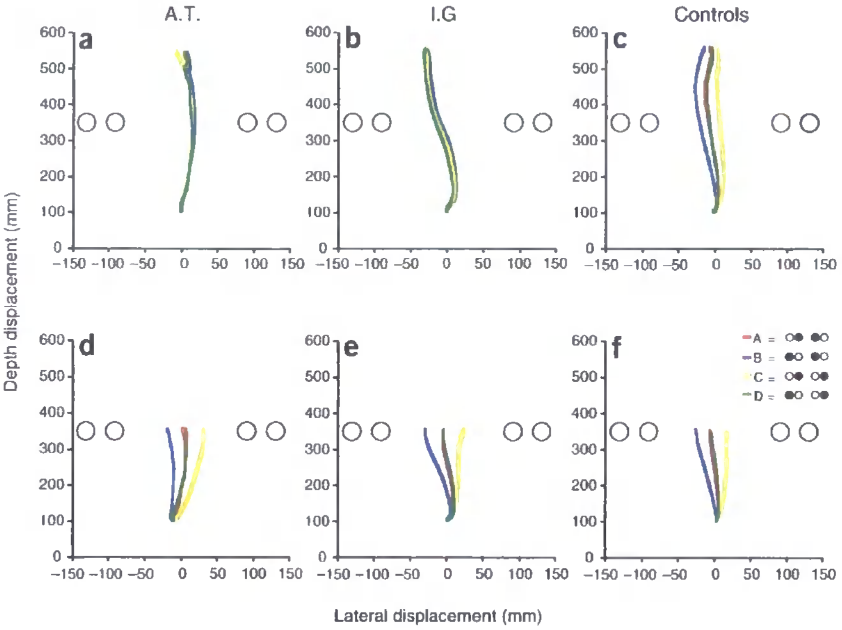

Figure 3 Mean trajectories of reaching (**a–c**) and bisection (**d–f**) movements made by the two patients, shown separately for each of the 4 different cylinder arrangements A, B, C and D (see **Fig. 2**). A, red; B, blue; C, yellow; D, green. Right, mean trajectories of the control group. The four cylinder configurations elicited appropriately different bisection movements in both patients (**d,e**), but failed to elicit different reaching movements (**a,b**). The reaches of the control subjects (top right) diverged maximally at a point approximately level with the cylinder locations, consistent with their treating the cylinders as potential obstacles.

Have we demonstrated anything new, or would our results simply follow from the well-attested problems that our patients have with target-directed reaching—in other words, their optic ataxia? Against this idea is the fact that like most patients with optic ataxia, A.T. and I.G. show little or no impairment for simple reaching to fixated targets[16,17]. Therefore our task, where the target for pointing (the gray strip) was fixated directly, should have presented no serious problem. Nevertheless, both patients did show a high variance in their reach trajectories, which would have led to a reduced *F*-value in any statistical comparison of their trajectories (such as on our measure *p*) across the four different cylinder configurations. This would not be true, however, of our analysis of the indices dp_L and dp_R, which were computed from mean values of the variable *p* and then compared directly between each patient and the controls. This analysis could not have been affected by trial-to-trial variability, and therefore gives the most unambiguous evidence of a loss of obstacle avoidance skill in A.T. and I.G.

The obstacle avoidance we have studied in this experiment is of one specific kind—an 'automatic' modification of reaching movements that allows people to minimize the risk of collision with a nontarget object without having to think about what they are doing. It is automatic in the sense of being quite unintentional; indeed the separations we used would pose very little risk of collision in healthy subjects. However, this behavior also seems to be automatic in the stronger sense of operating independently of visually awareness. In a recent study of a single patient suffering from visual extinction, we showed that conscious awareness of the obstacles during reaching is unnecessary for successful obstacle avoidance[18].

Of course in some circumstances we need to do more than minimize the risk of collision; we need to remove the risk entirely, either to protect the object or ourselves—for example when the potential obstacle is fragile or noxious, respectively. In this case, we can assume that perceptual processing, vested in the ventral visual stream[19,20], must be involved; otherwise the fragile or noxious nature of the obstacle could not be identified. The result will typically be a far more cautious navigation around the obstacle than otherwise, giving it a wider berth and slowing down more than usual[21]. This 'perceptual' form of obstacle avoidance will presumably often involve conscious monitoring of the hand as well as the obstacle during a reach, a scenario that thereby resembles our bisection task more than our reaching task. Such conscious control would be necessary also in situations where the clearance available to the hand is more limited than in our task, or where the obstacle lies directly in the path of the intended reaching movement.

If this reasoning is correct, then one would predict impairments of this second kind of obstacle avoidance in certain patients who are unimpaired on the kind tested here. For example, we would predict that patients with spatial neglect should paradoxically show an

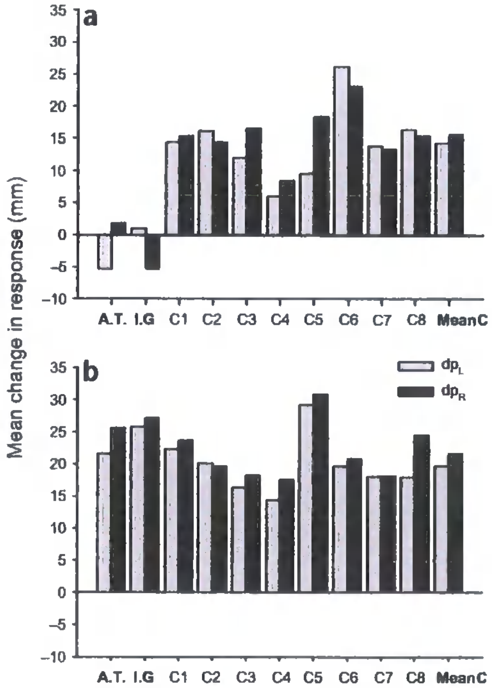

Figure 4 'Weightings' given to the two cylinders. The mean change in response induced by a 40 mm shift in the location of the left cylinder (dp_L) or right cylinder (dp_R) is plotted separately for the reaching task (**a**) and bisection task (**b**). Patients A.T. and I.G. are shown on the left of each graph, while the eight controls are shown individually, and also averaged as a group on the extreme right.

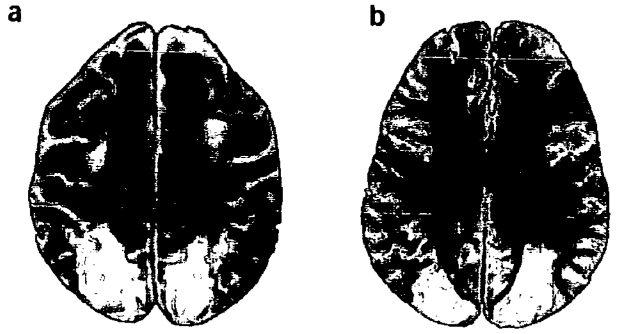

Figure 5 Axial slices through the parietal lesions of patient A.T. (**a**) and patient I.G. (**b**). More detailed information about both patients' lesions can be found elsewhere[24].

asymmetry in the influence of (for instance) delicate obstacles, giving these a wide berth only when they are on the right. The proposed distinction we are making is parallel to one made recently[16,22] in the context of error-correction during reaching. The authors distinguished two kinds of corrections that are made to a reach trajectory when the target is suddenly displaced during the reach. They observed many quick involuntary corrections in healthy subjects, which are all but abolished in patient I.G., and presumably depend on the integrity of the dorsal stream, just like the automatic obstacle avoidance we have studied in the present experiment. But in addition, they identified a separate category of slow voluntary corrections, which are unaffected in I.G. In contrast to I.G., they found that a patient with prefrontal damage did show impairment on this second kind of error correction[16,22]. One might predict a similar impairment if such a patient were to be tested on a task requiring the proposed 'perceptual' kind of obstacle avoidance.

