View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by YorkSpace

NEURAL MECHANISMS OF TRANSSACCADIC INTEGRATION OF VISUAL FEATURES

Bianca-Ruxandra Baltaretu

A THESIS SUBMITTED TO THE FACULTY OF GRADUATE STUDIES IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE

GRADUATE PROGRAM IN BIOLOGY

YORK UNIVERSITY

TORONTO, ONTARIO

February, 2016

© Bianca-Ruxandra Baltaretu, 2016

ABSTRACT

This thesis explores the neural mechanisms of transsaccadic integration of visual features. In the study, I investigated the cortical correlates of transsaccadic integration of object orientation in multiple reference frames. In a functional MRI adaptation (fMRIa) paradigm, participants viewed sets of two orientation stimuli in each trial and were asked to indicate if the orientations were the same (‘Repeat’ condition) or different (‘Novel’ condition). Stimuli were presented in one of three spatial conditions: 1) space-fixed, 2) retina-fixed and 3) frame-independent. Results indicate that, in addition to common activation in frontal motor cortical regions in all three spatial conditions, parietal and occipitotemporal regions are active in the space-fixed condition, parietofrontal regions are active in the retina-fixed condition, and parietofrontal and occipitotemporal regions are active in the frame-independent condition. In conclusion, these results indicate that transsaccadic integration involves differential activation of cortical areas, depending on the frame of reference.

DEDICATION

This thesis is dedicated to my parents.
Thank you for always supporting me and
encouraging me to fulfill all of my dreams.

ACKNOWLEDGEMENTS

I would like to express my immense gratitude to my supervisor, Dr. J. Douglas Crawford, who gave me the incredible opportunity to conduct neuroimaging research in his laboratory and who has provided unwavering support and guidance. Thank you for entrusting me with this project and for expanding my research horizons by allowing me to communicate to and with world-renowned researchers. I am also honoured to have been given the opportunity to be a part of an exciting and inspirational transatlantic collaborative program. It is more than I could ever have dreamed of and I feel truly grateful to have an exemplary academic role model such as you.

I would also like to thank my co-authors, Drs. Benjamin T. Dunkley, Simona Monaco and Ying Chen. Thank you very much for teaching me the steps to running a transsaccadic integration task, for teaching me how to analyze functional imaging data, and for always graciously answering any questions I had.

I would also like to thank the wonderful members of the Crawford Lab for the excellent atmosphere in which I always feel comfortable and encouraged to converse and think about research. Thank you for your help, time, feedback and for your comradery, all of which have helped me grow.

I would like to convey how privileged I feel to have pursued my graduate studies in the Centre for Vision Research, as I have been surrounded by leading researchers who have inspired me throughout my journey. From among them, I would especially like to thank the members of my examining committee, Drs. Joseph F. X. DeSouza, Keith A. Schneider and W. Dale Stevens who have taken the time to converse with me about research, for their helpful suggestions and feedback, and for their thoughtful questions.

TABLE OF CONTENTS

ABSTRACT ……. ii

DEDICATION …….. iii

ACKNOWLEDGEMENTS …….. iv

TABLE OF CONTENTS …….. v

LIST OF TABLES …… vi

LIST OF FIGURES …….. vii

CHAPTER 1: INTRODUCTION ……. 1

1.1 Introduction …… 2

1.2 Saccades ……. 2

1.2a Behavioural aspects ……. 3

1.2b Subcortical and cortical physiology ……. 6

1.3 Visual working memory …… 10

1.3a Behavioural aspects ……. 10

1.3b Cortical physiology ……... 12

1.4 Spatial updating during saccades…….. 14

1.4a Behavioural aspects ……. 14

1.4b Cortical physiology ……... 15

1.5 Perception and memory of object orientation …….. 16

1.5a Psychophysics …….. 17

1.5b Cortical physiology …….. 19

1.6 Transsaccadic feature integration …….. 22

1.6a Reference frames …….. 23

1.6b Theoretical explanations of transsaccadic integration …….. 24

1.6c Psychophysical studies …….. 25

1.6d Physiological studies (monkeys, fMRI, TMS) …….. 27

1.7 Functional magnetic resonance imaging adaptation (fMRIa)…….. 29

1.7a fMRIa basics…… 30

1.8 Aims and hypotheses of the study …….. 34

CHAPTER 2: TRANSSACCADIC INTEGRATION OF VISUAL FEATURES AND SPATIAL INFORMATION…….. 37

2.1 Introduction …….. 38

2.2 Orientation experiment …….. 40

2.2a Participants …….. 40

2.2b Experimental set-up and stimuli …….. 40

2.2c Imaging …….. 41

2.2d General paradigm/procedure …….. 43

2.2d.i Experiment …….. 43

2.3 Analysis …….. 44

2.3a Behavioural data ……..…. 44

2.3b Functional imaging data ……..…… 45

2.3.i Experimental data ……. 45

2.3.ii Localizer data ……..… 48

2.4 Results ……..…….. 50

2.4a Space-fixed condition ……..…... 50

2.4b Retina-fixed condition ……..…… 54

2.4c Frame-independent condition ……..…….... 56

2.4d Conjunction results ……..…….. 58

2.4e Time courses ……..…… 58

2.4f Localizer results ……..…….. 61

2.5 Discussion ……..…….. 62

2.5a Common areas ……..…. 63

2.5b Transsaccadic judgments of Space-fixed stimuli ……..…... 64

2.5c Transsaccadic judgments of Retina-fixed stimuli ……..... 66

2.5d Transsaccadic judgments of Frame-independent stimuli ……... 67

2.5e Integration of our 3 networks within the general transsaccadic network ……. 69

2.5f Conclusion: overall comparison of results from the three spatial conditions.……..…. 69

CHAPTER 3: GENERAL DISCUSSION ……. 71

3.1 Discussion …… 72

3.2 Contributions to transsaccadic literature ……..... 72

3.3 Unresolved questions.……... 74

3.4 Possible applications (medical, industrial, transportation safety) ……..... 76

3.5Future directions ……. 78

REFERENCES ……..……..…. 80

LIST OF TABLES

Table		Page
1	Cortical regions and their associated acronyms ……...	51
2	Talairach coordinates of cortical correlates ……..	52

LIST OF FIGURES

Figure		Page
1	Example rendering of the brain and associated cortical regions……..…	8
2	Transsaccadic integration example……..	22
3	fMRIa expectations for repetition suppression and enhancement……...	31
4	Reference frame examples (space-fixed, retina-fixed, frame-independent)	35
	Results from Experiment	
5	*5.1 Experimental set-up, paradigm, test combinations.*…….……	42
6	*5.2 Cortical correlates for space-fixed condition* ……	53
7	*5.3 Cortical correlates for retina-fixed condition* ……...	55
8	*5.4 Cortical correlates for frame-independent condition* ……...	57
9	*5.5 Cortical correlates for spatial condition conjunction analyses* ……	59
10	*5.6 Time courses for selected cortical areas* ……..……..	60
11	*5.7 Cortical correlates of saccade, retinotopic localizers* ……...	61
12	*5.8 Neural network model for the three frames* ……..……	68

CHAPTER 1

GENERAL INTRODUCTION

1.1 Introduction

Vision is a composite of the retinal information obtained from a series of fixations and movements of the eye. Within one fixation of the eye, we can obtain highly detailed information centrally through the fovea and less detailed, poorer visual acuity information peripherally. We sample our visual surroundings several times per second when we make saccades (Rayner, 1998). This behaviour allows us to re-orient the fovea to, ultimately, obtain a 'sharp' or detailed visual perception of our environment. We are able to maintain the information we capture from one fixation to the next and, somehow, integrate these pieces of information to obtain a complete view and understanding of our (visual) surroundings.

The type of information that we are able to extract within one fixation and integrate has been investigated previously. This type of research has focused on both low-level components of the visual world, or features, such as orientation, colour and luminance (Prime, Vesia, & Crawford, 2011), and more complex stimuli such as visual scenes/locations and faces (Epstein, Harris, Stanley, & Kanwisher, 1999; Kanwisher, McDermott, & Chun, 1997). Our ability to remember and combine information from one fixation to the next has also been investigated within an everyday task, such as reading (Irwin, McConkie, & Zola, 1980). These investigations suggest that we can extract different types of information from our visual surroundings within a fixation and integrate this information across a series of saccades. Here, I will consider the underlying processes in greater detail.

1.2 Saccades

Although the term, 'saccade,' in French refers to the jerky movement of a horse's head upon tugging on its reins, Javal (Javal, 1879; Leigh & Zee, 2005) and Landolt (Landolt, 1891;

Leigh & Zee, 2005) first used it in association with a particular type of eye movement. They used the term ‘saccade’ to refer specifically to rapid movements of the eye, such as those made while reading (Javal, 1879; Landolt, 1891; Leigh & Zee, 2005). Later, Dodge (1919) was able to distinguish saccades from other types of eye movements. Yarbus (1967) emphasized the role of saccades, with specific reference to looking at different aspects of the visual scene during visual search tasks for example. Yarbus (1967) also outlined the many types of saccades that are available in our saccadic repertoire: volitional (voluntary), predictive (made to a position where the target is anticipated to appear), memory-guided (relative to the remembered target position), those that are carried out in response to a command, reflexive, express (small amplitude, very rapid, involuntary eye movements), among others. Although they can be differentiated into different classes, they have also been shown to share certain behavioural traits. Moreover, the subcortical and cortical networks that are involved in programming and executing saccades have also been documented. I will discuss their behavioural characteristics, along with the subcortical and cortical networks involved in further detail below.

1.2a Behavioural aspects

Saccades can be characterized behaviourally in terms of their velocity, duration, reaction time/latency, as well as in terms of accuracy. To start off, certain characteristics of saccades have been linked, such as velocity/duration and amplitude (Abel, Troost, & Dell’Osso, 1983; Bahill, Clark, & Stark, 1975; Garbutt, Han, Kumar, Harwood, Harris, & Leigh, 2003). This relationship between these characteristics has been referred to as the ‘main sequence’; it describes a typical relationship between saccade velocity and amplitude or duration and amplitude (Bahill et al., 1975). The former relationships can be defined by an exponential equation or a power equation (Lebedev, Van Gelder, & Tsui, 1996). By using these characteristic curves/relationships, we can

derive a normal range of values (Sharpe, Troost, Dell'Osso & Daroff, 1975; Sharpe & Zackon, 1987). We can also make use of these values to classify behaviours within clinical populations. Other factors such as fatigue, luminance and the predictability of a target can play a role in altering those relationships (Becker & Fuchs, 1969; Fletcher & Sharpe, 1986; Sharpe et a., 1975; Smit, Van Gisbergen & Cools, 1987). Nevertheless, on average, saccade peak velocity can range from 30 to 700 degrees/second, whereas the duration of a saccade can be of 30 to 100 milliseconds for saccade amplitudes of 0.5° to 40° (Bahill et al., 1975; Smeets & Hooge, 2003; Smit et al., 1987). (However, once a saccade has been initiated, its velocity cannot be changed or controlled (Becker & Fuchs, 1969; Fletcher & Sharpe, 1986; Sharpe et al., 1975; Smit et al., 1987).) These relationships are similar for horizontal and vertical saccades, and are not altered by factors such as age (Huaman & Sharpe, 1993; Sharpe & Zackon, 1987).

Another characteristic of eye movements/saccades is the time to onset of a saccade after the presentation of a target or 'go' signal, i.e., latency (Leigh & Zee, 2005; Sharpe & Wong, 2005). Saccade latency is approximately 150 to 200 milliseconds (Sharpe & Wong, 2005). Saccade latency can be modulated by factors such as the type of target stimulus that is presented. For example, the latency may vary differentially in response to object features such as luminance, contrast, and size, just to name a few (Doma & Hallett, 1988; Groner & Groner, 1989). Motivation and attention can also influence saccade latency, as well the modality of the stimulus (visual or auditory, for example) (Carpenter, 2004; Reddi, Asrress & Carpenter, 2003; Zambieri, 2002). Also, the starting position of the eye relative to the end position or the predictability of the target stimulus can affect saccade latency (Shelhamer & Joiner, 2003). This characteristic of saccades has been probed previously using gap tasks/stimuli (Kalesnykas & Hallett, 1987). These experiments are conducted in a dark room, whereby participants are asked

to fixate on a stimulus initially. The fixation cross may disappear, signaling to the participant to move their eyes to a saccade target. The time from the 'go' signal until the presentation of the target stimulus is varied. Using this type of experimental set-up, it has been demonstrated that when the fixation light is turned off 100 to 400 milliseconds before the presentation of the target stimulus, saccade latencies are much shorter than when the fixation and target overlap, for example (Kalesnykas & Hallett, 1987).

Lastly, saccadic accuracy has also been intensely investigated. On average, saccades tend to be quite accurate; however, even under normal circumstances, saccades may undershoot (hypometria) or overshoot (hypermetria) the target (Weber & Daroff, 1971). The difference between the saccade target and actual landing position (i.e., dysmetria) may show as much as 10% of the total saccade amplitude (Becker & Fuchs, 1969; Troost, Weber & Daroff, 1974) for predictable saccades. More often than not, saccades tend to be hypometric (undershoot the target) if targets are presented in the periphery, whereas hypermetria (overshooting of the target) is more likely when targets are presented more centrally (Collewijn, Erkelens & Steinman, 1988). Luminance and size of targets can also influence saccadic accuracy by drawing the saccade toward a brighter or larger target stimulus (Deubel, 1989). Saccadic accuracy has also been tested in scenarios when the target is present or when it is required to remember the target. It turns out that accuracy is higher for visually-guided saccades than for memory-guided saccades (Opris, Barborica & Ferrera, 2003). If participants are fatigued or advanced in age, saccadic accuracy may be slightly compromised, showing more hypometry and secondary, corrective saccades (second or third saccades that bring the eye to look at the target) (Abel et al., 1983). Overall, saccades are quite accurate, but can be modulated by the type of stimulus presented, as well as by other factors such as fatigue and age.

1.2b Subcortical and cortical physiology

Saccades are generated through an intricate, yet clearly delineated subcortical neural network. The production of a saccade involves two important phases: 1) the actual movement of the eyes (the pulse) and 2) the stopping of the eye (the step). The progression of a saccade starts off with a gaze command from a midbrain structure, called the superior colliculus (SC) (Sparks & Mays, 1990). The SC projects to the brainstem and uses neural firing frequency to communicate information about saccade direction, amplitude and velocity, especially for visually-guided saccades (saccades that are made in response to a visible saccade target) (Sparks & Mays, 1990). In the brainstem, structures, such as the pons, generate signals that can produce the pulse phase of saccades, in many directions- horizontal, vertical and torsional (Horn & Buttner-Ennever, 1998; Horn, Buttner-Ennever, Suzuki, & Henn, 1995). Specifically, neurons within the paramedianpontine reticular formation are responsible for generating horizontal saccades (Hikosaka et al., 1978; Strassman, Highstein & McCrea, 1986), whereas neurons in the rostral interstitial nucleus of the medial longitudinal fasciculus are involved in generating vertical saccades (Buttner-Ennever & Buttner, 1978; Buttner, Buttner-Ennever & Henn, 1977; Horn & Buttner-Ennever, 1998; Shiraishi & Nakao, 1995). The pons can also indicate the size of the saccade, in addition to its direction (Hepp & Henn, 1979; Scudder, Kaneko, & Fuchs, 2002). In order to produce the step of the saccade, or the holding of the eye at a particular position, a neural integrator is required to calculate, based on eye position signals, how the eye has moved and how it needs to move (Sparks, 2002). The neural integrator has been found in the brainstem (nucleus interstitialis of Cajal, INC; and nucleus prepositus hypoglossi, NPH; Crawford & Vilis, 1993; Moschovakis, 1997; Moschovakis, Scudder & Highstein, 1991a; Moschovakis, Scudder & Highstein, 1991b). The signals passed on by the SC to brainstem burst neurons (to produce the

pulse) and those passed on from neural integrators (to produce the step) excite and inhibit motoneurons that control extraocular muscles (Sparks & Mays, 1990) to generate ultimately the saccade.

Now that we know how saccades are produced at the subcortical level, we can look at cortical modulation of saccades and their production. There are several cortical areas that have been shown to play a role in saccade generation. One area that has been implicated in saccade production is located within the parietal lobe, namely the parietal eye field (PEF; see Fig. 1) (Muri, Iba-Zizen, Derosier, Cabanis, & Pierrot-Desseiligny, 1996). In humans, it has been localized to a region within the mid-posterior intraparietal sulcus, mIPS (Muri et al., 1996; Vesia, Prime, Yan, Sergio, & Crawford, 2010). In monkeys, this area is also found within the parietal lobe; however, it is referred to as the lateral intraparietal area (LIP) in non-human primates (Andersen, Asanuma & Cowan, 1985). The LIP has been shown to process information that is obtained across saccades (such as the location of a visual target of interest) which might be important in planning an upcoming saccade towards a particular location in space (Andersen, Brotchie & Mazzoni, 1992). From lesion and stimulation studies, the PEF has been shown to play a role in helping to produce accurate eye movements in memory-guided saccade tasks (a visual target is presented, followed by a delay period where the target position must be remembered, and then an eye movement toward the remembered target must be made) (Gnadt & Anderson, 1988), and in visually-guided saccade tasks (eye movements are made towards the visual target while it is still visible or on the screen) (Gaymard, Ploner, Rivaud, Vermersch, & Pierrot-Deseillginy, 1998). However, the PEF is mainly known for its role in producing reflexive saccades (Pierrot-Deseilligny, Rivaud, Gaymard & Agid, 1991). Thus, in the parietal lobe, the

PEF seems to be involved in processing and in helping to plan saccades (especially reflexive rapid eye movements).

