Applied Cognitive Neuroscience:

An investigation into the dorsal and ventral visual streams

Jaimie Catherine Wilkie

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Abstract

The role of the dorsal and ventral visual streams in attentional orienting were examined in three experiments. The first a behavioural test, the second a high-density EEG, and the third a neuropsychological case study. Visual attention was examined by using peripheral cues that were either symbolic-semantic 'identity' or visuospatial 'landmark' cues to respond to a target. In experiment one, when cues were presented briefly (66ms), only landmark cues could facilitate the response time of locating a target. Identity cues were able to facilitate target detection only with a sustained cue presentation time of 133ms. This was interpreted in terms of the transient and sustained response characteristics of the dorsal M-cells and ventral streams P-cells respectively. The EEG showed stronger C1 waveforms for landmark cues in the parietal-occipital electrodes, overlaying dorsal areas (compared to the identity cues) and vice versa, the identity cues showed stronger waveforms in the temporo-occipital electrodes, overlaying ventral areas. The neuropsychological experiment showed a patient with a lesion in the dorsal area of the right parietal occipital junction, had a clear ability to use identity cues, but was unable to utilise landmark cues. This may be because of the damaged dorsal stream. Taken together these findings provide support for the unified model of vision and attention.

Dedication

This thesis is dedicated to my late grandmother Victoria Gordon.

Without your support and belief in me, I would never have made it this far.

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Firstly, I would like to thank FM, my clinical patient. FM you made this thesis a much more interesting place to be. Your joie de vivre, positivity and cooperation were inspiring. I really appreciate your time and our chats. I have learnt so much from you and about you!

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Table of Contents

Abstract iiiii

Dedication ivv

Acknowledgements v

Table of Contents vii

Preface iv

Thesis Structure x

Chapter 1. INTRODUCTION 1

Neuroanatomy 2

Dual streams of vision 7

Dual streams of visual attention 9

Unified model of vision and attention ..... 1**Error! Bookmark not defined.**

Chapter 2. CUE PRESENTATION TIME 14

Method 18

Results 21

Discussion 25

Chapter 3. ERPs of Landmark and Identity Cues ..... **Error! Bookmark not defined.**

C1 Activation 30

Method ..... **Error! Bookmark not defined.**3

Results ..... **Error! Bookmark not defined.**

Discussion 46

Chapter 4.Clinical Experiment.....50

Patient DF 52

Case Study 53

Neuropsychological Assessment .....**Error! Bookmark not defined.**8

Optic Ataxia.....61

Landmark Cueing Task.....**Error! Bookmark not defined.**

Visual Object Space Perception Tasks 70

Object Perception Test.....71

Space Perception Test.....74

Neglect 79

Orientation Agnosia.....82

Blindsight.....86

Summary of Results.....90

Discussion…….95

Chapter 5. General Discussion.....99

Overview of Thesis Results 99

Case study .....**Error! Bookmark not defined.**

EEG.....**Error! Bookmark not defined.**

Cue exposure.....**Error! Bookmark not defined.**

Unified model of vision and attention .....**Error! Bookmark not defined.**

In conclusion.....**Error! Bookmark not defined.**

References.....**Error! Bookmark not defined.**

Appendix A ASL Scan..... **Error! Bookmark not defined.**

Appendix B SPR Scan ..... **Error! Bookmark not defined.**

Appendix C Visual perimetry Left ..... **Error! Bookmark not defined.**

Appendix D Visual perimetry Right..... **Error! Bookmark not defined.**

Appendix E Bells task..... **Error! Bookmark not defined.**

Appendix F Line bisection task ..... **Error! Bookmark not defined.**

Appendix G Tumour checklist for GPs ..... **Error! Bookmark not defined.**

PREFACE

The scientist-practitioner model is a well-defined concept and pre-requisite of those studying clinical neuropsychology and my field of interest. I began my studies entrenched in the era of cognitive psychology, the rise of functional magnetic resonance imaging and the move away from discrete neural areas to connectivity. From the beginning, my love of neuropsychology and a good double dissociation came from my supervisor, Jeremy Tree in Exeter (now Durham university). The study of neuropsychology was a welcome relief from some of (what I found to be) grey areas in the psychological field. The brain did it or didn't, and we could test that objectively; with the ability to identify the brain activation through fMRI, EEG and now white matter tractography!

In New Zealand, I met Tony Lambert, who kindly took on a punt on me after we met. I was armed with my dissertation on face processing, and although Tony was not pursuing face processing anymore, we agreed I would continue Tony's research on vision and attention. To maintain my interest in the clinical field, Lynette Tippet was assigned as my co-supervisor. And so, my scientist-practitioner journey was born. Tony and my PhD predecessor, Narissa Marrett, had worked with patient DF and to provide a well-rounded body of evidence, we needed to find a patient with a dissociative condition to DF.

The major aim of this study was to bridge the field of cognitive neuroscience with the clinical world. Could the study of vision and attention neuroscience, bring knowledge that could be applied to the clinical world; firstly, in terms of knowledge, and secondly in a practical way?

Thesis Structure

The first part of this thesis introduces the two main topics of research, the dual process of vision and the dual process of attention. The first experimental chapter (chapter two) details the main behavioural experiment, marries the two dual processes together, and has a part to play in the conception of the Unified Model of Vision and Attention (Lambert, Wilkie, Greenwood, Ryckman, Scibberas-Lim, & Booker 2018). The third chapter is an electrophysiological examination, similar to the previous behavioural experiment, to understand the temporal basis for behavioural results. Chapter four is the clinical case study, of which the patient was also tested on the behavioural test, along with a battery of neuropsychological assessments. The final discussion chapter brings these two worlds of cognitive neuroscience and clinical together, in the view of the scientist-practitioner.

INTRODUCTION

The purpose of this investigation is to bridge the gap between cognitive neuroscience and psychological practice. Each field must constantly inform the other to provide patients with the best possible care. The overarching aim of the present research is to investigate the role of the dorsal and ventral visual pathways, and the dichotomy of endogenous and exogenous attention, with a particular focus on clinical evidence. Accordingly, the research in the following chapters explore the neural basis of early visual attention in healthy participants and a patient with a lesion in the dorsal stream. The studies that follow are designed to answer a number of questions, including a) will attention-shifting based on encoding the symbolic identity of cue stimuli rely on ventral stream encoding; b) will attention-shifting based on encoding the visual-spatial features of cues relies on dorsal stream encoding; c) would a patient with a lesion in the dorsal stream be less able to process visual-spatial cues; and d) can this research inform the clinical world and provide some kind of therapeutic measure?

The theoretical distinction between the two visual pathways have been extremely well researched over the last couple of decades (Mishkin & Ungerleider 1982; Milner & Goodale 2006 & 2008; Whitwell, Milner & Goodale, 2014; Milner 2017). The endogenous and exogenous attentional theories have also been well documented (Corbetta & Shulman 2011, Chica, Bartolomeo & Lupiáñez, 2013; Lambert, Wilkie, Greenwood, Ryckman, Scibberas-Lim & Booker 2018). Several studies from the Lambert lab found that cue duration could be the key for bringing together these two dichotomous theories (Lambert et al. 2018).

To begin the investigation, the first chapter will introduce dual process vison theory, and the dual process attentional theory. The neuroanatomy and rationale for testing cue duration, will

be explained, along with an explanation of the current research to date. The second chapter will describe the long and short cue duration, and a behavioural experiment will reveal attentional effects and how these can be mapped onto the dual process theory of vision. The third chapter is an electrophysiological investigation of the exogenous and endogenous cues and how they can be related to the neuroanatomy of early visual pathways. The evidence will be discussed in light of the unified model of vision and attention (Lambert et al. 2018). The fourth chapter presents the clinical evidence of a patient with a lesion in the dorsal visual stream and discuss the present research along with the evidence of a patient with a lesion in the ventral visual stream (Marrett, de-Wit, Roser, Kentridge, Milner & Lambert, (2011). The final chapter is the general discussion, bringing all the lines of evidence together and discussing them in the context of the dual vision process and the dual attention theory.

Throughout the thesis, the current clinical literature is described in conjunction with pioneering data from current cognitive neuroscience. A novel rehabilitation technique for clinical patients with vision loss is described. A world-wide issue with delayed diagnosis of brain tumours comes to light and so, an indicator list of symptoms for brain tumours is compiled for general practitioner doctors, along with an urgent plea for more neuropsychologists in New Zealand.

Neuroanatomy

Visual processing is first performed in the retina. Output from photoreceptors is processed in the bipolar cells, and then the ganglion cells (Gazzaniga, Ivry and Mangun, 2014). Axons of the ganglion cells form a bundle, called the optic nerve, before entering the brain, each optic nerve bundle from each retina splits into two parts; nasal and temporal. The temporal

branch continues to traverse along from the outer parts of the retina projecting ipsilaterally, the nasal branch crosses over the optic chiasm (Erskine & Herrera, 2014). In this way, each visual field is projected to the primary visual cortex in the contralateral hemisphere.

After entering the optic chiasm, each optic nerve divides into pathways that terminate in different areas of the subcortex, a small percentage of visual fibers in the optic nerve terminate in the superior colliculus and pulvinar nucleus (Ungerleider & Mishkin,1982; Kravitz, Kadharbatcha, Baker, Ungerleider, & Mishkin, 2013). This is known as the retino-collicular pathway and is sometimes viewed as a more primitive visual system (Gazzaniga et al, 2014). The retino-geniculate pathways projects from the retina, to the lateral geniculate nuclei (LGN) of the thalamus and then the bundle of axons exit from the LGN and ascend to the cortex, terminating in the primary visual area of the occipital lobe. This geniculo-cortical pathway contains more than 90% of the axons in the optic nerve and provides input to the cortex via the geniculo-cortical projections (Gazzaniga et al. 2014).

The architecture of the LGN is highly organized, containing six well defined layers. Each layer within the LGN receives input from the axons of the optical tract and sends outputs that terminate in the cortex (Savier, Chen & Cang, 2019). Layers 3 through to 6 contain the smaller neurons of the parvocellular system; layers 1 and 2 contain the larger neurons of the magnocellular system. The cell types of each layer have clear distinctions. The axons of cells within the first two layers are larger in diameter than the cells of the upper four layers. Because of their large size, the bottom layers are referred to as magnocellular, or M system and the smaller cells in the upper four layers make up the parvocelluar or P system (Ferrera, Nealey, & Maunsell, 1994).

The first cortical synapses for neurons carrying visual information are in the medial portion of the occipital lobe, area 17 in Brodmann's map, known as the striate cortex, primary visual cortex or V1. This receiving area is located medially and buried below the superficial surface of the cortex along the calcarine sulcus (Gazzaniga et al 2014). The segregation of the M and P pathways is maintained through to the cortex. Although both systems terminate in layer 4 of the cortex, the P pathway involves a second synapse on intracortical neurons and carries information through to layers 2 and 3. The P pathway has also been shown to have 2 branches blob and interblobs (Wong-Riley, 1979). Visual information is segregated into distinct pathways in V2 or the prestriate cortex. The M, P-blob and P-interblob arrangement continues into V2. Whether they are completely independent is uncertain. Visual information from the retina is processed in parallel through the superior colliculus and simultaneously from the LGN to V1 (Savier, Chen & Cang, 2019).

All cortical processing begins in V1, but there are two processing streams that extend dorsally to the parietal lobe, or ventrally to the temporal lobe. The stimulus required to produce optimal activation of a cell becomes more complex along the ventral stream. In addition, the size of these receptive fields of these cells increases, ranging from the 0.5 degree span of a V1 cell, to the 40 degree span of a cell in area TE (Desimone& Duncan, 1995).

The pathways carrying visual information from the retina to the cortex segregate into multiple processing stream. There is the partitioning of magno- and parvocellular pathways, followed by blob and interblob zones in the primary visual cortex. Output from the occipital lobe is primarily contained in two major fibre bundles called fasciculi. The inferior longitudinal fasciculus follows a ventral route into the temporal lobe (Ungerleider and Mishkin, 1982). The

superior longitudinal fasciculus takes a more dorsal path, with most of its terminations in the posterior regions of the parietal lobe.

Cells in the magnocellular pathway are very responsive to motion and very sensitive to contrast differences. Cells in the blob, thin stripe region of the parvocellular pathway also have high contrast sensitivity and are sharply tuned for colour. Cells in the interblob, interstripe regions of the P pathway are sensitive to location and orientation (Maunsell and Van Essen, 1983). Zeki (1993) showed different visual areas are activated when processing colour or motion. Although the spatial resolution of the PET was coarse, colour was activating anterior, inferior occipital lobe and motion was bilateral near the junction of the temporal, parietal and occipital cortices. They labeled the area for colour foci, V4 and motion V5 (or human MT). V4 is devoted to shape perception; colour can provide an important clue about shape perception, by facilitating form perception. The physiological evidence indicates the strongest segregation of function is in motion and colour perception (Mckeefry, Laviers& McGraw, 2005).

The retino-geniculate-cortical tract contains 90% of the fibers in the optic tract and subdivisions of this pathway provide the building blocks for form, colour and motion perception, allowing recognition of complex visual scenes (Danesh-Meyer, 2012). Damage to a part of the primary visual cortex, from strokes, injury, or disease renders a patient blind to stimuli falling in the receptive area. This deficit is known as a scotoma (a visual field cut), if the entire visual cortex is lesioned, the patient is unable to see anything in the contralesional hemifield (De Haan, Heytink, & Melis-Dankers 2015).

Hadjikhani (et al 1998) used high resolution MRI and transformed the folded cortical surface into a flattened 2-D map. They showed areas above the calcarine sulcus (primary visual

cortex) are active when a stimulus is in the lower visual field and below the calcarine sulcus activates when a stimulus is in the upper visual field. The retinotopic mapping of the visual field is replicated many times indicating separate topographic maps from V1 through to V4. The cortical representation of the fovea is quite large with a disproportionate amount of cortex encoding the fovea, compared to the peripheral visual field.

Many non-geniculate optical fibers terminate in the superior colliculus. This structure plays a critical role in eye movements. Schneider (1969) lesioned hamsters bilaterally in their visual cortices, or the optical fibers inputting the superior colliculus. Cortical lesions severely impaired visual identification, but collicular lesions impaired the ability to orient towards a stimulus. Weiskrantz (1986) found that a hemianopic patient (D.B.) could still detect the location of objects in his blind field; this blindsight may come from subcortical visual pathways, such as the superior colliculus. It is also possible that information can reach extrastriate visual areas in the cortex, either through direct geniculate projections or from other subcortical structures. Another possibility is that lesions in the primary visual cortex are incomplete and blindsight results from residual function in spared tissue (Campion, Latto & Smith, 1983).

Neurons in the temporal lobe have receptive fields encompassing the fovea, ideal for object recognition. Desimone (1984) found temporal cells respond to complex objects, not just lines or contrast. The same activity also holds, even if the stimulus is rotated 90 degrees. The parietal lobe is not likely to exhibit such specificity or spatial independence (Gazzaniga et al. 2002). 40% of parietal neurons have receptive fields near the fovea, the remaining 60% are peripheral, eccentric for detecting presence of stimuli entering the visual field, similar to the role of the superior colliculus (Quraishi, Heider & Siegel, 2006). The neurons are activated by any stimuli at all, but the activity is correlated with the size of the stimuli. Parietal lobe lesions result

in disturbance to perception of spatial layout and spatial relations of objects (Ackerman & Courtney, 2015).

Dual Streams of Vision

Ungerleider and Mishkin (1982) first proposed the highly cited what and where dual steam theory of vision. Their experiment on monkeys, they used an object discrimination task and a landmark task. In the object discrimination, the monkeys are presented with a familiar object and a new object. The monkey's task was to pick the new object, showing they recognize the original object and were rewarded if correct. In the second task, the landmark discrimination, monkeys were placed in front of a table that has two covered foodwells. A cylinder was placed next to one of the foodwells, if the monkeys chose the foodwell next to the cylinder, they were rewarded (Ungerleider &Mishkin, 1982).

After training, the monkeys had either bilateral removal of area TE in the temporal lobe or bilateral removal of the posterior parietal cortex. Those monkeys who have temporal lobe lesions were no longer able to perform the object discrimination task. Monkeys with parietal lesions were no longer able to perform the landmark discrimination task. In each case the monkeys were still able to perform the other task. This dissociation led the ventral visual stream being termed the 'what' pathway and the dorsal visual stream, the 'where' pathway.

The dorsal pathway is an occipitoparietal network that lies between the early visual cortex and specialized cortical structured involved in visually guided action, somatosensation, spatial audition, navigation and spatial working memory. The role of the dorsal stream has been debated over the years, but the role of the ventral stream as processing what an object is, has been unchallenged. The ventral visual pathway is a recurrent and highly interactive

occipitotemporal network, linking early visual areas with the anterior temporal cortex (Milner 2012). Both visual pathways are connected with the frontal eye fields, so eye movements initiated by one stream might also impact the other stream (Kravitz et al. 2013).

Ungerleider and Mishkin's (1982) conception of the dorsal and ventral visual streams is that they are specialised for encoding spatial relations and stimulus identity, respectively. However, in more recent decades, Ungerleider and Mishkin's (1982) approach has been to some extent superseded by the theory of Milner and Goodale (1992, 2006), which offers a rather different view of the functional distinction between the dorsal and ventral visual streams. According to Milner and Goodale (2006) the ventral stream delivers *'vision for perception'*. That is, the ventral stream provides visual representations that can become conscious and gain access to working memory. In contrast, the dorsal stream provides *'vision for action'*. According to Milner and Goodale's (2006) framework, visual representations encoded by the dorsal stream play a critical role in rapid, on-line control of visually guided actions. Moreover, Milner (2012) reviewed evidence in support of the proposal that the dorsal stream visual encoding that supports such movements is independent of, and indeed inaccessible to, conscious awareness. Much research attention and effort has been directed towards studying the role of the dorsal stream in visually guided actions of the hand and arm, especially grasping movements (Milner & Goodale, 2006).

Goodale and Milner (1992) reported patient DF who suffered bilateral lesions of the occipital lobes. DF has severe visual form agnosia, and could not identify the orientation of slots, but was able to orient her hand correctly towards them. This led to the reformation of what/where pathway to what/how. The ventral pathway, occipital-temporal cortex, allows the identification of objects and their semantic attributes. The dorsal pathway, following the

occipito-parietal cortex, allows the visual control of actions, the spatial localization of visual stimuli identification of spatial attributes, including orientation, depth and movement. The dorsal pathway also provides strong input to motor systems to compute how movement is produced.

An opposite dissociation is optic ataxia. With this impairment, patients can recognize objects, but can't orient towards them. The saccades direct inappropriately and fail to bring an object into the fovea. Recent research has shown the dorsal and ventral what/where dissociation continues into the midbrain. The entorhinal cortex is an area of the brain located in the medial temporal lobe and functioning as a hub in a widespread network for memory, navigation and the perception of time. Scultz, Sommer and Peters (2014) found spatial information connects the dorsal visual regions with the parahippocampal cortex, the posterior-medial EC and the hippocampus. Object information is carried between the ventral visual regions, the perirhinal cortex, the anterolateral EC and the hippocampus. An anterior circuit connects PRC to LEC, while a posterior circuit connects PHC to MEC.

Dual Theory of Visual Attention

Attention may be differentiated into "overt" versus "covert" orienting. Overt orienting is the act of selectively attending to an item or location over others by moving the eyes to point in that direction. Overt orienting can be directly observed in the form of eye movements. Although overt eye movements are quite common, there is a distinction that can be made between two types of eye movements; reflexive and controlled. Reflexive movements are commanded by the superior colliculus of the midbrain (Savier et al. 2019). These movements are fast and are activated by the sudden appearance of stimuli. In contrast, controlled eye movements are

commanded by areas in the frontal lobe; these movements are slow and voluntary (Terao, Fukuda, Hikosaka, 2017).

Covert orienting is the act of mentally shifting one's focus without moving one's eyes. Simply, it is changes in attention that are not attributable to overt eye movements. Attention can be voluntary or involuntary. Also known as endogenous or exogenous, it is either within our control or outside of our control (Posner, 1980). Endogenous attention can be sustained, but exogenous is transient (Lambert et al. 2018). The spatial cueing paradigm of Posner (1980) is often used to measure the response of covert attention. Participants are asked to respond to a target on a computer screen where the location is generally predicted by a cue of some form. When the target appears where it was cued, the response time is faster than when the target appears in an unexpected location. This effect is attributed to the influence of covert attention.

Unified Model of Vision and Attention

The Lambert lab has administered many variations of the Posner cueing effect to ascertain what factors cause or inhibit covert attention; and what role the dorsal and ventral streams play in attention (Lambert & Duddy, 2002, Lambert & Shin. Marrett & Lambert 2011, Lambert & Wootton 2017, Lambert et al. 2018). Symmetric cues were presented centrally or peripherally, and participants told that two letter cues, e.g. X-X's, indicate the target will likely appear on the right. As soon as the target is spotted, participants press the spacebar. If the target appears in the expected location it is a valid trial and response time is faster than if the target appears on the unexpected side, an invalid trial. This is known as the Posner effect. Generally, targets appear where cued 80% time.

The features of the cue play an important role in the ability to orient covert attention. If a cue is asymmetrical, then response time to the Posner cueing tasks is much faster than if it is symmetrical. The cueing effect, indexed by the difference in response time between valid and invalid trials, for this type of cue becomes apparent at much briefer stimulus onset asynchronies (SOA). Being able to differentiate the lateralisation of the cue enables orientation. That is, if some spatial feature of the cue corresponds to the side where a target is likely to appear, response time is faster. Classically attention from focused eye gaze (within the fovea) is thought to be associated with endogenous orienting. But when cues were presented centrally, the only reliable effect on orienting was symmetry (Lambert et al. 2002, 2010). Even at a long SOA where there should be ample time for endogenous orienting to take effect only spatial correspondence (feature-based cues) produced faster response times. Visually symmetric central cues had no reliable effects on orienting at either short or long SOAs. This was puzzling as other experiments in the literature, using centrally presented cues produced faster responses than peripheral cues (Fischer, Castel, Dodd & Pratt, 2003). At that time is was believed other work had found this association because traditionally central cues are arrows, which are highly over-learned symbols, producing automaticity in response. The difference here was the central cues were completely arbitrary (Lambert et al 2002, 2010).

In a further experiment Shin et al. (2011) tested automaticity in the form of the same arbitrary cues X and T, which predicted the target, but in this experiment half of the participants were informed of this relationship between cue and target and half were not. Interestingly cue validity effects were unaffected by strategic instructions. This means participants showed similar advantages in response times to valid cues whether they were aware of the relationship between cue and target or not. These results appeared to show that visual orienting of feature-based cues

are unconscious and therefore, possibly driven by dorsal stream encoding. The dorsal stream encoding has been reported to encode unconsciously (Milner, 2012).

As previously mentioned, the representation of foveal and peripheral vision is not analogous in the cortex. The parieto-occipital area receives a relatively greater contribution than the inferior temporal from inputs representing the peripheral, as compared with the central visual field (Quraishi, Heider & Siegel, 2006; Wandell, Dumoulin & Brewer, 2007). The inputs from central vision (i.e. the central 7 °) are more important (than those from peripheral vision) for the pattern discrimination functions of the temporal cortex, but in the case of visual spatial functions of parieto cortex, the inputs from central and peripheral vision are equally important (Mishkin & Ungerleider 1982). Put more simply, the central vision is represented well in the ventral visual stream, but not the dorsal stream. The dorsal stream receives inputs from both central and peripheral vision, but is more specialised for peripheral vision. The physiology of the visual representation is important for attentional cues being presented in the central or periphery of vision.

To continue the evidence towards unconscious processing of the dorsal stream, a study by Lambert and Shin (2010) reported that conscious perception of low contrast peripheral letters was massively impaired but there was no significant difference in orienting between low and high contrast letters. The orientating effects were still happening in the low contrast condition, despite participants being unable to perceive the cues.

Further evidence for unconscious processing of the dorsal stream comes from patient DF, who suffered carbon monoxide poisoning. MRI revealed bilateral damage to shape processing area LO, the ventral stream area responsible for basic form perception (Milner & Goodale, 2008). DF has severe visual form agnosia for object recognition but is able to perform visually

guided motor actions such as orienting her hand towards vertical or horizontal slots. DF carried out the cueing tasks and despite being unaware of the letter cues, she was able to orient towards targets presented at the cued locations (Marrett, de-Wit, Roser, Kentridge, Milner, & Lambert, 2011). Furthermore, the size of the cueing effect in DF did not differ from controls. Orientation of the cues must have been unconscious because DF was not able to consciously perceive the cues and because of the bilateral damage to her ventral stream, orientation must have been enabled via the dorsal stream.

Standard exogenous orienting in response to visuospatial peripheral cues, is non-semantic. The visual orienting effects appear to be determined by the symbolic or semantic information carried by the cue. Defining cues as semantic or visuospatial could hold a similar distinction to Ungerleider & Mishkin's "what" and "where" proposition. Orienting from the visual-spatial aspects of a cue might map on to the "where" or dorsal visual pathway and using the semantic features of a cue (e.g. X cues right) could relate to the "what" distinction of the ventral visual pathway.

This theory has been tested on a patient with a lesion in the ventral stream (Marrett et al. 2011). The ventrally damaged patient could not consciously see the visuo-spatial cues but could orient towards the cue effectively. Patients with a lesion in their dorsal stream are expected to be able to consciously perceive cues but not orient towards them. If so, this would give a double dissociation for the semantic versus visuospatial cue distinction, possibly being utilised separately by the two early visual pathways.

CHAPTER 2. CUE PRESENTATION TIME

INTRODUCTION

This chapter details the behavioural experiment of the effects of cue duration on attention. The purpose of this experiment is to compare effects of some visuospatial letter cues and some symbolic-semantic letter cues and vary the cue exposure time. The longer exposure time may allow for symbolic-semantic processing of the ventral stream, whereas the shorter cue exposure may only allow for rapid processing of the dorsal stream.

The time course of attention shifts has been investigated in a variety of conditions. A typical measurement is a pre-cue paradigm (Posner, 1980), where a cue informs the participants about the location of an upcoming target. This behavioural performance improves detection response time after cueing by several tens or hundreds of milliseconds.