Our conclusions also cannot be generalized to the avoidance of collision with obstacles during locomotion, as this skill is likely to present different demands from the reaching task used here. There is anecdotal evidence that patient I.G. does have such difficulties, for example in avoiding collisions with other people when walking through a busy railway station. Of course complex dynamic environments like this demand visual processing of not only static location but also of the movement trajectories of others, and indeed require a reading of other people's intentions.

METHODS

Subjects. Two patients with optic ataxia following bilateral parietal damage (A.T. and I.G.), along with 8 age-matched healthy controls (median age 39.5 years, range 32–50), took part in the experiment. All subjects were right-handed by self-report.

Patient A.T. was 48 years old at the time of testing, 14 years after an eclamptic attack that provoked a hemorrhagic softening in the territory of both parieto-occipital arteries (branches of the posterior cerebral arteries). Early structural MRI scans revealed bilateral parietal damage extending to the upper part of the occipital lobes and encroaching slightly into the medial part of the right premotor cortex. The calcarine area remained intact except for a part of the upper lip on the left side (Fig. 5a). At the time of the current testing, A.T. continued to show symptoms of Bálint's syndrome, including visual disorientation, simultanagnosia and a severe optic ataxia for targets in her peripheral visual field.

Patient I.G. was tested at the age of 33, after bilateral parieto-occipital infarction 3 years earlier. Shortly after the lesion, bilateral optic ataxia and simultanagnosia became apparent[23], but by the start of our testing the simultanagnosia had subsided, at least for presentations of up to three objects[16]. I.G. received a diagnosis of ischemic stroke, related to acute vasospastic angiopathy in the posterior cerebral arteries. MRI revealed near-symmetrical damage in the posterior parietal and upper and lateral occipital cortico-subcortical regions (Fig. 5b). The lesion involves mainly Brodmann's areas 7, 18 and 19, the intraparietal sulcus and part of area 39.

Additional sections through the lesions of both patients are published elsewhere[24].

Testing procedure. The subject sat facing a 60-cm-square white stimulus board placed flat on a table, with her right index finger at the start position (Fig. 1). Two dark gray cylinders made of sponge rubber (24.5 cm tall and 3.5 cm in diameter) could be fixed into the board, one on either side of the midline, at a distance of 25 cm from the start position. 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 locations thus created four stimulus configurations. A strip of 5-cm-wide gray tape spanned the far edge of the board, at a depth of 20 cm behind the cylinder locations. The bisection task and the reaching task were performed in separate blocks, with the order balanced across subjects within the control group. Patient I.G. was first tested on the reaching task and then the bisection, while A.T. was tested in the converse order. Responses were recorded by sampling the position of a marker attached to the nail of the right index finger, at a frequency of 86.1 Hz, using an electromagnetic motion analysis system (*Minibird*, Ascension Technology) for 3 s following movement onset. Every movement in both the reaching task and the bisection task was recorded in full.

Throughout testing on both tasks, subjects wore liquid-crystal shutter glasses. Subjects initiated each trial by depressing the start button with the right index finger, whereupon the shutter glasses cleared to allow them to see the apparatus. Viewing time was unrestricted. In preparation for responding, subjects were required to fixate a cross at the back of the board, located centrally 16 cm above the surface of the board. They were asked if they were ready, and were then given a verbal 'go' signal to respond. The shutter glasses closed immediately when the start button was released, so that subjects could see neither the fixation cross nor the cylinders when making their responses. Thus movements were performed entirely in visual open loop. The fixation procedure was used so that the cylinders would be seen in peripheral vision, which is where target stimuli elicit the most severe pointing errors in optic ataxia[16,17]. An experimenter was seated directly in front of subjects and checked their fixation.

Bisection task. Subjects were told that this was a test of "accuracy of judgment" and that their task was to point with the right index finger exactly midway between the two cylinders, following the 'go' signal. On every trial, a strip of white card was placed between the cylinders to prevent subjects from using any visible holes in the board to aid their judgments. Subjects were informed that the positions of the cylinders would vary from trial to trial, but that there would always be one on the left and one on the right. The end position of the finger was defined as that recorded on the frame at which hand velocity fell below a threshold of 50 mm/s. The dependent measure on each trial was the average lateral position (p) of the finger marker on this last frame, with respect to the midline of the stimulus board. Each subject made 48 bisection responses, 12 trials for each of the four cylinder configurations, in a fixed pseudo-random order.

Reaching task. Subjects were told that this was a test of "speed of movement" and that their task was to reach out and touch the gray strip with their right index finger as quickly as possible following the 'go' signal. They were permitted to touch any part of the target strip, to encourage them to make reaches that were geared more to obstacle avoidance than to end-point accuracy. Subjects 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 cylinders were not mentioned again during the rest of the experiment. The dependent measure was again the lateral position (p) of the 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, with 12 trials for each of the four cylinder configurations, and 12 trials in which no cylinder was present. The 12 no-cylinder trials were included to check for any systematic spatial biases when the reaching response was not constrained by potential obstacles. They were not included in the analyses presented here.

Analyses. The primary dependent variable p codes the absolute lateral position of each response, without reference to the center of the gap between the two cylinders presented on that trial. The main analyses were two sets of two-way repeated-measures ANOVAs of response positions p, with the factors left cylinder location (near, far) and right cylinder location (near, far). A separate ANOVA was carried out on the data of each individual subject.

A second set of analyses were made of the weighting indices dp_L and dp_R, which were calculated according to the following equations[11,14] (Fig. 2):

$$dp_L = (\text{mean } p \text{ in configurations A and C}) - (\text{mean } p \text{ in configurations B and D})$$

$$dp_R = (\text{mean } p \text{ in configurations C and D}) - (\text{mean } p \text{ in configurations A and B}).$$

A modified t-test[15] was used to make a separate statistical comparison between each patient and the control group on each of the two indices in each test condition.

In a third set of analyses, the variability of reaches was assessed by calculating the standard deviation of p scores for each of the four test configurations, and averaging these to give a mean variability score for each subject.

All of our analyses exploit the formal correspondence between our two tasks, without making any assumptions about causality in either case. The analyses simply treat both tasks as requiring a spatial response that depends simultaneously on the location of objects (cylinders) on the two sides of space.

ACKNOWLEDGMENTS
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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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Automatic avoidance of obstacles is a dorsal stream function: evidence from optic ataxia

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Nat. Neurosci. 7, 779–784 (2004)

Table 2 on page 781 contained a typographical error, a superfluous letter introduced into one of the numbers, which were otherwise correct. The corrected version appears below.