There are also frontal regions that are involved in saccade generation and processing. Medially, there are two frontal areas that are involved in production of saccades, namely the supplementary eye field (SEF; Schlag & Schlag-Rey, 1987; Schlag-Rey, Amador, Sanchez &

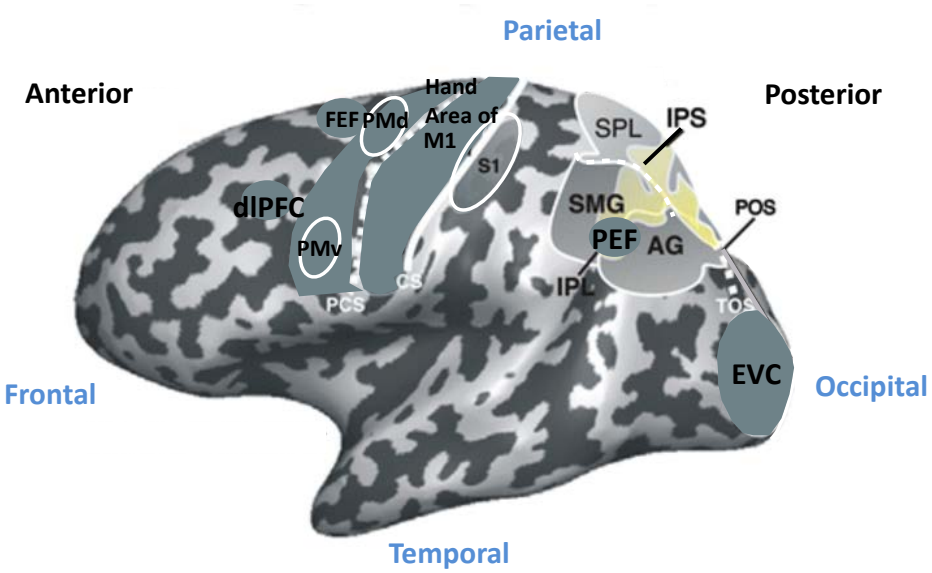

Figure 1. Inflated rendering of a typical human brain. The left, lateral side of the brain depicts the front of the brain (anterior) and the right side of the brain represents the back, or posterior, of the brain. Shown on the inflated brain are cortical regions that are described in text. The four lobes of the brain are shown (Frontal, Parietal, Occipital and Temporal). FEF: frontal eye field; PMd: dorsal premotor cortex; M1: primary motor cortex- the hand motor area; PMv: ventral premotor cortex; PCS: precentral sulcus; CS: central sulcus; S1: primary somatosensory cortex; SPL: superior parietal lobule; SMG: supramarginal gyrus; IPS: intraparietal sulcus; PEF: parietal eye field; IPL: inferior parietal lobule; AG: angular gyrus; POS: parieto-occipital sulcus; TOS: transverse occipital sulcus; EVC: early visual cortex; SC: superior colliculus, midbrain structure. Not shown on the medial side are SEF: supplementary eye field; ACC: anterior cingulate cortex; CEF: cingulate eye field. Modified from Vesia & Crawford, 2012.

Schlag, 1997) and the cingulate eye field (CEF) (Gaymard et al., 1998). The SEF has been shown to be involved in the production or control of the motor commands for eye movements (and/or for limb movements) (Pierrot-Deseilligny, Israel, Berthoz, Rivaud, & Gaymard, 1993), as well as in initiating saccades (Muri, Roesler & Hess, 1994). The CEF has also been

demonstrated to be implicated in making memory-guided saccades and in remembering visually-guided saccade sequences (Gaymard et al., 1998). The CEF has been shown to project to another, more lateral frontal area that is involved in saccade generation and processing, the frontal eye field (FEF; see Fig. 1) (Wang, Matsuzaka, Shima, & Tanji, 2004). The FEF is involved in generating volitional saccades, as well as in processing visuospatial information (Gaymard et al., 1998) to then create commands to generate saccades (Schall, 2002). It is less involved in the initiation of visually-guided saccades, as compared with memory-guided saccades; but, it has contributions to both types of saccades (Gaymard, Ploner, Rivaud-Pechoux & Pierrot-Deseilligny, 1999; Pierrot-Deseilligny et al., 1991). It has also been shown to have the most visual projections, compared with SEF and CEF (Pouget, Emeric, Stuphorn, Reis, & Schall, 2005). The FEF also has reciprocal projections to SEF and CEF, but more to the SEF (Pouget et al., 2005). FEF also projects to subcortical saccade system structures such as the pons and the SC, directly and indirectly (Sommer & Wurtz, 1998, 2004), which can modulate saccade production in response to visuospatial stimuli. FEF, SEF, CEF and PEF all connect with another frontal area that is mainly known for its role in the (spatial) working memory network, namely the dorsolateral prefrontal cortex (dlPFC; see Fig. 1) (Pierrot-Deseilligny, Muri, Nyffeler, & Milea, 2005). The dlPFC has been implicated in spatial short-term memory during memory-guided saccade tasks (Muri et al., 1996; Pierrot-Deseilligny et al., 1991). It has also been shown to inhibit reflexive saccades, prepare predictive saccades and play a role in the steps necessary to generate a saccade (Pierrot-Deseilligny et al., 2003). Lastly, dlPFC has been shown to be activated during target and saccade direction selection (Pierrot-Deseilligny et al., 2005). Overall, these parietal and frontal areas play a distinct role in the generation of saccades, each with a role

that is fine-tuned to different types of saccades. They are able to generate saccades, in addition to being able to process information obtained across rapid eye movements.

1.3 Visual working memory

After understanding how it is that we are able to make saccades and what neural mechanisms or networks are involved, the next question that arises is about how we are able to remember or use the information that we obtain from each successive fixation. In order to integrate the information to act upon it, for example, we need a (temporary) store of information, or a buffer. This temporary buffer is used to actively store (relevant) information (Baddeley, 2003). Together, the buffer and the process that is responsible for actively utilizing the information in the buffer are referred to as working memory (Jonides et al., 1993). The most relevant type of working memory to this thesis is a visuospatial, or visual, working memory, which maintains information with respect to object features, as well as to location information (Baddeley, 2003). The behavioural aspects of visuospatial working memory, as well as the cortical network behind it, will be discussed below.

1.3a Behavioral aspects

Baddeley and Hitch provided among the first works on how much and what type of information is stored and maintained in (short-term) working memory, of which they and others since have tried to identify additional, inherent properties (Baddeley, 2003). It was shown that working memory has specific characteristics, including a capacity limit of 4 +/- 3 items (Baddeley, 2003). As mentioned before, visuospatial working memory can keep track of object (feature) information (e.g., orientation), as well as spatial information (Baddeley, 2003). Luck and Vogel (1997) were interested in finding out more about this visual working memory,

specifically regarding its capacity for feature information. Using a classic design, they were able to probe visual working memory of single or multiple object features (colour, orientation, size and location). They were able to demonstrate that visual working memory of object features is very similar to working memory in capacity and in their ability to interact across dimensions (colour and orientation, for example).

Others have further dissected visual working memory relative to feature and spatial location information of objects (Courtney, Ungerleider, Keil & Haxby, 1996). For example, memory for object features, such as shape, colour and orientation, has been shown to occur in one cortical network (Desimone & Ungerleider, 1989), whereas spatial working memory has been associated with a different set of neural correlates (Chafee & Goldman-Rakic, 1998; Compte, Brunel, Goldman-Rakic & Wang, 2000; Haxby et al., 1994, 1991; Ungerleider & Haxby, 1994). Nevertheless, Luck and Vogel (1997) demonstrated that it is possible to integrate these two types of information from memory to make a unified decision. Further evidence for this claim comes from interference tasks that require processing of objects (e.g., symbols) at different spatial locations; results indicate that such processing comes at a cost of spatial sequential tasks (Guerard, Tremblay, & Saint-Aubin, 2009; Lawrence, Myerson & Abrams, 2004; Tremblay, Parmentier, Guarard, Nicholls, & Jones, 2006).

How is the combination of information from these two neural networks and their associated memory types accomplished? Hayhoe, Moeller, Ballard and Albano (1990) conducted a study where they were able to identify what signals the brain uses to compare pre-saccadic to post-saccadic information in order to make spatial working memory judgments. They discovered that the spatial working memory system is able to rely on signals from both eye position, as well as context about visual components (e.g., allocentric relationships- comparing the position of an

object to the position of another object). However, to be able to make a judgment or decision about pre- and post-saccadically acquired visual information, a comparison has to occur.

1.3b Cortical physiology

Now, we know that there are behavioural differences between spatial (location) and feature working memory (Courtney et al., 1996). It has also been demonstrated that there are different neural underpinnings or networks that contribute to maintaining sensory information about object features versus spatial, location information (Courtney et al., 1996). To get at the neural correlates involved in spatial working memory, tasks that involve or have a strong spatial component, such as mental rotation or spatial reasoning tasks, have been used and found a strong association with parietal (superior and inferior parietal) activation (Harris & Miniussi, 2003; Knauff, Mulack, Kassubek, Salih & Greenlee, 2002; Zacks, Gilliam & Ojemann, 2003). Patients with damage to the parietal cortex have also been shown to have deficits in spatial, mental rotation tasks (tasks wherein participants have to imagine an object and rotate it in their mind's eye to meet a certain criterion, such as rotate it until it is in the same position as the test object) and in spatial working memory (Karnath, Dick & Konczak, 1997). This supports the idea that the parietal cortex is involved in spatial encoding and working memory. When object location has to be maintained within the context of a visual scene over a delay period, activity correlated with processing this information has been shown in the medial temporal lobes (Crane & Milner, 2005; Pigott & Milner, 1993; Smith & Milner, 1989).

Other studies have also looked to differentiate the pathways between the spatial and feature aspects of visuospatial working memory, such as a study looking at retention of geometric objects in an object task vs. square configuration in a spatial task (Mecklinger & Pfeifer, 1996). Mecklinger and Pfeifer (1996) found that there was prefrontal cortical activity

associated with the former task, whereas parietal activity was associated with the latter task (Mecklinger & Pfeifer, 1996). However, prefrontal cortex has also been associated more with spatial working memory (Chafee & Goldman-Rakic, 1998; Compte et al., 2000) than with feature working memory. Specifically, imaging studies have identified a large swath of activation in prefrontal areas, in the inferior and superior frontal gyri, when participants were required to tap into spatial working memory (D'Esposito et al., 1998). D'Esposito et al. (1998) were able to localize prefrontal cortical activity to the right ventral prefrontal activity during spatial working memory tasks. By analyzing their own results and the results of others, D'Esposito et al. (1998) found that ventral prefrontal cortex is also activated during maintenance of spatial information, whereas dorsal prefrontal cortical areas are active during maintenance as well as any additional processing. In contrast to the idea that prefrontal areas are more involved with maintaining the acquired spatial information to then make decisions based on that, it has been purported that parietal areas are predominantly involved in transforming and storing spatial information (Levy & Goldman-Rakic, 2000).

Although it has been found that spatial working memory is associated with activation in the parietal cortex, can the same be said about non-spatial working memory? A positron emission tomography (PET) study, that contrasted object and spatial working memory information, found that there are distinct networks that process those two types of information (Courtney et al., 1996). Specifically, when participants were probed with facial information, there was an increase in PET activity within fusiform, parahippocampal, inferior frontal and anterior cingulate cortices, right thalamus and medial cerebellum. On the other hand, corroborating the previously mentioned findings, location working memory was associated with increased PET activity within inferior and superior parietal areas, as well as in the superior

frontal sulcus. To this end, previous work has demonstrated that ventral occipitotemporal activation is involved in object perception, whereas dorsal occipitoparietal activation is found in response to spatial information about objects (Mishkin, Ungerleider & Macko, 1983). This distinction is also found at the level of extrastriate processing (Haxby et al., 1991, 1994; Ungerleider & Haxby, 1994). Despite there being different neural networks involved in processing spatial and non-spatial/visual information, they can work together to allow us to make decisions in spatial navigation or visual search tasks for example.

1.4 Spatial updating during saccades

The comparison of pre- and post-saccadic visual/spatial information is well-studied and accomplished through spatial updating (Funahashi, 2013). It is a process that is able to take into consideration any changes in the relationship between an observer and its environment, as a function of any disturbances or movements that occur as a result of the observer (Wang et al., 2006). It is defined as the combination of a retinal signal and an extra-retinal signal, which conveys information about movement amplitude and direction, in order to produce a motor command that points the eye toward an object or target (Klier & Angelaki, 2008). This process is important, as it ensures visual constancy (Klier & Angelaki, 2008) and allows us to make inferences about the visual world. Here, I will discuss behavioural aspects and the cortical physiology behind spatial updating.

1.4a Behavioral aspects

Although spatial updating takes into account eye position signals and relative relationships between components of the visual scene, it does not necessarily make point-by-point updates of the visual scene with each movement (Irwin, Brown, & Sun, 1988; Irwin, Zacks, & Brown, 1990). Then, what does it update? Among the first studies showed, through the use of

a double-step task (fixate centrally and then make a saccade, which will then be followed by a second saccade), that with intervening changes in the second saccade target, humans are able to spatially update positions of targets horizontally and vertically (Hallett & Lightstone, 1976a, 1976b). Wang et al. (2006) were further interested in understanding the visual context (Hayhoe et al., 1990) in spatial updating. Specifically, using a virtual reality set-up, they were able to identify how spatial updating (within an allocentric or egocentric reference frame, where egocentric is relative to the self, be it relative to the eye) would be modulated by the amount of objects present in the visual environment. They tested one-, two- or three-object situations within the virtual reality set-up and discovered that spatial updating is dependent upon or responsive to the number of objects present within the visual environment. Melcher (2007) looked further into object features that can be spatially updated. Melcher (2007) found that feature information of form can be processed pre-saccadically and influence post-saccadic perceptions and judgments. Not only do we update information about the objects, but it has been shown that information that allows us to pinpoint where our bodies are relative to other objects or organisms has also been found to be involved in spatial updating (Wolbers, Hegarty, Buchel, & Loomis, 2008). Thus, spatial updating, itself, is reliant upon or responsive to many spatial processing/navigation signals that allows object and spatial information to be stored from one fixation to the next in visual/spatial working memory.

1.4b Cortical physiology

Spatial updating is reflective of a transfer of information (e.g., visual) from a particular neuronal population associated with stimuli at a specific position in space to a new neuronal population associated with a future position in space (Munoz, 2006). The onset of spatial updating may be due to acquired efference copy signals that are produced with executed eye

movements (Duhamel, Colby, & Goldberg, 1992a). Sommer and Wurtz (2004) identified that a copy of the eye motor command (corollary discharge) is, in fact, important in updating previous sensory (e.g., visual) information. More specifically, they demonstrated that there is a particular pathway (SC-thalamus-FEF) that is involved in utilizing corollary discharge to perform spatial updating. This process can also be found within other cortical regions, such as in the parietal cortex.

Single-step and double-step tasks, which require one saccade to the first fixation target and a second saccade to a remembered, second fixation target using updating, or remapping, have been proven ineffective in patients with parietal lobe damage (Duhamel, Goldberg, Fitzgibbon, Sirigu & Grafman, 1992b; Heide, Blankenburg, Zimmermann, & Kompf, 1995). This points to the involvement of the parietal lobe in spatial updating. More specifically, within the parietal lobe, spatial updating seems to activate the cortex differentially based on the stimulus type (i.e., visual, somatosensory motion stimuli activate monkey ventral intraparietal area, VIP) (Duhamel, Colby, & Goldberg, 1998) and task requirement (i.e., object identification activates anterior intraparietal area, AIP) (Sakata, Taira, Murata, & Mine, 1995). Additionally, spatial updating has been documented in parietal areas such as LIP in the monkey (Duhamel et al., 1992a) and human PPC (Medendorp et al., 2003), FEF (Goldberg & Bruce, 1990) and in early visual areas, V2 and V3 (Merriam, Genovese, & Colby, 2007; Nakamura & Colby, 2002).

1.5 Perception and memory of object orientation

It is crucial to know the spatial location of the object one might reach for, in addition to information about form, size and orientation of the object. These pieces of information will guide the brain in creating, ultimately, any prehensile gesture of the hand that will enable to efficiently and accurately grasp the object. Even if the output of neural processing of a visual scene will not

end up executing a motor command to lead to a specific action, such as grasping a coffee mug, the brain is still able to process all of the previously mentioned aspects. Here, however, I will focus on processing of object orientation, its perception and memory of this type of information.

1.5a Psychophysics

Objects contain simple or low-level feature information (i.e., orientation, colour) (Treisman & Gelade, 1980), as well as complex or high-level features (e.g., facial expression) (Suzuki & Cavanagh, 1995). Here, I will focus on low-level feature processing; specifically, orientation will be the main focus.

Do we or can we discriminate orientations of objects? Upon finding that there are cortical regions within the cat striate cortex that respond selectively to lines at particular orientations by Hubel and Wiesel (1962), there was subsequent fascination with how we are able to process line orientations in humans (Andrews, 1967). Andrews (1967) found that we are able to judge parallelism of lines very well, but that this process may involve multiple detectors or, orientation-selective cortical regions. Gilinksy (1968) also sought to further understand how psychophysical results revolving around orientation discrimination can be correlated with neurophysiological findings from Hubel and Wiesel (1962), for example. She suggested that the human visual system must be organized in such a way that cortical regions that respond to contours or lines should be orientation-specific and that they show light-and-dark adaptation (Gilinsky, 1968). (This line of research, however, stemmed from wanting to understand contour processing.) Later studies focused on the more fundamental aspect of orientation processing alone.

One study was interested in assessing human ability to discriminate line orientations (Westheimer, Shimamura & McKee, 1976). They showed that we are able to discriminate line orientation that is as little as approximately 0.3° away from the vertical (Regan & Beverly, 1985; Westheimer et al., 1976). Westheimer et al. (1976) also showed that orientation discrimination is impaired by the amount of line flankers (the more flankers, the more distraction and the harder it is to discriminate if the central line is vertical or not), presentation of distractor flankers (delayed presentation will interfere more than presentation before or after), and moving line flankers around the test line. Regan and Beverley (1985) were also interested in orientation discrimination, but simultaneously probed orientation detection. Using a sine wave grating, they found that only orientation discrimination is improved (not detection) when the first stimulus (adaptor) grating and the test grating are parallel, whereas detection is improved when the gratings differ by 10-20° (Regan & Beverly, 1985). Along the same lines, Carrasco and McElree (2001) used two tasks to determine visual processing. In the first, feature task, they presented one grating at a certain orientation among zero, three or seven distracter gratings and had participants indicate if a given patch was tilted to the left or the right (Carrasco & McElree, 2001). The second, conjunction task showed a grating with a specific orientation and spatial frequency combination among zero, three or seven distracters (tilted to the left or right, and half had a higher spatial frequency) (Carrasco & McElree, 2001). Their tasks demonstrated that when a cue is used to identify the grating that will be tested, not only is orientation discrimination improved, but so is the time it takes to process orientation information (Carrasco & McElree, 2001). (Thus far, orientation discrimination has been determined relative to Gabor patches, oriented lines, within the context of spatial frequency or contours. However, the orientation of letters, faces and

biological motion have also been investigated (Corballis & Cullen, 1986; Koriat & Norman, 1985; Shipley, 2003; Watson, 1966).)

Once we process object orientation information, how does it enter memory? How is it stored and how is it affected in order for us to make decisions or effectuate a motor command? These ideas were investigated by Tarr & Pinker (1989). They presented participants with an object at a particular initial orientation in the study phase. At test, they presented objects in orientations that were similar in rotation to the initially studied object orientation or in an increasingly different orientation. Results indicated that participants store the initial orientation of the object and then, they engage in mental rotation of the current object to match the initially studied orientation in order to make any further judgments. From this, we can gather that, when information about objects, such as orientation information, is stored, it is the initial orientation that is remembered and all subsequent pieces of information are compared to that orientation or to a canonical orientation of the object.