Early work in the Lambert lab found that orienting of covert visual attention can be driven by visual and spatial features of a letter cue, rather than the meaning or semantics of a cue (Marrett, de-Wit, Roser, Kentridge, Milner & Lambert, 2011; Lambert & Duddy, 2002 & Lambert & Shin, 2010). Rules for attending left or right in the classic Posner (1980) cueing task were learnt by associating visuospatial features of the cue and target location. For example, if the letter “d” meant the participant should attend left, the rounded edge of the letter is leftward, thereby directing covert attention to the left. The visual elements are “landmark” features, spatially associated with target location. The cueing effect of these landmark letters were compared with laterally symmetric letters (X and T), which did not have any landmark feature to pin spatial associations on.

The results of Shin et al. (2011) found the attentional effects of visually symmetric cues without landmark features did not influence attention at all. This was despite have a long SOA of around 500ms to prepare and shift attention. A puzzling result as many studies of orienting attention were successful with symmetric and asymmetric cues, that appear to be driven by semantic meaning of the cue, rather than landmark featured alone. An example of this, is the work by Fischer, Castel, Dodd and Pratt, (2003). They presented a high value single digit (eg eight or nine) as a central cue, which gave an automatic shift of attention to the right, whereas a low value digit (one or two), shifted attention to the left. This was discussed a reflection of the relationship between attention and the mental number line. Low numbers begin on the left and high numbers continue onto the right. Critically two of the stimuli utilised by Fischer et al. 2003, one and eight, were almost completely visually symmetric.

Fischer et al. (2003) found that number cues were spatially *and* semantically informative, due to the mental number line. A notable difference between Fischer's study and the work in the Lambert lab, was the cue presentation time. Lambert and colleagues used a very brief cue exposure of 66ms and Fischer et al (2003) had used a longer cue exposure time of 300ms. The stimulus onset asynchrony (SOA) has been varied in many papers over the years, but none have systematically tested the effects of cue presentation time on attention.

Why is cue presentation time important? Both physiological and clinical literature can help us to understand this question. The anatomical differences of the dorsal and ventral streams should show different response times for the symbolic-semantic (hereby referred to as identity) and visuo-spatial (hereby referred to a landmark) cueing, because of the different physiological characteristics. The vast majority of fibres in the dorsal stream carry signals that originate from the two magnocellular (M-cell) layers of the lateral geniculate nucleus (LGN). The ventral

stream contains projections originating from the four parvocellular (P-cell) layers of LGN and the also receives some M-cell input (Merigan and Maunsell, 1993).

These P and M cells have different characteristics. M-cell derived channels elicit a transient response to visual stimuli (Livingstone & Hubel, 1988; Robson & Kulikowski, 2012). The onset or offset of a stimulus elicits a transient response in these cells, after which firing rates return to a baseline level. In contrast, the P-cells of the LGN, which provide the majority of input to the ventral stream, fire a sustained response to visual stimuli (Livingstone & Hubel, 1988; Merigan & Maunsell, 1993). Therefore, M cells of the dorsal stream should respond to briefly presented cues and P cells of the ventral stream should respond to a sustained cue presentation.

The dissociation between the ventral and dorsal use of semantic understanding has been shown by a patient with bilateral lesions of the occipital-parietal areas (Vinckier, Naccache, Papiex, Forget, Hahn-Barma, Dehaene & Cohen, 2006). Meaning or semantics, were acquired through the patient's intact occipital-temporal routes, the ventral stream, but spatial and attentional impairments were noticed when using alternative reading strategies such as rotated words, mirrored words, separating letters with double spaces. The latter strategies are spatial and were disrupted in this patient because of the impaired spatial encoding from damage to the dorsal stream.

Furthermore, in split brain patients, a fully sectioned corpus callosum means little or no perceptual interaction can occur between hemispheres. Gazzaniga et al. (2014) show that semantic and visual information can be dissociated. The anterior part of the callosum transfers *semantic* information about a stimulus, but not about the stimulus itself. The posterior part of the

corpus callosum (which interconnects the occipital lobes around the temporal area), transfers only visual, auditory and tactile information.

Until recently all the work from our own lab on shifting attention in response to cues appears to have been driven by the dorsal stream encoding (Lambert et al., 2006; Shin et al., 2011). When cues are presented briefly, visual orienting is unable to utilise the identity features of a cue. Semantic associations are likely to be encoded in the ventral stream, which need a longer time to encode than the dorsal stream. but are unlikely to be encoded in the dorsal stream (Vinckeir et al. 2006; Milner & Goodale, 2006). If attentional learning can be determined by identity encoding, maybe identity encoding is driven by the ventral stream and landmark encoding is driven by the dorsal visual stream.

The types of cues used in the following experiment are letter cues, as used previously in our laboratory (Lambert et al. 2018, Lambert & Wootton, 2017 & Shin et al. 2011). There will be some symmetrical letters, e.g. X-T or V-O on either side of fixation, with instructions to which letter indicates the target location, so spatial correspondence can occur. For example, the letter X (or V), means a target will appear on the left. The same letters will be used to encourage identity learning. For example, X-X or T-T, two X's means the target will appear on the left, two T's means a target will appear on the right. As the letters are identical in the second cueing paradigm, spatial correspondence will be void and the participants will need to infer the semantic symbolization of the cue.

The large number of participants used in this experiment will hopefully reveal any small magnitude effects of identity cues in the brief exposure time condition. To paraphrase Ungerleider and Mishkin's (1982) model of vision, the hypothesis is that attentional behaviour in

this situation will be driven by encoding the identity of cue stimuli within the 'what pathway' (i.e. the ventral stream).

Attention shifting based on encoding the symbolic identity of cue stimuli relies on ventral stream encoding, and in particular on the P-cell inputs to the ventral stream; and attention shifting based on encoding the visual-spatial features of cues relies on dorsal stream encoding, and in particular on the M-cell inputs to the dorsal stream. The aim of this experiment was to test this interpretation, by assessing the effects of cue exposure time in two spatial orienting paradigms. Will the effects of landmark cues be strong, indexed by a large Posner response, when exposure time is reduced? Consistent with the proposal that these effects are mediated through visual encoding by M-cell channels, and their fast, transient response characteristics? On the other hand, will the validity effects of identity cues be smaller when exposure time is reduced, consistent with the suggestion that these effects are mediated by P-cell channels, which do not respond well to briefly exposed stimuli?

METHOD

Participants

75 adults from the community took part. Age range 21-67 years old, median age 29. All procedures were approved by the University of Auckland ethics board (ref 7835). Two made excessive anticipation errors and one excessive catch trial errors. 72 were used in the final analysis.

Apparatus

The experiment was performed using a Dell Inspiron lap-top PC, with a 15" LCD visual display. A chinrest was used to control optimal viewing distance (57cms). The cueing program was built in E-prime.

Stimuli

Cue stimuli comprised a pair of bilateral letters, presented on either side of the central fixation cross. The dimensions of each cue letters were 1° (visual degree) high and were extended 3.5° to the left and right from the central point. The cues were 2.5° above fixation for the upper visual field and 2.5° below for the lower visual field. In the Landmark Cueing (LM) condition, two different letters, either 'X' and 'T', or 'V' and 'O' were presented on every trial. In the Identity Cueing (ID), condition, two identical letters (X-T, V-O) were presented on every trial. The target was an asterisk, subtending 0.4^{o} x 0.4^{o}. The target was aligned with the fixation cross in the vertical-axis and was presented 7.3^{o} to the left or right of the screen centre.

Procedure

The experimental blocks were divided into two sessions of repeated measures experimental design. For the LM task, the participant was instructed that the target would appear on the same side as one of the stimuli (X or T) or in the case of the ID condition, that two XX's meant the target would appear on the left (and therefore two TT's meant the target would appear on the right), see figure 2.1

In the LM blocks, participants were informed that the target would usually appear on the same side as one of the letters. The ratio of valid to invalid cues was 4:1. For half the

participants, the letters ‘X’ and ‘T’ were used as LM cues; for the other half, the letters ‘V’ and ‘O’ were also LM cues. Within each of these groups, the letter used to cue target location was counterbalanced between participants. Hence, counter-balancing this aspect of the design required four groups, with equal numbers of participants shifting attention in response to each of the four letters (X, T, V, O).

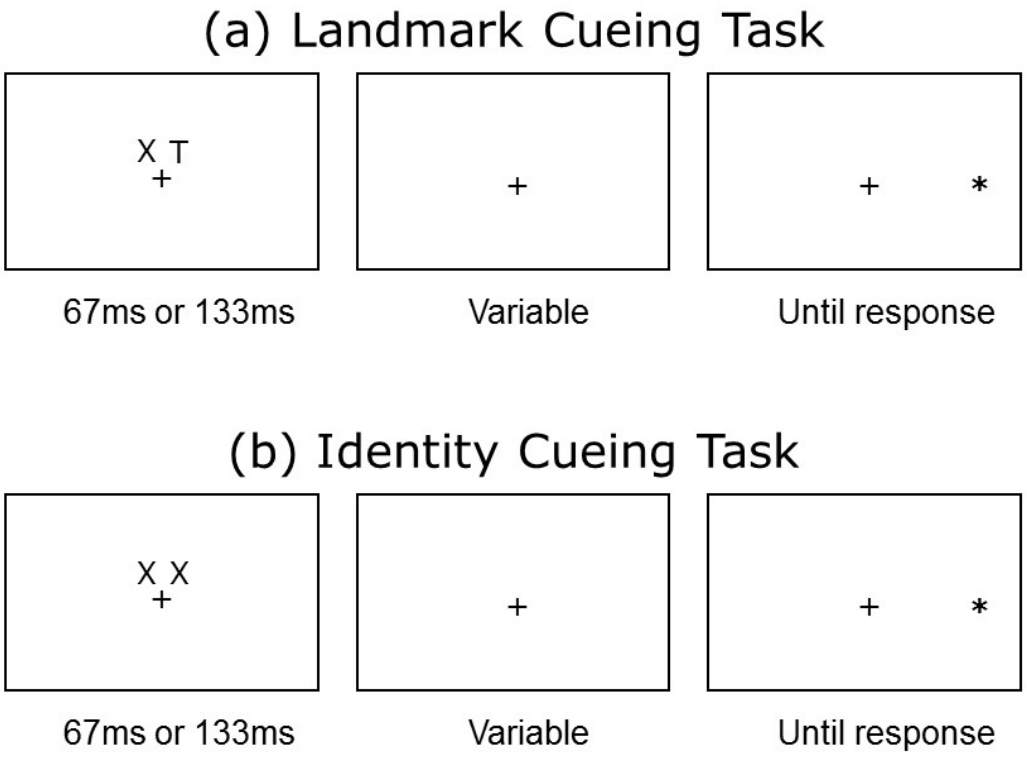


Figure 2.1. Both the LM and ID task. The LM using visuospatial cues and the ID using symbolic-semantic cues.

In the ID blocks, participants were informed that one letter pair signified that the next target would probably be presented on the right of the display, while the other indicated that the next target would probably be on the left. The two letters employed as ID cues were always

different to those used as LM cues. For half the participants, the letter pairs X-X and T-T were used as ID cues, while the letters V-V and O-O were ID cues for the remaining participants. There were four counter-balanced groups, with equal numbers of participants shifting attention left, or right in response to each of the four letters (X, T, V, O). Cue letters were presented for either 67ms or 133ms, with cue exposure time varying randomly from trial to trial. The stimulus onset asynchrony was also varied at either 150ms or 600ms delay before target appeared.

Design

Each participant performed 10 landmark cueing practice trials, followed by two blocks of 96 landmark cueing experimental trials; and 10 identity cueing practice trials, followed by two blocks of 96 identity cueing experimental trials. In each block of trials there was 64 valid trials, 16 invalid and 16 catch trials (no target was presented, to ensure participants were responding to target). The order of participating in the landmark cueing and identity cueing conditions was counter-balanced between participants.

RESULTS

The rate of anticipations (0.4%) and catch-trial errors (0.1%) for the 72 participants in the final dataset were acceptably low.

The graph in Figure 2.2 shows that the largest cueing advantage was indeed for the LM cueing with the shortest exposure time. There was also a clear cueing effect for the LM cues with a long exposure time. As predicted, for the ID cues, the Posner effect appears to be almost

completely wiped out in the brief cue exposure time, but there *does* appear to be a cueing advantage at the longer cue exposure time.

To ascertain significance, the mean response times were entered into a four-way, repeated measures analysis of variance with cueing paradigm (LM vs. ID), cue exposure time (67ms vs. 133ms), trial validity (valid vs. invalid), and SOA (150ms vs. 600ms) as factors (See figure 2.2). The main effect of trial validity, $F(1,71) = 15.27$, $p < .001$, $\eta^2_p = .18$, and the interaction between trial validity and SOA, $F(1,71) = 8.87$, $p = .004$, $\eta^2_p = .11$, were both significant.

This showed that overall, participants responded more rapidly on valid trials, and that the advantage for valid relative to invalid trials was greater in the long SOA condition (Valid RT = 368ms; Invalid RT = 381ms) than in the short SOA condition (Valid RT = 375ms; Invalid RT = 378ms).

Critically, the predicted interaction between cueing paradigm, cue exposure time, and trial validity was reliable statistically, $F(1,71) = 6.41$, $p = .014$, $\eta^2_p = .08$. Illustrated by the graph in figure 2.2.

The prediction that the Posner effect of LM cues have a strong validity effect with brief cue exposure times, while the effects of ID cues would collapse, was tested by analysing data from the brief cue exposure time condition. The predicted interaction between cueing paradigm and trial validity was significant, $F(1,71) = 6.09$, $p = .016$., $\eta^2_p = .08$. Moreover, in the brief exposure time condition, there were clear effects of landmark cues on attention. Briefly exposed LM cues elicited a main effect of trial validity, $F(1,71) = 9.62$, $p = .003$, $\eta^2_p = .12$, and an interaction between trial validity and SOA $F(1,71) = 4.00$, $p = .049$, $\eta^2_p = .05$ (see Figure 2.3(a)). Even with 72 participants, there was no attentional effect on briefly exposed ID cues. In the brief

exposure time condition with identity cues, the main effect of trial validity ($F < 1$, $\eta^2_p = .009$), and the interaction between validity and SOA ($F < 1$, $\eta^2_p = .005$) were both non-significant (see Figure 2.2(b)). Despite having more than 600ms to prepare and execute a shift of attention in response to the information provided by the cue, response times on valid and invalid trials were very similar (see Figure 2.3, part (b)).

In the long exposure time condition, the main effect of trial validity $F(1,71) = 10.88$, $p = .002$, $\eta^2_p = .13$ and the interaction between trial validity and SOA, $F(1,71) = 9.54$, $p = .003$, $\eta^2_p = .12$, were both significant, as in the omnibus analysis. Moreover, in the long exposure time condition, attentional effects of precues did not vary as a function of cueing paradigm: the interaction terms between cueing paradigm and trial validity ($F < 1$, $\eta^2_p = .001$), and between cueing paradigm, trial validity and SOA ($F < 1$, $\eta^2_p = .006$) were non-significant (see Figure 2.3, part c) and (d)).

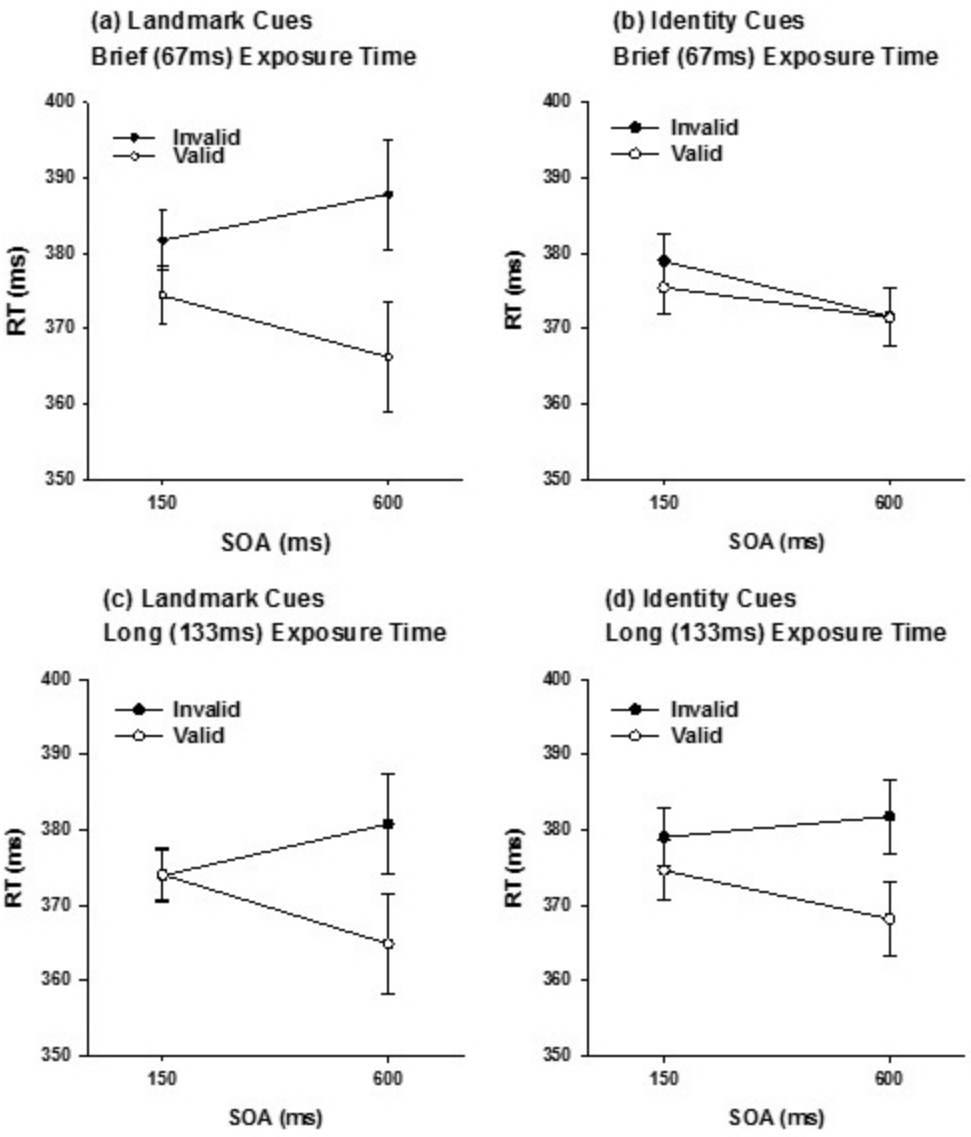


Figure 2.2. The four-way repeated measures ANOVA, showing the collapse of cueing effect for ID cues in brief exposure time, part (b).

DISCUSSION

Reducing cue exposure time nullified the attentional effects of identity cues. As predicted, identity cueing effects collapsed, and appear to have completely disappeared when the exposure time of the cue was reduced to 67ms. Attentional effects of landmark cues in the brief exposure time condition were at least as large those observed in the long exposure time condition.

The effects of landmark cues were robust when exposure time was reduced; consistent with the suggestion that these effects are mediated through visual encoding by M-cell channels, which should respond well to briefly presented stimuli, because of their transient response characteristics.

Secondly, the effects of identity cues collapsed when exposure time was reduced, there was no validity effect. This is consistent with the suggestion that these effects are mediated by P-cell channels, which respond poorly to briefly exposed stimuli

The dorsal stream has high contrast sensitivity, due to the M-cell inputs (Merigan & Maunsell, 1993). Lambert and Shin (2010) found landmark cues showed validity cueing effects with stimuli of both low and high contrast. Lambert & Duddy (2002) found that identity cueing effects were influenced by the visual eccentricity of cues, with stronger effects for centrally presented cues. This is consistent with ventral stream mediation, as the ventral stream has better representation of the foveal area (Merigan & Maunsell, 1993). The same experiment showed landmark cues exhibited a validity effect when they were presented centrally or peripherally. This is pertinent because the dorsal stream has uniform representation across the central and

peripheral vision (Merigan & Maunsell, 1993) i.e. there are connections to the dorsal stream from both central and peripheral vision.

A Unified Model of Vision and Attention

The two modes of orienting, endogenous and exogenous are now described as separate entities (Chica et al. 2013). But, are they separate entities of the same attentional system, or functionally separate attentional systems? Peelen, Heslenfeld and Theeuewes (2004) believe the exogenous and endogenous orienting processes are two encoding systems in constant competition for control of attention. However, Peelen et al. (2004) used as arrows as their cues in the fMRI study which showed the same large-scale networks. Arrows have since been understood to form a more automatic cue, or at the very least high highly overlearned stimuli and should not be used as an endogenous cue (Brignani, Guzzon, Miniussi, 2009). Chica et al. (2013) consider these two processes as two different attentional systems, which independently modulate performance to accommodate an individual's goals, as well as environmental factors, such as a danger approaching. Chica et al (2013) cite several compelling reasons for their theory, discovered from a meta-analysis of more than twenty orienting of attention papers and revealed fifteen dissociations. The following are most pertinent to the current research. Firstly, orienting is faster in the periphery (exogenous), than central vision (endogenous). Second, endogenous attention can be sustained for longer than exogenous attention. Third exogenous cues cannot be voluntarily suppressed. Fourth exogenous cues are more automatic than endogenous cues (which are under voluntary control).

The influential paper by Muller and Rabbitt (1989) also postulated early in the literature that the two types of attentional orienting were two different attentional mechanisms competing for the same limited-capacity attention system.

The ventral stream is the input pathway for symbolically driven, endogenous orienting, while the dorsal stream is the input pathway for rapid, non-conscious orienting in response to visual landmark features. Both proposals are well supported by evidence, and are consistent with contemporary theoretical characterisations, firstly of attention shifting mechanisms, and secondly of the contrasting functions of the ventral and dorsal visual stream. Therefore, we propose that there is a simple relationship between rapid, exogenous orienting in response to landmark cues, and slow, consciously controlled orienting in response to endogenous, symbolic cues, and the distinct functions performed by the dorsal and ventral visual streams.

Foxe and Simpson (2002) showed widespread activity in sensory parietal prefrontal areas in less than 30ms, and that activation spreads dorsally before ventrally. They stated that conscious perception depends on re-entrant pathways. An initial rapid pass through the visual hierarchy provides global framework and gist and may prime target object or locations. Attention is then focused back to early areas to allow a serial check and form representations that become consciously experienced (Foxe & Simpson 2002).

The evidence from this experiment, along with evidence cited in this discussion have formed the basis for the theory of a unified model for vision and attention (Lambert, Wilkie, Greenwood, Ryckman, Scibbera-Lim, Booker & Tahara-Eckl, 2018). That semantic and non-semantic orienting of attention may be driven by the ventral and dorsal streams respectively and possibly map on to the endogenous, exogenous two neural processes of attentional orienting

Chica, et al. (2013). Landmark cueing has much in common with exogenous cueing, they are both rapid, utilize peripheral vision and are non-conscious, but identity cueing has similar properties to endogenous cueing, its time course is slower, and it is consciously controlled (Lambert et al. 2018).

Previously, there has been good electrophysiological evidence for the activation of the dorsal stream in response to a target, after landmark cueing (Lambert & Wootton, 2017; Marrett et al. 2011). The ID cues have not yet been tested to show temporal activation. Would landmark cues elicit dorsal stream activation, and conversely would identity cues elicit ventral stream activation?

CHAPTER 3. EVENT RELATED POTENTIALS OF LANDMARK & IDENTITY

INTRODUCTION

To further support the unified model of vision and attention (Lambert et al. 2018), electrophysiological evidence for the landmark and identity cueing is required. As previously stated in chapter two; would LM cues elicit dorsal stream activation, and conversely would ID cues elicit ventral stream activation? The neural correlates of encoding ID cues have not been invetigated before. We predict that dorsal stream activation would be observed following the presentation of LM cues, and ventral stream activation in a task where participants orient in response to ID cues.

Lambert and Wootton (2017) carried out a very similar task to the landmark cueing, along with a perceptual discrimination task. The stimuli were placed in the upper visual field and the visual event-related potential (ERP) was measured at the parietal-occipital (dorsal) electrode sites, and the temporal-occipital (ventral) electrodes. The ERP responses showed both tasks elicited negative C1s and positive P1s at approximately 80ms and 120ms respectively (after stimulus onset). The C1 component was more strongly negative in response to landmark cues. Source localization showed widespread dorsal activation for the landmark task during the C1 epoch and widespread ventral stream activation became apparent later, during the phase of the P1. In summary, activation in the dorsal visual stream was seen with early shifts of attention. Dorsal stream activation associated with attention shifting had a quicker onset than ventral stream activation associated with conscious discrimination.

C1 Activation

The C1 is the earliest observable component of the visual ERP (Lambert & Wootton, 201). The component typically peaks around 50-100ms and its polarity and scalp distribution depend on where the stimulus is presented (Mangun, Hillyard & Luck, 1993). If the stimuli are presented in the upper visual field, the C1 will have negative polarity, but if stimuli are in the lower visual field, the C1 will show a positive polarity.

It is difficult to look at the C1 component on ERPs without being drawn into the debate of whether the C1 modulates attention. Foxe and Simpson (2002) first showed how initial visual activation was as widespread as prefrontal areas in less than 30ms. Activation is from the occipital cortex at 80ms and continues for 100-400ms before motor output, leaving plenty of time for feedback information. Foxe and Simpson (2002) proposed only the initial C1 (10-15ms C1e) is likely to represent predominantly V1 activity. Therefore, they propose the C1, P1 and N1 are all processing *after* higher level attention processes. The activation of the C1 would have had time for the first feedforward sweep of afferent visual information (30ms), and possible subsequent feedback, and re-entry to visual areas, armed with a biasing influence of top-down information.

On the other hand, discussion around early human visual system suggests the earliest ERP, the C1 component, was *unaffected* by attention (Russo, Martinez & Hillyard, 2003). It was observed that the C1 component (onset latency 50–60 ms) was not modified by spatial attention. Their ERP results suggest that the initial response in area V1 is not modulated by spatial attention and that the earliest attentional influences upon visual processing are in extrastriate areas starting at ~70–80 ms.