Table 2 Kinematic parameters of movements in the reach task

Subject	MT	PV	TPV
A.T.	830.7	1,033.6	324.7
I.G.	561.4	1,598.2	171.6
C1	480.3	1,757.8	189.9
C2	590.4	1,671.5	220.7
C3	656.2	1,458.1	207.4
C4	454.4	2,008.9	156.3
C5	711.1	1,295.2	209.8
C6	617.3	1,226.8	260.6
C7	601.3	1,365.3	251.2
C8	454.0	1,959.5	142.8
Mean C	570.6	1,592.9	204.8

MT, mean movement time (ms); PV, mean peak velocity in the horizontal (*x-y*) plane (mm/s); TPV, time to peak velocity in the *x-y* plane (ms). The start and end of each movement was defined as a rise or fall below a threshold velocity of 50 mm/s. Data are given individually for patients A.T. and I.G. and for 8 healthy control subjects (C1–C8).

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The role of V5/MT+ in the control of catching movements: an rTMS study

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Abstract

Milner and Goodale [Milner, A. D., & Goodale, M. A. (1995). *The visual brain in action*. Oxford: Oxford University Press] described a model which distinguishes between two visual streams in the brain. It is claimed that the ventral stream serves object recognition (i.e. vision for perception), and the dorsal streams provides visual information for the guidance of action (i.e. vision for action). This model is supported by evidence from the domain of spatial vision, but it remains unclear how motion vision fits into that model. More specifically, it is unclear how the motion complex V5/MT contributes to vision for perception and vision for action. We addressed this question in an earlier study with the V5-lesioned patient LM [Schenk, T., Mai, N., Ditterich, J., & Zihl, J. (2000). Can a motion-blind patient reach for moving objects? *European Journal of Neuroscience, 12*, 3351–3360]. We found that she is not only impaired in perceptual tasks but also in catching, suggesting a role for V5/MT+ in vision for both perception and action. However, LM's lesion goes beyond V5/MT+ into more dorsal regions. It is thus possible, that the catching deficit was not produced by damage to V5/MT+ itself. In this case, one would expect that selective interference with V5/MT+ would have no effect on catching. In the present study we tested this prediction by applying rTMS over V5/MT+ of the left hemisphere while healthy subjects were either performing a catching or a reaching task. We found that V5-TMS reduced the speed of the catching but not the reaching response. These results confirm that V5/MT+ is not only involved in perceptual but also in visuomotor tasks.

Keywords: Visual motion; Interception; Dorsal/ventral streams; Akinetopsia; Reach-to-grasp; Prehension

1. Introduction

Ungerleider and Haxby (1994) and Ungerleider and Mishkin (1982) suggested that the various areas of the visual brain could be separated into two visual streams, which are anatomically and functionally distinct. Both of these streams originate in the primary visual cortex, but then part company and go either towards the temporal cortex in the case of the ventral stream, or towards the parietal cortex, in the case of the dorsal stream. Ungerleider and Mishkin (1982) assumed that the ventral stream is primarily concerned with visual attributes that allow the identification of objects (e.g. colour and form), whereas the dorsal stream is concerned with visuo-spatial aspects (e.g. position and motion), and allows the localization of visual objects. More recently, Goodale and Milner (1992) and Milner and Goodale (1993) suggested a functional re-interpretation of the original two-stream hypothesis. They argue that the functional distinction between the two streams is not primarily based on the type of visual attributes, which are processed in these two streams (i.e. colour/form in ventral stream versus position and motion in the dorsal stream), but on the behavioural or cognitive function for which the visual information is used. More particularly they suggest that visual information which is used for object identification and scene identification, i.e. vision for perception, is processed in the ventral stream, whereas visual information used for the control of motor behaviour, i.e. vision for action, is processed in the dorsal stream. This model by Milner and Goodale received much support from neuropsychological and experimental studies (see Milner & Goodale, 1995). However, most of its evidence comes from experiments on intrinsic physical attributes such as form, size, and orientation perception (Norman, 2002). Other visual attributes (e.g. motion and depth perception) have been examined much less in this context, and it therefore remains unclear how these aspects of processing fit into the model (Goodale, 1993).

In the case of motion vision it is certainly conceivable that the distinction between vision for perception and ac-

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tion also applies, since it is obvious that motion vision is relevant for both object recognition and visuomotor control. For example, object recognition requires figure-ground segregation, for which motion is an important cue (Anstis, 1978; Sekuler et al., 1990). Similarly, visuomotor control tasks also include catching behaviour, and we would expect that successful catching behaviour is not possible without motion vision. Even manual movements towards stationary targets might involve motion vision, namely for the visual monitoring of the moving hand (Paillard, 1996). The question thus arises whether there are distinct brain areas processing visual motion information either for perceptual or visuomotor tasks. Functional imaging studies have shown that there is a whole set of motion-related areas in the human brain (Culham, He, Dukelow, & Verstraten, 2001). For most of those areas very little is known about their functional contribution, and therefore it is too early to decide whether this set of motion-related areas can be subdivided into a perceptual and a visuomotor stream.

However, one of those brain areas, namely the motion complex V5/MT+, has been examined much more extensively, and it is clear that this area makes an important contribution to a number of aspects of motion perception. For example it has been found that the preferred speed range of cells in V5/MT+ (Lagae, Raiguel, & Orban, 1993; Maunsell & Van Essen, 1983; Mikami, Newsome, & Wurtz, 1986; Rodman & Albright, 1987) correlates closely with psychophysical performance in speed-discrimination tasks (McKee, 1981; Orban, de Wolf, & Maes, 1984; Orban, Van Calenbergh, De Bruyn, & Maes, 1985), suggesting that V5/MT+ is the essential mechanism underlying this performance. This conclusion is confirmed by studies that show a degradation of speed discrimination after damage to V5 (Hess, Baker, & Zihl, 1989; Orban, Saunders, & Vandenbussche, 1995; Plant & Nakayama, 1993; Zihl, von Cramon, & Mai, 1983; Zihl, von Cramon, Mai, & Schmid, 1991). Similarly, for the perception of direction in global motion stimuli it has been found that activity in V5/MT+ is closely related to performance. In fact, it could be demonstrated that a bias in perceived direction can be induced by stimulating direction-specific cells in V5/MT+ (Salzman & Britten, 1990). Furthermore, it was found that damage to V5/MT+ leads to a performance drop in tasks involving the identification of direction in global motion stimuli (Baker, Hess, & Zihl, 1991; Newsome & Paré, 1988; Plant & Nakayama, 1993; Plant, Laxer, Barbaro, Schiffman, & Nakayama, 1993; Schenk & Zihl, 1997; Vaina, Cowey, Eskew, LeMay, & Kemper, 2001). It is thus well established that V5/MT+ plays an essential role in a variety of perceptual tasks.