1.5b Cortical physiology

If we are able to extract orientation information from the visual scene, where then does it get processed in the brain? First, information from the visual surroundings gets transmitted to the retina, and this information is then passed along to the lateral geniculate nucleus (LGN; to the simple cells that respond to orientations of objects, lines) (Hubel & Wiesel, 1961). From there, information is relayed to the early parts of the visual processing system. Specifically, this information is relayed to the early visual, striate cortex (Hubel & Wiesel, 1962, 1968). Hubel and Wiesel (1962, 1968) were able to demonstrate in the cat that the striate visual cortex is mapped topographically, according to the location of retinal stimulation. The columns of striate visual cortex respond to specific orientations (horizontal, vertical and obliquely oriented lines). The

topographic mapping has also been documented in humans, who show a very similarly mapped striate visual cortex (DeValois, Abrecht, & Thorell, 1982). DeValois et al. (1982) analyzed additionally to what the striate cortex of monkeys responds. They showed evidence for meridional anisotropy (more sensitivity in response to horizontal or vertical orientations, as compared with oblique orientations), as well as a differential response and location of response to foveal vs. parafoveal (around the fovea) stimuli (DeValois et al., 1982). Thus, when an object at a given orientation is perceived by the retina and passed on to the LGN, it will activate simple cells therein for the particular object orientation. This information will then be relayed to primary or early visual cortex. Now, what happens to this information after it has activated and been processed within the striate visual cortex? Where does it lead to in the brain?

Ungerleider and Mishkin (1982) discovered that there are two processing pathways for visual information, depending on the final output goal, that extend from the early visual cortex (EVC; Ungerleider & Haxby, 1994). The first pathway projects from the occipital lobe to the parietal lobe (also known as an occipitoparietal pathway; Milner & Goodale, 1992; Ungerleider & Haxby, 1994). More commonly, the occipitoparietal pathway is referred to as the 'dorsal' visual stream and is said to be involved in action planning (Milner & Goodale, 1992; Ungerleider & Haxby, 1994). More specifically, it is thought that the exact projections start off in primary visual area V1, which projects to V2, to V3 and then, middle temporal (MT), LIP/PPC, FEF and/or area 46 (Culham & Kanwisher, 2001; Goodale & Westwood, 2004; Munoz, 2002; Tong, 2003; Ungerleider & Haxby, 1994). Projections to frontal, parietal areas are useful in guiding action planning and decision-making (Tong, 2003). (Information that is processed about the object can also be passed along to areas such as anterior intraparietal area (AIP), which can then transform the information into a reference frame that is appropriate in order to effectuate a motor

command and ultimately, an action (James, Humphrey, Gati, Menon, & Goodale, 2002; Sakata, Taira, Kusunoki, Murata & Tanaka, 1997).)

On the other hand, object processing or recognition may enter a different, 'ventral' visual stream which projects from the occipital lobe to the temporal lobe (i.e., occipitotemporal pathway; Milner & Goodale, 1992; Ungerleider & Haxby, 1994). From V1, feature information about the object will be passed along to V2, to V4, and ultimately to inferotemporal (IT) cortex (i.e., anterior and posterior parts of the IT cortex, TE and TEO, respectively; Milner & Goodale, 1992, 1995; Tong, 2003; Ungerleider & Haxby, 1994). In a related vein, orientation and other feature information may end up in areas such as the lateral occipital complex (Grill-Spector, Kushnir, Hendler, & Malach, 2003; Malach, Levy & Hasson, 2002).

Although there may be different visual streams that can process the same object in different ways, the two streams need to work in conjunction with one another. A nice example of this situation is demonstrated by Valyear, Culham, Sharif, Westwood and Goodale (2006). In this study, an event-related averaging functional magnetic resonance imaging (fMRI) design was used to uncover the neural activity of participants when they are presented with objects (that are meant to be grasped) as the same initial image, as an object of slightly different identity, at a different orientation, or as a different identity and at a different orientation. They found activation in a parieto-occipital area within the 'dorsal' visual stream in response to a change in object orientation (which is exactly the opposite of what we would expect for strictly visual information processing), whereas they observed activation within a temporo-occipital area in response to a change in object identity. This may stem from the fact that the dorsal stream requires information about the size, form and orientation of an object in order to manipulate or interact with it (Culham et al., 2003; Goodale & Milner, 1992). As such, information is

processed in the visual stream as early as the striate visual cortex, is then passed on to extrastriate areas, and to parietal (posterior) cortex, and ultimately to motor cortical areas to carry out the motor command and produce the reaching or grasping behaviour. However, both visual streams should interact to accomplish this behaviour in a successful manner.

1.6 Transsaccadic feature integration

In an everyday situation, we make several eye movements (Rayner, 1998). The scope of these eye movements is to re-orient the fovea of the eye onto objects or part of the scene that are salient and important to some task that we might be completing. As such, it is important to piece together the discrete pieces of information that we acquire from each fixation of the eyes in order

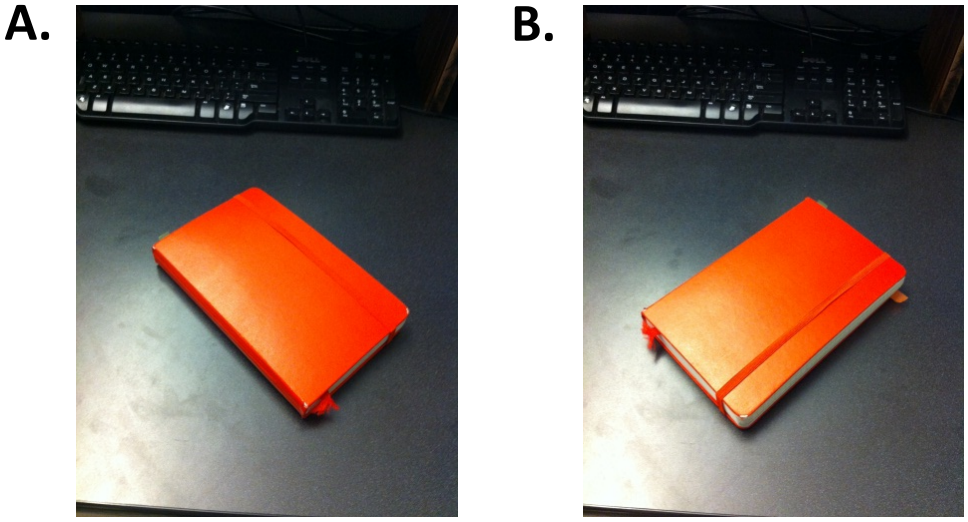

Figure 2. Transsaccadic integration example. We can survey our visual surroundings and if we need to find a notebook, for example, we have to be able to identify an object that possesses the features associated with a notebook. If we fixate on an object like the one shown in A), we can identify the shape of the object and compare it to what we generally associate with notebook shapes. However, if we then make an eye movement and the notebook happens to change its position, it will appear different on our retinas. Then, how do we conclude that it is still a notebook? For example, if we compare the orientation of the book on the left and the one on the right, we might conclude that they are not the same object. If the orientation of the notebook on the left and on the right were the same, we could conclude that they might be the same object. Thus, we have to be able to remember object features, bind them to their location and space, and make comparisons in order to decide if that is the notebook for which we are searching. This is a task that we do on a daily basis.

to make sense of the visual world and/or to be able to complete a desired goal or action (Rayner, 1998). Being able to store information from one fixation and integrate it with information from a successive fixation following an eye movement has been referred to as 'transsaccadic integration' (Henderson, 1997; Irwin, 1991, 1998; McConkie & Zola, 1979); see Fig. 2). Here, I will discuss the reference frames that we might use during transsaccadic integration, as well as the theories behind how we are able to integrate information from fixation to fixation, using psychophysics, transcranial magnetic stimulation, neurophysiological recordings, as well as functional imaging approaches.

1.6a Reference frames

In everyday life, we have to be able to maneuver through our surroundings with ease. One of the ways that we can do this is by knowing where we are in space and where objects are around us. How we relate these two things depends on the reference frame that we use to encode these relationships. First, a reference frame is a rigid body to which we attach a coordinate system (Crawford, Henriques, & Medendorp, 2011). We can relate other objects or rigid bodies to this coordinate-system-embedded rigid body, or reference frame. There are several types of rigid bodies that we can utilize to serve as reference frames which can be subdivided into two general categories. The first category of reference frames is an egocentric one, where we can use a part of the body as a rigid body to assign the coordinate system. Coding an object egocentrically can mean relating that object to a part of the body (i.e., the retina, eye, head or torso). However, the other way to encode spatial relationships between objects can be relative to one particular object in space which is referred to as an allocentric reference frame. If a reference frame based on the layout of objects in space is used, that is also referred to as a spatiotopic or space-fixed reference frame (Helmholtz, trans. 1963). More commonly, retinotopic or retina-

fixed reference frames and spatiotopic or space-fixed reference frames have been considered (see 1.5b, c, d). These reference frames are tested directly or indirectly in transsaccadic integration studies, which are outlined in the following sections. (However, there might be intermediate references frames that can be used to encode spatial relationships.)

1.6b Theoretical explanations of transsaccadic integration

One of the most fundamental aspects of vision is that, despite our eye movements and the retinal shift of objects from the visual scene with each movement of the eye, the visual world seems very stable with respect to space (Helmholtz, trans. 1963). A theory for how our visual system might work to produce this perception was proposed by von Helmholtz (trans. 1963). Specifically, he proposed the 'spatiotopic fusion hypothesis,' which suggests that we are able to encode objects with respect to their location in a spatially stable manner across eye movements (Irwin, 1993). He also purports that we are able to obtain and maintain a very detailed perception from one fixation to the next (Irwin, 1993). Very few people agree or believe that we are able to maintain such a rich, detailed view of the visual world within one fixation to the next. Many experiments have suggested that there is a limit to the amount of detail that we can carry across eye movements and integrate successfully (Bridgeman & Mayer, 1983; Henderson, Pollatsek & Rayner, 1987; Irwin et al., 1988; Irwin, Yantis & Jonides, 1983; Rayner, McConkie & Zola, 1980).

The spatiotopic fusion hypothesis was among the first hypotheses to explain what may be happening in transsaccadic integration. Since then, others have proposed that there is very little that we are able to maintain faithfully across eye movements (Bridgeman, 1981). This hypothesis indicates that, because the visual world contains all of the visual information that we need and readily so, we do not need to construct any frameworks that we can maintain and utilize across

eye movements (O'Regan, 1992). Additionally, the information that we receive within one fixation is overwritten by the information from the next fixation (O'Regan, 1992). Evidence for this hypothesis has come from an inherently difficult, top-down-heavy process that has allowed researchers to conclude that it is indeed difficult to maintain large amounts or a detailed level of information across eye movements (O'Regan, Deubel, Clark & Rensink, 2000; Rensink, O'Regan & Clark, 1997; Simons, 1996; Simons & Levin, 1997). However, this line of evidence is extracted from a change blindness task that may be too difficult in nature to extrapolate to other tasks.

Since then, a more comprehensive hypothesis has been proposed for transsaccadic integration. This hypothesis states that a limited capacity of information can be maintained across eye movements; however, this acts upon the basis of a buffer (that works very much like visual working memory) (Carlson-Radvansky, 1999; Irwin, 1991), as well as upon a process that allows information from one fixation to be integrated with the next set of information (a process like spatial updating or remapping) (Duhamel et al., 1992a). Although the properties of transsaccadic memory are not exactly like those of visual working memory, it does have similar properties that make it a good candidate as a component of our ability to store and compare information across saccades. Below, I discuss the properties of transsaccadic integration and memory.

1.6c Psychophysical studies

One of the aspects of transsaccadic information that has been looked into is the capacity of transsaccadic memory. Irwin (1992) demonstrated that transsaccadic memory has a limited capacity of approximately 3-4 items. Using a paradigm where participants had to remember arrays of 6 items or 10 items and then make a saccade to ultimately identify the letter indicated

by a memory probe afterwards, Irwin (1992) demonstrated that for a 6-item array, participants were able to indicate the letter in the array at an accuracy level of 70%. He calculated from this level of accuracy that transsaccadic memory has a capacity of approximately 3-4 items (Irwin, 1992). This finding was corroborated using images of real objects later (Irwin & Gordon, 1998; Irwin & Zelinsky, 2002).

Another point about what is remembered within the limited capacity transsaccadic memory is that the detail that is remembered can be simple features (orientation, colour, etc.) or it can be a combination of features, as long as they belong to a similar object or context (Lee & Chun, 2001; Luck & Vogel, 1997; Vogel, Woodman & Luck, 2001; Walker & Cuthbert, 1998). Prime, Tsotsos, Keith and Crawford (2007) conducted psychophysical studies to identify the capacity of transsaccadic memory of different object features: luminance, colour and orientation. They found that similar to previous findings, transsaccadic memory does have a limited capacity of 3-4 items for any of the tested object features. Melcher and Colby (2005) added to this idea with their study, where they also investigated the integration of features such as contrast, tilt and shape across eye movements. However, they also looked at this process in terms of which frame of reference is used to encode these features (Melcher & Colby, 2005). They did not find transsaccadic adaptation for contrast, but they did find such an effect for tilt and shape (Melcher & Colby, 2005). Moreover, they found that this information was encoded in a spatially-specific manner (Melcher & Colby, 2005). (This indicates that not only is object feature information important, but knowing the frame of reference in which this information is stored is also necessary.) Transsaccadic integration has also been tested using a line intersection task, where participants were presented with one line at a given orientation, followed by a line at a different orientation (Prime, Niemeier & Crawford, 2006). Participants were subsequently required to

indicate using a mouse click where the point of intersection occurred (Prime et al., 2006). These results show that the oculomotor system attempts to integrate location, as well as orientation information, but in an egocentric manner (Prime et al., 2006). This strengthens the idea that the frame in which object features are integrated is important and, perhaps, an inherent part of the transsaccadic integration process.

1.6d Physiological studies (monkeys, fMRI, TMS)

To identify the neural underpinnings of transsaccadic integration, research has made use of advancements in technology. Techniques that utilize technology such as single-unit recordings, transcranial magnetic stimulation (TMS) machines and magnetic resonance imaging (MRI) machines have been used to identify such neural correlates. These techniques, which include functional MRI or fMRI, have been used to study, for example, where motion information is integrated. In such a task, d'Avossa et al. (2007) asked participants to observe random dot patterns and determine the direction of motion. d'Avossa et al. (2007) found that motion information is integrated across saccades, specifically, and this is accomplished in a manner that is encoded relative to space or in a spatiotopic reference frame. They found this integration to occur in middle temporal (MT+) area in humans (d'Avossa et al., 2007).

Using another technique, TMS, Prime, Vesia and Crawford (2008) were interested in understanding how the posterior parietal cortex, specifically, is involved in the integration of object features across saccades. They applied TMS to right and left posterior parietal cortex (involved in visuospatial integration, maintenance of saccade-related information and contains the PEF, equivalent to LIP; Pierrot-Deseilligny et al., 2005) in order to inactivate these regions during a task where participants were required to compare orientations of a pre- to a post-saccadic stimulus at the same spatial location (in the presence of distractors) (Prime et al., 2008).

(By inactivating the brain region, it acts as a virtual lesion. This allows for the investigation of the system when this area is not active. If the end result is the same, then the inactivated area may not be important to the process or mechanism; if the outcome is an impaired or less-than-optimal one, then the inactivated area may be a part of the investigated mechanism.) They found that TMS over right PPC prohibited participants from remembering well the orientations across saccades, which indicates that right PPC may be a component part of processing spatial information about features during the transsaccadic integration process. TMS has also been applied to left and right FEF during a feature comparison task within a fixation and across a saccade (Prime, Vesia & Crawford, 2009). These results showed that TMS applied to left and right FEF disrupted optimal transsaccadic memory of object features, indicating that FEF is also involved in processing object features in space across eye movements (Prime et al., 2009). Furthermore, brain areas early in the visual stream, such as early visual cortex, have been investigated in terms of their role in transsaccadic integration (Malik, Dessing & Crawford, 2014). During a task where a Gabor patch is presented to the left or right visual quadrant, the corresponding left or right early visual cortex was stimulated using TMS (Malik et al., 2014). Their results showed that, when early visual cortex is disrupted, both transsaccadic comparison and memory suffered (Malik et al., 2014). This suggests that the visual stream (e.g., early visual cortex) has a role in spatial processing during transsaccadic integration of object features.

Neurophysiological evidence has also been utilized to point to areas within the brain that may be involved in transsaccadic integration of object features. Specifically, Subramaniam and Colby (2014) used a paradigm that was similar to that of Sereno and Maunsell (1998) in order to investigate how spatial updating (an important process involved in transsaccadic integration) of object features occurs. (Sereno and Maunsell (1998) utilized a task that involved identifying

shape-selective regions of LIP by flashing objects in a neuron's receptive field and secondly, identifying shape-selective behaviour in LIP via a delayed match-to-sample task, where the monkey is shown an object in the periphery and must saccade to the correct one from a group of objects.) Specifically, Subramanian and Colby (2014) looked at this process within an area in the parietal cortex of the monkey (i.e., LIP). They found that even within the monkey LIP, there is (modest) updating in a spatially specific manner of object features (Subramaniam & Colby, 2014). To date, only one fMRI study has looked into the cortical correlates of transsaccadic integration in humans.

This study looked into transsaccadic integration, specifically of object orientation information (Dunkley, Baltaretu, & Crawford, submitted). This study used fMRI adaptation (see below) as a way to identify areas involved in this process. Dunkley et al. (submitted) found that there are distinct areas within the posterior parietal cortex (specifically, the supramarginal gyrus) that are responsive to object orientation during fixation or across saccades. It was also discovered that these areas are adjacent to the saccade network, but not directly a part of it (Dunkley et al., submitted). This information is specific to integration within a spatiotopic frame of reference. Thus, some progress has been made in determining where in the brain transsaccadic integration occurs for features and relative to which frame of reference.

1.7 Functional magnetic resonance imaging adaptation (fMRIa)

As mentioned previously, Dunkley et al. (submitted) used an fMRIa technique to uncover the brain areas involved in transsaccadic integration. Here, I also used this technique to identify the neural correlates involved in a transsaccadic integration task in multiple reference frames. Thus, I will introduce functional MRI, as well as how it has been applied to transsaccadic integration.