Kelly et al. (2008) found C1 *was* modulated by attention when an attended location was diagonally opposed; thus, crossing the vertical and horizontal meridians of the visual field. They concluded early modulation may represent top-down anticipation, time-locked to the cue. However, a replication by Baumgartner, Graulty, Hillyard & Pitts, (2018), found that C1 component could not be modulated by spatial attention. They found C1 activations, but they did not differ from attended to unattended attention. The only difference between the two experiments was stimuli were diagonally opposed for Kelly et al. (2008), and Baumgartner et al's (2018) was horizontally opposed. Many authors disagreed with Baumgarter's results. Ding (2018) and Pourtois (2018) suggest that Baumgartner's use of a shorter distance between stimuli could be a disadvantage, and that's why the replication could not find modulations of the C1. Klien (2018) corroborates this because it's easier to avoid attending diagonal stimuli, than it is horizontal stimuli.

A key issue between Kelly et al (2008) and Baumgarter et al. (2018) replication is whether the V1 waveforms show polarity reversal. The retinotopic organization of V1 is not only a contralateral organization, where the left visual field is mapped onto the right hemisphere, but it is also inverted (Slotnic 2012). Stimuli in the upper visual field are mapped onto the lower bank of the calcarine sulcus and stimuli in the lower visual field, below the horizontal meridian, are mapped into the upper bank of the calcarine sulcus. Slotnick (2012) states that V1 is organized such that upper and lower visual field stimuli are processed by cortex oriented in opposite direction, so the corresponding ERP C1 components reverse in polarity. Other authors reject the view that polarity is confined to V1. Ding (2018) suggests that the V1 is not uniquely identified by polarity reversals to the upper and lower visual field. Another experiment using 3-D

modelling of conductivity of brain, skull and scalp showed V2 and V3 also had polarity reversals (Ales, Nates and Norcia, 2010).

One reason for the polarity issue, is the C1 is notoriously difficult to find because of known variability between participants C1 activation (Baumgartner et al 2018, Kelly et al 2008; Pourtois 2018, Klien 2018, Foxe and Simpson 2002). Scalp topography is extremely variable. Uniform measures of C1 may be underpowered and small amplitude modulations may be missed. Multivariate analysis of spatial sampling of more than 100 electrodes is suggested for concluding topographies of underlying brain sources (Foxe & Simpson, 2002; Alilović, Timmermans, Reteig,, van Gaal & Slagter, 2019) Using 128-channel electrode caps are more reliable that smaller channel caps, and caution must be taken when comparing electrode name and numbers across experimenters. As well as using 100+ electrode scalp caps, C1 activations have been observed under the following conditions: stimuli should be peripheral; in the upper visual field and be of unequal luminance to the background (Slotnick, 2018, Ding 2018).

The aim of the current experiment is to find out primarily whether the LM cueing will elicit a stronger wave form than ID cues, in the parietal-occipital electrodes (dorsal stream recruitment of the LM cueing). Vice-versa, will the ID cues elicit a stronger waveform in the temporo-parietal electrodes (ventral stream activation)? Will ID cues elicit a stronger activation in the later ERPs than for LM cues, due to the slower response of the P-cells in ventral stream. Conversely would landmark cues elicit stronger activation in earlier ERP epochs, because of the fast receptors of the M-cells? The hypotheses predict that LM cued activation should be faster than ID cued activation.

Regarding the current C1 debate, will cues presented in the upper visual field (UVF) show a negative going C1, and cues in the lower visual field (LVF) show a positive going C1? The prediction is that UVF stimuli will show a negative going C1, and the LVF a positive going C1 waveform, due to the polarity reversal of early visual areas.

METHOD

Participants

Sixteen participants were recruited in total; eleven individuals were included in the final analysis. Data from three participants were removed due to excessive artifacts in head and eye movements or possible interference with building work being carried out. Two participants showed no visible C1 waveforms, defined as a positive going waveform for LVF or negative for UVF in the 50-90ms epoch and were also removed from analysis. All participants spoke English fluently, had normal or corrected to normal visual acuity, with no history of neurological disorders. Participants underwent one EEG session, lasting approximately one hour and were remunerated with a $10 shopping voucher. All procedures were approved by the University of Auckland ethics board (ref 7835).

Apparatus

Scalp EEG was recorded using a 128-channel electrode cap (Electrical Geodesic Inc, EGI, Phillips). Matlab was used to complete the final analysis. Signals were resampled to 250Hz and filtered using ERPlab, with a recording bandpass of 0.1-40Hz. During recording, electrode Cz was used as the reference. Eye movements and blinks were monitored using left and right horizontal electrooculogram (HEOG) channels. To ensure participants'

maintained fixation, a custom written script was used to remove any horizontal eye movement artifacts. If the HEOG deviated by more than 70μV they were discarded before analysis. A visual inspection was carried out after this process, to reject any other artefacts that deviated wildly.

Stimuli

All stimuli were presented in E-prime, on a Dell PC. A grey background (RGB: 187, 187, 187) was used, with stimuli contrasting in white (RGB: 255, 255, 255), on a 1920 x 1200 pixel LCD screen.

Each cue letter was 1° (visual degree) high and was presented 3.5° to the left and right from the central point. The cues were 2.5° above fixation for the upper visual field and 2.5° below for the lower visual field. They were flashed simultaneously in either the upper or lower visual field for 100ms. There was a stimulus onset asynchrony of 300ms before the target, appeared in either the valid or invalid location. The target, an asterisk was 0.5° high and presented further out in the periphery at 7.5° on either the left or right, but in line with fixation. The target remained on screen for 2000ms or until response. On 75% of trials the target was in the valid location.

The participants completed 384 trials per condition, including the ID and LM trials which were counterbalanced to reduce practice effects. There were 288 valid trials, 48 invalid trials and 48 catch trials. Timing of the stimulus onset relative to the trigger codes was measured during piloting. A consistent delay of 21ms was detected and was corrected by shifting the timing by -21ms in the EEG analysis.

Procedure

The experimental blocks were divided into two sessions of repeated measures experimental design. For the landmark task, the participant was instructed that the target would appear on the same side as one of the stimuli (X or T) or in the case of the identity condition, that two XX's meant the target would appear on the left (and therefore two T-T's meant the target would appear on the right), see figure 3.1. The ratio of valid cues was 75% to 25% invalid. There 384 trials per person, 288 or which were valid.

The cues, X and T or V and O, were chosen for their symmetry. For the LM condition both pairs of cues (X-T and V-O) were shown to each participant and were counterbalanced across participants. For the ID condition the cue stimuli were the same letters to ensure consistency of size, contrast and luminosity (eg X-X, T-T or V-V and O-O). Participants sat at a distance of 57cm from the computer monitor, resting their chin on a headrest and responded by pressing spacebar, as soon as they saw the target. Participants maintained fixation on a central cross in the centre of the visual display monitor, using a chin rest. A brief blink (100ms) of the central fixation cross signaled the moment to covertly attend to either the left or right side of the screen in anticipation of the target appearing. The cue onset time was set at 100ms, and the SOA at 300ms. These times were chosen specifically to be a midpoint between the times of cue onset and SOA of the cue exposure time experiment. Participants were asked to respond as fast and as accurately as possible when they saw the target.

All events were randomized within blocks, so the order of a trial being valid or invalid, upper or lower hemifield or left or right quadrant cueing could not be predicted.
If the participant pressed the space bar too early, a warning message flashed up, to make sure

participants were not anticipating the cue and pressing the spacebar ahead of the target appearing.

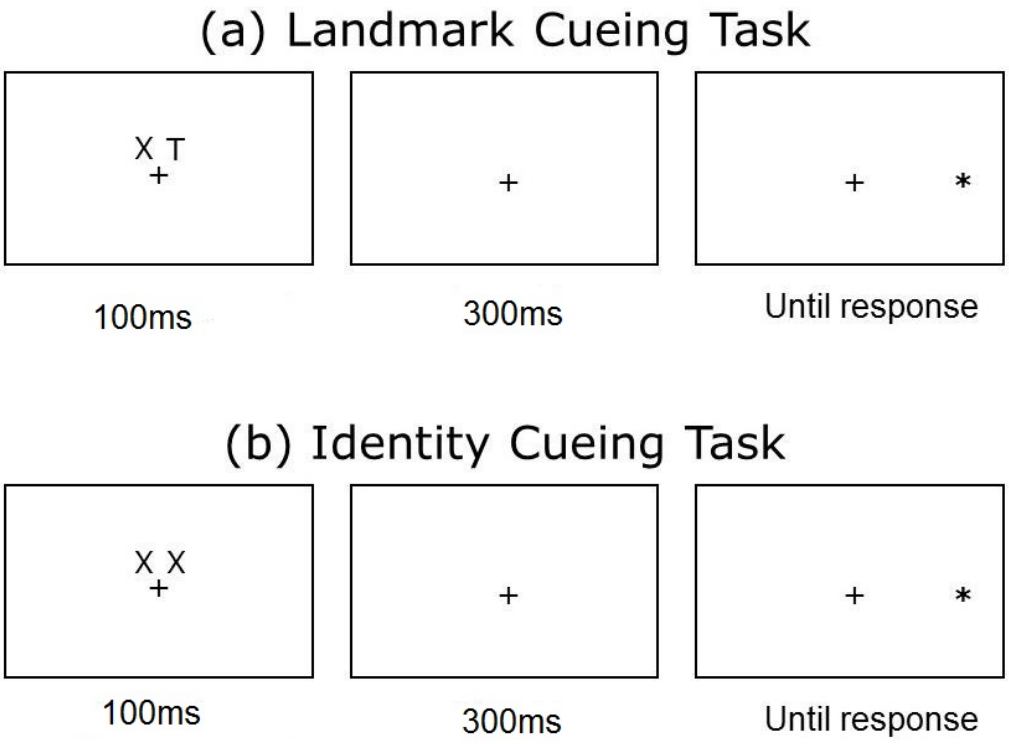


Figure 3.1: Stimulus example. A) Landmark valid trial using T as cue to predict target will appear on the same side as 'T'. B) Identity valid trial 2x X's predict target will appear on the right

RESULTS

Behavioural Results

The behavioural data for this experiment was analysed with a four-way repeated measures ANOVA, with factors of cue type (landmark-identity); visual field (upper-lower); visual field (left-right); and validity. The results show that validity effects varied reliably as a function of cue type and upper-lower visual field. We found the three way interaction between

cue type, upper-lower visual field and validity was significant, F(1,15) = 6.40, p = .023. This was the only statistically reliable effect in the analysis.

We examined this interaction in more detail by testing for validity effects in the upper and lower visual fields, for each cue type. These results showed that when participants oriented in response to landmark cues, validity effects were reliable when the cues were presented to the upper visual field, t(15) = 1.99, p = .033 (one-tailed), but not when they were presented to the lower visual field, t(15) = 1.33, n.s (see figure 3.2). However, when participants oriented in response to identity cues, validity effects were reliable when cues were presented to the lower visual field, t(15) = 2.26, p = .02, but not when they were presented to the upper visual field, t<1, n.s.

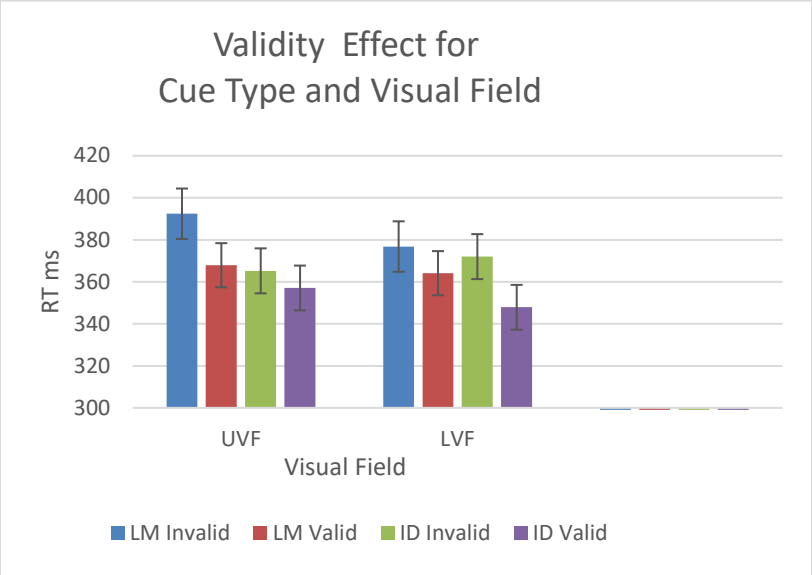


Figure 3.2. LM cues showed a significant validity effect in the UVF but not LVF
ID cues showed a validity effect in the LVF but not the UVF

C1 Waveforms for Dorsal Electrodes

The waveforms averaged across both identity and landmark tasks for the UVF and LVF are shown in figure 3.3. The ERPs measured are an average of parietal-occipital electrodes (61,

62 Pz, 67, 72 POz, 77, 78). Both the UVF and the LVF showed reverse polarity, as expected for V1 or early visual area activation. They diverge in polarity at an early stage, around 70ms after stimulus onset, this corresponds well with the timing of the C1 (pre 100ms). The stimuli presented in UVF has a negative going C1, and the LVF stimuli produced a positive going C1. The UVF appears to have a stronger P1 than the LVF. The early positive peak for the LVF possibly represents a P1, preceded by a positive going C1.

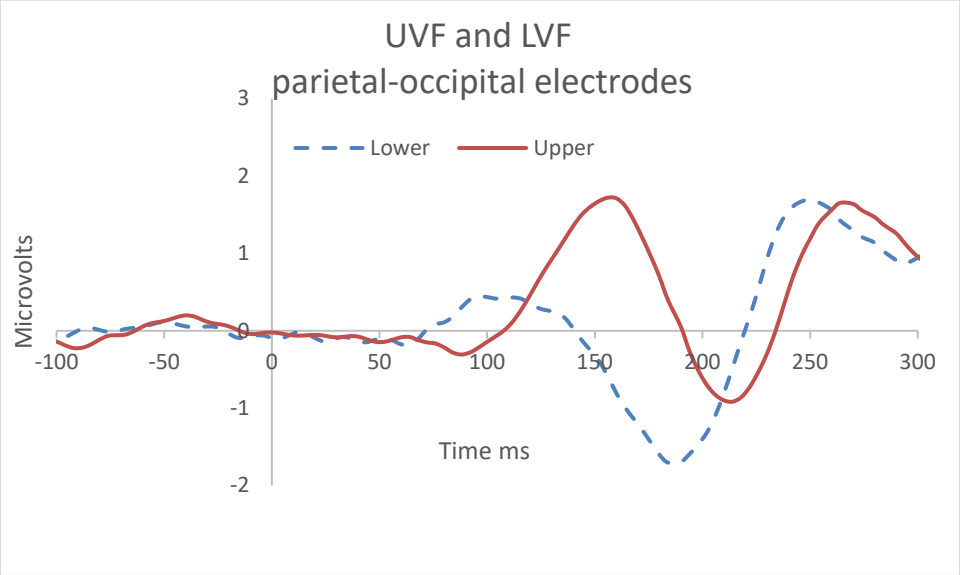


Figure 3.3. The waveforms averaged across tasks for LVF and UVF, showing a significant C1 waveform in the UVF ($p < .001$), and a clear polarity reversal from the C1 epoch, to the P1 epoch at 120ms

Analysis of the waveforms was modeled on the work carried out by Foxe and Simpson (2002) and Kelly et al. (2008). The Matlab output region of interest was selected at -121ms to 300ms (including the 21ms delay from the e-prime measure of time to the recorded measure), and was measured at every 4ms, giving 106 time points. The baseline epoch was measured from -60ms to 20ms, averaged and the standard deviation (SD) of the baseline epoch was calculated.

The baseline SD for the LVF was 0.184μV, and the UVF 0.226μV. ERPs that were sustained at 2.5 times larger than the baseline standard deviation, were considered as acceptably high and distinct from the baseline (Foxe & Simpson, 2002). For the LVF this mean voltage was reliably different at 80ms, and for UVF 84ms. The exact point of divergence was 68ms.

A running *t*-test (one-tailed, one sample) measured whether the mean of the C1 epoch for each visual field waveform was statistically different from zero. 12 time points were selected for the analysis of the C1 epoch, from 50ms to 90ms.

The *t*-test failed to reveal a statistically reliable difference of the LVF mean ERPs from zero (M = .025, SD = .192), t (10) = .453, $p > .05$. The one-tailed critical t value for 12 degrees freedom at 95% confidence is 2.179.

The *t*-test did reveal a statistically reliable difference of the UVF mean ERPs from zero (M = -.174, SD = .079), t (11) = -7.667, p = .000. Please note the different t values reflect the different number of time-points due to the length of ERP wave.

To give the best possible C1 waveform, a difference wave was created by taking the LVF away from the UVF. This removes overlapping components and gives a cleaner baseline. It accentuates activity from low level visual areas (V1-V3) and cancels out activity that does not differ from the upper and lower visual field (Slotnick, 2018), see Figure 3.4. The same running *t*-test as the first comparison checked for a reliable difference of ERP from zero, in the same C1 epoch, 50-90ms.

The *t*-test did reveal a statistically reliable difference of the difference wave mean ERPs from zero (M = -.199, SD = .268), t (11) = -2.574, $p < .05$, however this was not as large as the t value for the UVF alone.

The null result of the LVF and the weakened *t* value of the difference wave from the UVF suggest that there is no reliable C1 waveform for the LVF alone, however there are merits to including the LVF data to accentuate the small amplitudes of the C1 by cancelling out noise as guided by the very useful information from Slotnick (2018).

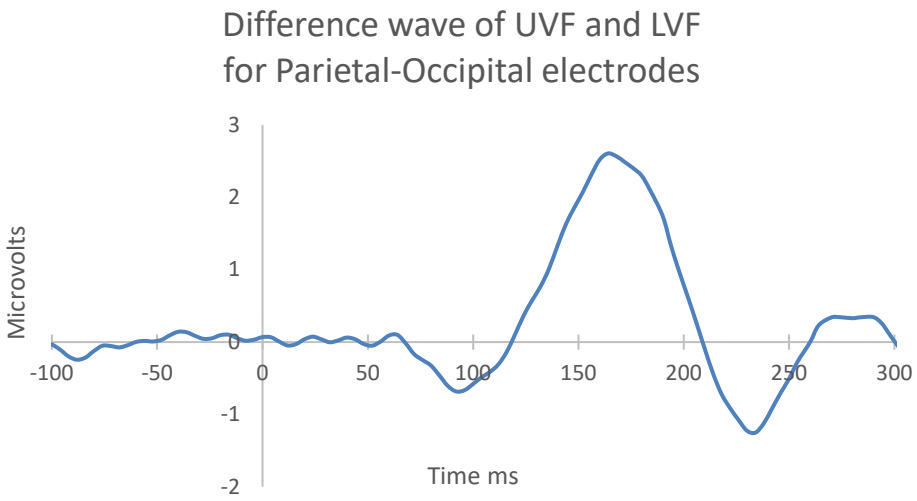


Figure 3.4. The difference wave was used to accentuate the C1 waveform, which showed a reliable ERP in the C1 epoch (50-90ms), $p < .05$

The difference wave showed a more prominent C1, which began sloping at 68ms and peaking at 92ms, measuring -0.68µV. The final peak is within the expected timing for the C1 (pre-100ms). The P1 peak is at 172ms (peaking at 2.489µV)

Identity Vs Landmark Waveforms at Parietal-Occipital Electrodes

The other hypothesis tested was that landmark cues would elicit a stronger waveform from the dorsal-parietal electrodes, than the identity cues. The data was collapsed across LVF and UVF and measured individually for the two cueing tasks.

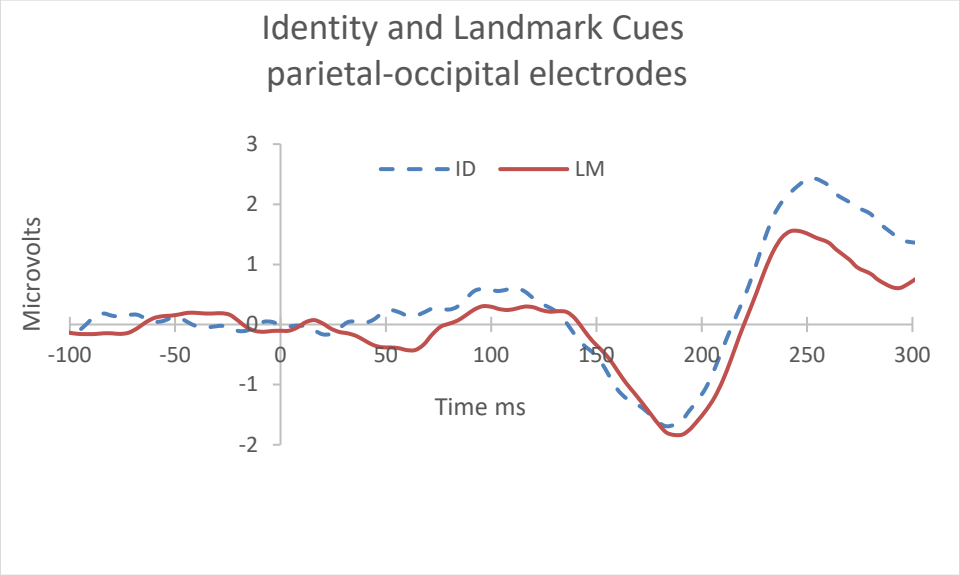


Figure 3.5. Both waveforms began to exceed baseline at 32ms, and was sustained during C1 epoch (50-90ms), the landmark waveform had a more negative voltage ($p < .001$) than the identity waveform during this period

The divergence of the two individual tests' waveforms began earlier than the lower and upper visual field waveforms, see figure 3.5. The identity cues showed a positive going waveform, which appeared to be weaker than the negative going landmark cueing task. Following the C1 epoch both waveforms for identity and landmark followed a very similar trajectory in time course and voltage for the P1 and N1, as reported in Lambert and Wootton (2017).

To test the hypothesis the standard deviations of the mean for the C1 epoch 50-90ms was calculated, and a one-tailed paired sample *t*-test was run. A one-tailed test was chosen because the prediction was directional; the landmark ERPs would be stronger than the identity cues.

The identity cues had a mean baseline calculation of -.0161 µV. Using Foxe and Simpson's (2002) estimation that an ERP should be 2.5 times the baseline microvolt, the identity voltage would need to exceed -.040µ. The landmark baseline was 0.120µV and the recommended 2.5 times SD was .144µV. Both the landmark and identity ERPs exceeded their values during the C1epoch 50-90ms. Interestingly both cue types began to exceed their respective values at 32ms.

Using the twelve time points taken from the ERPs for the C1 epoch (48-92ms), the *t*-test showed a statistically reliable difference in the strength of mean ERPs at the C1 for landmark cues (M = -.172, SD = .025) from the identity cues (M = 0.27, SD = .012), t (11) = 9.785, $p < .000$, at the parietal-occipital electrodes.

The early P1 peak was at 96ms for both ID and LM, the peak P1 was 116ms for ID and 120ms for LM. The twelve time points for the P1 epoch were 92-136ms and the *t*-test showed a significant difference in the strength of mean ERPs at the P1 for landmark cues (M = .256, SD = .341) from the identity cues (M = .440, SD = .193), t (11) = 3.764, p = .003, at the parietal-occipital electrodes.

Identity Vs Landmark Waveforms at Temporal-Occipital Electrodes

Waveforms for both the identity and the landmark cueing tasks were also analysed at the temporal-occipital electrodes (45 T3, 108 T4, 58 T5, 96 T6, 70 O1, and 83 O2).The mean baseline (-60-20ms) voltage for the identity condition was 0.472 (SD .039) µV and the landmark

baseline mean was 0.154 (SD.039) µV. Therefore, identity waveforms needed to exceed 1.188 µV and landmark waveforms needed to exceed 0.039 µV. This occurred at 60ms through to 72ms for the ID waveform (see figure 3.6). The LM waveform did not exceed the threshold amplitude during the C1 epoch. A paired-sample *t*-test comparing the means of the twelve time points for the C1 epoch (48-92ms) for the identity cues (M = .094, SD = .0262) and landmark (M = .005, SD = .0261) waveforms were significantly different from each other $t(11) = 6.566$, $p < 0.001$.

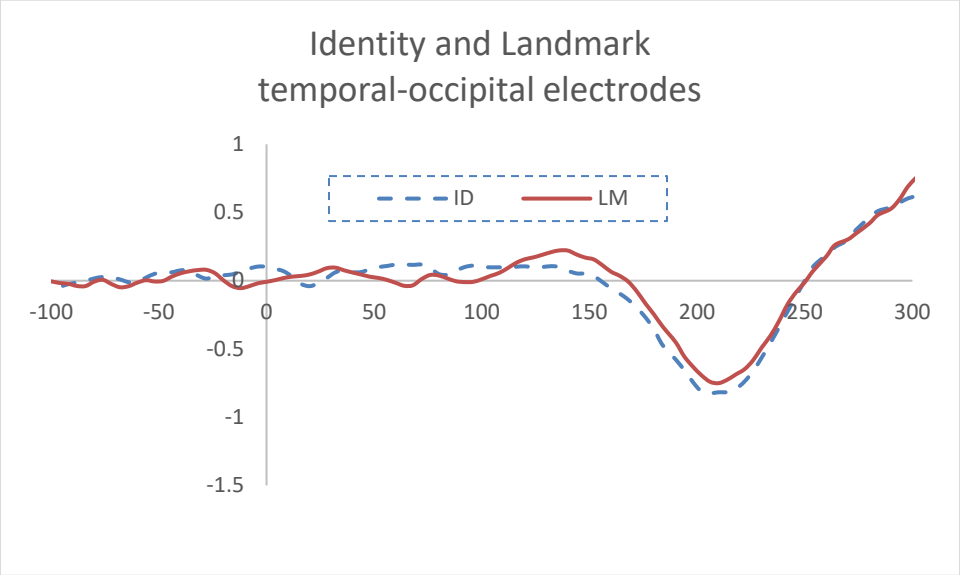


Figure 3.6. The ID waveform showed a C1 amplitude above threshold at 60-72ms, the LM waveform did not reach above the baseline threshold at any point during the epoch. There is a polarity reversal at 48ms, again at 112ms.

During the P1 epoch of 90 -130ms the identity waveform did not exceed baseline amplitude. The landmark waveform reached an acceptably high voltage at 108ms through to 112ms. The two waveforms showed means during the twelve time points of the P1 epoch (92-

136ms) were not significantly different, confirmed by a *t* test of identity cues ERPs (M = .101, SD .004) and landmark (M = .105, SD = .086), *t* (11) -.129, p = .900.