However, V5/MT+'s role in visuomotor tasks is still unclear. We addressed this question in a recent study with the motion-blind patient LM (Schenk, Mai, Ditterich, & Zihl, 2000). LM's brain damage includes V5/MT+ in both hemispheres, and consequently her ability to perceive visual motion is severely impaired (Zihl et al., 1983, 1991). In our study, we found that she is also impaired in a catching task (Schenk, Mai, et al., 2000). This seems to suggest that V5/MT+ contributes both to perceptual and visuomotor tasks. There is, however, a problem with this conclusion in that LM's lesions go beyond V5/MT+ and extend into surrounding areas (Shipp, de Jong, Zihl, Frackowiak, & Zeki, 1994). The lesions extend dorsally to the intraparietal sulcus, infringing on area 39 at least in her right hemisphere. Her lesions might therefore also include the superior temporal sulcus and the motion-responsive areas in the intraparietal sulcus. These regions have been found in functional imaging studies to respond selectively to visual motion stimuli (Culham et al., 2001).

Given the extent of LM's lesion, it is therefore quite possible that areas other than V5/MT+ are responsible for her deficits. With respect to the perceptual deficits, LM's results have been confirmed by various studies that used transcranial magnetic stimulation (TMS) to induce transient disruptions in V5/MT+. These TMS studies showed that a selective disruption of V5/MT+ produces deficits in the perception of visual motion that are similar to LM's deficits (Beckers & Hömberg, 1992; Beckers & Zeki, 1995; Walsh, Ellison, Battelli, & Cowey, 1998). However, similar TMS studies using visuomotor tasks have not yet been conducted, and it is, therefore, unknown whether a selective disruption of V5/MT+ would also suffice to produce a visuomotor deficit.

It was the aim of the present study to examine this question. We compared the effects of repetitive TMS (rTMS) over V5/MT+ with the effects obtained after stimulation over a control site (vertex) or a site that is approximately 2 cm dorsal to V5/MT+. Two visuomotor tasks were used: a catching task using a moving target object, and a standard reach-to-grasp task with a stationary target object. We expected that if V5 is involved in visuomotor processing, TMS over V5 should interfere with the subjects' ability to predict the course of the target's movement, and thereby impair their catching performance.

2. Methods

2.1. TMS stimulation

We used a MagStim 200 Super Rapid Stimulator with a figure of eight coil (diameter 90 mm; Magstim, Whitland, Dyffed, Wales, UK), which was placed tangential to the surface of the skull with the coil handle pointing backwards at approximately 45° to the spinal cord. The coil was held to the skull by the experimenter using the right hand to hold the coil, and the left hand to stabilize the head against the coil. A head and chin rest was used to minimize head movements during the experiment. After each trial the position of the coil was checked. In three subjects head movements during the experiments were measured and found to be negligible. For these head movement measurements, we used a 3D movement registration system which uses ultrasonic markers. This system is described in more detail below. One marker (coil-marker) was placed at the centre of the coil, the other marker (reference marker) was placed at the centre of the dorsal surface of the skull (i.e. vertex). We recorded head movements for both the catching and the reach-to-grasp task. Three subjects and 10 trials per subject and task were recorded. To assess the extent of coil-displacement during the period of TMS stimulation, we determined the maximum value of change in the distance between the coil- and the reference marker during the 500 ms Stimulation period. The average value of maximal displacement was less than 0.7 mm (SD: 0.16) during the catching task, and less than 0.8 mm (SD: 0.29) during the reach-to-grasp task.

Repetitive pulse TMS (rTMS) was delivered at 10 Hz for 500 ms at 65% of stimulator output (corresponding to 1.3 T or 110% of the average TMS motor thresholds of our subjects), beginning at the onset of the trial, which was indicated by the opening of the LC shutter glasses (see below).

We stimulated at three different sites: V5, vertex, and a site which was approximately 2 cm dorsal to V5 (dorsal site, DS). To stimulate V5 the centre of the coil is typically positioned 3 cm above the mastoid-inion line and 5 cm lateral to the midline in the sagittal plane (Walsh et al., 1998). However, since it is known that the locus of V5 varies between individuals (Watson et al., 1993), we used the perception of TMS-induced moving phosphenes to confirm the correct position for stimulation in each individual (Stewart, Battelli, Walsh, & Cowey, 1999). The chosen position was typically near the conventional coordinates V5 stimulation (see above). However, deviations of up to 1.5 cm in either direction were found. In five out of six subjects the position of V5 could also be checked anatomically. For those subjects structural MRI scans were available, and it was confirmed with a frameless stereotaxic system (Brainsight™, Rogue Research, Montreal, Canada) that the chosen stimulation site was near the anatomical landmark for V5 (Dumoulin et al., 2000), namely the intersection of the ascending limb and the posterior continuation of the inferior temporal sulcus. V5 was stimulated unilaterally on the left hemisphere, because previous TMS studies found effects across both hemifields when stimulating over the left hemisphere (Stewart, Ellison, Walsh, & Cowey, 2001). Left hemisphere stimulation, thereby, produces perceptual deficits that are similar to the deficits observed in patient LM (Walsh et al., 1998).

Our second stimulation site was at the vertex. Location of the vertex was determined by finding the intersection of the mid sagittal plane (defined by the nasion to inion line) and the mid coronal plane (defined by the line between the intertrachial notches of the ears). This location corresponds to the position Cz of the 10–20 International EEG system. Stimulation over the vertex provides a good control condition since it evokes all of the unspecific TMS-effects (e.g. noise and tickling sensation), without inducing currents in specific brain areas. In addition we introduced a second control condition to determine the spatial specificity of any effects, which might be found after V5 stimulation. For this purpose we chose a control site that was near to V5, but clearly outside of its borders. To determine the position for this control site, we first localized the V5 site, and then moved the coil dorsally along the surface of the skull until moving phosphenes could no longer be induced. The position of this site (dorsal site, DS) was on average 1.8 cm dorsal (SD: 0.4) to the position of V5.

2.2. Subjects

Six subjects (aged 21–38, three female, three male) participated in this study. All subjects were right-handed, had normal vision, and reported an absence of epilepsy in their family medical history. They consented to take part in the study after they had received information about safety issues relating to TMS and rTMS. Local ethical committee approval was granted for all procedures.

2.3. Tasks and procedures

Two visuomotor tasks were used. The first task was a catching task using a target object that moved away from the subject either to the right or to the left (see Fig. 1A). Two different speed conditions were used (object speed = 0.25 or 0.50 m/s). The parameters of the catching task were the same as those used in the experiment with LM (Schenk, Mai, et al., 2000). The second task was a reach-to-grasp task, in which the target object was stationary (see Fig. 1B). The spatial measurements for the trajectories in the catching task, and the positions of the object in the reach-to-grasp task are presented in Fig. 1. The two tasks were similar with respect to the demands on the motor system, but quite different with respect to their demands on the visual system. In both tasks, subjects had to produce rapid grasping movements. However, only in the catching task, the subject had to take visual information about the target's movement into account. Since V5 is primarily involved in the coding of visual motion, it was expected that V5-specific effects should be found primarily in the catching task.