1.7a fMRIa basics

Functional magnetic resonance imaging (fMRI) utilizes blood-oxygen level dependent (BOLD) signals in order to determine indirectly the level of activity a brain region is exhibiting during a particular task, which was first demonstrated by Roy and Sherrington in 1890 (as cited in Logothetis, 2002). By this logic, if a region of the brain shows high BOLD signals in response to an event or to a condition (as tested in event-related fMRI or block-design fMRI, respectively), it would be interpreted that this area is doing more processing and engaged in the event or condition (e.g., type of process explored, such as face perception). If we then ask participants to engage in an experiment that allows us to correlate an area's activity with the performance on one task (or event) as compared with another task, we can draw conclusions about whether the area is involved in the first task or in the latter. Neuroimaging researchers have utilized this relationship between BOLD signal and experimental tasks.

fMRI studies have generally involved presentation of a stimulus and a subsequent correlation of neural activity with the presentation event. However, Grill-Spector and Malach (2001) modified this standard neuroimaging sequence to identify neural correlates within specific tasks. It was noticed that when a stimulus is repeated multiple times, on a short timescale (milliseconds; Sobotka & Ringo, 1996), on a longer timescale (minutes, days; Henson, Shallice, & Dolan, 2000; van Turennout, Ellmore, & Martin, 2000) or interspersed with other stimulus presentations, brain areas that respond to the initial presentation of the stimulus will decrease in BOLD activity with (all) subsequent presentations of the stimulus (Sobotka & Ringo, 1996; Miller & Desimone, 1994; Li, Miller, & Desimone, 1993). This reduced BOLD signal in response to a repeated stimulus has been defined as 'adaptation' (Grill-Spector & Malach, 2001;

Ringo, 1996; Sobotka & Ringo, 1994), 'repetition suppression' (see Fig. 3) (Desimone, 1996) and/or 'neural priming' (Maccotta & Buckner, 2004).

Reduced neural responses resulting from repeated stimulus presentation have also been documented using neurophysiological studies in areas such as inferior temporal (IT) cortex (Brown & Xiang, 1998; Ringo, 1996; Miller et al., 1993; Desimone, 1996; Sobotka & Ringo, 1994). One important aspect about this is that not all of the neural populations do or can show repetition suppression (Ringo, 1996; Miller & Desimone, 1994). For example, it has been suggested that approximately 50-67% of neurons in IT, for example, show repetition suppression (Ringo, 1996; Miller & Desimone, 1994).

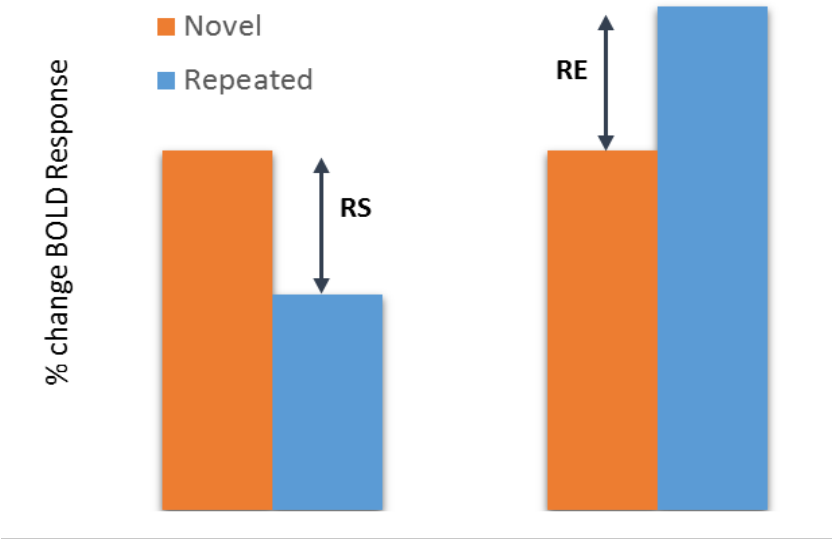

Figure 3. Graphical representation of repetition suppression (RS) and repetition enhancement (RE) effects in fMRI adaptation. On the left-hand side, the orange bar depicts the difference in BOLD signal during a Novel condition (i.e., in a series of stimulus presentations, the second stimulus is different than the first) as being higher than the difference for the Repeated condition response. When the BOLD activity is higher for the Novel condition, as compared with the Repeated condition, this is known as repetition suppression. On the right-hand side, the BOLD percent change is higher for the Repeated condition, as compared with the Novel condition. This effect, on the other hand, is known as repetition enhancement (higher BOLD activity in response to a repeated stimulus presentation). These differences are observed when such effects are reported.

Although it is still uncertain what the underlying process of repetition suppression is, one possibility is that repetition suppression is indicative of a decrease in neural activity in response to subsequent, repeated stimuli (Henson & Rugg, 2003; Race, Shanker, & Wagner, 2009; Schacter & Buckner, 1998; Wiggs & Martin, 1998). Models that try to explain the possible underpinnings or neural mechanisms for the observed repetition suppression effect have been put forth. The first, fatigue model suggests that neuronal firing will wane as a result of fatigue from responding to the stimulus; however, the tuning curve of the neurons will remain unaltered (Avidan, Hasson, Hendler, Zohary, & Malach, 2002; Li et al., 1993). In the second, sharpening model, repetition suppression is explained by way of the type of encoding in which neurons can engage (Segaert, Weber, de Lange, Petersson, & Hagoort, 2013). Specifically, if a stimulus elicits an increase in firing in a particular population of neurons, perhaps some of those neurons were not specific to the stimulus characteristics. On subsequent presentations of the stimulus, any irrelevant encoding neurons will not fire to the same extent, if at all, thereby resulting in a tuned population of neurons that respond to the stimulus (Wiggs & Martin, 1998). The third, facilitation model proposes that, in fact, with each subsequent presentation of the stimulus, the ability to process the information occurs with increasing rapidity and the fMRI BOLD signal cannot capture the time scale at which this occurs (James & Gauthier, 2006). A fourth possible mechanism that has been purported is a response-learning mechanism (Dobbins, Schnyder, Verfaellie, & Schacter, 2004). Dobbins et al. (2004) suggest that response learning can account for neural priming. Specifically, when classifying objects, participants can learn which responses are appropriate which are associated with priming responses to novel vs. highly primed stimuli (whereas task switching reduces this priming effect; Dobbins et al., 2004). A last explanation described here for repetition suppression is provided by the neural synchrony model (as cited in

Gotts, Chow, & Martin, 2012). This model suggests that, with repetition of a stimulus, there will be decreased firing per unit time (i.e., firing rates) in response to subsequent presentations, in addition to an increase in neuronal synchronization (as cited in Gotts, Chow, & Martin, 2012). Overall, to date, several models have been proposed to explain repetition suppression which may, ultimately, allow us to make inferences about the processes that are being investigated.

fMRI adaptation (fMRIa) has been utilized to study many cognitive processes, especially those surrounding objects. Specifically, fMRIa has been used to identify where in the brain object size, position, viewpoint and luminance are processed (Grill-Spector et al., 1999). From this work, it was found that an area within the ventral stream, LO or LO complex, LOC, is involved in object perception (Grill-Spector et al., 1999). This area has been shown to also be involved in transformations of objects. fMRIa has also been utilized in identifying whether the (scene-responsive) parahippocampal place area responds to images in a viewpoint-dependent manner (Epstein, Graham & Downing, 2003) and in identifying the face area proper within humans (Krekelberg, Boynton, van Wezel, 2006). Even where and how language is processed has been tackled with fMRI adaptation (Gagnepain et al., 2008; Glezer, Jiang & Riesenhuber, 2009). Thus, it has proven that fMRIa can be a useful method or technique to try to uncover neuronal correlates involved in a particular experimental task or condition.

One aspect of fMRIa is that, upon repetition of a stimulus, a decreased neuronal firing or BOLD response is not the only response. There has been documentation of an increased BOLD response as a result of stimulus presentation repetition (Segaert, Weber, de Lange, Petersson & Hagoort, 2013). This is referred to as repetition enhancement (see Fig. 3), though it has been less commonly observed and has proven to be more difficult to explain. Some of the contributing factors that have been suggested to play a role in driving repetition enhancement instead of

repetition suppression include attention, learning and expectation to name a few (Segaert et al., 2013). Several models have also been put forth in an attempt to explain what may be happening to produce a repetition enhancement effect. Such models include the accumulation model (James & Gauthier, 2006), the predictive model (Friston, 2005) and the novel network formation model (Henson, Shallice & Dolan, 2000). Segaert et al. (2013) suggest that, perhaps, it is not a single model that can account for repetition enhancement; rather, it might be a contribution of several of these models. Nevertheless, when conducting fMRI adaptation studies, we may observe either repetition suppression, repetition enhancement, or both.

1.8 Aims and hypotheses of the study

Previously, we saw that the visual system is able integrate information across eye movements and commit this information to memory (Prime et al., 2007, 2008, 2009, 2011). This has been studied for object features (Luck & Vogel, 1997; Prime et al., 2008, 2009, 2011), as well as how these features can be bound and integrated to spatial locations (Irwin et al., 1988; Melcher & Colby, 2008; Ross, Morrone, Goldberg, & Burr, 2001). From this line of research, the suggestion is that transsaccadic integration is not just a simple object feature integration process and rather, a feature-spatial location binding problem. To look at this issue, a recent fMRI adaptation study by Dunkley et al. (submitted) was conducted and found that integrating of object orientation can be done in a spatially-specific manner (i.e., in a spatiotopic reference frame).

In the study that I conducted, I went further and wanted to test transsaccadic integration within multiple reference frames. We saw that there are many ways in which visual information (e.g., object features) can be encoded (egocentrically or allocentrically). However, we have not yet discovered the neural correlates or networks involved in encoding object features in

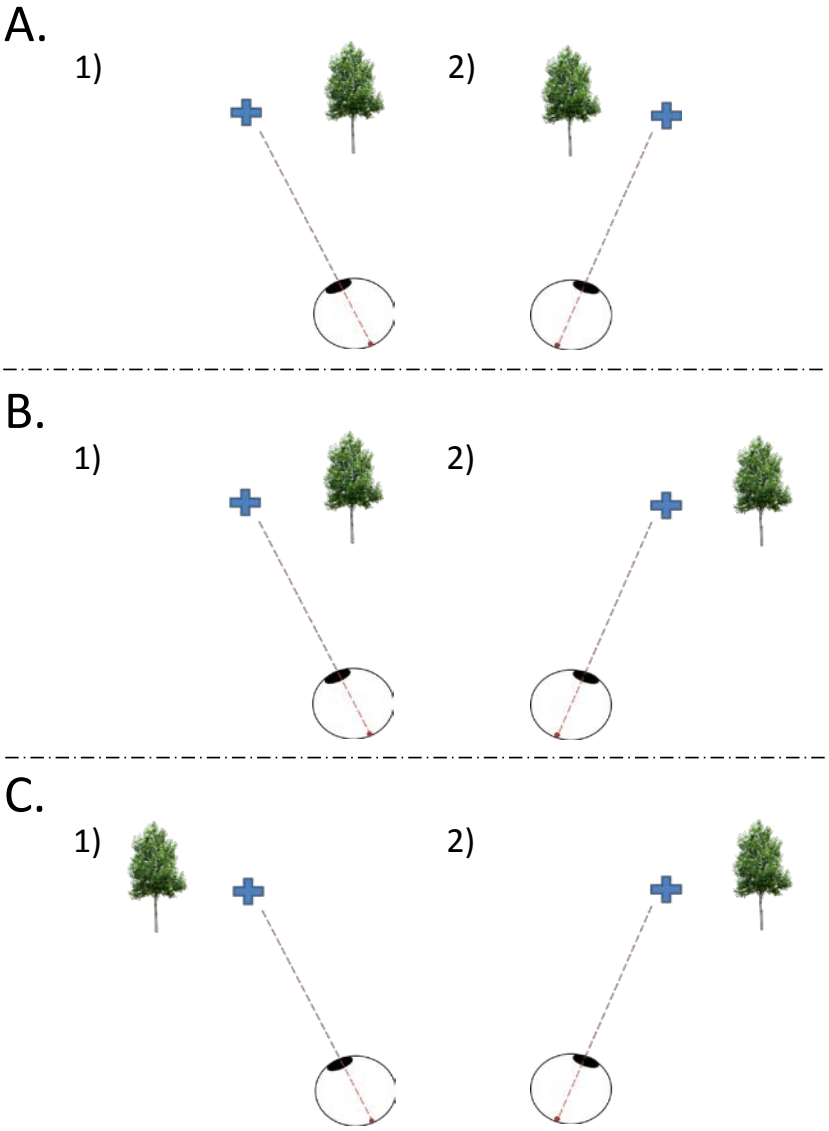

Figure 4. Examples of three reference frames. ***A***. Space-fixed frame of reference. In this example, we see the eye fixating initially to the left (blue fixation cross) of a tree that is far away (1). Then, we see the eye moving to the right of the tree (2). In this frame, the tree has changed its retinal position (red dot on the back of the eye where the line of gaze meets the fovea), but is still in the same position in space. Therefore, object feature information, for example, would be encoded relative to the fixed spatial position of the tree and not with respect to the changing retinal position. ***B***. Retina-fixed frame of reference. This example shows the eye fixating initially to the left of the tree (1) and then, moving to the right (2). However, the tree corresponds to the same position relative to gaze (the tree is to the right of gaze in both (1) and (2)), although the tree has changed in its spatial position. The tree, therefore, maintains its position on the retina, but not in space. Therefore, object features could be coded relative to the fixed retinal position, not to the changing spatial position of the tree. ***C***. Frame-independent. Lastly, an intermediate reference could be used. In this example, the eye is initially looking to the left (1) and the tree is to the left of gaze (where the fixation cross is). The eye then moves to the right (2) and this time, the tree is to the right of gaze. Now, the tree has not only changed its spatial position, but also position relative to the retina. Presumably, a different, or intermediate reference frame has to be used to be able to encode object features of the tree.

particular frames of reference. I chose to look at the common frames of reference that have been studied previously (i.e., retina-fixed and space-fixed) and also look at a different reference frame (that might be an intermediate) that is neither of space-fixed, nor retina-fixed (see Fig. 4). I hypothesized that areas within the parietal cortex (specifically, saccade-activated SMG) and perhaps, extrastriate areas may play a role in integration of orientation information, at least in a spatiotopic or space-fixed reference frame. Within a retina-fixed frame of reference, activity in early visual areas, but not in parietal or frontal areas was expected. Lastly, in the control, frame-independent condition (neither space-fixed, nor retina-fixed), I expected that neither occipital regions, nor frontal, parietal regions would be activated in integrating orientation information across saccades, or that all of the previously mentioned cortical regions would show activation. I present a study wherein all three spatial configurations are tested during a transsaccadic integration task of object orientation information.

The following chapter describes an fMRI adaptation study on the transsaccadic integration of object orientation within three spatial conditions: 1) Space-fixed, 2) Retina-fixed and 3) Frame-independent (i.e., neither Space-fixed, nor Retina-fixed). The objective of this study is to uncover the neural networks involved in transsaccadic integration within multiple frames of reference.

In Chapter 3, I bring into light the findings from the study presented here in view of the current ideology surrounding transsaccadic integration. Also, I discuss questions that linger even after the results (the neural networks) discovered within each of the spatial conditions that I tested. I also describe possible applications for the findings from this line of research within medicine, industry and transportation safety. Lastly, I present future research avenues that I plan to pursue following the work presented here.

CHAPTER 2

TRANSSACCADIC INTEGRATION OF VISUAL FEATURES AND SPATIAL INFORMATION

2.1 Introduction

Every second humans and other primates make several saccades, displacing the retinal image from one fixation point to the next. Not only do we perceive the visual world as continuous, the visual system is able to correctly fuse or compare information between different fixations. This process, whereby visual feature and location information is retained, updated, and integrated across saccades, is called transsaccadic integration (Irwin, 1996; Melcher & Colby, 2008). Transsaccadic integration has been demonstrated to involve a limited capacity memory storage mechanism similar to visual working memory (Irwin, 1996; Irwin & Gordon, 1998; Prime, Tsotsos, Keith, & Crawford, 2007). Transsaccadic integration is also able to integrate spatial and non-spatial information across naturally space-fixed stimuli (Hayhoe et al., 1991; Melcher, 2009; Prime et al., 2006), possibly using mechanisms similar to spatial updating across saccades (Hamker, Zirnsak, Ziesche & Lappe, 2011; Melcher & Colby, 2008; Prime et al., 2011). However, there are some transsaccadic tasks where subject performance is superior when pre- and post-saccadic stimuli appear at the same retinal location (Golomb, Chun & Mazer, 2008; Golomb & Kanwisher, 2012; Golomb, Pulido, Albrecht, Chun & Mazer, 2010). Moreover, there are some other tasks (such pre/post-saccadic comparisons in a single isolated stimulus) where spatial information is not necessary to solve the task, and here performance is relatively immune to experimental manipulations of spatial cognition (Prime et al., 2008).

Little is known about the neural mechanisms subserving these sensory-motor processes, but it has been shown that some aspects of transsaccadic integration can be disrupted by transcranial magnetic stimulation (TMS) over posterior parietal cortex (Prime et al., 2008), dorsolateral prefrontal cortex (Tanaka, Dessing, Malik, Prime, & Crawford, 2014), and early visual cortex (Malik et al., 2015). Direct evidence for transsaccadic feature integration by way of

neural function in neurons is scant, but monkey lateral intraparietal cortex (LIP) shows signs of modest spatial updating of rudimentary shape information (Subramanian & Colby, 2014). In addition, a recent functional magnetic resonance imaging adaptation (fMRIa) paradigm showed transsaccadic interactions between feature orientations in human supramarginal gyrus (SMG; adjacent to the human equivalent to LIP) and extrastriate cortex (Dunkley et al., submitted). These areas were saccade-specific (i.e., they did not show significant feature-specific interactions during fixation), whereas other areas showed the opposite: modulations during fixation, but not across saccades (Dunkley et al., submitted).

The studies described in the previous paragraph only employed transsaccadic stimuli that were space-fixed. Other studies have identified retina-fixed mechanisms for visual memory (e.g., Fecteau & Munoz, 2005; Harrison & Tong, 2009; Talsma, White, Mathôt, Munoz & Theeuwes, 2013), and of course many other studies have looked at feature memory and interactions in the absence of saccades (Averbach & Coriell, 1986; Irwin, 1992; Johnson, Hollingworth & Luck, 2008; Logothetis, Pauls & Poggio, 1995; Motter, 1994; Prime et al., 2007); the use of different methods and approaches in previous studies makes it difficult to compare the neural mechanisms involved in space as opposed to retina-fixed frames of reference. However, to date, no study has compared the mechanisms for transsaccadic feature interactions across situations where the stimuli were spatially arranged to be space-fixed, retina-fixed, or frame-independent.