Source Localisation

The source localisation analysis, sLORETA, was used to inspect where activity is happening during the C1, P1e and P1 epochs for the LM and ID task. Activity has been shown in the dorsal stream regions for spatial correspondence LM cueing (Marrett et al. 2011, Lambert & Wootton, 2017), this is the first EEG experiment using the symbolic-semantic coding of the ID cues, but activation is expected in the ventral stream for early epochs.

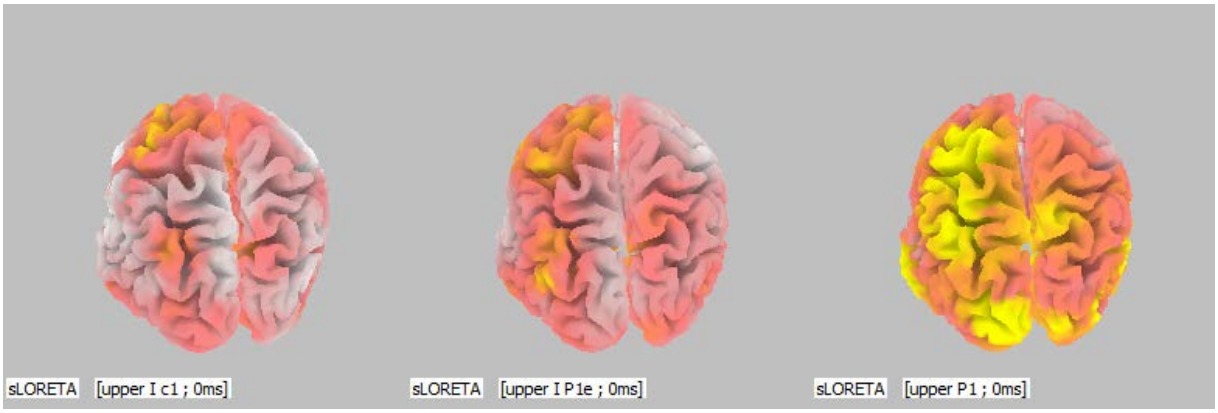


Figure 3.7. sLORETA analysis of activation of Identity cues at C1, P1e and P1 epoch. Threshold analysis was not significant. Activation at middle frontal gyrus during C1, P1e and P1, with some temporal and occipital activation during the latter epoch

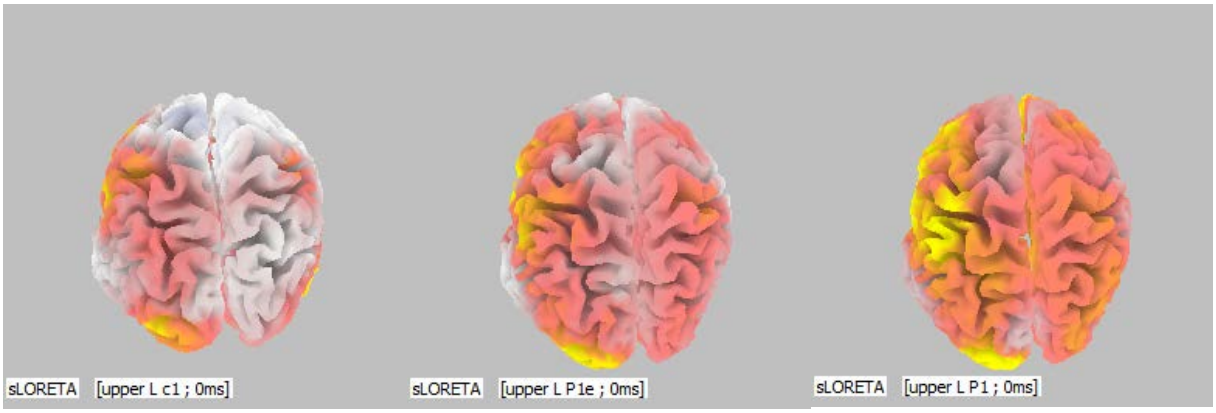


Figure 3.8. sLORETA analysis of activation of Landmark cues at C1, P1e and P1 epoch. Threshold analysis was not significant. Activation is mainly pre-central gyrus with some activity becoming noticeable in temporal areas at P1

sLORETA threshold analysis compared activity in 20ms epochs of 70-90ms for C1, 90-110ms for P1e and 130-150ms for P1, to a baseline epoch of -20-0ms. Figure 3.7 shows a 3D pictorial representation of the output. The LM C1 and P1 epoch showed 1 voxel at significance in the frontal lobe, the precentral gyrus. The LM P1e had 36 significant voxels ($p < .05$), 24 at precentral gyrus. LM P1 had 51 voxels, with the majority split between the middle temporal gyrus, middle frontal gyrus and precentral gyrus.

	Landmark N supra-threshold voxels ($p < .05$) Total voxels = 88	Identity N supra-threshold voxels ($p < .05$) Total voxels = 57
C1 (70-90ms)	1 Precentral Gyrus	0
P1e (90-110ms)	24 Precentral Gyrus	0
P1 (110-130ms)	11 Middle Temporal Gyrus 12 Precentral Gyrus 5 Occipital Cuneus	9 Post Central Gyrus 10 Occipital Cuneus 8 Middle Temporal Gyrus

Table 3.1. Supra-threshold voxels and location during 20ms epochs compared to baseline -20-0ms

The ID C1 and P1e had no significant voxels, the P1 epoch showed 57, with 8, 9 and 10 voxels attributed to the middle temporal gyrus, post central gyrus and occipital cuneus respectively (table 3.1). The lack of activation in the dorsal stream area is most puzzling as the LM cue has shown robust activation in the superior parietal lobule during the same epochs (Marrett et al. 2011, Lambert & Wootton, 2017). Although this is the first EEG from the Lambert lab using the specific ID cues, activation was expected to be ventral, temporal areas.

DISCUSSION

This study provides further evidence of dipole differentiation of V1. Information from the UVF reaching V1 is below the calcarine sulcus and producing a negative waveform. Conversely LVF information is projected above the calcarine sulcus and produces a positive going wave. The C1 waveform was weaker in the LVF. However, other authors have also found the LVF to be weaker than the UVF. Slotnick (2018) has championed the use of a difference wave to eliminate noise not attributable to the UVF and LVF. The use of a difference wave made a smoother line that was easier to define the C1 from the P1e. Many papers have used the attended versus unattended stimuli to distinguish C1 components (Foxe, Kelly at al. 2008, Baumgartner et al. 2018), but using cues designed to maximize potentials of the dorsal and ventral visual stream have given clear cut C1 modulations (Lambert and Wootton, 2017, Lambert et al. 2018). This concurs with Foxe and Simpson's (2002) influential data of very early activation hitting the frontal areas within 30ms. Other have suggested the re-entrant process begins at ~100ms, along with the subjective experience of seeing (Koivisto, Revonsuo, & Lehtonen, 2006).

At the parietal-occipital electrodes, the C1 was stronger for the landmark cueing task. The divergence of polarity for the two visual evoked potentials for the landmark and identity waveforms began at 32ms. Around the time Foxe and Simpson (2002) proposed the feed forward re-entrance sweep may have returned to the occipital area. At the temporal-occipital electrodes, the ID waveform showed a C1 amplitude, the LM waveform did not. This is a nice dissociation of possible ventral and dorsal cueing activation. This temporal activation is line with the behavioural data. The LM cues showed reliable attention-shifting in the UVF (see figure 3.2) and figure 3.5 showed a strong negative C1 waveform at the parietal-occipital electrodes (dorsal area). With the reverse in polarity, it may be the UVF cues that drove the negative C1 waveform.

The absolute opposite results were shown for the ID cues, which showed reliable attention-shifting in the LVF (figure 3.2), and a more positive C1 waveform in the temporo-occipital electrodes (ventral area).

Silson, Reynolds, Kravitz and Baker (2018) reported the upper visual field is processed ventrally, and the lower visual field is processed dorsally. The landmark cued waveform in this experiment showed a negative going wave and the identity cueing a positive waveform in the C1 epoch. If the dorsal stream has inputs from the lower visual field, then the opposite dipole of the early visual cortex should have rendered the dorsally represented wave positively. Vice versa for the identity, where the ventral representation is in the upper field. The suggestion of Silson et al. (2018) is also troubling for the behavioural data reported earlier in this chapter. The ventral/dorsal representation in Silson et al. (2018) work is a quote from Wandell, Dumoulin & Brewer's (2007) paper, which showed a dorsal and ventral white matter connection with the V3 visual map. As Wandell et al. (2007, p367) notes "spatial representation of an image is preserved and repeated multiple times within the cortex"; they document at least five separate maps by V5/MT. If the very early V1 map is where the C1 is located, then our dipole activation is likely to be opposite of that in V3.

Both P1 and N1 visual evoked potentials were very similar, so extra-striate activation and control of attention at this point were indistinguishable from landmark and identity cueing. The latency of the P1 is slightly later than expected, but in line with the data from Lambert and Wootton (2017). The Lambert and Wootton data found a stronger C1 for landmark compared to the perceptual discrimination task. The theory predicts that landmark cueing will elicit stronger parietal-occipital activation than identity cues. The evidence from the current study shows a double dissociation a) landmark cues showing a stronger C1 activation in the parietal-occipital

electrodes and b) the identity cues showing stronger C1 activation at the temporo-parietal electrodes.

The source localization was unclear. Both Marret et al. (2011) and Lambert and Wootton (2107) have shown clear dorsal activation in the early epoch and ventral in the later epoch. The current study was underpowered with only 11 participants. What we could see, was the activation of the post central gyrus for identity cues. Chen, Wang, Yu & Liu (2017) showed the pre-central gyrus was activated in the aware part of an aware versus unaware attentional task, during a 150-200ms epoch. This area has been implicated in low cognitive demand of attention and implicated as a mediator for dorsal and ventral streams (Falkenberg, Specht &Westerhausen, 2011; Chen et al. 2017). Mainly frontal areas are activated for the landmark cues, particularly the middle frontal gyrus which shows a similar story, a place where the dorsal and ventral stream converge (Jappe, Holiday, Satyshur, Mukai & Ungerleider, 2015). Snider and Chatterjee (2006) showed that damage to the dorsolateral prefrontal cortex resulted in sluggish exogenous attention. The main areas of activation for this sLoreta data are frontal attentional areas and cannot be used to discern any dorsal or ventral stream activation conclusively.

Overall the discovery of a C1 at the ventral areas for the ID waveform, but not the LM and a stronger C1 for LM, compared to ID at the dorsal area is a lovely dissociation in support of identity cues being encoded by the ventral stream, landmark being encoded by the dorsal stream and both of these attentional effects being influenced at the point of C1 activation. We propose, therefore that C1 is modulated by attentional effects and this is subsequent to a feedforward sweep and re-entrance of information biased by top down attentional influences.

The final piece of the puzzle for this investigation and in support of the unified model of vision and attention is to assess some clinical data for a patient with a lesion in the dorsal stream.

Prior evidence for the unified model of vision and attention came from clinical evidence of patient DF, with bilateral ventral stream damage. She can shift attention normally in response to LM cues, despite being unaware of them (Marrett et al., 2011). This is consistent with dorsal stream encoding of LM cues, because DF has sustained bilateral damage to area LO, disrupting ventral stream input. Interestingly, DF's ability to consciously distinguish between letters was extremely poor but was able to orient in the LM task. What the current research seeks to find out, is could orienting of attention be dissociated in the dorsal stream from the ventral stream, in the same way as vision? What would happen if we tested this theory on a patient with a lesion in the dorsal stream?

CHAPTER 4. CLINICAL EXPERIMENT

INTRODUCTION

The final experimental chapter of this thesis was designed to test the unified model of vision and attention in a clinical setting. Marrett et al (2011) showed how a patient with a bilateral ventral stream lesion was able to orient towards valid letter cues, despite being unable to consciously perceive them. To ascertain strong support for the unified model requires observing a double dissociation. The work of Marrett et al. (2011) showed a single dissociation. To observe a possible double dissociation, we needed to study the attentional behaviour of a patient with a lesion in the dorsal stream, exhibiting signs of optic ataxia (this is the opposing deficit to DF's visual form agnosia). We would expect an ability to discern shapes and consciously perceive them but be unable to use landmark information for visual orienting.

This chapter will describe patient FM and her results. The case study of FM will be detailed, and it will then give a description of deficits from the clinical literature, of patients who have lesions in the dorsal stream. The results of FM's attention test and the other clinical investigation into her deficits are noted. How FM's results influence the unified model of vision and attention will be discussed.

The famous case of patient DF (Goodale & Milner, 1992) led to the dissociation of conscious perception and control of action. DF could not consciously ascertain whether a slot was horizontal or vertical due to agnosia from the bilateral lesions in her ventral visual stream. However, when instructed to insert a card into a slot, DF produced the correct action without hesitation. This case led Milner and Goodale (1992) to propose that information accessible to action systems can be dissociated from information accessible to knowledge and consciousness.

We now know the two pathways communicate extensively (Milner & Goodale, 2008; Milner 2012). The parietal lobe plays a critical role in the guiding of action, including saccadic eye movements, and spatial information (Milner & Goodale, 2008, Op de Beeck, Torfs, & Johan Wagemans, 2008; Cavina-Pretesi, Connolly & Milner, 2013; Meyberg, Sommer & Dimigen, 2017).

The opposite dissociation to DF's problem can be found in the clinical literature. Patients with optic ataxia can recognise objects but cannot use visual information to guide their actions. These patients have the inverse problem of DF. In accord with what we expect from the dorsal-ventral dichotomy, optic ataxia is associated with lesions in the parietal cortex, the termination of the dorsal 'where' pathway.

Patient DF completed the Lambert lab's cueing paradigm and showed a traditional Posner effect, with a benefit for locating a target when it was cued correctly. This was despite being unable to discriminate the letters used as cues (Marrett et al. 2011). The aim of the current work was to provide a further test for the unified model of vision and attention, with the cooperation of a patient with a lesion in the dorsal stream, who showed optic ataxia. We predicted that this dorsal stream lesioned patient would be able to name the letter cues without problem, but may be impaired at utilising the cues unconsciously, indexed by a slower visual-spatial priming or non-existent effect. Specifically, the question arising from the clinical literature was, could a patient with a lesion in the dorsal stream encode dorsal-biased landmark cues? If not, evidence from the two opposing clinical cases would provide a double dissociation in support of the well-known visual dorsal-ventral distinction *and* the unified model of vision and attention. The secondary question pertinent to this chapter is, can the research of the unified model of vision and attention be applied to the rehabilitation of persons with deficits of the visual system?

To answer these questions, we canvassed a pool of participants with brain injury from the Centre for Brain Research, Auckland. FM responded, who has a lesion in the parietal-occipital junction following surgery for a brain tumour. This patient underwent a series of neuropsychological tests to determine if she was a suitable candidate in terms of ability to complete the cueing paradigm and if she showed signs of optic ataxia. These results were compared with those of DF and other control participants. From these tests a visual rehabilitation technique emerged.

The content of this chapter will begin with describing the test Lambert lab carried out on DF (Marrett et al. 2011). It will then introduce the information regarding brain tumours and issues for patients with a lesion in parietal and occipital areas and specifically a visual field cut, which FM has. There will be an in-depth case report and then each neuropsychological assessment will be described, followed by the results for that test.

Patient DF

Patient DF was tested initially by Milner and Goodale back in 1992, when DF was around 36 years old. DF was 56 at the time of our lab's testing (Marret et al. 2011), so not much older than FM, who was 49 during the initial testing phase. DF performed an attention test virtually identical to the landmark EEG test reported in this thesis. The X and T cues presented to DF were onscreen for 150ms, followed immediately by the target. Our current research cues were presented for 67ms or 133ms with a mid-range SOA of 300ms. DF showed a significant cueing effect that did not differ from controls (despite being unable to consciously perceive the cues). The second experiment DF completed was a perception test, the same cues were presented, but after a 700ms SOA, was required to indicate whether a designated letter was on the left or right of the display. This experiment was very difficult for DF and her performance

was very poor. These results may have been mediated by the dorsal stream, consistent with the mediation of spatial priming in the attention task by the dorsal visual stream; and mediation of the perception task by the ventral stream.

Case Report

A right-handed female, born in 1968 (FM), worked as a chartered accountant. In 2005 she reported headaches, fatigue and an inability to remember where she had parked her car. The symptoms slowly worsened, with flashing lights in the visual field and fragmented vision, “as though looking through jagged glass” through the lower left quadrant. FM reported intense feelings of déjà vu and “a sick feeling rising up” through her body occasionally when entering her place of work. Accounting became very difficult as FM kept “losing the ends of numbers”. One million was seen as one thousand (1,000,000 to 1,000). Eventually she crashed her car. Diagnosis from the GP was stress.

In 2010, FM became pregnant, and in September her son was born. In October FM collapsed. During hospitalisation, FM was diagnosed with an anaplastic oligodendroglioma or astrocytoma, WHO grade II. An oligodendroglioma is a tumour of the glial cells accounting for 2-5% of all brain tumours (Ahmet, Serkan, Selin, Alaattin, Ozgur, Ali, Ayse, Hakan, & Gulten, 2012). It is a rare because of the type of IDH mutation (metabolic enzymes) in solid and blood cancers, and virtually never found in patients over 55 years old (Freilich, 2020). Glia or neuroglia are non-neuronal cells found in the brain and spinal cord, oligodendrocytes and astrocytes are types of glial cells (Gazzaniga et al. 2014). FM’s tumour involved the posterior and medial aspect of the right cerebral hemisphere, and took up nearly all the space in the posterior right quadrant of the brain, pushing the posterior lateral ventricle almost through to the

left side (see patient's copy of original scans, appendix A and B). Surgery was scheduled for late November 2010. Most of the tumour was removed, but not all, due to the close proximity of the optic radiations. Chemotherapy and radiation were prescribed to ensure all cancerous cells were ablated.

Immediately post-surgery, and for the following month, FM presented with neglect, frank hallucinations and severe loss of direction. She was unable to traverse hospital corridors alone, as she could not find her way back. Patterns on the hospital curtains first appeared to her as black and white, when looking again "colour appeared". At that time FM was unable to complete the blanket stitch exercise, a simple stitch used as neurological test that requires fine motor control, and orientation. She was prescribed respiradone (for hallucinations) and dexamethasone to treat the swelling associated with a brain tumour.

MRI analysis at 8 years post-surgery shows a distorted brain shape, with extensive white matter damage throughout right-sided posterior, medial and inferior parietal and occipital areas, extending into the posterior temporal area. High flair, the very bright areas in figure 4.1 reveals gliosis (inflammation of glial cells), most likely from chemotherapy and radiation. There is a lesion of 23 mm and loss of grey matter in the parietal-occipital junction (POJ) where the resection took place (see figure 4.1, part C, D). There is dense white matter atrophy around the lesion area (POJ), extending into the posterior part of the inferior horn (or temporal horn) of the lateral ventricle (see figure 4.1, part A). The T2 scans show very dark spots of an oedema filled cavity (see figure 4.1, part A, B and C). The enlarged right ventricle has a faint septum, likely separating it from the lesioned area (see figure 4.1, part A). Damage does not appear to extend into the midbrain (any further than medial parietal areas). Parahippocampal and hippocampi structures are normal.

For 8 years, FM's condition remained stable until mid-2018. FM recently reported a resurgence of headaches, these were attributed to cerebral spinal fluid pressure build up (by her general practitioner), a common side effect of chemotherapy and radiotherapy.

A tumour in the posterior part of the right hemisphere can lead to many different symptoms. Patients can have deficits in visuo-spatial attention, executive functions, visual planning and neglect (Lee, 2009; Goodwin, 2014; Perez & Chokron 2014; Marin et al, 2017).

Damage to a part of the primary visual cortex, from strokes, injury, disease or a tumour renders a patient blind to stimuli falling in the receptive area (Schärli, Harman & Hogben (1999). If the entire hemisphere's visual cortex is lesioned, or any part of it, the patient is unable to see anything in the contralesional hemifield. Quadrantanopia is the loss of vision in a quadrant of visual field. Homonymous inferior is a loss of vision in the lower field of both eyes, homonymous superior is the loss of vision in the upper visual field (sometimes referred to altitudinal defects, Papageorgiou et al. 2018). Homonymous denotes a condition which affects the same portion of the visual field of each eye.

Quadrantanopia is a loss of vision in the same lower quadrant of visual field in both eyes. Homonymous quadrantanopia in the lower field specifically affects the ability to drive or read and has a significant effect on a person's quality of life (Goodwin 2014; Perez & Chokron 2014; Marin et al, 2017). Different to a scotoma (an area of missing vision), an interesting aspect of quadrantanopia is that there exists a distinct and sharp border between the intact and damaged visual fields, due to an anatomical separation of the quadrants of the visual field. This is the type of vision loss experienced by FM, she has lost the lower left visual quadrant, due to the tumour and subsequent lesion of the upper right area of the occipital lobe, bordering on the parietal area (see appendices C and D for visual perimetry results denoting blind field).

Despite the cortical loss of vision, the patients are alleged to be able to detect light within the damaged visual field (Danckert, & Culham, 2010). If a lesion is restricted to the lower bank of the calcarine fissure, the loss of vision is limited to the upper quadrant of the hemifield, known as a superior quadrantanopia. If the lesion is in one hemifield, on the upper bank of the calcarine fissure the loss of vision will be in the lower quadrant of the contralesional visual field, inferior quadrantanopia. The loss of vision will be identical for each eye, because the lesions are in the cortex. Patients presenting with quadrantanopia from cortical lesions posterior to the optic chiasm and beyond Meyer's loop will have spared foveal vision (Jacobson, 1997). Visual field defects are comorbid with phosphenes, anomia, reading disorders and memory deficits (Kraft et al. 2014).

The prospects of recovering vision in the affected field are bleak. Occasionally, patients will spontaneously recover vision in the affected field within the first three months after the brain injury; however, vision loss remaining after this period of spontaneous recovery is traditionally thought to be permanent (Schofield & Leff, 2009). A common assumption from healthcare professionals is that objective recovery from visual field loss is impossible (Perez & Chokron (2014).

An exception to this issue is blindsight, which broadly refers to the condition where patients with a visual field defect due to a cortical lesion, demonstrate residual visual sensitivity within their field cut (Weiskrantz, Warrington, Sanders & Marshall, 1974; Dankert & Rossetti 2005). Weiskrantz identified two types of blindsight. Type one, having no awareness of vision whatsoever, yet responding to priming, motion, form or light; or type two, having a feeling, some kind of quale, without any conscious visual perception (Weiskrantz et al.1974). There has been suggestion of blindsight being a product of visual information coming from the superior

colliculus and from there to the pulvinar nucleus, or even from the lateral geniculate nucleus to the middle temporal area (Danckert & Rossetti, 2005).

Parietal lobe lesions result in disturbance to perception of spatial layout and spatial relations of objects (Gazzaniga, Ivry & Mangun, 2014). The dorsal pathway, following the occipito-parietal cortex, allows the visual control of actions, the spatial localization of visual stimuli, and identification of spatial attributes, including orientation, depth and movement. The dorsal pathway provides strong input to motor systems to compute how movement is produced (Gazzaniga et al, 2014 Milner & Goodale, 2006)

Optic ataxia *(*OA), a deficit of visually guided hand movements, is a high order deficit in reaching to visual goals that occurs with posterior parietal cortex lesions (McIntosh, Mulroe, Blangero, Pisella & Rossetti, 2011). With this impairment, patients can recognize objects, but can't orient towards them. Optic ataxia is generally considered the opposite or dissociative condition to patient DF with visual form agnosia, who can accurately grasp and calibrate movements, but cannot perceive objects (Milner & Goodale, 2008). One possible reason is that the saccades direct inappropriately and fail to bring an object into the fovea; the parietal occipital sulcus is thought to be involved in error correction of saccades (Gobel, Calabria, Rosetti, 2006). An elaboration of this is a contralesional deficit for visuo-spatial processing affecting both hand and eye movements (Pisella, Sergio, Blangero, Torchin, Vighetto & Rosetti, 2009; McIntosh et al. 2011).

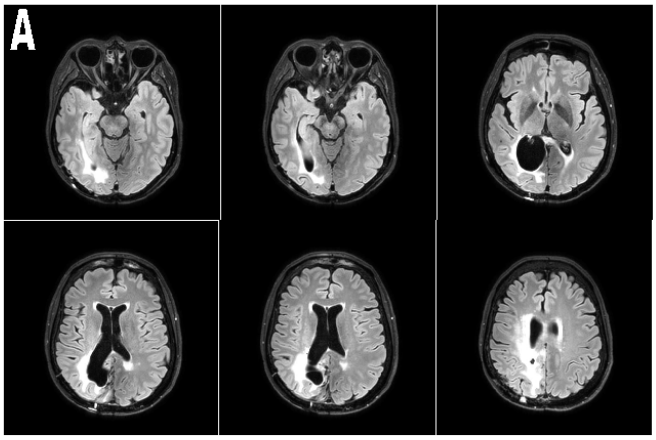
Neuropsychological assessment

FM's cognitive evaluations began in 2018 (8 years post-surgery), after responding to our advert for participants with lesions in the dorsal stream. A series of standardized tests were

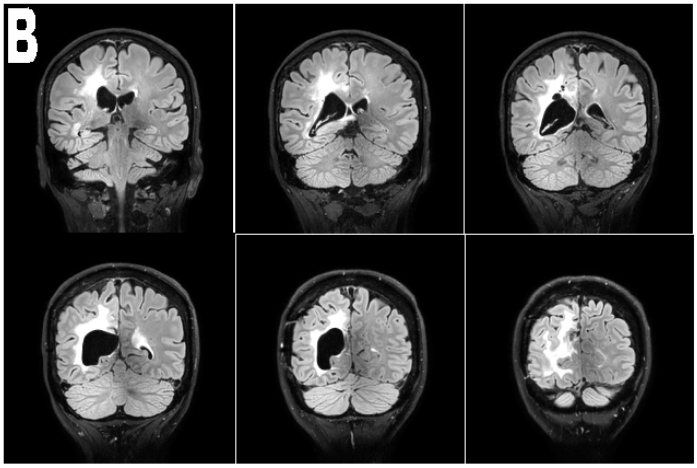
performed; to ascertain if FM was going to be suitable for the dissociation of the dorsal stream lesion, to compare with DF's lesion of the ventral stream. Firstly, the National Adult Reading Test (NART, Nelson, 1982) was given to check FM's general IQ. An optic ataxia test was carried out to check visually guided hand movements. The Visual Object Space Perception battery (VOSP, Warrington & James, 1991) was used to test the ventral and dorsal specialisations. Lastly some standardised neglect tests were prescribed to understand why FM could not see multi-digit numbers. The VOSP tests showed deficits, so some further tests were performed; the Mirror and Orientation Test (MOAT, Martinaud et al. 2016) and the Benton Judgement of Line Orientation test (JLOT, Benton (1994)). A blindsight test was devised to ascertain whether FM may benefit from a visual rehabilitation program.