In both tasks, subjects were instructed to use their right hand. To ensure that the temporal parameters of the subjects' responses were comparable in the two tasks, subjects were asked in both tasks to move as fast as possible. To prevent head movements the subject's head was constrained by a head and chin rest. Ear plugs suppressed the noise coming from the TMS coil and the moving object. At the start of each trial, the subject's right hand rested on a plate (start switch) in front of the body. Subjects wore LC shutter glasses (Plato System, Translucent Technologies, Toronto, Canada), which opened at the beginning of the trial. At the same time the rTMS-sequence was triggered, and in the case of the catching task the object started to move. The LC shutter glasses stayed either open for 100 ms (observation time, OT = 100 ms) or for 800 ms (OT = 800 ms). With an OT of 100 ms, subjects saw the start of the trial, but not the movement of their hand. With an OT of 800 ms, subjects saw the object for the entire duration of the trial, and could also observe the movement of their hand. In the case of LM, we had found that the duration

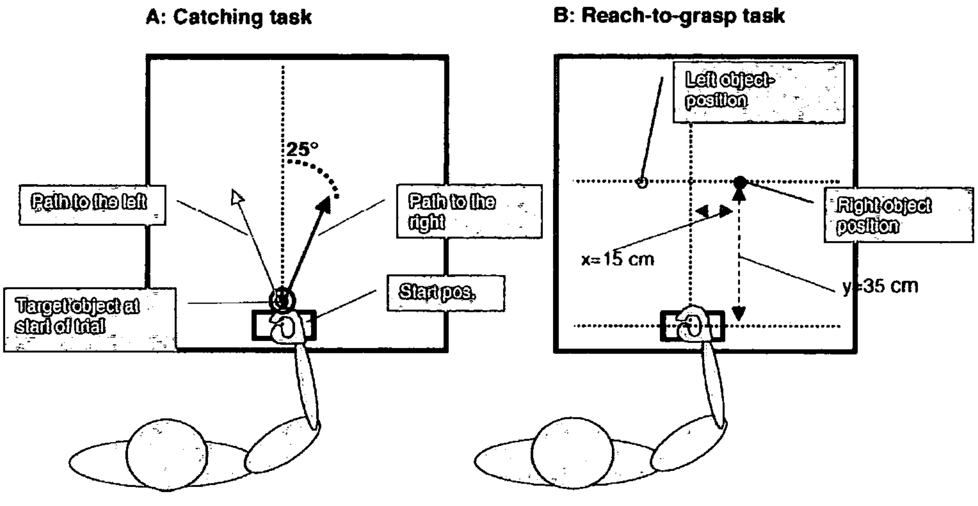

Fig. 1. Set-up for the catching (A) and the reach-to-grasp task (B).

of the OT had a significant effect on her performance. LM caught significantly more objects if she could observe the object for a longer period, and if she could see her hand (Schenk, Mai, et al., 2000).

In each condition 40 trials were presented. The three different TMS conditions (V5, vertex, DS) and the two different visual conditions (100 ms versus 800 ms) were presented in separate blocks. Each block was presented twice; blocks for the different conditions were presented in an interleaved order. The order of the blocks and thus the order of the TMS and visual conditions were counterbalanced across the subjects. Within each block, different types of trials were randomly mixed. In the case of the catching task the trials differed with respect to the direction and speed of the target. In the case of the reach-to-grasp task the trials differed with respect to the position of the object. The two tasks were presented in two separate sessions. At the start of each experimental session, the skull positions for the TMS were determined, and the task was practised for 15 min (40 trials). Each session lasted for approximately 90 min. A short break of approximately 10 min was provided after the first half of the session.

2.4. Apparatus

In this section, we provide a description of the machine that was used to generate the object motion, and the devices used to record the temporal and spatial aspects of the manual response.

2.4.1. System to generate 2D motion of real objects (servo-object-controller, SOC)

This system uses two motor-driven linear axes to move a target object within a horizontal area that covers an area of 1 m^2. The linear axes are covered by a metal plate. Magnets transfer the movement of the linear axes to an object carrier that sits on the surface of the metal plate. The target object itself (small cylinder: weight 15 g, height 6 cm, diameter 4 cm) also contains a weak magnet and sits on the object carrier. This system is controlled by a PC, which also triggers all other events (e.g. opening and closing of LC shutter glasses, start of rTMS-sequence). A detailed description of that system has been provided elsewhere (Schenk, Philipp, et al., 2000).

2.4.2. Measuring the manual response

At the start of each trial subjects rested their hand on a start button which was on the table in front of the centre of their body (see Fig. 1A and B). This start button contained an electronic switch which signalled the beginning of the manual response. The end of the manual response was indicated by another switch that was contained within the target object. As soon as the subject grasped the object the switch within the object was released, and a signal was transmitted to the PC.

In addition a 3D movement registration device was used to record the trajectory of the arm and fingers during the subject's manual response. This registration device employs ultrasonic loudspeakers as markers and a panel with embedded microphones as receivers for the ultrasonic signals. This system (CMS 70, Fa. Zebris, Germany) has a spatial resolution of 0.1 mm and achieves a sampling frequency of 50 Hz when three markers are used. We used three markers to measure both the hand's transport to the target (marker on the wrist, above the styloid process of the ulna) and the opening and closing of the fingers during the grasp (markers on the nails of the index finger and the thumb).

2.5. Data analysis and statistics

Our choice of performance measures was partly based on the results from our study with LM, and partly on the results from other TMS studies, and included measures of accuracy and movement timing. Accuracy was measured by computing the percentage of trials (%error) in which the subject could catch or grasp the target object. A grasp was only considered to be successful, if the subject could lift the object from the object carrier without dropping it. In our study with LM, we found that her success rate in the catching task was significantly lower than that of healthy subjects. But even in those trials in which LM was able to catch the target object, her performance was not normal. In particular, we found that her reaching speed was lower and more variable than that of healthy subjects (Schenk, Mai, et al., 2000). We therefore decided to compute average *reaching speed* (*RS*) and *peak reaching speed* (V_{max}) as a further performance measure in the present study. We also measured the *relative time when the peak velocity occurred* (Tv_{max}; this variable is computed in the following way: [time of peak velocity/time of reaching movement] × 100). This variable is often used to assess the relative duration of the acceleration and deceleration phase of the reaching movements. It has been found that the deceleration phase is selectively prolonged in the absence of visual feedback from the moving hand (for a review, see Churchill, Hopkins, Roenqvist, & Vogt, 2000). This suggests that the relative duration of the deceleration phase, and accordingly $\%Tv_{max}$ could be used to check for TMS-induced changes in the use of visual feedback from the moving hand. Our last performance measure was reaction time. *Reaction time* (*RT*) is a measure that is frequently used in TMS studies, because it provides a sensitive indication of TMS-induced processing delays.

A further index, that expressed the amplitude of the TMS-effect, was computed for variables that proved to be significantly affected by TMS in one or more conditions. To calculate this index, called %TMS-effect, the following formula was used: $\%\text{TMS-effect}_{\text{PM}}(i) = (\text{PM}_v - \text{PM}_i) \times 100/\text{mean}(\text{PM}_v, \text{PM}_i)$. In this formula PM stands for a performance measure (i.e. %error, RS or RT), i indicates the TMS-site for which %TMS-effect was computed (i.e. either V5 or DS), and subscript v indicates that vertex was used as the reference condition. This index expresses the TMS-effect relative to the performance in the control condition (i.e. vertex) as a normalized percentage-difference.