Here, we investigated the neural mechanisms involved in object orientation in multiple reference frames using an fMRIa approach (Grill-Spector & Malach, 2001). Specifically, participants were presented with the same orientation or different orientations and were required to indicate via button-press if the orientations were the same or different. Such a protocol is capable of producing both repetition suppression (RS: different > same) or repetition

enhancement (RE: same > different) effects in cortical regions sensitive to the manipulated feature (Grill-Spector, Henson, & Martin, 2006; Grill-Spector & Malach, 2001; James & Gauthier, 2006; Krekelberg et al., 2006). We tested transsaccadic integration of orientation in three spatial configurations: 1) a Space-fixed condition, 2) a Retina-fixed condition and 3) a Frame-independent condition. Overall, our Space-fixed results showed activity in parietal and occipitotemporal areas similar to those reported by Dunkley et al. (submitted), but the Retina-fixed and Frame-independent conditions produced quite different patterns of cortical activation, suggesting that the mechanisms for transsaccadic comparison of feature information (at least, of object orientation) are highly dependent on the spatial nature of the task.

2.2 Orientation experiment

2.2a Participants

Participants were graduate students or employees at York University, Toronto, Ontario, Canada with normal or corrected-to-normal vision. 17 volunteers participated in the study initially (11 females, 6 males, 21-42 years of age, 16 right-handed) and provided informed consent. They had no history of neurological disorders. However, based on exclusion criteria described below, 5 participants' data were excluded. Analyses presented in this study are based on 12 of these participants (10 females, 2 males, age 21-42, 11 right-handed individuals). All experiments were approved by York University Human Participants Review Subcommittee.

2.2b Experimental set-up and stimuli

After passing initial MRI safety screening, participants were then informed about the task. Once they understood the task, they lay supine on the MRI table, with their head resting flat within the 32-channel head coil (Fig. 1, A). They were then fit with a head-mounted apparatus

containing a mirror to reflect images on the screen (within the MRI bore) and an MRI-compatible eye-tracker (i ViewX, SensoMotoric Instruments). This was used to record eye position from the right eye. Behavioral responses were recorded using a 'button box' held in the right hand, with the index finger resting on the leftmost button and the middle finger on the adjacent button (Figure 1, A). All button press responses were recorded in a MATLAB .mat file for offline analysis.

While in the scanner, participants were presented with stimuli consisting of circles 6° in diameter that were filled with an isoluminant Gabor pattern presented either at a 45° angle or a 135° angle in standard polar coordinates. The stimuli were presented in the centre of the screen or 12° to the right or left of centre on a light gray background, depending on the spatial condition being tested. The stimuli created with MATLAB (The Mathworks, Inc.) were projected onto a screen in the magnetic bore that was reflected using a mirror onto the participants' eyes (Fig.1, A).

2.2c Imaging

A 3T Siemens Magnetom TIM Trio magnetic resonance imaging scanner was used to acquire functional data using echo-planar imaging (EPI) sequence (repetition time [TR]= 2000 ms; echo time [TE]= 30 ms; flip angle [FA]= 90°; field of view [FOV]= 192 x 192 mm, matrix size= 64 x 64 with an in-slice resolution of 3 mm x 3 mm; slice thickness= 3mm, no gap) throughout each of the six functional runs in ascending and interleaved order. Thirty-three slices were acquired per volume for a total of 280 volumes of functional data. Within an experimental session, a T1-weighted anatomical reference volume was obtained through an MPRAGE sequence (TR= 1900 ms; FA= 256 mm x 256 mm x 256 mm; voxel size= 1 x 1 x 1 mm^3). 192 slices were acquired per volume of anatomical data were acquired.

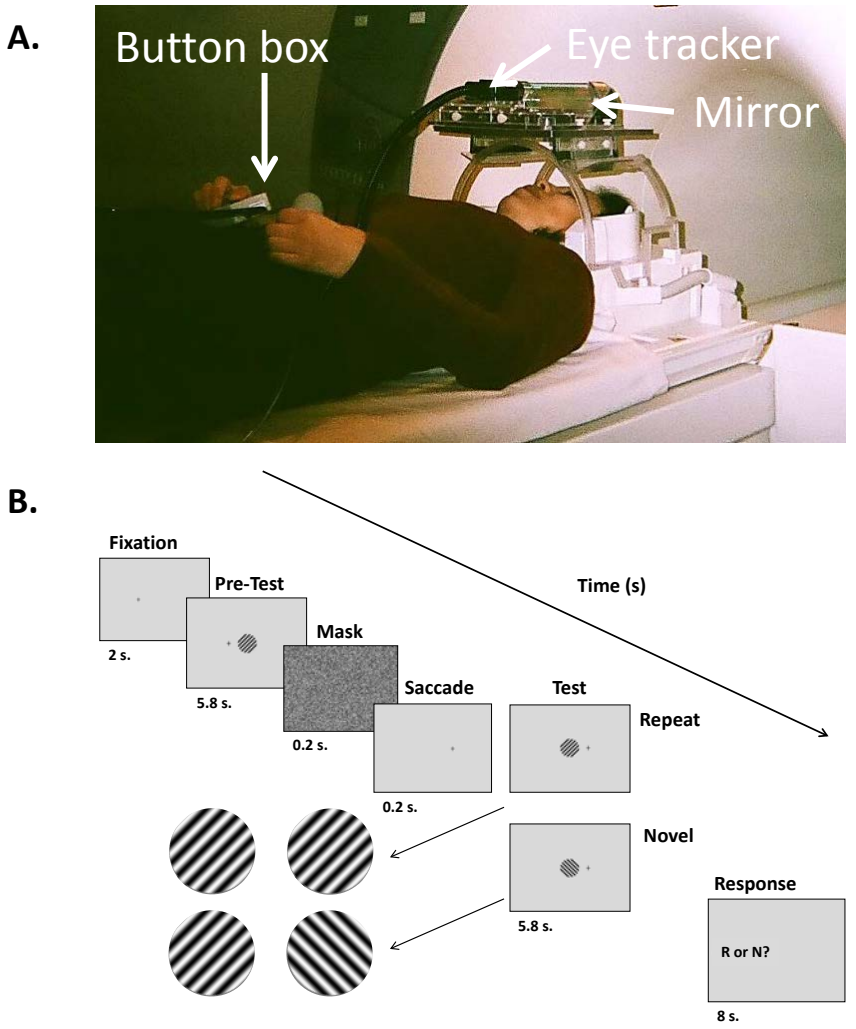

Figure 5. Experimental set-up, paradigm and pre-test, test combinations. ***A.*** Experimental set-up showing participant lying supine on MRI table with head mount containing mirror and eye tracker. Button box is held in right hand with index and middle fingers on first two buttons from left to answer during task. ***B.*** A typical trial sequence is depicted through time (22 s) for any one of the three spatial condition types (retina-fixed, space-fixed or frame-independent). Stimulus orientations are presented at 45° or 135° and are repeated ('Repeat' condition) or are different ('Novel' condition). ***C.*** The possible combinations of spatial feature (orientation angle) and location during the first stimulus presentation ('Pre-test') and the second stimulus presentation ('Test') for the three spatial conditions.

2.2d General paradigm/procedure

2.2d.i Experiment

We used an fMRIa paradigm to test for adaptation to object orientation by presenting a pre-test stimulus at one of two possible orientations (45° or 135°) and a test stimulus whose orientation could be repeated or novel. Each trial (Figure 1, B) started with a 2 s fixation period on a cross at one of two possible positions (6° left or right of centre). This was followed by the presentation of the pre-test stimulus (i.e., the first presentation of the oriented grating) for 5.8 s after which a 200 ms mask appeared (to prevent processing of retinal afterimages, and afterimages themselves), and this was followed by the appearance of a fixation cross at the other fixation cross position for 200 ms prompting participants to make a saccade. The test stimulus was presented for 5.8 s at the same orientation as the pre-test stimulus ('Repeat' condition) or at a perpendicular orientation ('Novel' condition). The final phase of the trial was a written prompt ('R or N?') for 8 s to allow the haemodynamic response to return to baseline as well as to instruct participants to make a response by pressing a button with the right hand to indicate if the orientation of the test stimulus was repeated or novel compared to the pre-test. The first, most-left button was used to indicate that the orientations had been the same ('Repeat' condition). The second button was used to indicate that the orientations had been different ('Novel' condition).

The presentations of the pre-test and test stimuli were manipulated to depict the spatial conditions probed (Figure 1, C). In the Space-fixed condition, the stimuli appeared in the same position on the screen (i.e., in space), but changed relative to the retina upon making the saccade after test presentation (Figure 1, C). In the Retina-fixed condition, two possible permutations could be tested: If the fixation cross was initially presented 6° to the left of center, the pre-test stimulus would appear to the left of the fixation cross; then, the fixation cross would

subsequently appear 6° to the right of center before the presentation of the test stimulus, which would appear directly in the center of the screen. The opposite could also occur (i.e., the first fixation cross appears 6° to the right of center and the pre-test stimulus appears to the right of the fixation cross; then, the fixation cross moves to 6° to the left of center and the test stimulus appears in the center of the screen). Lastly, in the Frame-independent condition, if the fixation cross appeared 6° to the left of center, the pre-test stimulus would appear to the left of the fixation cross; then, the fixation cross would move to 6° to the right of center and the test stimulus would appear to the right of the fixation cross (and vice versa). Overall, there were 8 trials for the Space-fixed, 16 trials for the Retina-fixed (to allow for all the permutations that allow the test to end up in the center) and 8 trials for the Frame-independent conditions, for a total of 32 trials in one run, which lasted for ~ 9 min. in one complete testing sequence, or run. All condition and trial types had been counterbalanced and randomly intermingled throughout each run. At the beginning and end of each run, participants were required to fixate centrally for 12 s. There was a total of 6 runs in the entire experiment. The paradigm was modified from Dunkley & Crawford (submitted) and Turi & Burr (2012).

2.3 Analysis

2.3a Behavioural data

All eye and button press data were analyzed after image acquisition was completed to ensure that the task was being done correctly. Eye position data for each trial were inspected visually to confirm that the eye fixated on the fixation crosses and moved at the required times. Any trials in which the eye broke fixation at an inappropriate time were excluded from any further analyses by being designated as confound predictors in fMRI analysis.

Button press responses were also inspected after the experiment. Only trials where button presses correctly indicated the feature condition (Repeat vs. Novel) were included in the analysis. Trials that showed errors in eye and/or button press response were excluded from additional analysis by being designated confound predictors. On this basis of incorrect eye and/or button press responses, the whole data set from one participant who had chance level (50% correct) performance in 5 out of 6 runs was excluded from the analyses. That left 12 participants' data: three runs were included from one of these participants who had at least 96 correct trials (88.9% of the total trials, four runs were included from another participant with at least 125 correct trials (97.7% of the total trials) and five runs were included from a third participant who had at least 127 correct trials (79.4% of the total trials). The entire data set (all six runs) of the other nine participants were included in analyses, at least 171 correct trials (89.1% of the total trials).

2.3b Functional imaging data

2.3b.i Experimental data

For each participant, we used a general linear model (GLM) that included 16 predictors. We used a predictor ("Fixate") for the presentation of the first fixation cross. In the Pre-test phase, we used two predictors: one for a stimulus presented in the left visual field, "Adapt_LVF", one for a stimulus presented in the right visual field, "Adapt_RVF". In the test phase, we considered three factors: 3 spatial conditions (Space-fixed, Retina-fixed, Frame-independent) x 2 orientations (Repeat, Novel) x 2 visual hemifields (left: LVF and right: RVF), which resulted in 12 predictors of interest: Space-fixed_Repeat_LVF, Space-fixed_Repeat_RVF, Space-fixed_Novel_LVF, Space-fixed_Novel_RVF, Retina-fixed_Repeat_LVF, Retina-fixed_Repeat_RVF, Retina-fixed_Novel_LVF, Retina-

fixed_Novel_RVF, Frame-independent_Repeat_LVF, Frame-independent_Repeat_RVF, Frame-independent_Novel_LVF and Frame-independent_Novel_RVF. We also used a predictor ("Response") for the button press response. The "Fixate" predictor was 2 s or 1 volume in duration, pre-test predictors were 6 s or 3 volumes in duration, test predictors were 6 s or 3 volumes in duration, and the response predictor was 8 s or 4 volumes long. Predictors were used to generate GLMs for each run for each participant (BrainVoyager QX 2.8, Brain Innovation). A haemodynamic response function was convolved with the predictor variables. The haemodynamic response function that was modeled was a standard two-gamma function model (Dunkley et al., submitted). GLMs were then amended to exclude any trials that had incorrect button responses, improper or incorrect eye movement trials and/or trials during which excessive motion was observed after motion correction. Only those trials that met these criteria were included in further functional analyses. Any GLMs for which over 50% of the trials were excluded had the entire run excluded from further functional data analysis.

Functional data for each run for all participants were preprocessed. (Motion correction parameters were also included as predictors of no interest in the GLM.) Preprocessing of functional data involved slice scan time correction (cubic spline), temporal filtering (for removal of frequencies <2 cycles/run) and 3D motion correction (trilinear/sinc). On the basis of motion correction results for each run, data for runs that indicated abrupt movement over 2 mm were excluded from further analyses. The whole data set of four participants was not included in statistical analyses due to head motion exceeding our set threshold. Anatomical data was transformed to a Talairach template (Talairach & Tournoux, 1988). The remaining 12 participants' functional data were coregistered using gradient-based affine alignment (translation,

rotation, scale affine transformation) to the raw anatomical data. Functional data were spatially smoothed using an FWHM of 8 mm.

From the final 12 participants' data, a random effects (RFX) GLM was conducted on the compiled data. The result of the RFX GLM produced a statistical map of activation whereby positive activation showed a repetition suppression (RS) effect (i.e., higher activation in response to 'Novel' orientation trials over 'Repeat' orientation trials) and negative activation showed a repetition enhancement (RE) effect (i.e., higher activation in response to 'Repeat' orientation trials over 'Novel' orientation trials). A statistical threshold of $p<0.05$ ($t_{(11)}=2.25$, $p=0.04589$) was utilized. To correct for the multiple comparisons problem, a BrainVoyager QX cluster threshold correction plugin was used and applied to each of the three spatial conditions (Forman et al., 1995). Cortical regions that survived cluster threshold correction at $p<0.05$ ($t_{(11)}=2.25$, $p=0.04589$) within each of the three spatial conditions were deemed to be statistically significant (cluster threshold for Space-fixed condition=131 voxels; cluster threshold for Retina-fixed condition=172 voxels; and cluster threshold for Frame-independent condition=170 voxels). Areas that did not survive cluster threshold correction but survived a threshold of $p<0.05$ ($t_{(11)}=2.25$, $p=0.04589$) were deemed to show a trend toward significance (and are denoted through the use of a white triangle in Figures 2, 3, 4). Both types of areas were included in further analyses (specifically, for time course inspection and beta weight statistical analysis).

The results shown in this manuscript are from the voxelwise analysis of the beta weights during the 'test' stimulus presentation period, in order to identify areas that show adaptation (RS or RE effects) to orientation in the three spatial conditions tested. From areas that showed such adaptation effects, time courses were then extracted and inspected. Based on inspection of the data, the typical time course was expected to have an initial increase in BOLD activity in

response to the first presentation of the stimulus, a second increase in activity in response to the second presentation of the stimulus, and a third increase or plateau in activity during the button press response period. Beta weight values were also extracted from these areas for further statistical analyses to determine if the observed areas were shared among the spatial conditions or were condition-specific. Areas that are mentioned hereafter met all of the criteria mentioned above. Statistical values (t-statistic and p-values) will be indicated for each of the t-tests run for each brain area (i.e., $t_{(df)s}$ and p_s represent the t-statistic and p-value, respectively, for a t-test conducted on the Novel and Repeat beta weights within a given area for the Space-fixed condition; $t_{(df)r}$ and p_r for the Retina-fixed condition and $t_{(df)f\text{-}i}$ and $p_{f\text{-}i}$ for the Frame-independent condition).

2.3b.ii Localizer data

To localize cortical areas involved in saccadic movements, we employed a task that has specifically revealed the 'parietal eye field' (Dunkley et al., submitted). This task required participants to fixate centrally for 2 s. Then, two fixation crosses appeared simultaneously 12° apart along the middle of a black screen. Participants were required to make self-paced saccades between the two fixation crosses for 2 s. A series of fixation followed by self-paced saccades took place for 256 s (128 volumes). For the saccade-associated functional localizer, 33 slices were acquired and a total of 128 functional volumes of data were acquired (TR= 2000 ms, TE = 30 ms; in-slice resolution of 3 mm x 3 mm; slice thickness= 3mm, no gap).

The retinotopic localizer commenced with a baseline of 12 s of central fixation on a black screen. A checkered wedge appeared and rotated through the eight angles counterclockwise for 48 s (24 volumes) per block, with 8 blocks in total. Central fixation for the final 12 s signaled the end of the trials and the localizer. Participants were required to maintain central fixation

throughout the 6 min 48 s retinotopic localizer task. For the retinotopic localizer task, 33 slices were acquired and a total of 204 functional volumes were obtained (TR= 2000 ms; TE= 30 ms; in-slice resolution of 3 mm x 3 mm; slice thickness= 3mm, no gap).

During anatomical image acquisition and localizer image acquisition, the experimental set-up was kept the same as described above with the exception of the use of an anterior 4-channel head mount and the exclusion of the 'button box'. Functional runs for independent localizers (saccades and retinotopy) were preprocessed in the same way as experimental functional runs are preprocessed (see 2.3b.i). The GLM for the saccade localizer included two predictors: One predictor ("Fixate") modeled the haemodynamic response for the fixation (2 s), whereas the second predictor (for saccades, "Sacc") modeled the response for the saccade period (4 s). The fixation-saccade pattern was repeated for a total duration of 256 s. A GLM was created using this protocol file for the saccade localizer. To determine the areas that are involved in self-paced saccades within our tested participants, a fixed effects (FFX) GLM was run on the compiled data of 9 participants'. From this GLM, a contrast was conducted to identify "Sacc" responsive areas.

The GLM for the retinotopic localizer contained a predictor of interest for each of the 8 angles through which the wedge traversed ("Wedge1," "Wedge 2," Wedge 3," "Wedge 4," "Wedge 5," "Wedge 6," "Wedge 7," and "Wedge 8") for 6 s each. There were 8 angles per run and 8 runs in total. The GLMs for the retinotopic localizer for each functional run for 10 participants were created. For this retinotopic localizer, a cross-correlation analysis was conducted on the eight wedge predictors (time course segmentation size= 10 volumes (20 s); cross correlation lags= 24 (3 volumes for each wedge, 8 wedges in total per run)). The results

were then thresholded (r>0.22, t=0.219) to show areas in the brain that code in a retinotopic manner.