NART

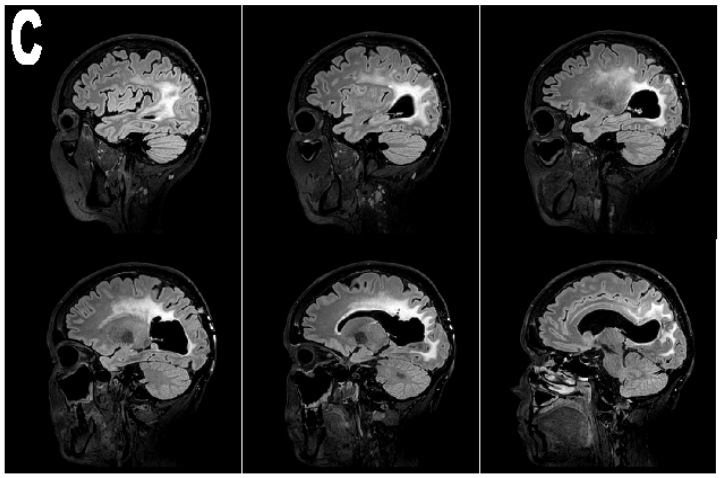
FM completed The National Adult Reading Test (Nelson, 1982,) which is a premorbid neuropsychological assessment of intelligence. Patients are asked to pronounce 50 irregularly spelled words. Response correlates highly with IQ (Barker-Collo, Bartle, Clarke, van Toledo, Vykopal, & Willetts, 2008). FM performed slightly better than average, with 13 errors (normative mean errors = 17.27, SD 6.64, Barker-Collo et al. 2008). IQ was sufficient to commence testing. It must be noted here, that the NART is a measure of premorbid IQ, so the above average performance is likely to be an underestimate (Tippett, 2020). Suffice to say more than enough to continue with the experimental process.



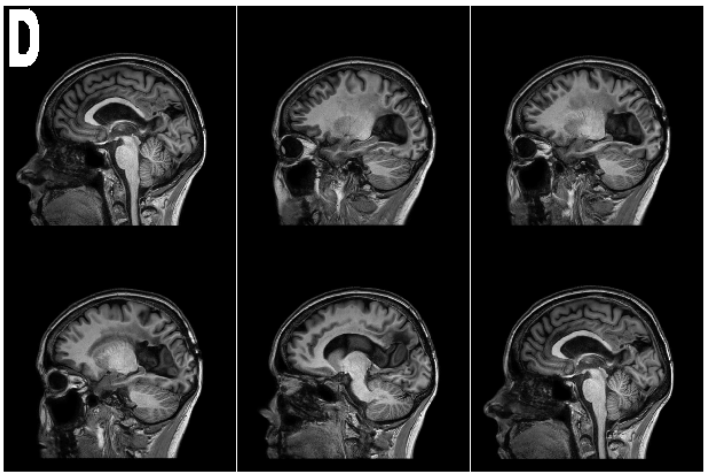
(A) Flair axial MRI (through feet)



(B) Flair coronal (through nose)



(C) Sagittal 3D flair (left ear to right), all showing matter atrophy (very bright white) and fluid as black holes



(D) T1 sagittal showing hypointense lesions (left ear through to right)

Figure 4.1. Brain imaging of the patient in 2018, eight years post-surgery. Lesion of the parietaloccipital junction.

Optic Ataxia

Object ataxia is a neurological symptom resulting in gross mis-reaching in the peripheral field. The defining characteristic is the contrast between spatial errors in the reaching movements to targets in the periphery, compared to unimpaired movements to targets in the central visual field. The lateral and medial portions of the parietal-occipital junction are specifically affected in a lesion analysis reported in Borchers, Müller, Synofzik & Himmelbach (2013). The procedure followed was the same as Borchers et al. (2013) guidelines for the diagnosis of optic ataxia.

Method

The participant sits comfortably with the upper body up right and arms able to move freely. There are two tests, a fixation and a saccade condition. The examiner stands behind the patient and presents the pole over their shoulder. The target presentation varies between the elbow height of the patient and the top of their head. In the fixation condition the participant is instructed to look straight ahead at a fixation cross on computer display monitor, and grasp a pole using peripheral vision. The saccade task allows the patient to move their eyes to see the pole and grasp, so using the foveal vision. Both conditions use the following procedure.

The examiner stands behind the participant and holds a wooden pole to the side of their body for them to grasp. The pole is presented between the line of the patient's head and elbow, at a frontal horizontal angle of 30 to 60° in front and to the left or right side of the body, with the arm not being fully extended to grasp the pole. The pole was always presented in an upright orientation, to both visual hemifields and grasped with a power grip. Both the left and right hand are used to grasp in each visual hemifield, so four different hand/field combinations are executed. Left visual field, grasping with the right and left hand, and right visual field, grasping

with the right and left hand. After each trial the patient moves their hand back to a resting position on the thigh. For each trial the patient's grasping ability is rated from 0 through to 3 points, no errors or gross errors, uncorrected or corrected movements. 0 is perfect grasping in one fluent movement. 1 point means the patient grasped the pole, but not with maximum 3 fingers or falters or hesitates before grasping. 2 points are given if the patient neither grasps or touches pole with first movement, or jolts pole with back of hand, but correctly grasps in the second movement. 3 points are recorded if pole is not grasped in first or following movement.

After all trials are carried out, the scores are summed up per visual condition and transformed into a percentage score relative to possible maximum score. A difference value was calculated by subtracting the percentage score of the fixation condition of one hand/field combination from the saccade condition of the same hand/field combination. This is done to cancel out variables such as hemiparesis or tremor (Borchers et al. 2013). To summarise, the *fixation* condition is where the patient fixates and uses peripheral vision to grasp the pole. This is contrasted with the results of the *saccade* condition, where the patient may move their eyes to view the pole in their foveal view and then make the grasping movement.

Optic Ataxia Results

The results of both the fixation and saccade conditions are illustrated in figure 4.2. With the fixation condition, the left hand grasping in her left visual field (LVF), FM made more than 60% errors in grasping. This was expected as it is FM's blind field. The results were similar for grasping with her right hand in her blind LVF. Using her left hand in her right visual field (RVF), FM made a few errors and had less difficulty grasping with her right hand in her RVF in her peripheral vision. For the saccade condition, FM made a large number of errors grasping

with either hand in the blind LVF, she made slightly more errors when she was able to saccade towards the target in the LVF, also to be expected as the blind spot is in FM's peripheral vision. FM made less errors grasping with her left hand in to the RVF but made considerably more errors grasping with the right hand into the RVF, while making a saccadic response.

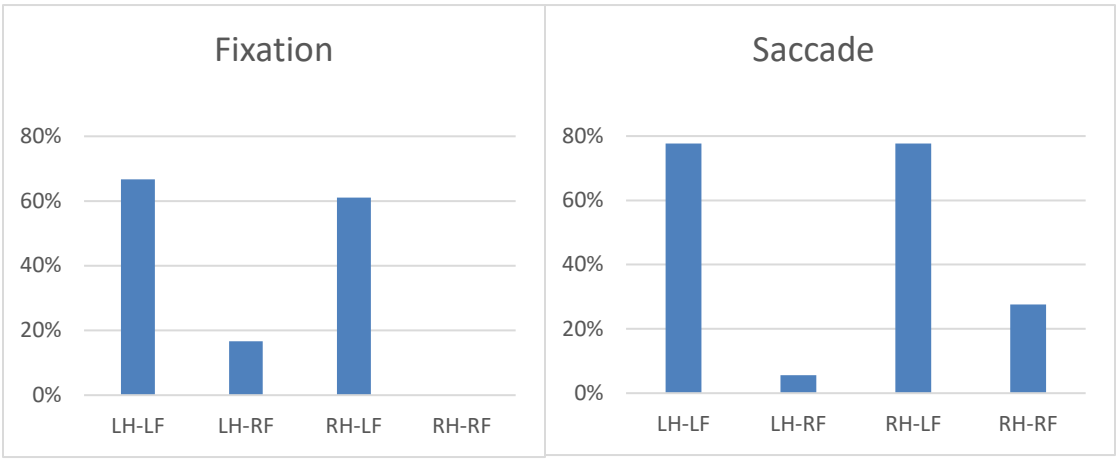


Figure 4.2. Congruent hand/field show more errors in saccade compared to fixation condition.

LH Left Hand, LF Left Visual Field, RH Right Hand, RF Right Visual Field

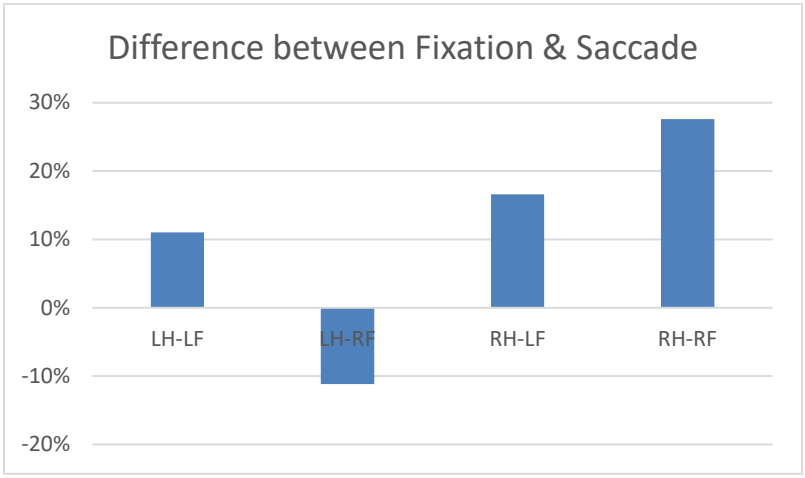
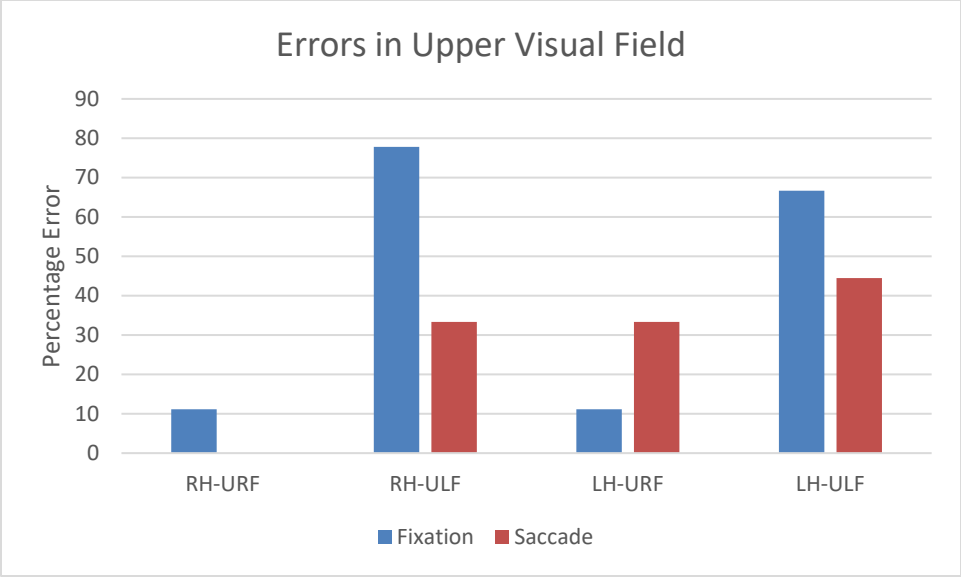


Figure 4.3. Congruent conditions reveal biggest difference is ipsilesional; right hand, reaching into right visual field

To ascertain a diagnosis of optic ataxia, there needs to be a difference of more than 13% ($p < .05$) or 16% ($p < .001$) between the fixation and saccade of the same (congruent) hand/visual field combination (Borchers et al. 2013). This assessment was made by comparing the results with healthy controls using adjusted t-test statistics as suggested by Crawford and Garthwaite (2005), using their program SINGLIMS. Borchers et al (2013) have calculated the cut-off scores using their data of 36 healthy controls.

The difference scores of LH/LF (contralesional) with RF/RF (ipsilesional) for FM were 11.03% and 27.6%. The ipsilesional difference is above significance, but one needs to be mindful the difference should be worse for the *fixation* condition (peripheral vision), not the *saccadic*. The saccadic condition showed a difficulty reaching, even when permitted to turn and look for the target with her foveal vision. This is most likely to be because of her visual field cut condition. FM has the lower left quadrant of her vision missing, so a diagnosis of optic ataxia on this basis of these scores is not possible.

The scoring method employed in this test may be inadequate for those with a blind field. To discover whether FM truly has optic ataxia or if the results are confounded by the blind field, the results will be re-analysed using data from the upper visual field only. This is because FM's upper visual field is intact, the field cut is in the lower left quadrant.



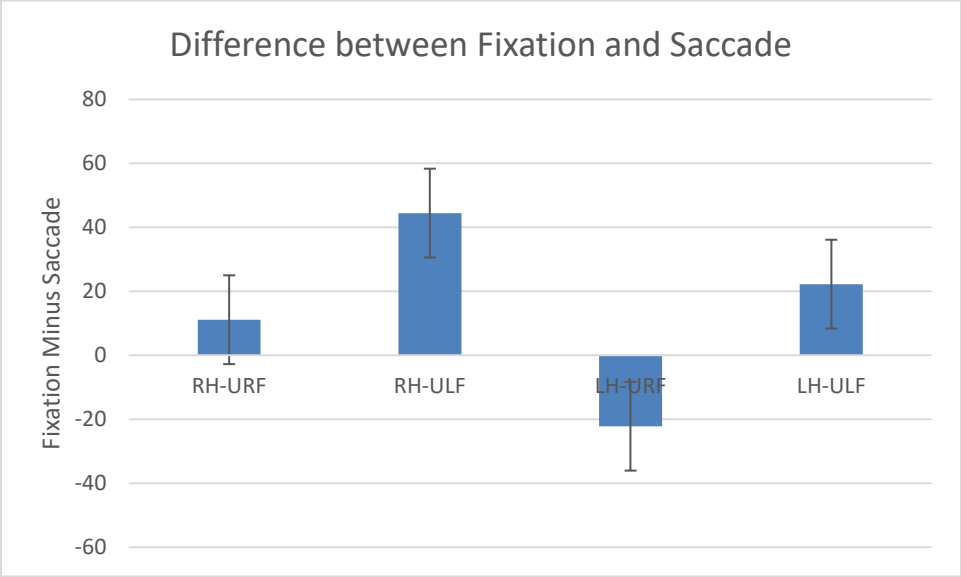


Figure 4.4 Errors in upper visual field, showing congruent contra-lesional fixation (peripheral) vision worse than saccade (foveal), LH-ULF $p < .001$, left hand reaching into upper left visual field

Using data from the upper visual field only, gave a much clearer picture, unconfounded by FM's peripheral blind spot. The congruent condition of right hand paired with upper right visual field (RH-URF), in the ipsilesional area (shown in figure 4.4), is not reaching significance. The congruent left hand and left upper visual field, for the contralesional side showed a

difference of 22.23% (>16%), so significant at $p < .001$. Borchers et al. (2013, p5) state "the impairment in OA patients should differ primarily between the combinations of contralesional hand/contralesional field and ipsilesional hand/ipsilesional field", ie congruent. So, although the incongruent "right hand-left visual field" condition is above threshold, it is not considered an impairment for OA. The impairment should be contralesional in patients with neurological deficits (Borchers et al. 2013).

To summarise, (with blind spot aside) FM fulfils the criterion set by Borchers et al. (2013) to diagnose OA. FM meets the criteria of optic ataxia, and has a lesion in the dorsal stream, so she is a good candidate to compare her ability to perform the landmark and identity cueing tests with patient DF (Marrett et al. 2011)

Landmark and Identity Cueing Task

Participants

FM completed a cueing task, identical to the one described in the EEG methods section. The same participants for that experiment were used as controls. All procedures were approved by the University of Auckland ethics board (ref 7835).

Apparatus

The experiment was performed using a Dell Inspiron lap-top PC, with a 15” LCD visual display. A chinrest was used to control viewing distance (57cms).

Stimuli

The stimuli, apparatus and procedure were the same as documented in the ERP Chapter, on the same Dell computer, in the room of the EEG lab. Except FM completed the experiment behaviourally (without using the ERP electrode cap). FM was aged 49 at the time of testing. The data from the sixteen participants who completed the ERP experiment were used as the controls (for this experiment only; the following clinical experiments used age-matched controls). The data was also compared with the results of DF, published by Marret et al. (2011).

Results

Four outliers were removed from the data set. Each of these were extremely long response times that were more than three standard deviations from the mean. Overall, FM showed a cueing advantage of similar magnitude to the control participants and DF (see figure 4.6). Critically the cueing difference by FM was not statistically different from controls, $p = .89$ (Crawford & Garthwaite, 2002).

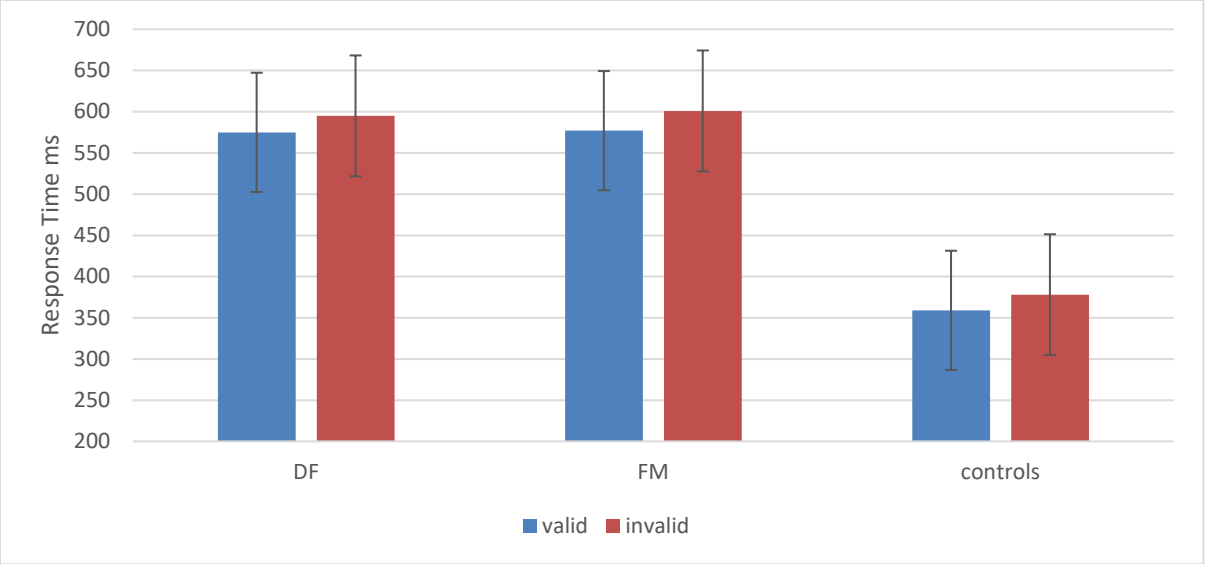


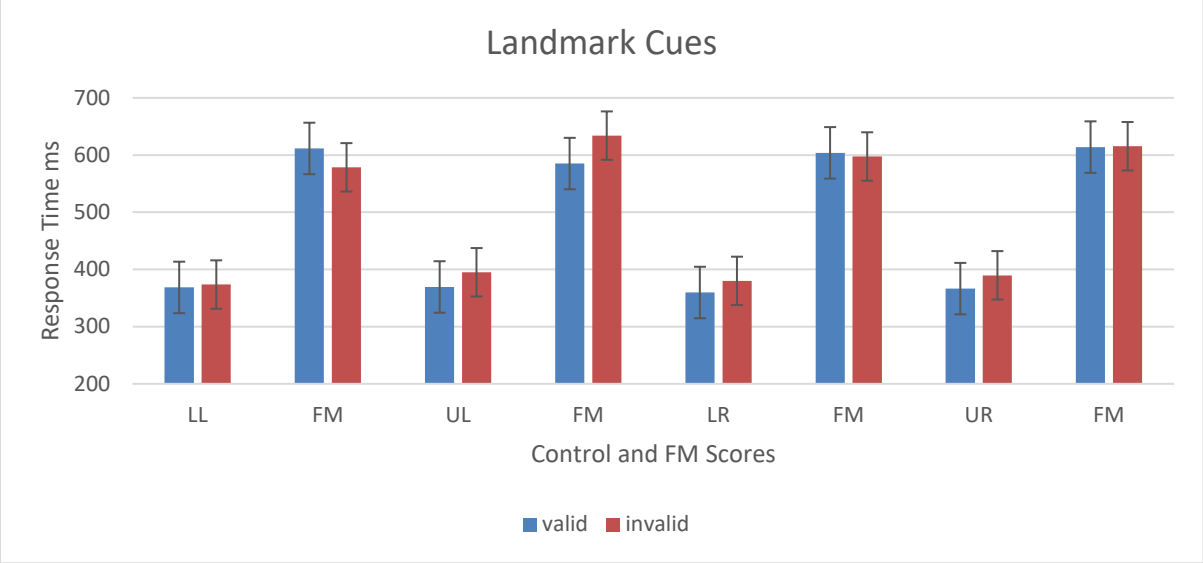
Figure 4.5. Valid compared to invalid reaction times. Both patients took longer to respond, but neither a ventral nor dorsal stream lesioned patient's overall cueing response is different from controls

DF p = .87 (Marret et al. 2011), FM p = .89

Analysing the cue information seperately for FM has shown an interesting difference. For valid cues presented in FM's blind field, there was no cueing advantage (see the graph, lower left "LL", for both landmark and identity cues, in figure 4.5). This was to be expected, of course, as she couldn't see them! Whilst these *predictive* cues were in her blind field, FM did not appear to utilise the secondary cue (on the other side of her field of vision) to help her attend to the target. This was a possibility that had been considered in the lab as a possible method for identifying cues. Perhaps participants were biasing attention towards the predictive cue, but maybe participants also used the non-predicitive cue to inform target location. Not so in FM's case.

A three-way independent groups ANOVA was performed on FM's data, the three factors were cue type, visual field quadrant and validity. The three-way interaction between cue, validity and visual field were not significant, $F(3,325) = 1.464$, $p = .224$. However, the two-way interaction between cue and validity was highly significant, $F(1,325) = 12.24$, $p = .001$.

Individual *t*-tests compared the effects of validity for each cue type, in each visual quadrant (see table 4.1). FM was able to use the ID cues in the three visual quadrants unaffected by the lesion, but was not able to utilise the LM cues, there were no reliable differences in validity for any of the quadrants for LM cues (see figure 4.6).



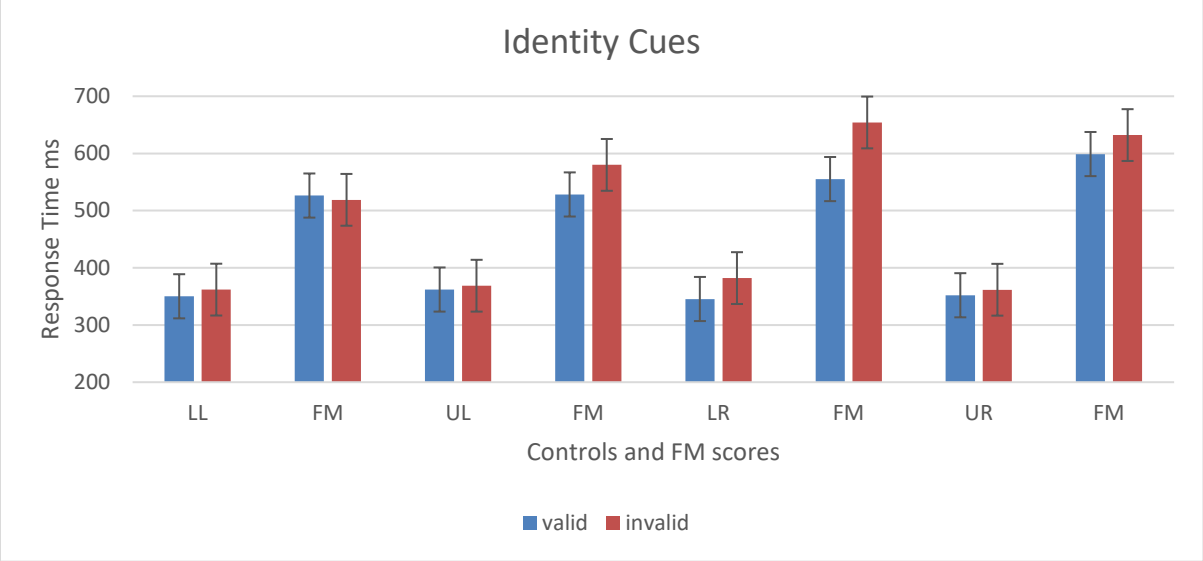


Figure 4.6. The identity cues showed more of an advantage for FM (p = .011), than the landmark cues (p = .827)

Both identity and landmark cues, in the lower-left visual field, have faster responses for *invalid* cues (figure 4.7). However, the same cues in the other visual field quadrants *are* showing a cueing advantage for the identity condition. So if, FM is able to see and utilise the identity cues in her intact parts of peripheral vision, why can't she use utilise the landmark cues? As FM has a lesion in her dorsal stream, perhaps she is less able to utilise landmark cues than controls, and less able to use landmark cues over identity cues, which may be recruited by FM's intact ventral visual stream.