For the computation of %errors all trials were used. For the computation of the kinematic measures (i.e. RS, V_{max}, $\%Tv_{max}$, and RT) some trials had to be discarded, namely those trials in which the subject did not grasp or catch the object, or which contained recording artefacts. However, 94% of the trials could be used. Before reaching speed could be computed, the recording traces had to be filtered using a non-parametric regression method (Marquardt & Mai, 1994). The results from the catching and reach-to-grasp tasks were analysed separately. For the catching task, an ANOVA with the three within-subject factors *TMS* (V5, vertex, DS), *observation time* (100, 800 ms), and *motion direction* (leftward, rightward) was conducted. A similar ANOVA was used for the results from the reach-to-grasp task. Instead of the factor motion direction, the factor *object position* (left, right) was employed. Bonferroni-corrections were used for post-hoc comparisons. A significance-threshold of 5% was adopted.

3. Results

3.1. Task 1: catching task

The factor TMS-site had a significant effect on average reaching speed (RS, $F(2/10) = 9.98$, $P < 0.004$), and peak reaching speed (V_{max}, $F(2/10) = 14.91$, $P < 0.001$). Post-hoc comparisons confirmed that V5 stimulation produced a reduction in RS and V_{max} when compared to stimulation at either of the two control sites (see also Table 1). It should be noted that the factor TMS-site had no effect on %error or on RT.

The factor observation time had a significant effect on %error ($F(1/10) = 7.98$, $P < 0.37$), and RT ($F(1/10) = 18.18$, $P < 0.008$), but not on RS, V_{max}, or $\%Tv_{max}$. Shorter observation times led to higher error rates (at 100 ms (mean, S.D.): 6.17%, 2.76; at 800 ms: 1.73%, 1.92), and shorter reaction times (at 100 ms (mean, SD): 182.89 ms, 53.29; at 800 ms: 188.94 ms, 49.36). These effects of observation time are probably best explained if one assumes that subjects produce their best performance when they are able to view the target for more than 100 ms. If subjects are deprived of this option,

Table 1
Catching task: effect of TMS-site

Observation time	TMS	Errors (%)		RT (ms)		RS (m/s)		V_{max} (m/s)		$\%Tv_{max}$	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
100.00	V5	6.25	2.31	181.45	50.49	1.11	0.41	1.86	0.18	51.36	7.39
	Vertex	6.24	2.76	179.59	56.43	1.31	0.41	2.01	0.12	51.20	10.45
	DS	6.01	4.06	187.77	52.18	1.32	0.55	2.01	1.82	51.06	7.78
800.00	V5	1.29	1.50	178.94	42.04	0.99	0.29	1.83	1.84	46.14	6.18
	Vertex	1.07	1.92	187.53	50.90	1.13	0.32	1.95	1.60	46.63	9.55
	DS	2.84	2.96	199.72	52.29	1.18	0.34	1.93	1.37	48.04	8.94

Note: These values represent the mean and standard deviations across the group of subjects. As can be seen, the absolute values for RS vary considerably between subjects. Regardless of this variability in RS, the effect of TMS-site on RS was quite consistent. To see this, it is necessary to compute the difference of RS in the different TMS conditions for each subject separately. This has been done to compute %TMS-effect. Fig. 2, which presents the values for the variable %TMS-effect, therefore provides a much more accurate picture of the effect of TMS-site on performance.

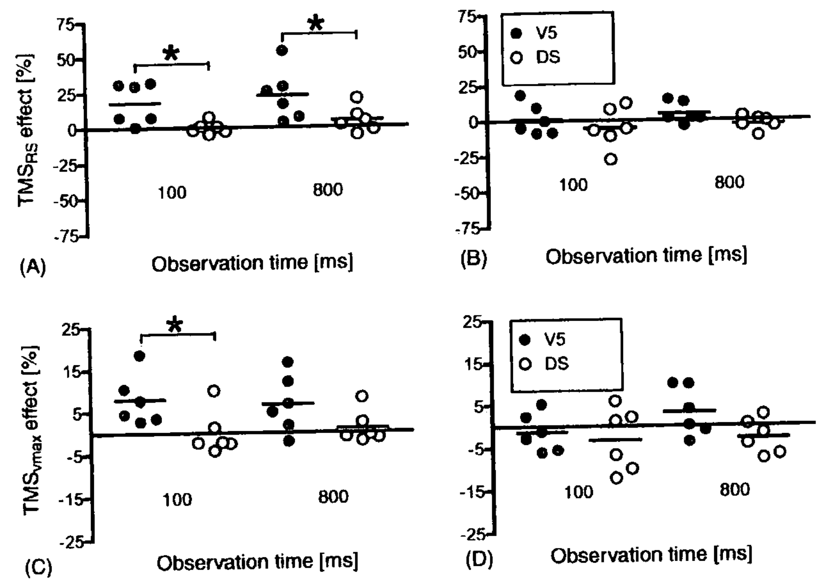

Fig. 2. Comparing the %TMS-effect for stimulation at V5 and DS. A definition of the variable %TMS$_{\mathrm{RS}}$ and %TMS$_{V_{\max}}$ effect is provided in Section 2. (A) and (B) %TMS$_{\mathrm{RS}}$ effect for catching (A) and reach-to-grasp task (B). (C) and (D) %TMS$_{V_{\max}}$ effect for catching (C) and reach-to-grasp task (D).

the accuracy of their movements will suffer (i.e. higher error rates), but at the same time they will be able to initiate their response earlier (i.e. reduced RTs). An alternative explanation could be that subjects launched their reaching movements faster when they anticipated an early closure of the glasses (i.e. OT = 100 ms). In this case, we could also expect that accuracy would drop as a consequence of the well-known speed-accuracy trade-off. Therefore, this explanation would also be consistent with the observed effect of observation time on RTs and error rates. The factor observation time did not modulate the effect of TMS (i.e. no interaction between the factors TMS-site and OT for any of the dependent measures). This result contrasts with the significant effect of OT on LM's catching performance. On the basis of LM's results it might have been expected that TMS stimulation of V5 would lead to more pronounced deficits when the observation time was restricted to 100 ms. The fact that we did not find this effect in this study suggests interesting differences in the behavioural consequences of TMS and lesions. We will explore the reasons for these differences in Section 4.

The factor motion direction did not produce any significant effects, nor were there any significant interaction effects involving the factor motion direction. In particular, the lack of an interaction between the factors TMS-site and motion direction might be unexpected given the fact that we stimulated unilaterally over the left hemisphere. One might therefore have expected to see more pronounced V5-TMS-effects with objects moving to the contralateral hemispace, i.e. the right hemispace. We will return to this issue in Section 4. The results are summarized in Table 1.