Lastly, to identify areas that show visual field-specific neural correlates (directional selectivity localizer), we used a contrast on the experimental predictors, Adapt_LVF > Adapt_RVF, on the 12 participants' data ($t_{(11)}$=2.25, p=0.04589).

2.4 Results

Our objective, in this study, was to identify and compare areas that show adaptation to object orientation in three spatial conditions (Space-fixed, Retina-fixed and Frame-independent). In the following sections, we will first describe the cortical areas that showed repetition suppression (RS) or enhancement (RE) effects derived from each condition separately, compare the Novel vs. Repeat activations of these areas across the different conditions, and finally describe the areas that were common to all spatial conditions. (Please see Table 1 below for a list of the acronyms used in the following results sections, as well as Table 2 for the Talairach coordinates of each cortical area mentioned in the text.)

2.4a Space-fixed condition

We used a Novel > Repeat contrast for all Space-fixed trials (i.e., (Space-fixed_Novel_LVF + Space-fixed_Novel_RVF) > (Space-fixed_Repeat_LVF + Space-fixed_Repeat_RVF)) to identify brain regions that show adaptation to orientation in a space-fixed condition. The *left panel* of Figure 2 shows an activation map overlaid on an 'inflated brain' rendering of an exemplary participant in the top two images and horizontal slices of an average brain of the 12 participants in the bottom two images. Figure 2 (*right column*) shows the

corresponding beta weights derived from these 'Space-fixed' areas, and also compares these to the beta weights derived from the same areas in the other tasks.

As seen in the left panel of Figure 2, in the Space-fixed condition, RS effects (orange) were observed in parietal areas including the supramarginal gyrus (SMG; $t_{(11)s}$= 2.66, p_s= 0.011, $t_{(11)r}$= -0.58, p_r= 0.288, $t_{(11)f\text{-}i}$= 1.53, $p_{f\text{-}i}$=0.077) and the intraparietal sulcus (IPS; $t_{(11)s}$= 3.27, p_s= 0.004, $t_{(11)r}$= 2.04, p_r= 0.033, $t_{(11)f\text{-}i}$= 2.34, $p_{f\text{-}i}$=0.020) in the left hemisphere (SMG in the right

Acronym	**Full name**
SMG	Supramarginal Gyrus
LOtG	Lateral Occipitotemporal Gyrus
lBA 7	Lateral Brodmann Area 7
mBA 7	Medial Brodmann Area 7
LIP	Lateral Intraparietal Cortex
IPS	Intraparietal Sulcus
aIPS	Anterior Intraparietal Sulcus
mIPS	Middle Intraparietal Sulcus
pmIPS	Posterior Middle Intraparietal Sulcus
PMd	Doral Premotor Cortex
M1	Primary Motor Cortex
Pre-SMA	Presupplementary Motor Area
SMA	Supplementary Motor Area
PreCS	Precentral Sulcus
IFG	Inferior Frontal Gyrus
FEF	Frontal Eye Field

Table 1. List of acronyms of cortical regions mentioned throughout this article and their corresponding, full names.

hemisphere did not approach significance). We also observed RS effects in left hemisphere frontal motor areas including primary motor cortex (PMd/M1; $t_{(11)s}$= 3.56, p_s= 0.002, $t_{(11)r}$= 1.82, p_r= 0.048, $t_{(11)f\text{-}i}$= 3.78, $p_{f\text{-}i}$=0.002), pre-supplementary motor area (pre-SMA, SMA; $t_{(11)s}$=3.43 , p_s= 0.003, $t_{(11)r}$= 2.75, p_r= 0.009, $t_{(11)f\text{-}i}$= 2.80, $p_{f\text{-}i}$= 0.009) and SMA($t_{(11)s}$= -2.68, p_s= 0.011, $t_{(11)r}$= -3.32, p_r= 0.003, $t_{(11)f\text{-}i}$= -2.70, $p_{f\text{-}i}$= 0.010). RE effects (blue) were observed in the lateral occipitotemporal gyrus (LOtG; $t_{(11)s}$= 4.44, p_s= 0.0005, $t_{(11)r}$= 1.16, p_r= 0.135, $t_{(11)f\text{-}i}$= 1.23,

p_{fi}=0.122) in the left hemisphere. (For all of the areas mentioned here, the associated Talairach coordinates may be found in Table 2.)

Area of Interest	Mean x	Mean y	Mean Z	Stdev X	Stdev Y	Stdev Z	Nr of Voxels
PreCS_RET_NovVsRep	-38.71	-9.9	56.32	2.1	2.03	2.34	413
PreSMA_RET_NovVsRep	-4.08	7.29	50.86	2.55	2.79	2.49	708
SMA_RET_NovVsRep	-7.23	-4.86	57.28	2.84	2.75	2.86	908
IPS_RET_NovVsRep	-39.77	-47.49	36.44	2.54	2.53	2.37	639
IFG_RET_NovVsRep	-37.61	19.6	34.76	2.59	2.27	2.17	529
PrecentralSulcus_RET_NovVsRep	-56.5	-10.51	37.77	2.45	2.02	1.64	308
lBA7_RET_NovVsRep	-30.32	-59.42	50.73	1.44	2.22	0.88	107
PreSMA_SPAT_NovVsRep	-5.81	4.54	53.34	2.65	2.37	2.09	543
SMA_SPAT_NovVsRep	-8.95	-6.53	54.53	1.27	2.37	1.81	98
PMd/M1_SPAT_NovVsRep	-29.47	-18.18	50.1	2.3	2.48	2.59	647
PrecentralSulcus_SPAT_NovVsRep	-55.93	-5.12	40.98	1.93	1.78	2.41	349
aIPS_SPAT_NovVsREP	-43.54	-40.96	36.4	2.74	1.08	1.31	97
SMG_SPAT_NovVsRep	-58.37	-45.87	36.26	1.78	2.21	2.3	325
IPS_SPAT_NovVsRep	-39.2	-54.9	36.79	1.82	1.3	2.1	206
PreSMA_UNMAT_NovVsRep	-5.83	3.91	51.56	2.82	2.66	2.32	680
SMA_UNMAT_NovVsRep	-1.73	-11.6	63.46	2.82	2.68	2.72	849
FEF_UNMAT_NovVsRep	-28.59	-10.74	57.72	2.85	2.78	2.81	941
PMd/M1_UNMAT_NovVsRep	-30.75	-20.22	52.44	2.81	2.76	2.82	927
IPS_UNMAT_NovVsRep	-37.54	-50.69	34.69	2.83	2.79	2.81	948
mBA7_UNMAT_NovVsRep	-13.53	-67.21	41.63	2.73	2.67	2.77	869
PreCS_NovVsRep_UNMAT	-42.11	-11.6	55.1	2.77	2.83	2.7	887
LOtG_SPAT_RepvsNov	-36	-40.95	-21.73	2.23	2.21	2.14	439
LOtG_UNMAT_RepvsNov_RH	46.35	-44.78	-17.44	2.62	2.62	2.29	601
PreSMA_Shared_NovVsRep	-7.18	2.77	52.42	2.58	2.39	1.61	403
PMd/M1_Shared_NovVsRep	-25.5	-16.92	52.33	0.65	0.49	1.18	12
pmIPS_Shared_NovVsRep	-38.44	-53	38.89	1.07	0	0.74	9

Table 2. Talairach coordinates of areas of interest resulting from RS or RE effects. In the first column, the cortical region is referred to by its acronym (see Table 1), followed by the spatial condition in which it was found (i.e., RET refers to the Retina-fixed condition, SPAT refers to the Space-fixed condition, and UNMAT refers to the Frame-independent condition), which is subsequently followed by the contrast that was conducted (i.e., NovVsRep refers to the activity in response to Novel (Nov) trials versus Repeat (Rep) trials). If not indicated after the contrast (i.e., NovVsRep), the area was found in the left hemisphere (otherwise, RH refers to an area found within the right hemisphere).

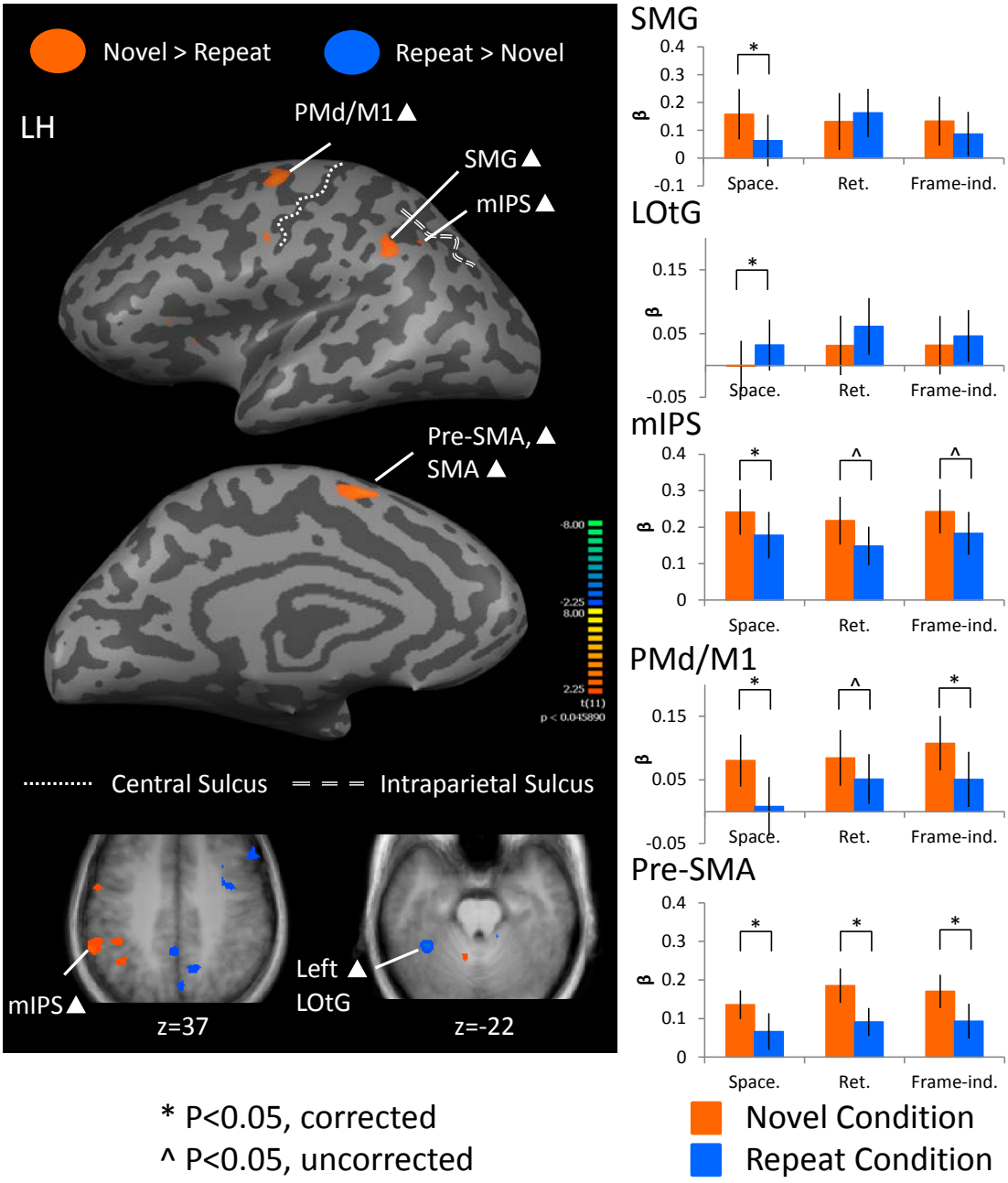

Figure 6. Voxelwise statistical map obtained using an RFX GLM (n=12) for Novel > Repeat in the Space-fixed condition (p<0.05). *Left column*: Activation map is displayed on inflated brain of a representative subject. Activation in orange depicts Repetition Suppression (RS) effects (i.e., where activation is higher for Novel > Repeat), whereas activation in blue depicts Repetition Enhancement (RE) effects (i.e., where activation is higher for Repeat > Novel). Additional slices at bottom show full extent of mIPS and LOtG activation. Areas of interest included SMG: Supramarginal Gyrus, LOtG: Lateral Occipitotemporal Gyrus, mIPS: middle Intraparietal Sulcus, PMd/M1: dorsal Premotor, Primary Motor Cortex, Pre-SMA: Pre-Supplementary Motor Area and SMA: Supplementary Motor Area. *Right column*: Beta weights on the right compare peak voxels from the Space-fixed condition to the Retina-fixed, and Frame-independent conditions. Specificity for the Space-fixed condition was found in SMG and LOtG. White triangles indicate cortical regions that passed a p<0.05, but did not pass cluster threshold correction in the left panel. * indicate statistically significant (corrected) differences between Novel and Repeat β weights on the graphs in the right panel, whereas ^ indicate statistically significant differences (uncorrected).

Turning to the beta weights for these areas in the right column of Figure 2, there was (by definition) always a significant difference between Novel and Repeat conditions in the spatial condition (from which these regions were derived), but this was not necessarily the case for the other spatial conditions. SMG and LOtG showed Space-fixed-specific results, whereas the RS effects in mIPS, PMd/M1 and pre-SMA were common to all three conditions. Overall, our Space-fixed condition produced very specific feature-specific modulations in the left hemisphere, with RS effects in parietal and frontal areas, whereas RE effects were in occipitotemporal regions.

2.4b Retina-fixed condition

Retina-fixed trials, a Novel > Repeat contrast was used (i.e., (Retina-fixed_Novel_LVF + Retina-fixed_Novel_RVF) > (Retina-fixed_Repeat_LVF + Retina-fixed_Repeat_RVF)) to identify areas showing adaptation to orientation in a retina-fixed condition. Figure 3 shows activation maps are depicted on an inflated brain (*left panel*) and bar graphs of beta weights *(right column*) from retina-fixed trials. RS effects were observed in parietal areas such as the IPS (IPS; $t_{(11)s}$= 2.20, p_s= 0.025, $t_{(11)r}$= 2.38, p_r= 0.018, $t_{(11)f\text{-}i}$= 2.81, $p_{f\text{-}i}$=0.009) and lateral BA 7 (lBA 7; $t_{(11)s}$= -1.08, p_s= 0.153, $t_{(11)r}$= -2.65, p_r= 0.011, $t_{(11)f\text{-}i}$= -1.79, $p_{f\text{-}i}$= 0.051) in the left hemisphere. Areas in frontal cortex, including M1 ($t_{(11)s}$= 1.59, p_s= 0.070, $t_{(11)r}$= 2.75, p_r= 0.009, $t_{(11)f\text{-}i}$= 2.65, $p_{f\text{-}i}$= 0.011), pre-SMA ($t_{(11)s}$= 1.98, p_s= 0.036, $t_{(11)r}$= 2.78, p_r= 0.009, $t_{(11)f\text{-}i}$= 2.49, $p_{f\text{-}i}$= 0.015), SMA ($t_{(11)s}$= -2.15, p_s= 0.027, $t_{(11)r}$= -3.63, p_r= 0.002, $t_{(11)f\text{-}i}$= -3.11, $p_{f\text{-}i}$= 0.005), precentral sulcus (preCS; $t_{(11)s}$= 0.536, p_s= 0.301, $t_{(11)r}$= 2.16, p_r= 0.027, $t_{(11)f\text{-}i}$= 2.97, $p_{f\text{-}i}$= 0.006) and inferior frontal gyrus (IFG; $t_{(11)s}$= 0.403, p_s= 0.347, $t_{(11)r}$= 3.10, p_r= 0.005, $t_{(11)f\text{-}i}$= 1.39, $p_{f\text{-}i}$= 0.096) in the left hemisphere also showed RS effects. RE effects were not observed in this spatial condition. Our beta weight analysis suggests that lBA 7, and IFG, showed RS effects specific to the Retina-

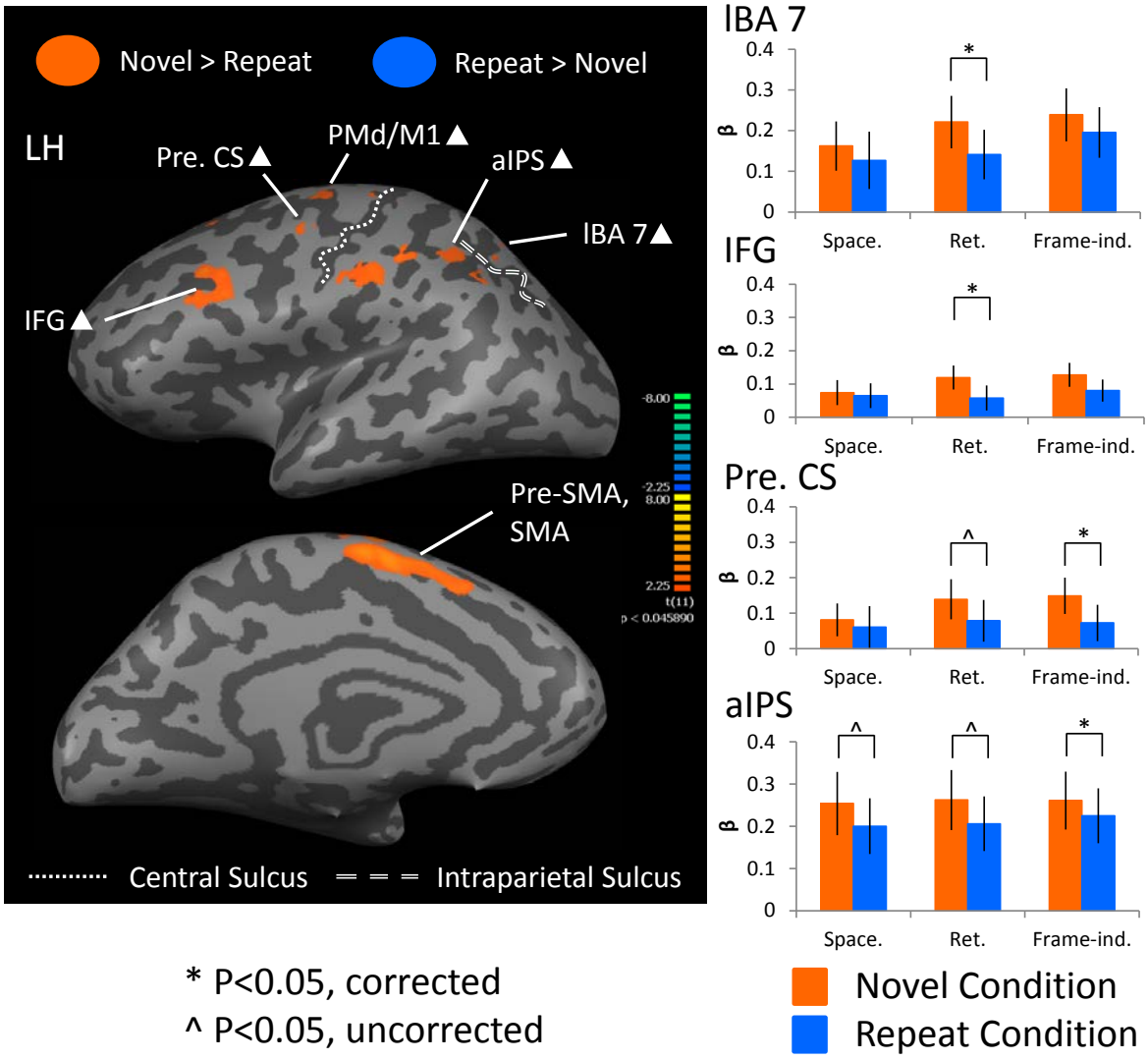

Figure 7. Voxelwise statistical map obtained using an RFX GLM (n=12) for Novel > Repeat in the Retina-fixed condition (p<0.05). *Left column*: Activation map is displayed on inflated brain of a representative subject. Activation in orange depicts Repetition Suppression (RS) effects (i.e., where activation is higher for Novel > Repeat), whereas activation in blue depicts Repetition Enhancement (RE) effects (i.e., where activation is higher for Repeat > Novel). Areas of interest included lBA 7: lateral Brodmann area 7, aIPS: anterior Intraparietal Sulcus, PMd/M1, Pre. CS: Precentral Sulcus, IFG: Inferior Frontal Gyrus, Pre-SMA and SMA. *Right column*: Beta weights on the right compare peak voxels from the Retina-fixed condition to the Space-fixed, and Frame-independent conditions. We found specificity for the Retina-fixed condition in l BA 7 and IFG. White triangles indicate cortical regions that passed a p<0.05, but did not pass cluster threshold correction in the left panel. * indicate statistically significant (corrected) differences between Novel and Repeat β weights on the graphs in the right panel, whereas ^ indicate statistically significant differences (uncorrected).

fixed task, whereas preCS, aIPS, and again PMd/M1/PreSMA/SMA (not repeated here) showed significant feature modulations across all three tasks. In summary, our Retina-fixed task only

produced RS effects in the left parietal and frontal cortex, but involved a slightly larger, more continuous swath of cortical tissue (compared to Space-fixed) running from IPS to IFG.