Cue and Visual Field	*t* value (df)	Significance
LM Upper Right	-.025 (39)	p = .980
LM Upper Left	.284 (41)	p = .778
LM Lower Right	-.692(39)	p = .493
ID Upper Right	2.932	p = .006
ID Upper Left	2.337	p = .024
ID Lower Right	3.543	p = .001

Table 4.1. The ID cues showed a reliable validity effect in all of FM's unaffected visual quadrants, but the LM cues did not show any effects

Visual Object and Space Perception

The Visual Object and Space Perception battery (VOSP) was devised by Elizabeth Warrington. A large sample of healthy control, right-brain damaged, and left-brain damaged data was collected (Warrington & James. 1991) and analysed to establish sensitivity and selectivity of the VOSP tests. To take into account the minor effects of aging, the control groups were divided in to two age bands, age band 1 <50, age band 2 >50. For each test and each age band, a Mann

Whitney U Test were used to determine a 5% cut-off score that reflects a deficit. This test was chosen because FM was expected to do poorly in the space perception tests as they are meant to recruit the dorsal stream. The VOSP consists of eight tests, plus a screening test. The first four are designed to tap object perception and the final four, space perception.

Detection Screening Test

This test is administered to check if patients have enough visual acuity and adequate shape discrimination. Test stimuli are degraded X's superimposed on random pattern backgrounds (see figure 4.2). Some cards have an X and some don't. Patients are asked if they can see an X. Patients scoring less than 15/20 do not have enough visual acuity to complete the VOSP test. FM scored 19/20. X's present were correctly identified, except for one, so we were able to proceed with the tests.

Object Perception Tests

Test 1: Incomplete letters.

If the perceptual clarity of a letter is degraded, it becomes more difficult to identify. For example, handwritten script is more difficult to read than typed. Neuropsychological studies have established patients with right hemisphere lesions, particularly right-posterior lesions, may have a selective deficit reading degraded letters (Warrington & James, 1986). Twenty cards were shown to the patient, with varying degrees of degradation. The letter on each card was to be read aloud by the patient (see figure 4.7).

FM scored 19/20, scoring as normal (mean score for <50 19.3). FM struggled to identify the practice card, which was an upside-down F. The only letter in the test to be inverted.

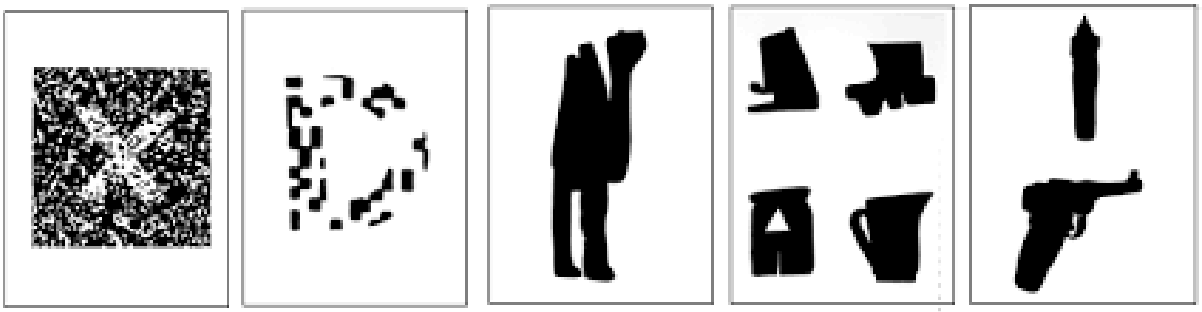


Figure 4.7. Object Perception Battery and the screening test, a) Visual Acuity test cards, b) Incomplete Letters c) Silhouettes d) Object Decision e) Progressive Silhouettes
(picture courtesy of Annegarn, F. 2017, University of Amsterdam).

Test 2. Silhouettes.

Recognition of common objects photographed from an unusual view may be selectively impaired in patients with lesions in the posterior part of the right hemisphere. Distinctive parts needed to be visible for identification in some participants, but not in others (Warrington & James, 1986). The silhouettes were drawn from an outline of each object, rotated through the lateral axis in varying degrees. The tests consisted of 15 animal and 15 inanimate objects, ranging in order of difficulty (see figure 4.7, middle picture). The patient was shown the first animal silhouette and told it is a drawing of an animal, then asked to name it. The procedure is repeated, then the patient was informed the next set of pictures were all common objects. The total number of silhouettes correctly named or identified is recorded as the score. FM scored 18/30. The age band normative data is 23.1. A score between 16 and 20 is between the 5% and 25% (respectively) cut off score for normal data, so FM is showing a deficit for this task. Her score is in line with the right hemisphere lesioned data collection from Warrington & James (1991) at 18.4.

Test 3: Object Decision.

The object perception test was designed after perceptual processing deficits were observed in patients with right hemisphere lesions and semantic processing deficits with left hemisphere lesions. To avoid problems with verbal responses or identification of objects (dysphasia and visual agnosia), the task requires selection of a real object from an array of distractor objects. Warrington and James (1991) found right hemisphere lesioned patients had difficulty recognizing 3D rotated shadow images. In the test, two-dimensional shadow drawings of objects were rotated at an angle of rotation which approximately 75% of a normal control group could identify. They are minimal views, meaning they are 2-D shadow images with minimal perceptual cues. One real object is placed on a card with three distractor items (see figure 4.7). The participant is shown the test card and asked to point at the real object. The number of correct choices out of 20 is recorded. FM scored 10/20 and found this test extremely difficult and tiring. The age band normative data is 18.6. The 5% cut off score to show a deficit is 15. FM was severely impaired at this task ($p < .001$) and performed worse than the group of right lesioned patients in Warrington and James' (1991) data, which have a mean score of 16.2 (with a standard deviation of 3).

Test 4. Progressive silhouettes.

When an object is shown at a lateral view (from the side), it is easily identifiable. If rotated 90°, critical distinctive features are not visible, and it is not so easy to identify (Warrington and James, 1986). A series of ten silhouettes was constructed by varying the angle of view from 90 rotation through to 0° rotation of the lateral axis (see figure 4.7, last picture). The tests consist of two series, a gun and a trumpet. The first silhouette is shown, and the patient

is told the picture is a silhouette of a real object, which will get progressively easier to identify on each page. As each page is shown, the patient is asked whether they can identify the object. The number of trials required to identify each object are summed and recorded as the total score (maximum score = 10+10). A lower score is a faster response, therefore the higher the score, the more impaired.

FM scored 13, 7 trials for the gun and 6 for the trumpet. Mean score of the control group <50 = 9.8. Please note, the aim of the test is to identify the silhouette as fast as possible, therefore identifying the object in as few cards as possible. The mean of the patient group with right hemisphere lesion is 12.3. The healthy control group average is 9.8. FM scored 13 which was significantly different from controls ($p < .05$) and scored as a grade three deficit in this test (four being a small deficit and one being the largest) according to Warrington & James (1991).

Space Perception Tests

Test 5**.** Dot Counting.

The first of the space perception test was designed to tap a dissociation between knowing where an object is respect to oneself and knowing where an object is in relation to other objects. The test provides a screening for visual disorientation and a simple spatial scanning task. The test stimuli consists of arrays of black dots on a white card. There are two arrays of five, six, seven, eight and nine dots, arranged to make a random pattern. The dots were between 10 and 120mm from the centre of the card (see figure 4.8). The patient is asked “Tell me, how many dots are on this card?”. FM scored 9/10. The mean sample of healthy controls <50 is = 9.9, the 5% cut off score is 8. The mean right hemisphere lesioned group score is 9.3, SD = 1.2 ($p=2.32$). As this test

is extremely easy, the assessment of an individual should use only pass or fail, with the five percent cut off score to be meaningful. Many patients score within the normal range.

Test 6**.** Position Discrimination.

The ability to perceive the relative position of objects in a two-dimensional space in healthy controls is extremely good. A misalignment of less then 1° of visual angle can be detected (Warrington & James, 1991). This test consists of two adjacent horizontal squares, one with a black dot printed exactly in the centre and one with a black dot off centre (see figure 4.8). In each of the twenty cards, the dot off centre is in a different position within the square, and the off centre dot is counterbalanced with ten on the left and ten on the right. The participant is told one of the dots is exactly in the centre and could they point to which one that is. The number of correct responses is recorded. FM scored 19/20. The mean control score at matched age is 19.7. The 5% cut off score is 18. The patient group score for right hemisphere lesion is 18.7, the standard deviation is 2.1, p = 2.14. Therefore many of the patient control group scored within the normal range. FM was not impaired at this task.

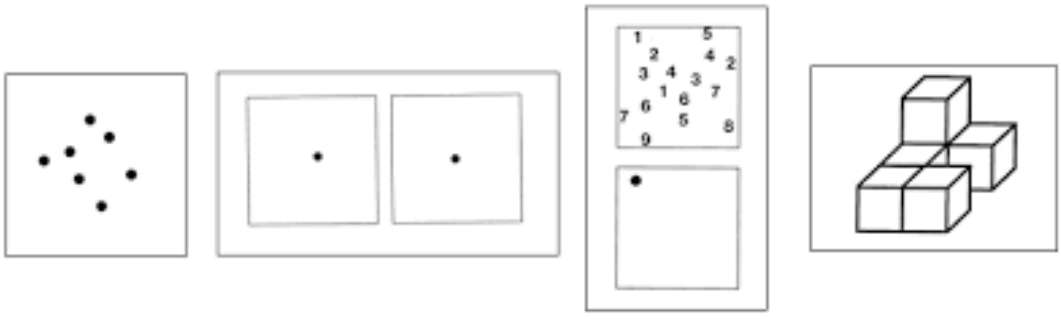


Figure 4.8. Space Perception Battery a) Dot Counting b) Position Discrimination

c) Number Location d) Cube Analysis

(picture courtesy of Annegarn, F. 2017, University of Amsterdam).

Test 7. Number location.

This test is designed to be a more demanding test of spatial perception. Ten test cards consist of two squares one above the other. The top square contains randomly placed numbers from 1-9 and the bottom square a single black dot corresponding to the position of one of the numbers (see figure 4.8). The position of the dot is different in each stimulus and there are four different number arrays. The task is to identify the number that is in the same position as the single dot. The number chosen is noted and the correct response is recorded.

FM scored 8/10. The was no difference between the two age bands, both <50 and >50 healthy control groups have a mean score of 9.4. 5% cut off score is 7. Mean score for right hemisphere group is 8.4. FM was not impaired for this task.

Test 8**.** Cube analysis.

The final test is a 3D interpretation which may involve more complex perception than discrimination of location. Based on the test by Binet, that was included in the Stanford-Binet intelligence scale for spatial abilities. The test stimulus is a drawing of square bricks representing a 3D arrangement. There are two test cards with a simple set of three bricks. The ten stimuli are graded in difficulty by increasing the number of bricks from five up to twelve, and includes hidden bricks (see figure 4.8). The patient is told the drawing is made up of a nuber of solid brick; how many solid bricks are represented in this drawing? If a ‘hidden” brick is not counted, the experimenter may remind the patient there are hidden bricks to count. FM scored 10/10. The mean for age band 1 <50 is 9.3. FM performed extremely well on this test, better than the average control and higher than the right lesioned group, who have a mean score of 8 (SD 2.4).

Visual Object and Space Perception Results

The four space perception tests (cube analysis through to dot counting, tests 5-8) were very easy for FM. FM completed all these tasks well, although there was very little difference between the scores of FM, the controls and the right hemisphere lesioned group. The object perception battery appears to be a better set of tests for showing differences between the right brain lesioned group and control data. The incomplete letters test was not a problem for FM.

The three tests consisting of degraded stimuli did not appear to have enough perceptual information for FM to ascertain the objects. Silhouettes as a stimuli were more difficult for the right brain lesioned group than controls, and FM showed scores in line with the lesioned group. FM's silhouette task and progressive silhouette scores were statistically different from controls. The object decision task was extremely difficult for FM. This task involved deciding which silhouette (from a group of four) was the real object (see Figure 4.3) and the test cards in our VOSP kit were inverted, that is the shapes were generally up-side down. Discerning shape is more commonly associated with the inferior temporal cortex, than the right hemisphere (Milner & Goodale, 1992; Walsh & Butler, 1996). Many of the images were rotated, so FM's problem could either be a difficulty with rotated stimuli or discerning shape or both. Because of these results an orientation test was tested later.

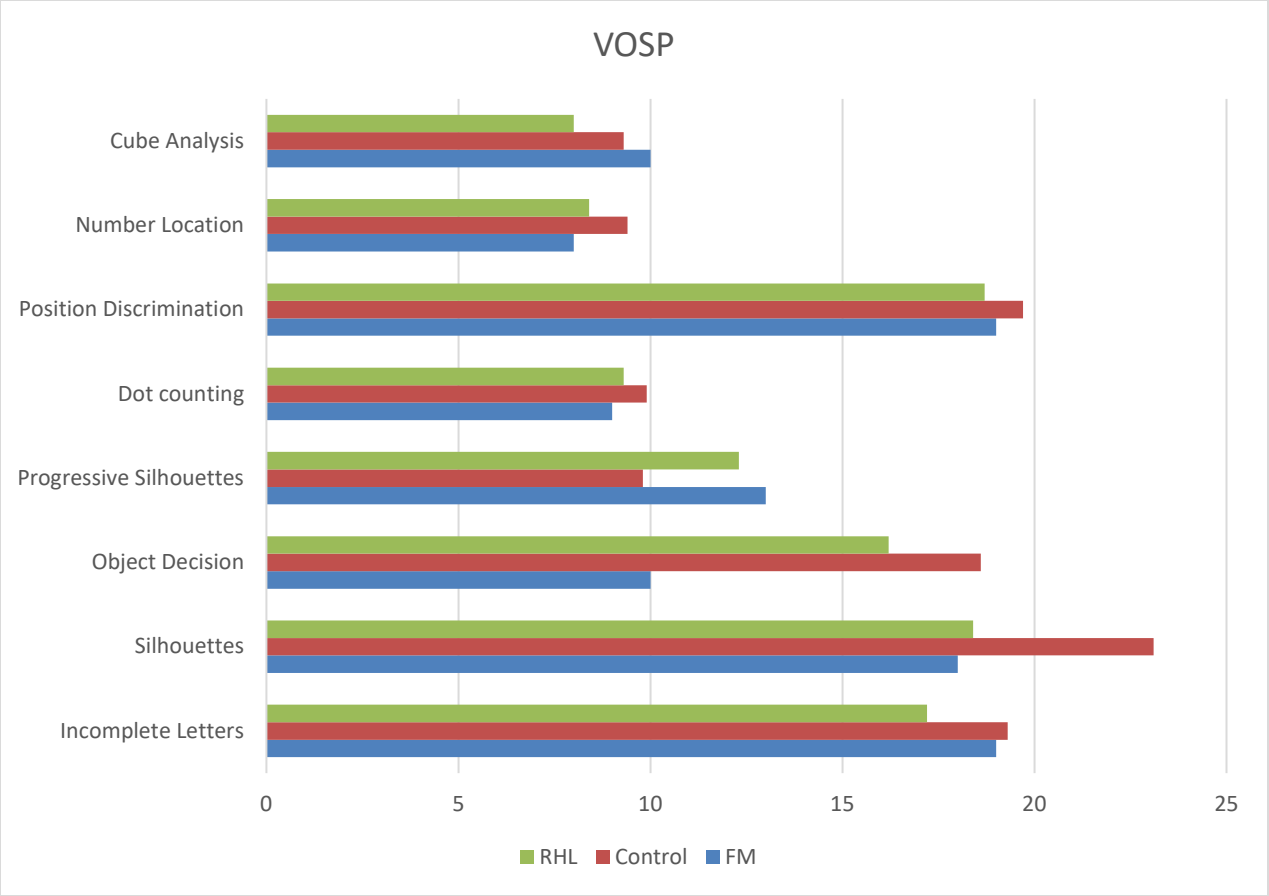


Figure 4.9. Summary of VOSP Space and Object battery. Object Decision task took significantly more cues to guess than controls ($p<.001$). Progressive Silhouettes and Silhouettes were difficult for FM to identify ($p<.05$)

RHL Right Hemisphere Lesioned patients (Warrington)

Neglect

Three tests were used to see if FM's inability to correctly name large numbers was due to neglect. The Bells cancellation task, the Ogden scene drawing, and a physical line bisection task were administered.

Procedure

The Bells test and Ogden scene drawing are behavioural tests commonly used to assess spatial neglect (Chen, Hreha, Fortis, Goedert, & Barrett 2012). The Bells test consists of an array of 35 bells and 280 distracter symbols such cars, trees, birds and teapots covering an A4 sheet of paper. In a maximum of 5 minutes, the patient is required to cancel (draw a strike line through) as many bells as possible. Scoring of the Bells test consists of three methods: asymmetry score, total cancellation score and time taken, as described by (Mancuso, Damora, Abbruzzese, Navarrete, Basagni, Galardi, Caputo et al. 2019).

The first score is the total number of crossed-out targets and is taken as a measure of selective attention (all target items are considered in this score). The total score ranges from 0 to 35 and indicates how accurate the participant is able to detect targets among distractors. The pathological performance (number of errors) expected for people aged 50 years old, with 8 years of formal education (Macuso et al. 2019 normative study) is 3 errors

The second is the asymmetry score, the difference is calculated between the target cancellations on the left-hand side of the sheet, compared to the right. Positive values indicate that more targets are crossed-out on the right than on the left side (left hemispatial neglect) and negative values indicate the opposite (right hemispatial neglect). Based on a 95% confidence limit, a cut-off deficit score of 2 was obtained (Macuso et al.2019). Therefore, individual performances in which the difference between left and right total omissions was equal to, or above 3, should be considered pathological. Finally, time taken to complete cancellations at maximum execution time is 216 seconds (Macuso et al. 2019). Any time taken over this limit should be considered as a deficit.

The Ogden scene is a simple drawing of a house, tree and picket fence. The target drawing is then copied, and any omissions noted.

The physical line bisection task is often used to diagnose unilateral visuospatial neglect. With right brain damage, patients generally show unilateral neglect of visual information on the left side; in particular, when asked to mark the midpoint of a physical line, they usually place it to the right (Bisiach, Bulgarelli, Strezi & Vallar, 1983). Healthy controls often bisect the line towards the left, known as pseudoneglect (Zago, Petit, Jobard, Hay, Mazoyer, Tzourio-Mazoyer, Karnath, & Mellet (2017). This healthy leftward bisection is approximately 1-2 mm or 1.6% for healthy controls (Lezak, 1990). Twenty-six horizontal lines were bisected by the patient, in a simple paper and pen exercise (see appendix F). The lines were of varying lengths, from 10mm to 300mm. The subjective midpoint is taken away from the objective midpoint to calculate the mean displacement. Displacement to the left is measured as a negative and displacement to the right as positive. The displacement score is then converted into a percentage deviance, following the Lezak (1990) method, as shown below:

$$\frac{\text{Measured left half} - \text{True half}}{\text{True half}} \times 100$$

The percentage scores are put in one of three groups, either left, right or centre and the average of each group is calculated.

Results

The Ogden scene drawing was copied with no omissions.

At first glance, the Bells cancellation appears to be performed well, with only 5 bells out of 35 not cancelled (see appendix E). But the cut-off specified for a deficit by Macuso et al (2019) was

missing more than 3 bells among distractors. Furthermore, using the second stage of analysis, all 5 of the missed bells were on the right-hand side of the page, giving an asymmetry score of -5, and a diagnosis of right hemispatial neglect. The third and final stage was the time taken. FM considered the Bells test for 300 seconds, until she felt she had finished. This was well over Macuso et al's (2019) recommended 216 seconds.

The fourth neglect task was the physical line bisection task. FM showed a considerable leftward bias at an average of 10.20% for fourteen lines. This was more marked on longer lines. Shorter lines were generally bisected to the right, with nine lines showing a rightward deviation of 4.91%. Three lines were marked perfectly in the centre by FM. These results are unexpected, as most right-hemisphere lesioned patients show a rightward bias, neglecting information contra-lesional to the damaged area of the brain (Bisiach, et al. 1983; Lezak, 1990; Zago et al. 2017). The neglect results are perplexing as one would expect a mainly right hemisphere lesion to show left hemispatial neglect. But the bells task showed a right hemispatial neglect and the line bisection task showed a right hemispatial neglect. Both of these results are in line with FM's self-report of losing the ends (right-hand side) of numbers.

Orientation Agnosia

The popular Judgement of Line Orientation Task (JLOT) by Benton (1994), and the Mirror and Orientation Agnosia test (MOAT) by Martinaud et al. (2016) were chosen to ascertain if FM exhibits orientation agnosia. Martinaud et al. (2016) have shown that deficits with mirrored stimuli can be dissociated from deficits with rotated stimuli. They tested thirty-four stroke patients with right parietal damage. Nearly half of these patients had agnosia for mirrored stimuli, with 59% of the patients showing a deficit for at least one of the six

orientations. One patient had very similar lesions to FM and also presented with lower left quadrantanopia. This patient showed a significant deficit for every single type of orientation, but most markedly for mirrored stimuli.

The JLOT is a series of cards with an array of lines, similar to a protractor. On each card there is the protractor-type arrangement of lines and one line separately which matches one of the lines. There are two tests, which are the same, with the same questions, but in a different order, both start easy and increase in difficulty. The patient is asked which numbered line matches the single line. On this task, right hemisphere damaged patients are significantly more impaired than left hemisphere damaged patients, suggesting a dominant role of the right hemisphere in discriminating line orientation (Treccani, Torri & Cubelli, 2005). FM showed "superior to average performance" on the JLOT test, gaining 23 correct answers out of 30 on form H, according to Benton's (1994) normative data. Therefore, showing no difficulty with the orientation of lines per se.

Participants

Alongside FM, who was 50 at the time of testing, 4 age-matched controls took part in the MOAT. Age range 49-51 years old, one male. All procedures were approved by the University of Auckland ethics board (ref 7835).

Apparatus

The experiment was performed using a Dell Inspiron lap-top PC, with a 15" LCD visual display. A chinrest was used to control viewing distance (57cms).

Stimuli

Each trial contains five different line drawings of the same object, four set at the same orientation and a fifth target object rotated or mirrored. The first four conditions showed the four regular stimuli appearing at the standard 0° everyday view (see figure 4.6). The mirror condition had the target stimuli as a mirrored image in the vertical plane (B). The up-down mirror condition shows the stimuli mirrored in the horizontal plane (C). The 90° condition showed the target rotated 90° clockwise from the other stimuli and 180° condition rotated the target 180° clockwise (D&E). The 45°+ 90° showed the distractor stimuli rotated at 45° clockwise from 0°, with the target stimuli rotated a further 90° (F). The final identity condition showed all five drawings at the same 0°, but the target stimulus was a different drawing (A). The identity condition was to ensure to patient did not have visual form agnosia. The stimuli were numbered one through to five and shown on a PC.

The order of stimuli presented was randomised and the target appeared in equal frequency in every spatial position, for a total of fifty-five trials for each condition.

Procedure

The participants were asked to detect the stimulus that was different from the others and press the corresponding number on the number pad on the right of the keyboard.

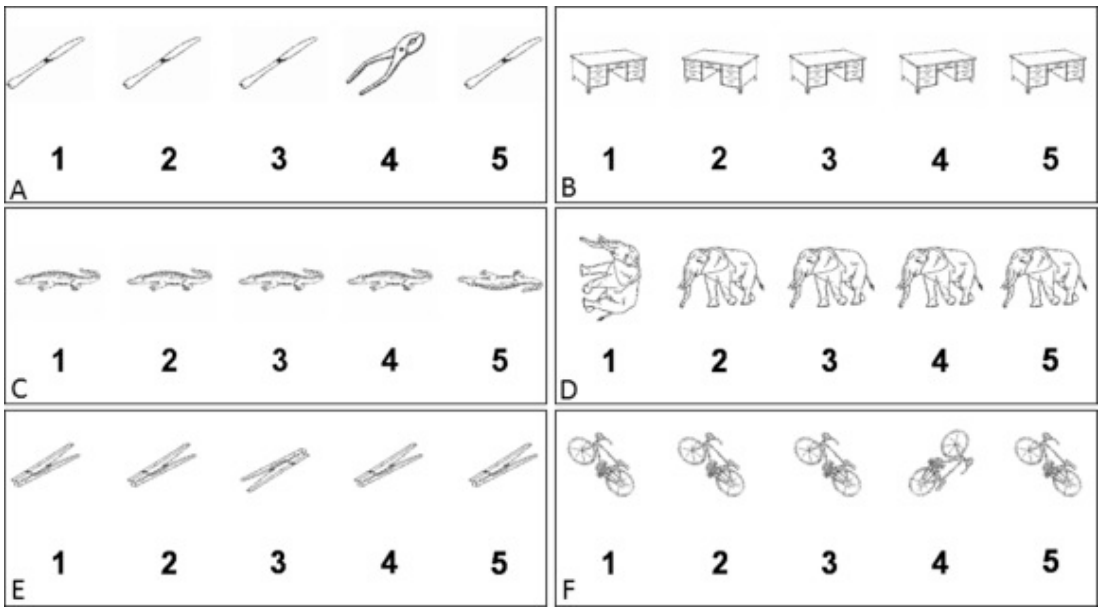


Figure 4.10 Stimuli for MOAT (Martinaud et al 2016).

A) Identity. B) Mirror. C) Up-down mirror. D) 90°. E) 180°. F) 45°+90

Correct scores for each condition were converted into an average percentage correct to be able to compare the data of four controls with FM. The patient's performance on each condition was compared to the mean and standard deviation (SD) of the control sample, using the Singlims ES test (Crawford, Garthwaite & Porter, 2010). Martinaud et al. (2016) suggest agnosia for mirrored stimuli can be considered when score is pathological in either vertical or horizontal condition, orientation agnosia was considered in either of the three remaining conditions (90°, 180°, 45°+90°). To identify selective deficits, only one condition should be `A`affected and the impairment should be significantly greater than all other conditions, using a modified t-test allowing comparison of one patient against a moderate sized control group (Crawford, Garthwaite & Gray 2003).

Results

The results show FM has agnosia for mirrored stimuli (the traditional mirror view, flipped in the vertical plane, $p < .05$) and orientation agnosia for the 45°+ 90° condition ($p < .001$). The mirror scores were 97.9% correct for FM (7 errors), and 99.7% (3 errors across all controls) for age-matched controls (see figure 4.11).