To see whether the effect of the factor TMS-site on average and peak reaching speed was specific to stimulation of V5, we conducted a further analysis in which we used %TMS$_{\mathrm{RS}}$ and %TMS$_{V_{\max}}$ (see Section 2, for a definition of %TMS-effect) as the dependent variables for a repeated measures ANOVA with the factors TMS-site (V5 versus DS) and observation time (100 versus 800 ms). A significant effect of factor TMS-site was obtained for both %TMS$_{\mathrm{RS}}$ ($F(1/5) = 10.46$, $P < 0.023$) and %TMS$_{V_{\max}}$ ($F(1/5) = 28.94$, $P < 0.003$). This confirms that the reduction in reaching speed was significantly more pronounced after V5 stimulation than after DS-stimulation. Moreover, one-sample t-tests showed that the %TMS-effect differed significantly from zero only in the case of V5 [for H_0 %TMS$_{\mathrm{RS}}$(V5) = 0, $P < 0.03$; for H_0 %TMS$_{V_{\max}}$(V5) = 0, $P < 0.025$], but not in the case of DS-stimulation. The %TMS-effects for the two sites and the two observation times are presented in Fig. 2A. No significant effect of factor observation time, and no interaction effect (TMS-site × observation time) was found.

3.2. *Task 2: reaching for a stationary object*

The factor TMS-site had no significant effect (see Table 2 and Fig. 2B). Observation time had a significant effect on %$T_{V_{\max}}$ ($F(1/5) = 21.609$, $P < 0.006$), reflecting the fact that peak reaching speed occurred in an earlier portion of the movement, when observation was shorter [%$T_{V_{\max}}$ (means, S.D.) OT = 100: 30.48%, 4.08; OT = 800: 33.51, 4.02]. This means that the deceleration phase was comparatively prolonged in the short-observation time condition. Since the short-observation time condition corresponds to an open-loop condition (i.e. condition where subjects were unable to see their reaching movements), this finding is consistent with that of earlier studies where it was shown that the withdrawal of visual feedback leads to a prolonged duration of the deceler-

Table 2
Reach-to-grasp task: effect of TMS-site

Observation time	TMS	RT (ms)		RS (m/s)		V_{max} (m/s)		$\%T_{V_{max}}$	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
100.00	V5	192.76	50.89	1.06	0.27	1.80	0.25	29.62	4.34
	Vertex	199.94	40.91	1.11	0.18	1.77	0.22	30.55	4.19
	DS	194.28	38.93	1.06	0.22	1.82	0.19	31.28	4.40
800.00	V5	177.54	52.52	1.13	0.32	1.82	0.34	33.07	4.42
	Vertex	188.67	44.11	1.21	0.30	1.87	0.31	33.50	3.75
	DS	185.62	36.80	1.17	0.28	1.92	0.29	33.95	4.40

Table 3
Reach-to-grasp task: effect of object position and observation time

Observation time	Object position	RT (ms)		RS (m/s)	
		Mean	S.D.	Mean	S.D.
100.00	Right	182.91	35.12	1.21	0.25
	Left	208.41	45.50	0.94	0.18
800.00	Right	178.63	46.35	1.30	0.35
	Left	189.26	39.86	1.03	0.26

ation phase (Churchill et al., 2000). Otherwise no significant effects of observation time were obtained.

The factor object position had a significant effect on RT ($F(1/5)=10.16$, $P<0.024$), and RS ($F(1/5)=44.19$, $P<0.001$). Subjects responded earlier and faster to objects on their right than to objects on their left side [RT (mean, S.D.), right pos.: 180.77 ms, 40.73; left pos.: 198.33 ms, 42.68; RS (mean, S.D.), right pos.: 1.26 m/s, 0.30; left pos.: 0.99 m/s, 0.22, see also Table 3]. We assume that this effect of object position reflects the fact that the head rest slightly hampered movements of the (right) hand towards positions in the left hemispace.

Furthermore, a significant interaction between the factors object position and observation time was found for RT ($F(1/5)=7.97$, $P<0.037$). This interaction reflects the fact that RTs for movements towards the leftward position are even more prolonged when the observation time is reduced to 100 ms (see Table 3). We can only speculate why this is the case. We assume that most subjects are even more hesitant to start their movement in the short-observation time condition, because in this condition, they cannot see their response, and therefore subjects might feel that the risk of colliding with the head rest is further increased.

4. Discussion

The results from this TMS study suggest that it is indeed the disruption of processing in V5/MT+ and not the disruption of more dorsal areas that was responsible for LM's catching deficits. By using rTMS we could show that selective interference with V5/MT+ is sufficient to cause a reduction in catching speed. Moreover, we found that stimulation in nearby dorsal regions does not affect catching performance. These findings broadly confirm the findings obtained in our earlier study with the motion-blind patient LM (Schenk, Mai, et al., 2000), and suggest that V5/MT+ is not only involved in purely perceptual but also in visuomotor tasks. One might therefore conclude that V5/MT+ provides visual motion input to both the ventral and the dorsal visual streams.

However, there were also some differences in the findings obtained in the patient and with TMS. The most obvious difference relates to the effect of observation time. LM's performance but not the performance of the healthy subjects was significantly affected by the duration of the observation interval. Her catching performance dropped to subnormal levels if the duration of the observation interval was less than 400 ms (Schenk, Mai, et al., 2000). Accordingly, one might have expected that the effect of V5-TMS would be more pronounced for shorter observation times. However, such an interaction between TMS and observation time was not found. At this stage we can only speculate why this difference occurs. We think the most likely explanation is that LM's dependence on long observation times reflects a compensatory strategy, which she acquired to use her intact spatial vision in order to compensate for her loss of motion vision. Long observation times allowed her to use the length of the path travelled by the moving object during the observation period to estimate the velocity of that object. It is likely that such a compensatory strategy only evolves over time and only in response to the experience of behavioural problems. In the TMS study, subjects had neither the time nor the need to develop a compensatory strategy, since the effect of TMS was only transient and did not produce a dramatic drop in performance.

This leads on to the second difference between the findings in LM and in our TMS study. Whereas LM's deficits were reflected in a decrease in catching speed and in an increase in catching errors, the TMS deficits were only reflected in a decrease in catching speed. This seems to suggest that a catching deficit induced by V5-TMS is much more subtle than a deficit that is caused by a lesion to this area. This is probably not surprising if one considers the fact that rTMS only induces a transient increase of noise in the affected area (Walsh & Rushworth, 1999), and therefore does not faithfully mimic the total disruption of information flow that results from structural brain damage.

Another reason why LM's deficit is more pronounced than the deficit found after V5-TMS might be that the spatial extent of LM's lesion certainly exceeded the extent of the area which was affected in our rTMS study. Moreover, LM's lesion was bilateral, whereas the stimulation in the present study was only unilateral. Any of these factors could explain why LM's deficit was more pronounced than the deficit which we observed after V5-TMS.