2.4c Frame-independent condition

In the Frame-independent condition, a Novel > Repeat contrast was used (i.e., (Frame-independent_Novel_LVF + Frame-independent_Novel_RVF) > (Frame- independent _Repeat_LVF + Frame-independent_Repeat_RVF)) to identify brain regions that show adaptation to orientation. Activation maps are overlaid onto an inflated brain/horizontal brain slice and on an average brain and bar graphs of beta weights are shown (Figure 4, left and right, respectively). RS effects were observed in parietal areas such as IPS ($t_{(11)s}$= 2.65, p_s= 0.011, $t_{(11)r}$= 2.13, p_r= 0.028, $t_{(11)f\text{-}i}$= 2.63, $p_{f\text{-}i}$= 0.012) and medial BA 7 (mBA 7; $t_{(11)s}$= 0.825, p_s= 0.213, $t_{(11)r}$= 0.729, p_r= 0.241, $t_{(11)f\text{-}i}$= 2.91, $p_{f\text{-}i}$= 0.007) in the left hemisphere. Additionally, RS effects were observed in frontal areas such as preCS ($t_{(11)s}$= 0.607, p_s= 0.278, $t_{(11)r}$= 1.89, p_r= 0.042, $t_{(11)f\text{-}i}$= 3.55, $p_{f\text{-}i}$= 0.002), M1 ($t_{(11)s}$= 3.39, p_s= 0.003, $t_{(11)r}$= 2.05, p_r= 0.032, $t_{(11)f\text{-}i}$= 4.74, $p_{f\text{-}i}$= 0.0003), pre-SMA ($t_{(11)s}$= 3.26, p_s= 0.004, $t_{(11)r}$= 2.74, p_r= 0.01, $t_{(11)f\text{-}i}$= 2.85, $p_{f\text{-}i}$= 0.008), SMA ($t_{(11)s}$= -0.807, p_s= 0.218, $t_{(11)r}$= -1.59, p_r= 0.070, $t_{(11)f\text{-}i}$= -3.97, $p_{f\text{-}i}$= 0.001) and frontal eye fields (FEF; $t_{(11)s}$= 1.16, p_s= 0.135, $t_{(11)r}$= 1.10, p_r= 0.148, $t_{(11)f\text{-}i}$= 3.91, $p_{f\text{-}i}$= 0.001) in the left hemisphere. On the other hand, RE effects were observed in LOtG ($t_{(11)s}$= 0.128, p_s= 0.450, $t_{(11)r}$= -0.094, p_r= 0.463, $t_{(11)f\text{-}i}$= 4.18, $p_{f\text{-}i}$= 0.0008) in the right hemisphere. Here, mBA 7, FEF and LOtG showed Frame-independent condition-specific effects. Overall, RS effects in this condition are found within a parietofrontal network (in this case, more widespread network than either of the preceding tasks), whereas RE effects are depicted in right occipital cortex.

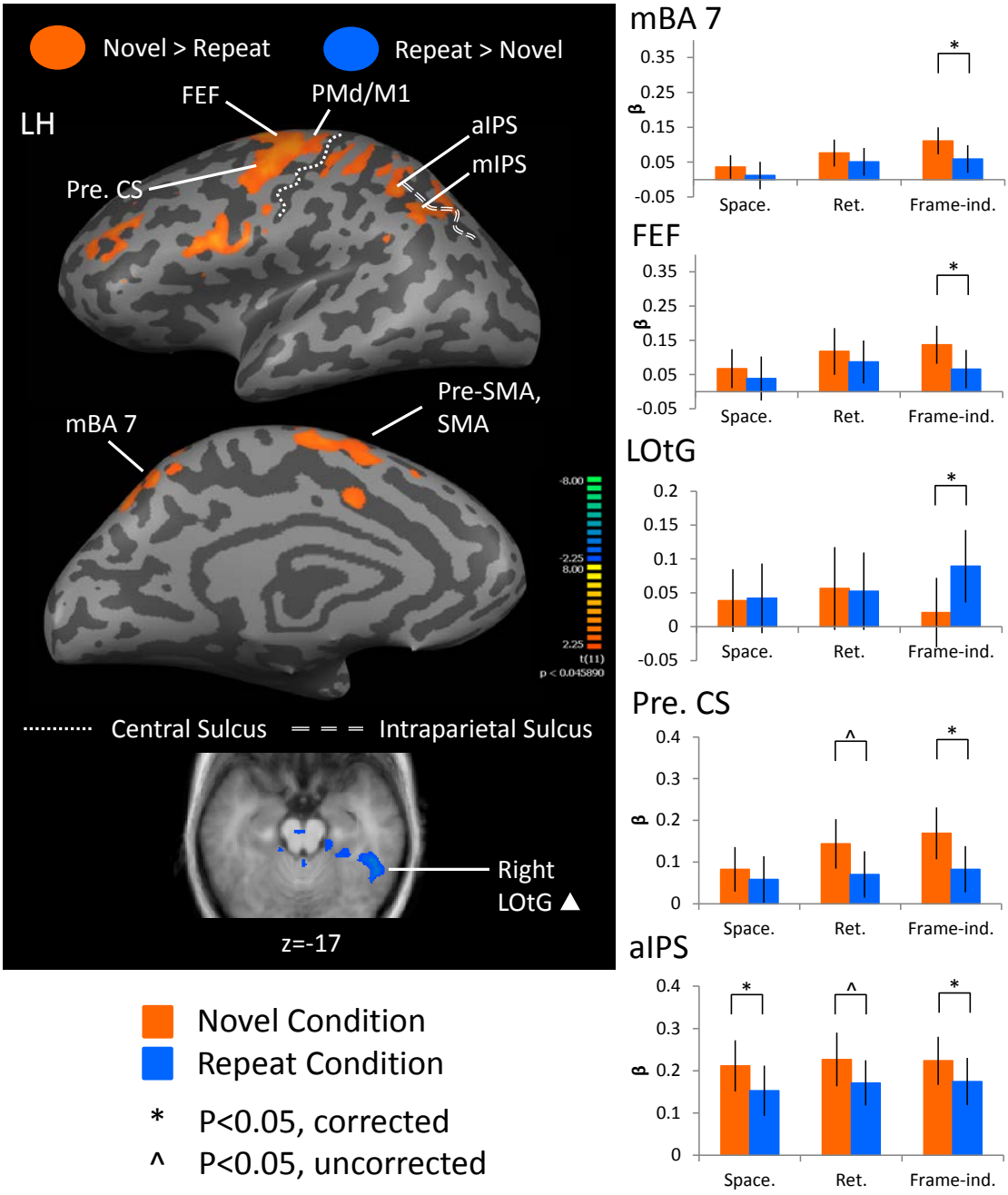

Figure 8. Voxelwise statistical map obtained using an RFX GLM (n=12) for Novel > Repeat in the Frame-independent condition (p<0.05). *Left column*: Activation map is displayed on inflated brain of a representative subject. Activation in orange depicts Repetition Suppression (RS) effects (i.e., where activation is higher for Novel > Repeat), whereas activation in blue depicts Repetition Enhancement (RE) effects (i.e., where activation is higher for Repeat > Novel). An additional slice at bottom shows full extent of LOtG activation. Areas of interest included SPL, mIPS, aIPS, PMd/M1, FEF: Frontal Eye Field, Pre. CS, Pre-SMA, SMA and LOtG. *Right column*: Beta weights on the right compare peak voxels from the Frame-independent condition to the Space-fixed condition, and the Retina-fixed conditions. We found specificity for the Frame-independent condition in mBA 7 (medial BA 7), FEF and LOtG. White triangles indicate cortical regions that passed a p<0.05, but did not pass cluster threshold correction in the left panel. * indicate statistically significant (corrected) differences between Novel and Repeat β weights on the graphs in the right panel, whereas ^ indicate statistically significant differences (uncorrected).

2.4d Conjunction results

Conjunction analyses were used to identify cortical regions that are feature-sensitive and common to all three spatial conditions tested here. Novel > Repeat and Repeat > Novel contrasts were used and subsequently, two condition and three condition conjunctions were conducted to identify the extent of overlap with any of the two-condition conjunctions, as the three-way conjunction results identified small areas of activation showing overlap in all three spatial conditions (Figure 5). Activation maps are shown on an average brain (Figure 5). RS effects were common in motor areas in the left hemisphere such as PMd/M1 ($t_{(11)s}$= 3.02, p_s= 0.006, $t_{(11)r}$= 2.53, p_r= 0.014, $t_{(11)f\text{-}i}$= 3.08, $p_{f\text{-}i}$= 0.005) and pre-SMA ($t_{(11)s}$= -3.59, p_s= 0.002, $t_{(11)r}$= -2.70, p_r= 0.010, $t_{(11)f\text{-}i}$= -2.65, $p_{f\text{-}i}$= 0.011). In the parietal cortex in the left hemisphere, a very small portion of the posterior portion of mIPS (pmIPS; $t_{(11)s}$= 3.04, p_s= 0.006, $t_{(11)r}$= 2.25, p_r= 0.023, $t_{(11)f\text{-}i}$= 2.23, $p_{f\text{-}i}$= 0.024), showed a common RS effect in all three spatial conditions.

2.4e Time courses

Figure 6 shows representative time courses derived from selected regions extracted from the previous analyses, all from the left hemisphere (LH) including pmIPS as a common area (A), SMG and LOtG as unique ‘Space-fixed’ areas (B), lBA 7 as a unique ‘Retina-fixed’ area (C), and mBA 7 and FEF as unique ‘Frame-independent’ areas (D). In most cases, one can detect an initial peak BOLD response late in the pre-test phase (6 s after presentation of the test stimulus). This is followed by a second peak BOLD response at the end of the test phase, 4-6 s after presentation of the test stimulus. This is then followed by a third peak (probably related to the behavioral response) about 4 s after the cue to respond. Importantly, the initial separation between Novel (orange) and Repeat (blue) conditions coincides with the second visual peak – as expected if this is related to early processing of the difference – and continues approximately

until the peak of the behavioral response. This is why these areas emerge from our analysis of the GLM/β weights locked to the 2nd, test stimulus.

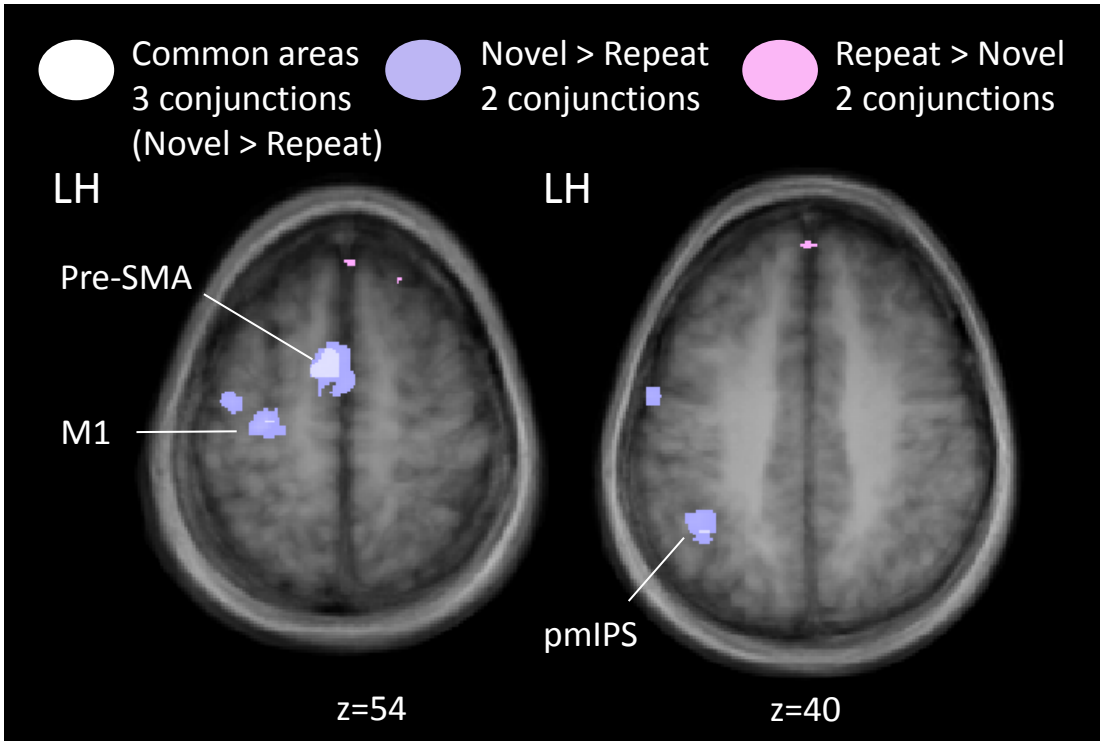

Figure 9. Voxelwise statistical map obtained from an FFX GLM (n=12) for Novel > Repeat in a multiple conjunction analysis. Areas depicted in purple show any two conjunctions using Novel > Repeat contrast (i.e., Space-fixed U Retina-fixed, Space-fixed U Frame-independent and/or Retina-fixed U Frame-independent). Similar conjunctions are shown in pink for a Repeat > Novel contrast. Three-way conjunction analysis results are shown in white for a contrast of Novel > Repeat (i.e., Space-fixed U Retina-fixed U Frame-independent). The specific contrasts used are two-condition and three-condition conjunctions (two-way: 1) (Space-fixed_Novel_LVF + Space-fixed_Novel_RVF) > (Space-fixed_Repeat_LVF + Space-fixed_Repeat_RVF) U (Retina-fixed_Novel_LVF + Retina-fixed_Novel_RVF) > (Retina-fixed_Repeat_LVF + Retina-fixed_Repeat_RVF); 2) (Space-fixed_Novel_LVF + Space-fixed_Novel_RVF) > (Space-fixed_Repeat_LVF + Space-fixed_Repeat_RVF) U (Frame-independent_Novel_LVF + Frame-independent_Novel_RVF) > (Frame-independent_Repeat_LVF + Frame-independent_Repeat_RVF); 3) (Retina-fixed_Novel_LVF + Retina-fixed_Novel_RVF) > (Retina-fixed_Repeat_LVF + Retina-fixed_Repeat_RVF) U (Frame-independent_Novel_LVF + Frame-independent_Novel_RVF) > (Frame-independent_Repeat_LVF + Frame-independent_Repeat_RVF); three-way: (Space-fixed_Novel_LVF + Space-fixed_Novel_RVF) > (Space-fixed_Repeat_LVF + Space-fixed_Repeat_RVF) U (Retina-fixed_Novel_LVF + Retina-fixed_Novel_RVF) > (Retina-fixed_Repeat_LVF + Retina-fixed_Repeat_RVF) U (Frame-independent_Novel_LVF + Frame-independent_Novel_RVF) > (Frame-independent_Repeat_LVF + Frame-independent_Repeat_RVF)).