For the 45°+ 90° condition, FM scored 94.2% correct and the control group scored 97.4%. This double rotation condition was the hardest condition overall with control participants making around 6 errors each, but FM far superseded those with 19 errors. The response time data showed a similar story. A *t*-test was used to compare differences between FM's own response times. The mirror condition ($M= 4895ms$, $p < .05$) and the 45°+ 90° ($M= 4711.18ms$, $p < .001$) had a significantly slower response time, than the other conditions 180° ($M=2741.74$), up mirror ($M=2987.26$), 90° ($M=2416.25$ and identity ($M=1959.07$).

In comparison with Martinaud et al's (2016) patient (#16), FM is presenting with the same visual field defect, but without agnosia in every single orientation as patient #16 does. From the images in their supplementary data, patient #16 has a POJ lesion that is more discreet than FM's, but also had some small infarction spots more interiorly in the parietal area, bordering on inferior frontal.

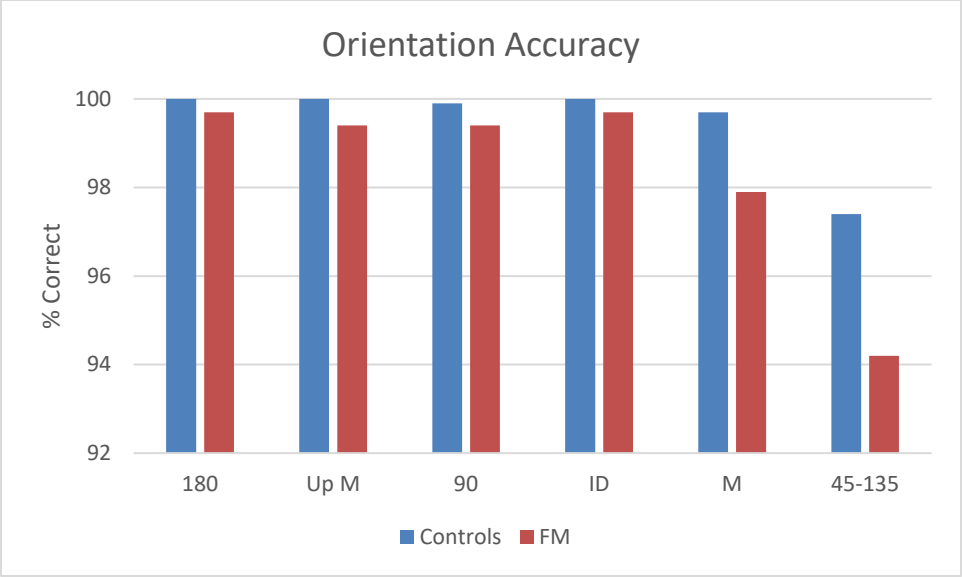


Figure 4.11 Percentage accuracy showing FM's deficit for mirror rotated stimuli ($p < .05$) and stimuli oriented at 45° + 90° ($p < .001$). 180°, Up Mirror, 90°, Identity, Mirror, 45°+135°

Blindsight

Blindsight is a phenomenon described initially by Weiskrantz et al. (1974). It is the ability to of people who are cortically blind due to lesions in the primary visual cortex, to respond to visual stimuli that they cannot "see". Blindsight had been thought to be spared islands of vision or dependent on the visual signals directly from the superior colliculus and lateral geniculate body (Campion et al. 1983). Normal function of the direct connection to the visual association areas from the lateral geniculate body and superior colliculi is to orient our attention to unusual visual events like a flash of light. It initiates the reflex action to draw attention to potentially harmful stimuli/events. These signals do not relay in the primary visual cortex V1 and thus this action is carried out non-consciously.

Participants

Alongside FM, 4 age-matched controls took part in the blindsight test. Age range 49-51 years old, one male. All procedures were approved by the University of Auckland ethics board (ref 7835).

Apparatus

The experiment was performed using a Dell Inspiron lap-top PC, with a 15” LCD visual display. A chinrest was used to control viewing distance (40cms).

Stimuli

The test stimuli created for FM consisted of two circular grating patterns, horizontal or vertical, which flashed up individually in a visual quadrant. There was a fixation cross in the centre of the screen. After a 30ms “blink”, extinguishing of the fixation cross, an arrow appeared predicting the position of the grating 75% of the time. The circular grating was black and white stripes on a grey background. The circle had a diameter 10° and was placed in the absolute corner of the visual display monitor, 20° diagonally away from the fixation cross. A 10° circle may seem a little large, but this is smaller than FM’s blind field. FM was also tested on a pilot study of variable sized circles to see which fell inside her blind field. The program was adjusted many times, because in the pilot study FM could see the grating. We also had to sit FM closer to the screen to get the stimuli in a position where she could not consciously see something. There were 128 trials per participant, and the arrow position and grating positions were completely randomised.

Procedure

The stimulus was left on the screen until a response, so FM knew if she could not see anything, and the arrow was pointing to her blind lower left quadrant, or a blank visual field, then the circle must be in her blind field. If the grating was horizontal, then the response was to press the "left" arrow key (horizontally facing), in between the letters and the number keypad. If the grating was showing vertical stripes, then the response key was the "up" arrow (pointing vertically). FM was instructed to make a forced-choice response, even if she couldn't see anything.

To decide if FM was able to show a type I or type II blindsight, visual awareness was made verbally before each response. These responses were noted and correlated with correct or incorrect answers. FM was asked to respond "yes" if she could see something, "no" if she could see nothing, or "aware" if she had a feeling that something was there. The verbal responses were not carried out with the control participants.

All participants were asked to keep their gaze fixated on the central cross. Only FM's gaze was analysed using an eye tracker. The number of eye movements that exceeded 5° was less than 3%, and these were removed from the final analysis.

Results

The accuracy of participants' choices were analysed along with mean response time and a measure of whether the predictive arrow increased accuracy. The percentage of correct answers is illustrated in (figure 4.12). The percentage correct for each visual quadrant was put into a *t*-test. The bottom left quadrant, FM's blindfield was not significantly different from the other visual quadrants ($p = .103$).

	No of Trials	No. Correct
Aware	115	112
No	10	2
Yes	3	1

Table 4.2. FM felt aware something was in her blind field 89.84% of the time

The validity effect of a predictive arrow increased the accuracy of correct responses for the control group, but not for FM (see figure 4.13). FM's response time was five times slower; 4563ms compared to 868ms for the controls. The average time for FM to respond to stimuli in the blindfield was 6852ms.

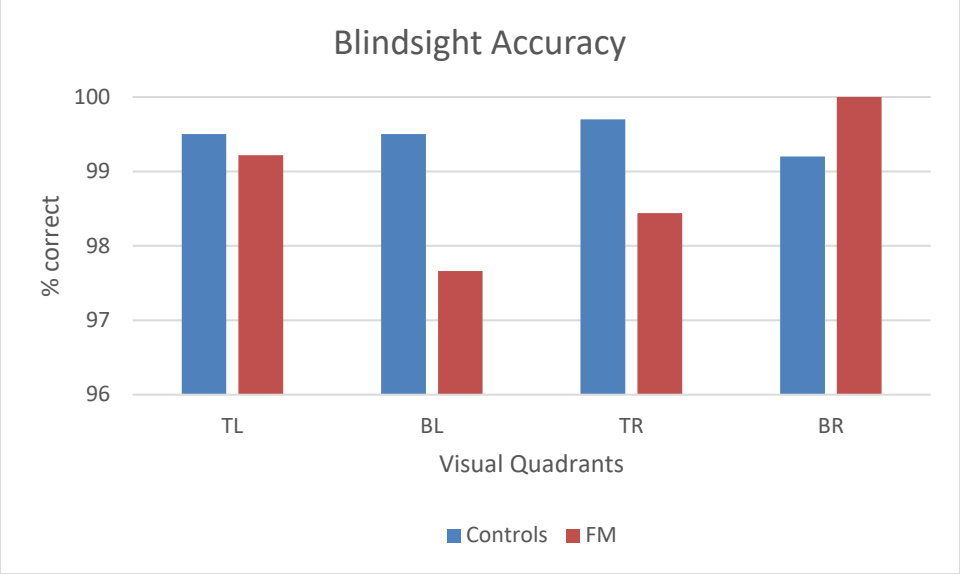


Figure 4.12. The accuracy of the bottom left blind visual quadrant did not differ from the other three quadrants (p =.103)

FM's verbal responses to every trial showed a clear awareness that something was in her blind field (see table 4.2). 89.84% of trials FM claimed to be able to "see' something. But was adamant that she could not tell whether there was a circle, or if there was a horizontal or vertical stripe.

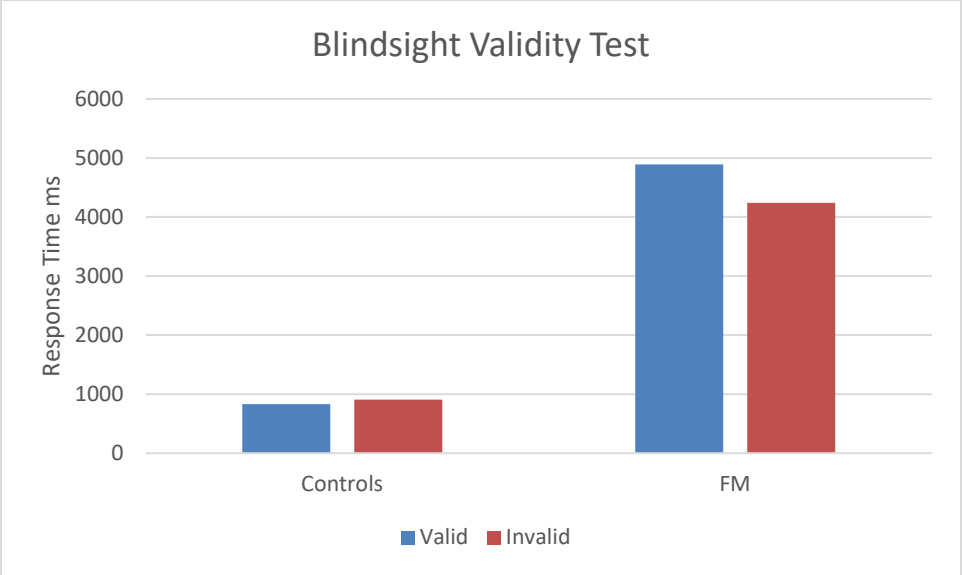


Figure 4.13. There was no predictive value of an arrow for FM. Response times 5x slower than controls for stimuli falling in non-blind field

SUMMARY OF RESULTS

The results of the clinical investigation were extremely surprising. FM had more deficits than we had possibly assumed from her aetiology. She has optic ataxia (that has controlled for her visual field cut), she has agnosia for mirrored and oriented stimuli, difficulty identifying degraded stimuli and ipsilesional neglect. Each of these tests will be discussed in turn. For the landmark and identity cueing test, FM showed more of a cueing advantage for the identity cues, than the landmark cues.

Neglect

Left sided neglect was expected from right brain damage, however the right hemispatial neglect is consistent throughout the Bells task, the line bisection task and with FM's self-reports of "losing the ends of numbers". There does not appear to be any damage to parietal areas on the left side of the brain which would normally indicate right-sided neglect. The foveal range of sight for FM is intact, the quadrantanopia affects only the lower left periphery, and therefore this anomaly cannot be attributed to FM's visual field cut.

Right parietal and frontal white matter tracts have been linked to neglect symptoms (Maarten, Saj, Loublad, 2016). Fiber tracts projecting from these locations indicated that posterior parts of the superior longitudinal fasciculus (SLF), as well as nearby callosal fibers connecting ipsilateral and contralateral parietal areas, were associated with perceptual spatial deficits, whereas more anterior parts of SLF and inferior fronto-occipital fasciculus (IFOF) were predominantly associated with object-centered deficits. In addition, connections between frontal areas and superior colliculus were found to be associated with the exploratory deficits.

Shimozaki, Kingston & Olk (2006) used the cueing effect to assess two patiemts with neglect from right hemisphere lesions. Both patients had difficulty with left (contralesional) signals when preceded by a right (ipsi-lesional) cue. This pattern is similar to extinction. Despite similar behavioural results, the patients' estimates in the left field suggested two different types of attentional deficits. CM disrupted selective attention and HL uncertainty locating the target, regardless of the cue's field.

Riestra, Wormack & Crucian (2002) invetsigated whether neglect was perceptual problems correlated with assessing the resulting size of the two sections. They concluded the

perceptual deficit was from lesions in the dorsal stream and comparing the length of two sections, might be mediated by the ventral stream.

A wide research of the literature revealed only two papers with ipsilesional neglect. The first paper, Vallar (2011), found that lesions of the posterior parietal cortex, specifically the right temporal-parietal junction led to a bias of spatial representation and unilateral neglect of the ipsilateral space, with impaired visuospatial short-term memory. The lesion corresponds with FM's and FM had also reported impaired short-term memory, especially when trying to recall numbers, such as her bank account.

The other has been reported in a very large study carried out in the Netherlands. 335 stroke patients with neglect were tested and classified into left or right hemispatial neglect regardless of lesion area (Ten Brink, Verwer, Biesbroek, Visser-Meily & Nijboer, 2017). Left hemispatial neglect correlated only with a right hemisphere lesion, but right hemispatial neglect arose from both left and right hemisphere lesions, but always in the temporoparietal area.

Only one paper describes the phenomena of right hemispatial neglect after a left sided tumour resection. The patient (unnamed) showed clear right sided neglect and transcortical sensory aphasia (DeDios-Stern, Durkin & Soble, 2019). This is a kind of aphasia that involves damage to specific areas of the temporal lobe of the brain, resulting in symptoms such as poor auditory comprehension, relatively intact repetition, and fluent speech with semantic paraphasias (a word semantically similar to the intended word). His tumour was perfectly opposite to FM's, in the left temporoccipitalpareital lesion

It is possible FM is less able to make corrective saccades to the RVF. This theory could explain FM's unusual right sided neglect as shown in the Bells task and her self-report of

“missing the ends of numbers”. Anderson (1997) has shown a ‘crossover effect’. The crossover effect is where line bisection of one hemispatial side, crosses over to the other hemispatial side in shorter lines. This could explain FM’s line bisection erring towards the right with shorter lines, in contrast with the left bisection of the longer lines. As the scoring method controlled for line length by converting to percentages, it is possible this right biased neglect is a crossover effect.

Optic Ataxia

Optic ataxia is difficulty reaching into the contra-lesional space. Could this be related to right-sided neglect? A study has shown more difficulties when reaching with hand and target in lower visual field (Bartolo, Angela; Rossetti, 2018; Patrice; 2013). The case of MH reported by Cavina-Pratesi, Connolly, & Milner (2013) showed deficits in the contralesional space, when using his peripheral vision. Pisella ,Sergio, Blangerp, Torchin, Vighetto and Rossetti (2009) report contralesional misreaching. The IPS and POJ has been implicated in many papers for optic ataxia (Kanrath & Perenin, 2005; Pisella et al. 2009; Cavina-Pratesi et al 2013). Pisella et al. (2009, 3039) states “ the optic ataxia is erroneous spatial coding of the peripheral targets due to lesions of the POJ”. Earlier work from Battaglia-Mayer & Caminiti (2002) implicate the SPL and suggest optic ataxia is due to a breakdown of hand, eye information in the parietal neurons. As previously mentioned, the parietal-occipital sulcus is thought to be involved in error correction of saccades. This may be the route of cause of FM’s OA due to the lesion in parietaloccipital cortex.

VOSP

FM appears to have difficulty forming perceptual wholes with degraded stimuli. This task is likely to reflect connectivity, as naming and shape processing is involved in the task. Functional connectivity of the left and right medial lateral occipital cortex was implicated in a patient impaired in object recognition (Milner & Goodale, 1992; Walsh & Butler, 1996; Ptak, Lazeyras 2019). Warrington and James (1991) described this a pre-semantic perceptual processing problem. FM had more difficulty processing 'shape envelopes' or silhouettes of artefacts over natural object (animals). Processing shape configuration is more demanding for artefacts than for natural objects and stimulus degradation, including silhouettes, has more devastating effects on the recognition of natural objects than on the recognition of artefacts (Peelen & Caramazza, 2012).

Orientation Agnosia

FM was unable to identify the "real" object out of 3 distractors, but these objects were all upside down. FM's orientation agnosia was confirmed after carrying out the MOAT. As expected with a parietal occipital lesion, she showed mirror agnosia and orientation agnosia, specifically for rotated stimuli. The mirrored stimuli deficit was reported to be associated with the right inferior parietal sulcus, extending to the intraparietal sulcus and the superior temporal gyrus (Martinaud et al's 2016). This evidence correlates well with FM's lesion.

Blindsight

FM showed a clear ability, well above chance to report whether a grating was horizontal or vertical. Danckert & Culham (2010), have shown that extraocular light scatter can fall on to portions of the retina that still have vision intact. It is likely that FM could see some light coming into her blind field. The stimuli were a fairly high contrast of gray and black stripes. However, this experiment has equal amounts of light in both grating conditions, so it not conclusive that the accuracy of responses could be due to extraocular light. Because of the nature of grating the striped grating, the light would have to reflect exactly, rather than "scatter" to give a true result of extraocular light scatter.

The accuracy of the results in FM's blind field, plus the feeling of seeing something, with eye movements controlled for (Weiskrantz et al, 1974), leads to a diagnosis of type II blindsight.

DISCUSSION

Marin et al (2017) show right hemisphere tumours are synonymous with neglect, visuo-spatial attention and visual planning. A battery of clinical tests has revealed FM has not only the pre-diagnosed quadrantanopia, but also a right-sided ipsilesional neglect, agnosia for mirrored stimuli, orientation agnosia, optic ataxia and blind-sight.

The case study revealed an onset of tumour symptoms such as headaches, gastric uprising (nausea), déjà vu, confusion, loss of direction, phosphenes, neglect, as well as fragmented or loss of vision. Immediately post-surgery, FM experienced colour anomia, loss of direction and severe neglect symptoms (which diminished over a month or so). With the benefit of hindsight, the evidence of a simple partial, or more recently termed "focal" (awareness maintained) form of epilepsy (Stafstrom & Carmant, 2015) was clear in FM's symptoms leading up to the diagnosis

of her tumour. The déjà vu is a psychological symptom of epilepsy. Ictal (the period of a seizure, Huffman & Stern, 2010) déjà vu is the type that comes from temporal lobe epilepsy, from simple partial epilepsy (Illman, Butler, Souchay & Moulin, 2012). Coined as “dreamy states” by Hughlings-Jackson (1888) to describe the nebulous mental states that occur as part of simple partial seizures. Illman et al. (2012) note this déjà vu most common from familiar places, fitting with FM’s description of this feeling occurring at work. This regularly happened when she reached the top of the stairs at work, so perhaps blood pressure may have triggered this, especially as vessels would have highly compressed due to the size of the growing tumour. The autonomic symptom of gastric rising was the nauseas or unpleasant feeling “rising up from the stomach”. The phosphenes or flashing lights were most likely an aura, the name attributed to a sensory, but not motor symptom of epiliepsy. FM did not report any convulsions or motor behaviours that could have represented a more obvious form of epilepsy. But there could have been a motor symptom present as well. Even the rigidity of a little finger would suffice as a symptom (Scott, 2019). Tumour related epilepsy is the most common cause of hospitalisation for patients with malignant gliomas (Wasilewski, Serventi, Ibegbu, 2019). The sudden onset of hemineglect can be caused by non-convulsive seizures (Schomer & Drisland, 2015). Education for GPs of these warning symptoms would be instrumental in a faster diagnosis and reduction of stress for the patient.

The six-year delayed diagnosis for FM most likely incurred a considerable growth of tumour, and increased severity of symptoms. Delayed diagnosis of brain tumours is very common. Statistics in the UK show most patients visit their GP three times before being diagnosed (Scott, 2019). FM visited six times, before giving up.

Neglect is a graded extinction of stimuli, a continuum of gradually decreased attention and vision, this is in stark contrast to the field cut, which has sharp demarcation of its borders (Villumier, 2007). Left sided neglect was expected from right brain damage, but FM showed conclusive right hemispatial neglect throughout the two main neglect tasks, corroborated further with FM's self-report. Corbetta and Shulman (2011) explain neglect by the dysfunction of distributed cortical networks for the control of attention. Structural damage to the ventral area of the right parietal and frontal cortex produces neglect.

Right parietal and frontal white matter tracts have been linked to neglect symptoms (Maarten, Saj, Loublad, 2016). Fiber tracts connecting ipsilateral and contralateral parietal areas were associated with perceptual spatial deficits, connections between frontal areas and superior colliculus were found to be associated with the exploratory deficits (Maarten, Saj, Loublad, 2016). With regards to the current literature on ipsilesional neglect, it is likely FM's ipsilesional neglect is damage to white matter tracts, which would require tractography imaging to determine. But FM clearly has a lesion in the temporoparietaloccipital area, a region through which various white matter tracts pass (De Benedictis, Duffau, Paradiso, Grandi, Balbi, Granieri, Colarusso et al. 2014). The sudden onset of hemineglect can also be caused by non-convulsive seizures (Schomer & Drisland, 2015). As FM's neglect was apparent before her surgery, in her words "losing then ends of numbers", it possible the ispilesional neglect was caused by a non-convulsive seizure or the tumour pressing on the POJ, an area classically associated with neglect (Bisaiach; Husain 2001

The parietal occipital junction has been implicated in many papers for optic ataxia (Kanrath & Perenin, 2005; Pisella et al. 2009; Cavina-Pratesi et al 2013). Battaglia-Mayer & Caminiti (2002) suggest optic ataxia is due to a breakdown of hand, eye information in the

parietal neurons. As previously mentioned, the parietal-occipital sulcus is thought to be involved in error correction of saccades (Guillame, Fuller & Curtis, 2018). It is possible FM is less able to make corrective saccades to the RVF, causing this disruption of attention to the right hemifield and hand-eye coordinated movements as demonstrated in her optic ataxia. Patients with a visual field loss have been reported to make extra saccades towards their blindfield, unless there is evidence of neglect (Scholfield & Leff, 2009). In which case, saccades are biased an estimate away from the neglected field. In this case FM would be making uncorrected saccades away from both her blind field and her neglected side.

The results of the VOSP test were difficult to attribute to a difficulty in processing perceptual wholes, or whether merely orientation agnosia for FM. Functional connectivity of the left and right medial lateral occipital cortex was implicated in a patient impaired in object recognition (Nordhjem, Blake, Meppelink, Redhed, de Jong, Leeders et al. 2015). How is this different from silhouettes? The pre-semantic perceptual processing (Warrinton & James, 1992) has not been further researched or clarified this millennium. FM's large lesion does extend into the inferior temporal cortex, which the current literature shows association with shape processing (Milner & Goodale, 1992; Walsh & Butler, 1996; Op de Beeck, Torfs, Wagemans, 2008; Peelen & Caramazza, 2012). Although current research may have superseded the early work by Warrington, the visual test has been an excellent starting place for neuropsychological testing of this patient and has been critical in the discovery of her orientation agnosia.

CHAPTER 5. GENERAL DISCUSSION

This thesis presents three main experiments that systematically explore the role of dorsal stream in exogenous and endogenous cueing. This chapter will review the main findings from the experimental chapters and consider the theoretical significance of the findings, including avenues for future research.

Overview of thesis findings

Chapter one showed the that brief exposure of cues had no validity effect for ID cues. LM cues were robust under brief exposure. The following chapter used EEG to ascertain a clear C1 during the 50-100ms epoch. The LM cues showed a larger C1 waveform at the dorsal electrode placements, compared to the ID cues. Conversely the C1 waveform from the ventral stream electrodes showed a higher voltage for the ID cues, than the LM cues. sLoreta revealed little activation at C1 and only general visual areas at the P1. Our patient with a dorsal stream lesion was diagnosed with OA, after a new method was devised for controlling for a visual field cut. FM showed a larger cueing advantage for ID cues, than for LM. FM was subsequently diagnosed with ipsi-lesional neglect, orientation and mirror agnosia, but also showed clear evidence of blindsight. This makes her an ideal candidate for a novel and portable visual rehabilitation technique described.

Case Study

FM showed a clear ability, well above chance to report whether a grating was horizontal or vertical in her blind field. Whether this result is due to plasticity of the eight-year post surgery or spared island of visual cortex, then fact remains it is possible to use this phenomenon to

encourage FM to “look” into her blind field. The reason this would be beneficial is to stop neuronal connections dying off in this area, and possibly increase her field of vision. Optical therapies such as prism lenses, which FM currently uses, can cause distortion of the visual field (Scholfield & Leff, 2009). Visual field restitution, bringing stimuli into the damaged field (similar to the blindsight experiment designed for this thesis) have shown modest improvements, but the digital equipment has been expensive and difficult for patients to access in centres regularly (Scholfield & Leff, 2009). Perez and Chokron (2014) have stressed the importance of early diagnosis and an urgent need for rehabilitating therapy for patients with visual field loss, either hemianopia or quadrantanopia. Their experiment showed that harnessing unconscious visual capacities can aid with restoring conscious visual perception in the blind field.

As a suggestion for further study and a rehabilitation technique for FM and others in a similar situation is to utilise the tests made for the present study. The presence of blindsight opens the possibility of a new therapeutic regime for those with a similar type of visual field loss. Blindsight does not have to involve saccades to the area of visual loss, which is the current method employed for visual rehabilitation, and is notoriously difficult for this with visual field loss. Instead covert attention can be used to strengthen the neural pathways to or around the lesioned area.

The behavioural task of landmark and identity used cues present in all four quadrants of the visual field, so consistently encouraging the patient to “see” stimuli in any blind field, whether quadrantanopia or hemianopia or a smaller scotoma of any kind and use this cue to facilitate faster responses to the cue. The orientation task can also be used in a similar way, if the patient is instructed to focus on the middle picture only, so the left and rightward pictures fall into the periphery and a quadrant of visual field loss. The program can adjusted to fit any area of

the visual field. Finally, the blindsight test allows for practise of judgements made about stimuli in the blindfield. The patient is encouraged to tap into the unconscious perception by use of forced choice judgements. The patient could also check results to get an idea of progression and an ability to turn guessing into accuracy. The accuracy results would be a measure of improvement. Each test is easily downloaded onto a patients' laptop to convenience and ability to use daily without difficulty. The computer-generated programs designed for this thesis can easily be distributed to patients on their own laptops, enabling therapeutic design with minimal cost and ease of use. Therefore, circumventing any financial issues or difficulties accessing therapy. The patient would need to be motivated, of course. The number of trials and dates completed would all be recorded in the E-prime data, so this information would be monitored.