It is in fact rather surprising that the TMS-induced deficits were found equally for objects travelling to both the right and the left hemispace despite the TMS stimulation being restricted to the left hemisphere. This is surprising since we know from electrophysiological (Maunsell & Van Essen, 1987; Van Essen, 1985; Zeki, 1974, 1980) and lesion studies (Newsome & Paré, 1988; Plant & Nakayama, 1993; Plant et al., 1993; Schenk & Zihl, 1997; Vaina et al., 2001) that V5 on each hemisphere contains only a representation of the contralateral visual field. Accordingly one would expect that unilateral TMS of V5 should lead to strictly contralateral deficits. Although some studies confirmed this expectation (Beckers & Hömberg, 1992; Beckers & Zeki, 1995; Stewart et al., 1999), others found whole-field deficits after unilateral TMS (Hotson, Braun, Herzberg, & Boman, 1994; Walsh et al., 1998). One way of explaining such whole-field deficits after unilateral stimulation is by assuming that unilateral TMS disrupts not only the processing in the underlying cortical area but also affects the activity in connected brain areas in the same but also the opposite brain hemisphere (including the area which is homotopic to the stimulated area). In fact, it has been shown in a number of studies that TMS-induced activity is transferred to such connected areas, including the homotopic area of the contralateral hemisphere (Cracco, Amassian, Maccabee, & Cracco, 1989; Ilmoniemi et al., 1997; Komssi et al., 2002; Paus et al., 1997). However, in a combined TMS-ERP study, it was found that although stimulation over left motor cortex induced activity in right-hemispheric sensorimotor areas, this activity was much smaller than the activity in the left hemisphere (Nikulin, Kicicacute, Kahkonen, & Ilmoniemi, 2003). It is therefore quite likely that the induced activity in the opposite hemisphere is too small to cause any disruption of processing and thus too small to cause any performance deficits. The same might be true for area V5. This means that the transfer of activity to the opposite hemisphere offers a possible, but at the moment not very plausible explanation for the observed whole-field deficits after unilateral V5 stimulation.

At least in our study a more plausible explanation for the lack of hemispace differences has to do with fact that subjects in our experiments were free to move their eyes. Since the object always started from a central position, it is quite likely that subjects directed their eyes first towards that central start position, and then followed the object with their eyes during the object's movement to the right or left. In this case the object's image would always be near the centre of the visual field, and consequently no hemispace differences should be expected.

Finally, we would like to return to the effect of V5-TMS on catching performance, and ask more specifically what aspect of the visuomotor processing has been disrupted by interfering with V5/MT+. In principle there are two sources of visual motion during the catching task, which might have been affected by the interference with the processing in the visual motion area V5/MT+. The first and more obvious source is the moving target object; the second source is the movement of the hand during the catching response.

There are three arguments which suggest that it is not the interference with the perception of the moving hand (i.e. on-line visual feedback) that caused the catching deficits. First, if the disruption of visual feedback were to blame for the catching deficits, then similar deficits should have been found in the reach-to-grasp task. This, however, was not the case. Secondly, we would expect that the deficits would only be found when visual feedback is provided. But in fact the TMS-induced catching deficits were also found in the 100 ms condition; yet during that condition on-line visual feedback was not available. Thirdly, we showed recently that visual feedback is not used in the control of catching behaviour (Schenk, Mair, & Zihl, 2003). It would therefore be difficult to explain the TMS-induced changes in catching behaviour, if TMS interferes primarily with the use of visual feedback. Furthermore, it is possible to examine the time-course of the reaching movement to look for changes which might betray effects of TMS on the use of visual feedback. Changes in the time-course have been described in a number of studies in which the effect of visual feedback was examined. In particular, it was found that the deceleration phase is relatively prolonged when visual feedback is withdrawn (for a review, see Churchill et al., 2000). Thus, if we had found a TMS-induced increase in the deceleration phase, this might indicate that the TMS has interfered with the use of visual feedback. However, no such TMS-induced prolongation of the deceleration phase was found. Taken together, our findings suggest that it is not interference with the use of on-line visual feedback, but with the perception of the target's movement that is responsible for the observed V5-TMS-effects.

More specifically, we would like to suggest that it is the degradation of information on the target's speed and not its movement direction that caused the TMS-induced changes in catching speed. This reduction in catching speed most probably reflects an underestimation of the speed of the target object that is induced by interference with V5. Such an underestimation of the speed of visual targets after damage to V5 has been found both for patient LM (Hess et al., 1989; Zihl et al., 1991) and for patients who suffered unilateral damage to V5 (Plant & Nakayama, 1993). Moreover, evidence from neurophysiological and behavioural studies suggests that V5 plays a unique role in velocity perception, whereas V5's contribution to the identification of unambiguous motion direction is much less essential. The range of velocities that are represented in V5 (Lagae et al., 1993; Maunsell & Van Essen, 1983; Mikami et al., 1986; Rodman & Albright, 1987; Van Essen, 1985) extends to much higher values than that for cells in either V1 (Newsome, Mikami, & Wurtz, 1986; Orban, Kennedy, & Bullier, 1986) or V3 (Felleman & Van

Essen, 1987). This means that since disruption of V5 disables the cell-population that codes higher velocities, such velocities are instead coded in lower-velocity cells in V1 or V3, and consequently velocity is underestimated. In contrast faithful direction discrimination can be found not just in V5, but in many more visual areas including V1 and V3 (Van Essen, 1985). Accordingly, disruption of V5 will not lead to a significant deficit in the identification of the direction of a single moving object. This has been confirmed in lesion studies (Baker et al., 1991; Hess et al., 1989; Shipp et al., 1994). We would not expect, therefore, that V5-TMS would cause deficits in the identification of the direction of the target object in our catching task. However, it should be noted that for other types of direction-discrimination tasks, which involve ambiguous stimuli (e.g. random kinematograms or so-called moving plaid patterns), V5 seems to make a unique contribution. This has been found in single-unit studies (Movshon, Adelson, Gizzi, & Newsome, 1985; Salzman & Britten, 1990; Snowden, Treue, & Andersen, 1992), and has been confirmed in lesion (Baker et al., 1991; Marcar, Zihl, & Cowey, 1997) and TMS studies (Beckers & Hömberg, 1992; Beckers & Zeki, 1995).

5. Conclusions

The results from this study confirm that V5/MT+ plays a role not just in perceptual but also in visuomotor tasks that require the processing of visual motion information. It is interesting that although anatomically V5/MT+ is often regarded as part of the dorsal stream, most of the functional studies have focussed on V5's role in purely perceptual tasks. Our results confirm that V5/MT+ also plays a role in vision for action, and thus seems to contribute to both dorsal- and ventral-stream functions. V5's functional contribution to the two streams is consistent with the well-established anatomical fact that V5 projects to areas within both the dorsal and the ventral streams (Felleman & Van Essen, 1991).

Thus, mostly this TMS-study confirms the findings from our earlier study with patient LM. There are, however, also informative differences between the two studies. Most importantly, the dependence on extended observation times that was found in patient LM was not found as a consequence of disrupting V5/MT+ by TMS. It seems that this dependence is only found in the context of a chronic V5 deficit, and is therefore probably not a direct effect of a V5 impairment, but an indirect effect of the long-term adaptation to the motion-blindness resulting from a chronic V5 lesion. This study along with similar studies (Walsh et al., 1998) suggests that the comparison between the effects of TMS and lesions may provide a method to discriminate between the direct behavioural consequences of a lesion that reflect the loss of a specific brain mechanism, and the indirect consequences, which result from neural or behavioural changes that take place in response to the lost brain capacity.

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