This would be ideally supplemented with some systematic visual scanning techniques. Those who use a greater number and larger amplitude of head and eye movements after training can avoid obstacles and have an increase in locating targets by up to 30˚ (Goodwin, 2014).

FM is currently too sick to undertake a longitudinal rehabilitation of these visual tests. Success of the vision being increased could be measured by pre and post visual acuity tests, which may show a reduced blind field or increased field of vision.

The lack of neurological assessment has significantly impacted FM's life. The diagnosis of neglect, orientation agnosia and optic ataxia could have led to a more informed rehabilitation and better quality of life. This case study highlights the urgent need for more neuropsychologists in New Zealand. Currently there are only 8 ACC registered neuropsychologists in Auckland and assessments can have up to a six-month waiting list (Hill, 2018). This unacceptably long wait misses the optimum three-month plasticity window. To train up more neuropsychologists,

Auckland University could devise a fast track neuropsychology training program. The current system produces only 11 clinical psychologists each year and approximately 1-2% of those are neuropsychologists (George, 2018). If Auckland University followed the program similar to Melbourne University, Auckland could produce many more. This proposition has the backing of Sir Richard Faull of the Centre for Brain Research, who has generously offered to match Auckland University dollar for dollar to run this program and increase the number of neuropsychologists in New Zealand.

EEG

Electrophysiological studies of ERPs are consistent with dorsal visual stream encoding of cue stimuli in the landmark task (Lambert & Wootton, 2017; Lambert et al., 2014; Marrett et al., 2011). Marrett et al. (2011) applied source localization to the early phase of the P1 ERP component elicited by landmark stimuli, and found evidence of activation in a structure associated with the dorsal stream, the SPL. When participants discriminated consciously between the stimuli used as landmark cues, source localization applied to the same ERP component (early P1) revealed evidence of activation in two structures associated with the ventral stream, ITG and FFG.

The electrophysiological experiment provided some evidence on the possible activation of temporal areas with the symbolic-semantic cueing. This was not clear cut, because of the sparse activity shown in sLoreta and small number of participants and data trials. Amending the EEG with upper visual field stimuli served to confuse the results further, this may be because the difference wave is the clearest way to discern small amplitudinal differences of the C1 (Slotnick, 2018). The ERP did provide good evidence for the anatomical separation of the cortical area V1. At the parietal-occipital electrodes, the C1 was stronger for the landmark cueing task. The

divergence of polarity for the two visual evoked potentials for the landmark and identity waveforms began at 32ms. At the temporal-occipital electrodes, the ID waveform showed a C1 amplitude, the LM waveform did not. This was a nice dissociation of support of the endogenous and exogenous attentional systems mapping onto ventral and dorsal stream, as shown by the ERP waveforms.

At the parietal-occipital electrodes, the C1 was stronger for the landmark cueing task. The divergence of polarity for the two visual evoked potentials for the landmark and identity showed a dissociation of ventral and dorsal stream activation. Both P1 and N1 visual evoked potentials were very similar, so extra-striate activation and control of attention were indistinguishable from landmark and identity cueing, which is to be expected with the proposed very early differentiation of the visual cues in attention. The latency of the P1 revealed plenty of time for visual input to have been fed forward, modulated and fed back.

Cue exposure time

The current results indicate that cue exposure time is also a key stimulus parameter in studies of visual orienting. When cues were exposed for a relatively long period, orienting effects were independent of cue visual-spatial (landmark) features, and were driven instead by its symbolic identity as a signal indicating the likely location of the target; and conversely, when cues were exposed briefly, (66 ms or less), orienting effects were driven by landmark features, independently of symbolic identity.

Visual-spatial features of the stimuli employed as cues are crucially important. For example, Kincade et al. (2005) investigated the neural correlates of attention shifting in response

to exogenous and endogenous spatial cues, using an event-related fMRI design. However, in their endogenous orienting condition, the cue stimulus comprised the transient brightening of two sides of a diamond-shape, forming an arrow-head cue pointing to the left or right. From the perspective presented here, this stimulus is clearly a landmark cue, and would be likely to recruit dorsal-stream mediated orienting, which shares many features with exogenous orienting in response to peripheral onsets, and is quite distinct from symbolic (endogenous), ventral-stream mediated orienting.

A Unified Model of Vision and Attention

Are symbolic semantic cues are mediated by the ventral stream and spatial correspondence cues are mediated by the dorsal stream? And does this data map on to the exogenous and endogenous distinction of attention? Previous research showed dorsal stream activation with the landmark cues (Marret et al 2011; Lambert & Wootton, 2017). Both also showed temporal activation with centrally presented single letter cue.

The evidence from this behavioural experiment, along with evidence cited in the discussion for that chapter have formed the basis for the theory of a unified model for vision and attention (Lambert et al. 2018). The semantic and non-semantic orienting of attention may be driven by the ventral and dorsal streams respectively and possibly map on to the endogenous, exogenous two neural processes of attentional orienting (Chica et al. 2013).

Landmark cueing has much in common with exogenous cueing, they are both rapid, utilize peripheral vision and are non-conscious. Identity cueing on the other hand, has similar properties to endogenous cueing, its time course is slower, and it is consciously controlled

(Lambert et al. 2018). The briefly presented cues were only able to be utilised in the context of landmark cueing. The identity cues only showed the Posner effect at a much longer cue presentation time. This fast, automatic attention fits with the distinction of rapid dorsal processing and slow controlled attention with focused ventral stream processing.

The target of the dorsal stream, parietal cortex, is of course, strongly associated with attention, so it seems highly likely that dorsal stream encoding of environmental cues will interact with parietal attention circuits. We propose that spatial expectancies, represented in these parietal regions (Ungerleider & Mishkin, 1982), interact with the outcome of dorsal stream visual encoding, leading to top-down facilitation of target processing at the cued location (Corbetta,& Shulman, 2011).

Clinical evidence from patient DF's ventral stream damage (Marrett et al, 2011) corroborated this hypothesis. The evidence from FM in this thesis showed a marked improvement in identity cueing, and proposed ventral route, compared to the landmark cueing and proposed dorsal stream activation.

One problem for the clinical evidence cited here is if FM could not process landmark cues because of a dorsal stream lesion, then DF should not have been able to process identity cues because of her ventral stream lesion. Perhaps the single letter perceptual cueing used in Marrett et al's (2011) was markedly different from the dual letter identity cues used currently. The proximity of FM's lesion bordering the temporal area should not have any bearing on the situation as she was clearly able to distinguish all letters. Both clinical patients described here have suffered diffuse damage to their cortices. DF is now showing dorsal stream damage from hypoxia to the POJ (Windfell, Milner and Goodale 2014). FM's damage to the temporal area

white mater tracts from radiation, illustrate the difficulties of brain injuries rarely being clearly defined or discreet. Despite the increasing size of boundaries of these patients' lesions, their behavioural outputs or motor controls remain static and well defined. DF cannot estimate aperture with her finger and thumb, but consistently, unconsciously scales her forefinger and thumb to grip the estimated object (Windfell et al. 2014). FM showed significant signs of OA.

However, that being said, we know that there are direct pathways from the occipito-parietal dorsal stream, to subcortical structures such as the superior colliculus, and to other brainstem structures that control the eye muscles and parts of the spinal cord that control the limbs (Glickstein et al. 1985; Baizer et al. 1993; Borra et al. 2014). Areas in the occipito-temporal ventral stream have few or none of these direct connections with motor systems, instead, the ventral stream interfaces with structures in the temporal and frontal lobes (Milner, 2017). Milner himself notes that "DF's problems are a result depleted interstream communications", rather than thinking of the streams as separate. Their functions are divergent, but the streams themselves are highly convergent.

The two-stream visual theory suggests that the visual information is divided. As mentioned earlier, one stimulus is clearly a landmark cue, and would be likely to recruit dorsal-stream mediated orienting, which shares many features with exogenous orienting in response to peripheral onsets. If a person has a lesion in the dorsal stream, then this dorsally mediated orienting is less able to be processed by the dorsal stream, hence to slower response to LM cues in this case, than the ID cues.

To sum up, attention-shifting based on encoding the symbolic identity of cue stimuli appears to rely on ventral stream encoding. This was shown by stronger ERPs of semantic or symbolic cues and the ability of a patient with an intact ventral stream to utilise them to respond faster to a cued target. The attention-shifting based on encoding the visual-spatial features of cues seems to rely on dorsal stream encoding, evidenced by rapid responses to visuospatial cue, a stronger C1 waveform in the dorsal area and the inability of a patient with a lesion in the dorsal stream to utilise these cues. The neuropsychological tests administered in this research are able to inform the clinical world and provide some kind of therapeutic measure.

CONCLUSION

The aim of this thesis was to bridge the two psychological schools of cognitive neuroscience and clinical psychology. The results have revealed several new strands of neuroscientific evidence to be woven into the growing body of research in support of the Unified Model of Vision and Attention (Lambert et al. 2018).

Brief cue exposure times appear only to be processed by rapid firing dorsal neurons, not slow and sustained ventral neurons. The very early attentional C1 waveforms are larger for LM cues in the dorsal areas and larger for ID cues in the ventral areas. A clinical patient with a mainly dorsal stream lesion in POJ, utilised ID cues (ventrally biased attention cues), but was unable to utilise the LM cues (dorsally biased attention-biased cues).

The sound clinical testing of this patient revealed a rare neuropsychological disorder (ipsi-lesional neglect), and the attention and visually based paradigm sowed the seeds for a novel visual rehabilitation technique, which may serve to increase the visual field of cortically

blind patients after a period of at least three months. Further testing is needed, but gives a clear clinical direction to follow, in the spirit of the scientist-practitioner.

The wide range of tumour symptoms listed in this thesis would provide an ideal checklist for GP's when dealing with patients of possible tumour cases. This would ideally be communicated throughout the health care community.

Thorough and faster neuropsychological testing for our patients in NZ, within the early and most life changing window of plasticity, is essential.

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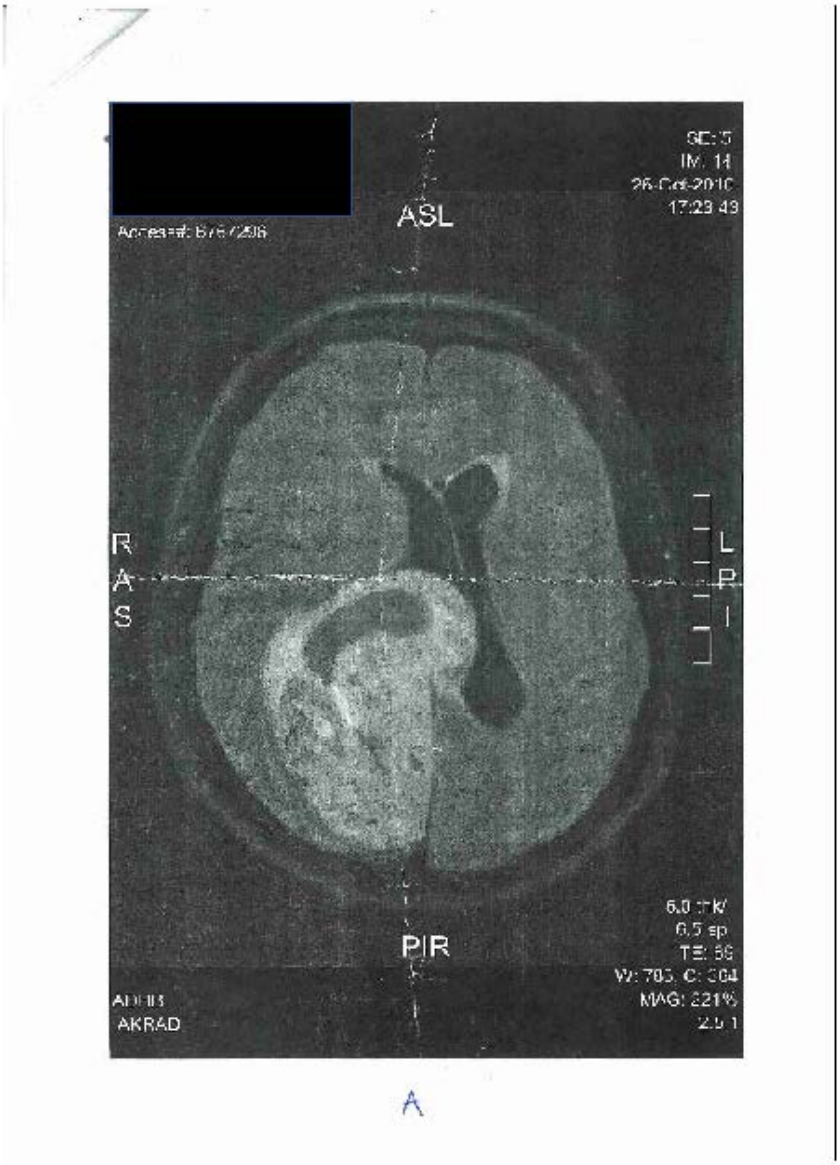
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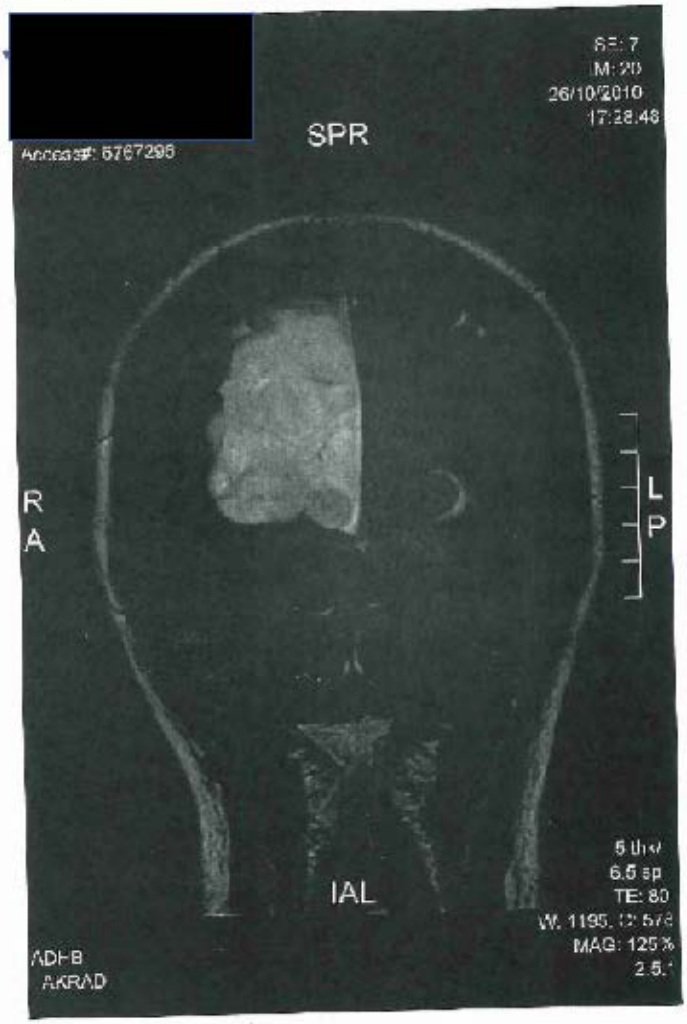


B

Patient: [redacted]
Date of Birth: Jan 08, 1968
Gender: Female
Patient ID: 1717927083

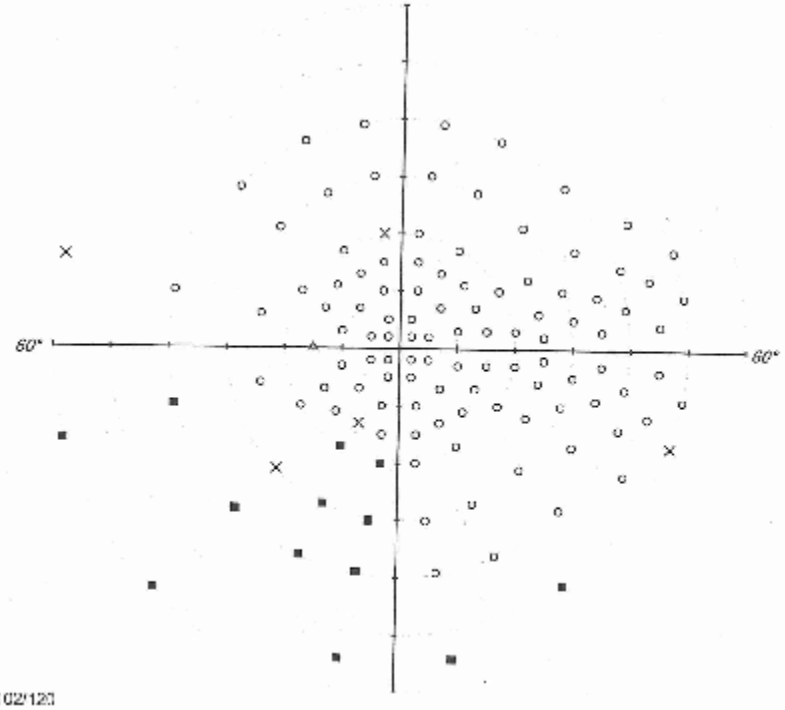
ZEISS
University Of Auckland

LEFT

OS Suprathreshold Full Field 120 Point Suprathreshold Test

Fixation Monitor:	Gaze/Blind Spot	Stimulus:	III, White	Date:	Jul 27, 2017
Fixation Target:	Central	Background:	31.5 asb	Time:	11:58 AM
Fixation Losses:	0/19	Strategy:	Three Zone	Age:	49
False POS Errors:	0/14	Test Mode:	Age Corrected		
False NEG Errors:	0/13	Pupil Diameter:			
Test Duration:	07:00	Visual Acuity:			
		Rx:	-5.50 DS		

Central Reference: 33dB
Peripheral Reference: 33dB



o Seen 102/120
× Defect 5/120
■ Not Seen 13/120
△ Blind Spot

Comments

ZEISS

C

Patient: [redacted]
Date of Birth: Jan 08, 1968
Gender: Female
Patient ID: 1717927083

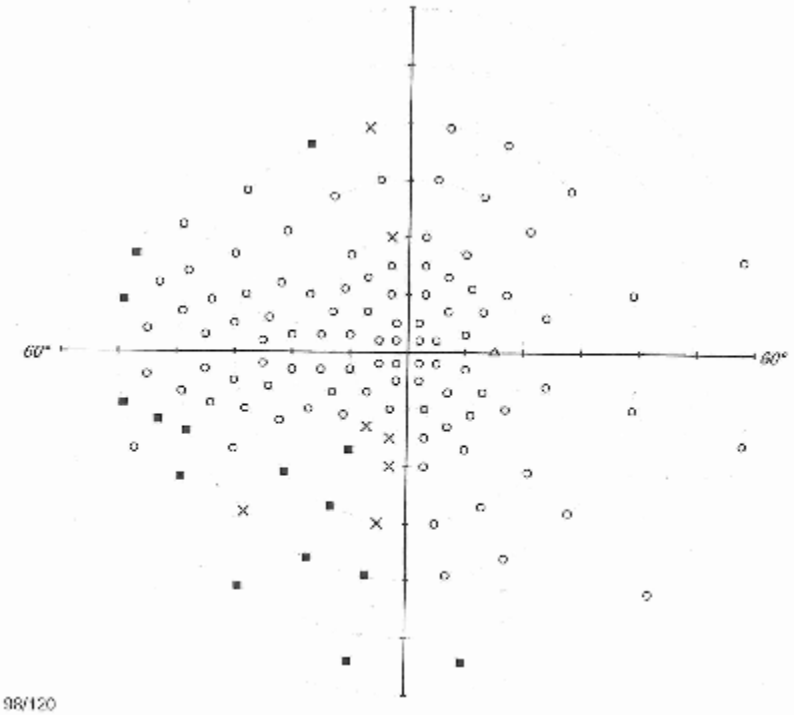
ZEISS
University Of Auckland

RIGHT

OD Suprathreshold Full Field 120 Point Suprathreshold Test

Fixation Monitor:	Gaze/Blind Spot	Stimulus:	III, White	Date:	Jul 27, 2017
Fixation Target:	Central	Background:	31.5 asb	Time:	11:47 AM
Fixation Losses:	0/18	Strategy:	Three Zone	Age:	49
False POS Errors:	0/15	Test Mode:	Age Corrected		
False NEG Errors:	0/13	Pupil Diameter:			
Test Duration:	07:06	Visual Acuity:			

Central Reference: 33dB
Peripheral Reference: 33dB
Rx: -5.25 DS -1.50 DC X 82



○ Seen 98/120
X Defect 7/120
■ Not Seen 15/120
△ Blind Spot

Comments

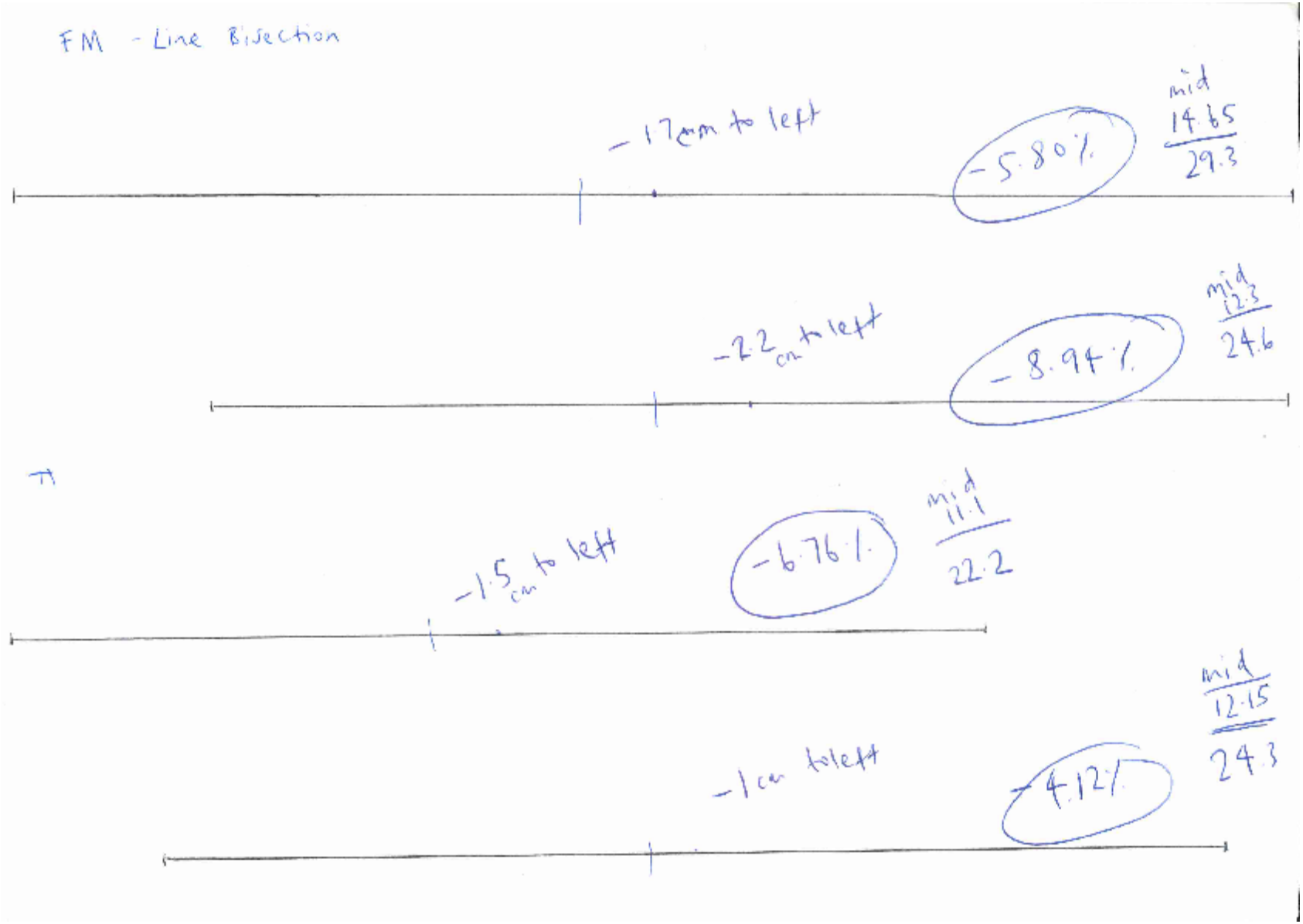
ZEISS

Version 2.40.0

Page 1 of 1

D

FM
Examiner
30
35
E


FM - Line Bisection
-1.7cm to left
-5.80%
mid
14.65
29.3
-2.2cm to left
-8.94%
mid
12.3
24.6
-1.5cm to left
-6.76%
mid
11.1
22.2
-1cm to left
-4.12%
mid
12.15
24.3

Appendix G

BRAIN TUMOUR CHECKLIST (Mnemonic – HEEMM)

HEADACHES

- persistent headaches, particularly if the person has no history of severe headaches
- headaches that increase in intensity over time
- headaches that are worse in the morning
- headaches that wake people up from sleep

EPILEPSY

- odd feelings, often indescribable
- unusual smells, tastes
- unusual feelings or experiences – "out-of-body" sensations; feeling detached; body looks or feels different; situations or people look unexpectedly familiar or strange; Déjà vu
- feeling spacey, fuzzy, or confused
- periods of forgetfulness or memory lapses
- daydreaming episodes
- jerking movements of a finger, arm, leg, or body
- falling
- tingling, numbness, or feelings of electricity in part of the body
- unexplained confusion, sleepiness, weakness
- losing control of urine or stool unexpectedly

- gastric uprising, nausea

EYE SIGHT

- vision problems

MOOD

- changes in personality
- memory loss
- mood swings
- fatigue
- anxiety or depression
- difficulty concentrating
- difficulty communicating as usual

MOVEMENT

- tingling or stiffness on one side of the body
- loss of balance
- loss of coordination
- muscle weakness
- feeling confused or disorientated