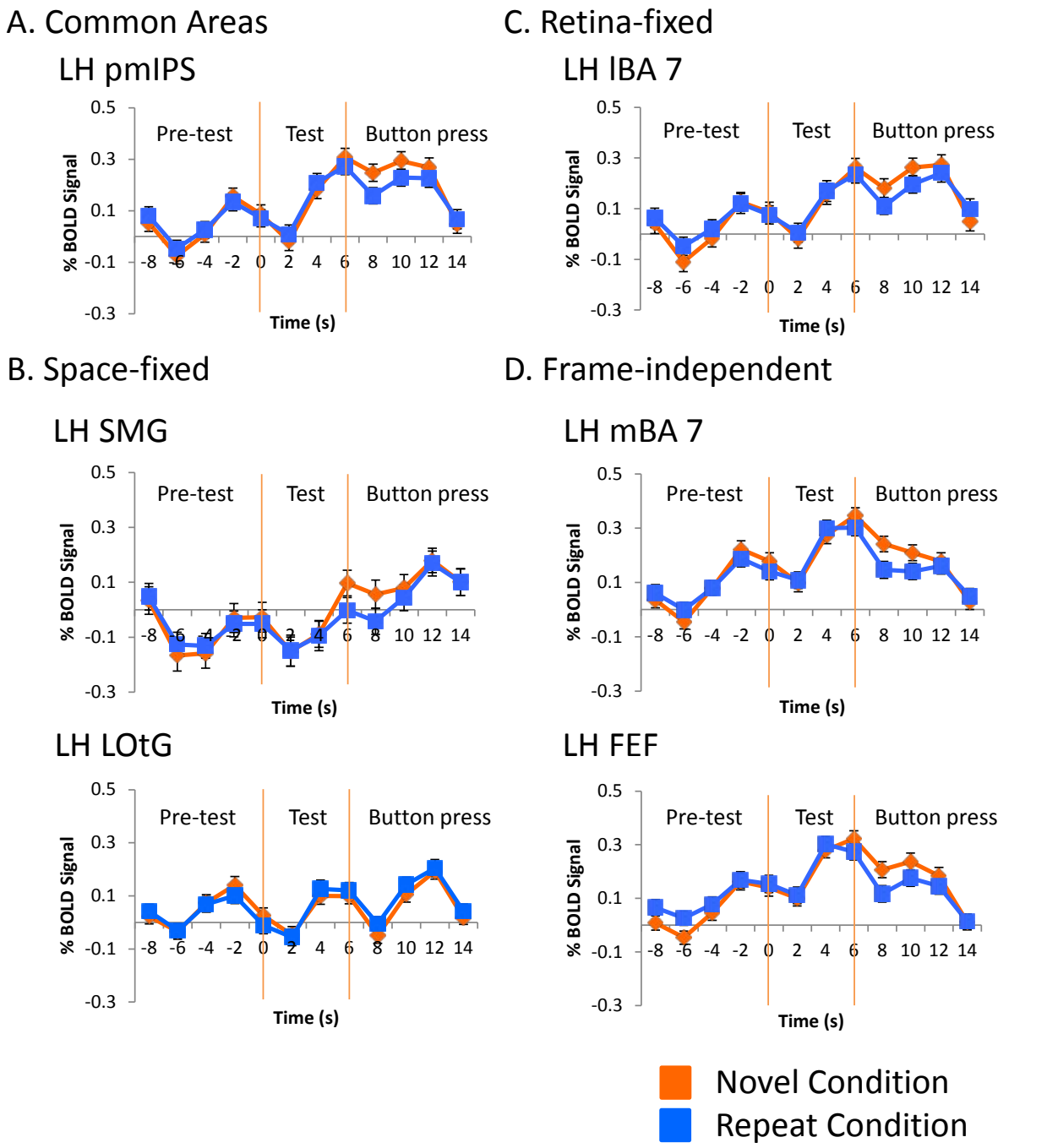

Figure 10. Event-related average time courses for cortical regions that show adaptation (repetition suppression or enhancement) to object orientation in areas shared by Space-fixed, Retina-fixed and Frame-independent spatial conditions, as well as within each of the spatial conditions. *A.* Averaged percent BOLD signal change (%BSC) shown for the pmIPS, an area that shows adaptation among all three spatial conditions. *B.* Averaged %BSC shown for areas that show Space-fixed-specific adaptation, SMG and LOtG. *C.* Averaged %BSC depicted for the lBA 7, which shows Retina-fixed-specific adaptation effects. *D.* Averaged %BSC shown for areas that demonstrate Frame-independent-specific adaptation effects, mBA 7 and FEF. All event-related average time courses extracted from peak voxels within each of the areas shown. Presentation of pre-test stimulus occurs at -6 s. Test stimuli are presented at 0 s. Lastly, the button press prompt occurs at 6 s. Orange vertical lines demarcate the beginning and end of the test stimulus presentation period, and separate it from the pre-test stimulus presentation period and the button press response period. pmIPS: posterior middle Intraparietal Sulcus.

2.4f Localizer results

Figure 7 summarizes the cortical locations of some of our main findings relative to three types of localizer. Each panel (A, B, C) shows activation maps plotted over an inflated brain rendering of the left hemisphere where we obtained most of our data. The brain areas identified by the three localizer tasks are indicated by purple, whereas the brain areas observed in the three experimental conditions are indicated in a different colour in Figure 7. Only experimental areas that were near to or overlapped with the localizer data are labeled.

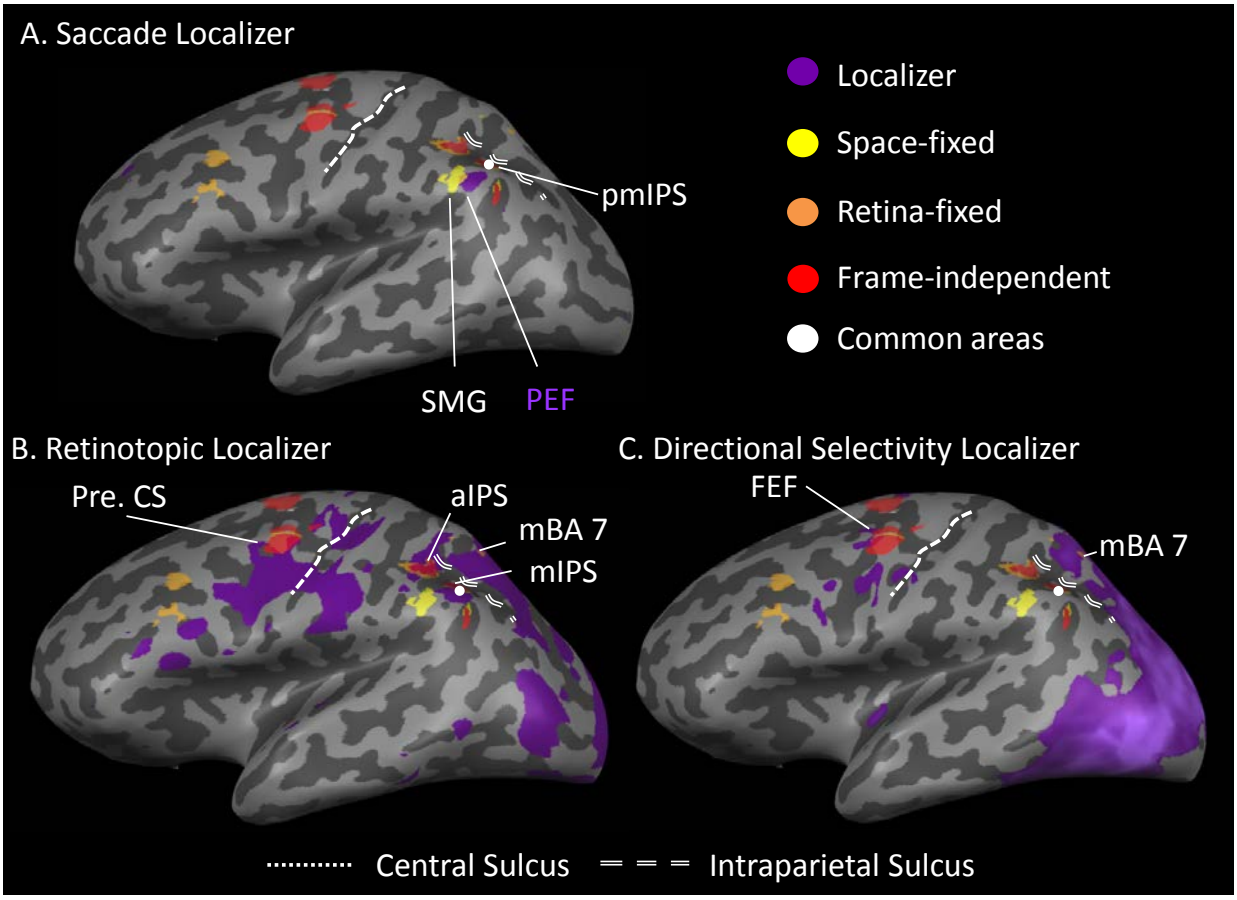

Figure 11. Functional localizer data for saccades and retinotopic mapping. ***A.*** Activation map is displayed on an inflated brain of a representative participant for saccade localizer. Activation in purple depicts areas that show activation during saccade activity > fixation. ***B.*** Activation map is displayed on average brain (n=12) for retinotopic localizer. Activation in purple depicts retinotopic mapping in areas that respond to the left visual field within the left hemisphere. ***C.*** Activation map is displayed on inflated brain of representative participant for directional selectivity localizer. Using contrast for Left Visual Field > Right Visual Field in the pre-test stimulus presentation, areas that are directionally selective are denoted by the purple colour.

As shown in Figure 7A, the location of the parietal eye field (PEF) was identified by our independent saccade localizer task. Relative to the PEF, pmIPS was medially adjacent and SMG was laterally adjacent, but neither area overlapped with PEF. Figure 7B shows the data from our independent localizer for retinotopy (using a conservative statistical threshold of $r>0.22$, $t=0.219$). Areas mIPS, lBA 7, aIPS and the precentral sulcus showed partial overlap with those localized retinotopic brain regions. Finally, to determine which, if any, areas show visual field specificity within the confines of our task, we used a contrast (Adapt_LVF > Adapt_RVF) on data from the first stimulus presentation across all tasks. These data, shown in Figure 7C, were generally similar patterns to the standard retinotopy localizer, but were weighted more toward the posterior cortex. Here, mBA 7 and FEF showed partial overlap with the field-specific areas.

2.5 Discussion

In this study, we aimed to identify the cortical regions that are involved in transsaccadic comparison of object orientation in three different spatial tasks. We found that in our Space-fixed condition, there is adaptation within the left parietal cortex (Repetition suppression) as well as within an occipitotemporal cortex in the left hemisphere (Repetition enhancement). In the Retina-fixed condition, we observed adaptation in a parietofrontal network (Repetition suppression) in the left hemisphere. Lastly, in our third, Frame-independent condition, we found an adaptation effect in a parietofrontal network (Repetition suppression) and in an occipitotemporal network (Repetition enhancement). We also showed that there is adaptation in common, frontal motor areas, which we reckon is due to the button press response, as well as within a region in the parietal cortex (perhaps, as a result of the transsaccadic task). Thus, in this study, we were able to determine the cortical correlates (and networks) involved in transsaccadic

processing of object orientation, although one cannot assume that these findings extend directly to transsaccadic judgements of other types of objects and features.

It is important to note that our three tasks (Space-fixed, Retina-fixed, and Frame-independent) were not designed to reveal specific Space-fixed, Retina-fixed, and Frame-independent mechanisms within the brain. This misunderstanding could lead to absurd conclusions (e.g., that the dorsal visual stream is predominated by frame-independent mechanisms) (Figure 4), which would contrast what we know about this system (Buneo & Andersen, 2006; Crawford et al., 2011; Goodale & Milner, 2008, 1992). Instead, our study was designed to test if different cortical networks (possibly using multiple intrinsic spatial coding mechanisms) are involved in solving a similar transsaccadic task when the compared stimuli are paired in different spatial arrangements.

2.5a Common areas

In our experiment, frontal motor areas, such as pre-SMA, SMA and PMd/M1, were consistently activated in all three spatial conditions. Traditionally, these frontal motor areas have been thought of as responsible for motor output processing, and have not been identified as potentially being involved in transsaccadic integration or memory. For example, pre-SMA and and SMA have been implicated in learning of movement sequences (Leigh & Kennard, 2005). Moreover, pre-SMA plays a role in making motor plans for effectors in response to visual information, as well as updating them based on new information (Shima, Mushiake, Saito, & Tanji, 1996), whereas SMA or PMd/M1 are involved in executing manual motor plans (Grafton, Hazeltine, & Ivry, 1998; Matsuzaka, Aizawa, & Tanji, 1992). The coordinates for PMd/M1 are also consistent with activation in the hand motor area those found by Dechent and Frahm (2003), as well as by neuromagnetic recordings (Cheyne, Kristeva, & Deecke, 1991). Thus, it seems

most likely that these areas were not involved in transsaccadic integration. Our interpretation of these commonly activated areas in the three spatial conditions that we probed is that they may actually be reflecting motor-related activity for the button press response.

Another common area that we observed within all three spatial conditions is an area within the intraparietal sulcus, namely pmIPS. Area mIPS (possibly equivalent to LIP/MIP in the monkey) has been demonstrated to perform reference frame transformations related to visuomotor transformations for saccades and reach (Mullette-Gillman, Cohen, & Groh, 2009, 2005; Snyder, Grieve, Brotchie & Andersen, 1998; Vesia & Crawford, 2012). Area pmIPS is just medial to the functionally localized parietal eye field (PEF), which might place it within a portion of the human 'parietal reach region' (Connolly, Andersen & Goodale, 2003; Gertz & Fiehler, 2015; Vesia & Crawford, 2012). This would be consistent with a role for this area in transforming information in various frames from our tasks into signals for the frontal hand motor areas described above. However, given the proximity of this area to our saccade localizer data, we cannot exclude the possibility that it was involved somehow in integrating saccade and feature information in all three tasks (Subramanian & Colby, 2014).

2.5b Transsaccadic judgments of Space-fixed stimuli

Our Space-fixed condition was very similar to that in our previous study (Dunkley et al., submitted), with the exception that we previously used larger Gabor patch stimuli (18º as opposed to 6º in the current study). In general, the results of these two experiments were similar (i.e., both found RS in SMG and RE in extrastriate occipital cortex). Importantly, Dunkley et al. (submitted) also showed that these transsaccadic areas were not modulated by same/different features during fixation (a condition we did not repeat here because of the need for time to do our other tasks).

However, the details of our findings were different. In particular, Dunkley et al. (submitted) found a significant transsaccadic RS effect in right SMG (with a similar trend in left SMG), whereas we obtained a significant effect in left SMG. In addition, Dunkley et al. (submitted) found activation in a smaller area (330 mm^3 to 15,525 mm^3 here). These differences might be accounted for by differences in the stimuli, and the greater overall complexity of the different tasks required of our subjects during the experimental period. Importantly, the right SMG has been implicated in saccades, attending to the left side of space, and (when lesioned) with hemi-neglect (Perry & Zeki, 2000), whereas the left SMG has been implicated in short-term memory (Russ, Mack, Grama, Lanfermann, & Knopf, 2003). SMG has also been implicated in reading (Stoeckel, Gough, Watkins, & Devlin, 2009), and other tasks involving spatial processing, such as spatial perception orientation (Kheradmand, Lasker, & Zee, 2003) as well as in visual search (Taylor, Muggleton, Kalla, Walsh, & Eimer, 2011). All of these functions relate closely to the notion of transsaccadic feature memory.

The details of our occipital findings also differed. Although both studies –Dunkley et al. (submitted) and the current study- showed transsaccadic RE effects in right extrastriate occipitial cortex again, the previous study found this in right cortex in an area overlapping with putative V4, whereas we localized our effect to a more lateral area (LOtG) in left cortex. LOtG is thought to be involved in recognizing gestures (Decety et al., 1997; Peigneux et al., 2000), although it is found within the lateral occipital complex (LOC) which is involved in judging the familiarity of shapes and features (Kanwisher, Woods, Iacobini, & Mazziotta, 1997; Malach et al., 1995). This latter function seems to be more relevant for our task and might explain the RE effect.

2.5c Transsaccadic judgments of Retina-fixed stimuli

The unique (non-motor) areas that showed RS in the Retina-fixed condition were lateral BA 7 and inferior frontal gyrus. BA 7 is thought to be involved in processing spatial information (Binkofski et al., 1999; Haxby et al., 1991), and our lateral area was located amongst regions running medial to the intraparietal sulcus involved in sensorimotor transformations for reach (see Vesia and Crawford 2012 for a graphic review). Area aIPS is best known for its role in grasping (Gallivan & Culham, 2015; Monaco et al., 2014; Murata, Gallese, Luppino, Kaseda, & Sakata, 2000). Precentral sulcus is also associated with the skeletomotor system, although some areas show saccadic signals (Rosano et al., 2002), and our particular area overlapped with the retinotopic localizer data. Lastly, activity in the inferior frontal gyrus has been related to executive and inhibition control, which has been hypothesized to work in conjunction with the posterior parietal cortex and preSMA to respond in task-difficult and -relevant manner (Duann, Ide, Luo, & Li, 2009; Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). Taken together, these results seem to implicate involvement from the grasp system in solving this task.

It might seem odd that the grasp system seems to have been evoked to help solve a retinotopic orientation judgement task, but the brain might tap into any available mechanism to solve an unusual task (given that stimuli are normally space-fixed in real life). This is not entirely out of place, because the grasp system is replete with stimulus orientation information in humans (Gallivan & Culham, 2015; Monaco et al., 2014) and macaques (Baumann, Fluet, & Scherberger, 2009). In addition, multivoxel pattern analysis has recently shown that the human aIPS has a gaze-centered representation of visual targets for grasping (Leoné, Monaco, Henriques, Toni, & Medendorp, 2015). And again, the use of this system might have been influenced by the behavioral output in our task: a button push. However, visual and visuomotor

systems show widespread gaze-fixed and retinotopic mechanisms, some of which have been implicated in memory (Fecteau & Munoz, 2005; Pratte & Tong, 2014; Talsma, White, Mathôt, Munoz & Theeuwes, 2013). Many of these areas show up in our retinotopic localizer, but would not show RS or RE effects in our main task unless they were specifically involved in retaining orientation memory. However, working in conjunction with areas that do show orientation retention (like those discussed above), they would provide massive support for solving a retinotopic task.

2.5d Transsaccadic judgments of Frame-independent stimuli

Our Frame-independent task evoked the widest area of RS effects in parietofrontal cortex, including unique areas FEF, mBA 7, as well as aIPS and mIPS and frontal precentral sulcus. We also observed RE effects in LOtG, except this time in the right hemisphere. Most of these areas we have already discussed above. FEF is famously involved in gaze control and working memory (Dias & Segraves, 1999; Goldberg & Bruce, 1990; O'Sullivan, Jenkins, Henderson, Kennard & Brooks, 1995), and is known to primarily utilize gaze-centred signals (Goldberg & Bruce, 1990; Sajad et al., 2015). FEF is thought to provide an efference copy signal of saccade motion to update space-fixed object locations (Prime et al., 2010; Duhamel et al., 1992a), so this would need to be suppressed here. Medial posterior parietal cortex has been associated with the use of multiple coordinate frames, including visual coordinates and allocentric coordinates (Fernandez-Ruiz, Goltz, DeSouza, Vilis, & Crawford, 2007; Uchimara, Nakano, Morito, Ando & Kitazawa, 2015). It is possible that subjects used the saccade fixation points as allocentric cues for the sequential task, or updated the first stimulus with eye position (Colby & Goldberg, 1992; Medendorp, Goltz, Vilis & Crawford, 2003; Merriam, Genovese &

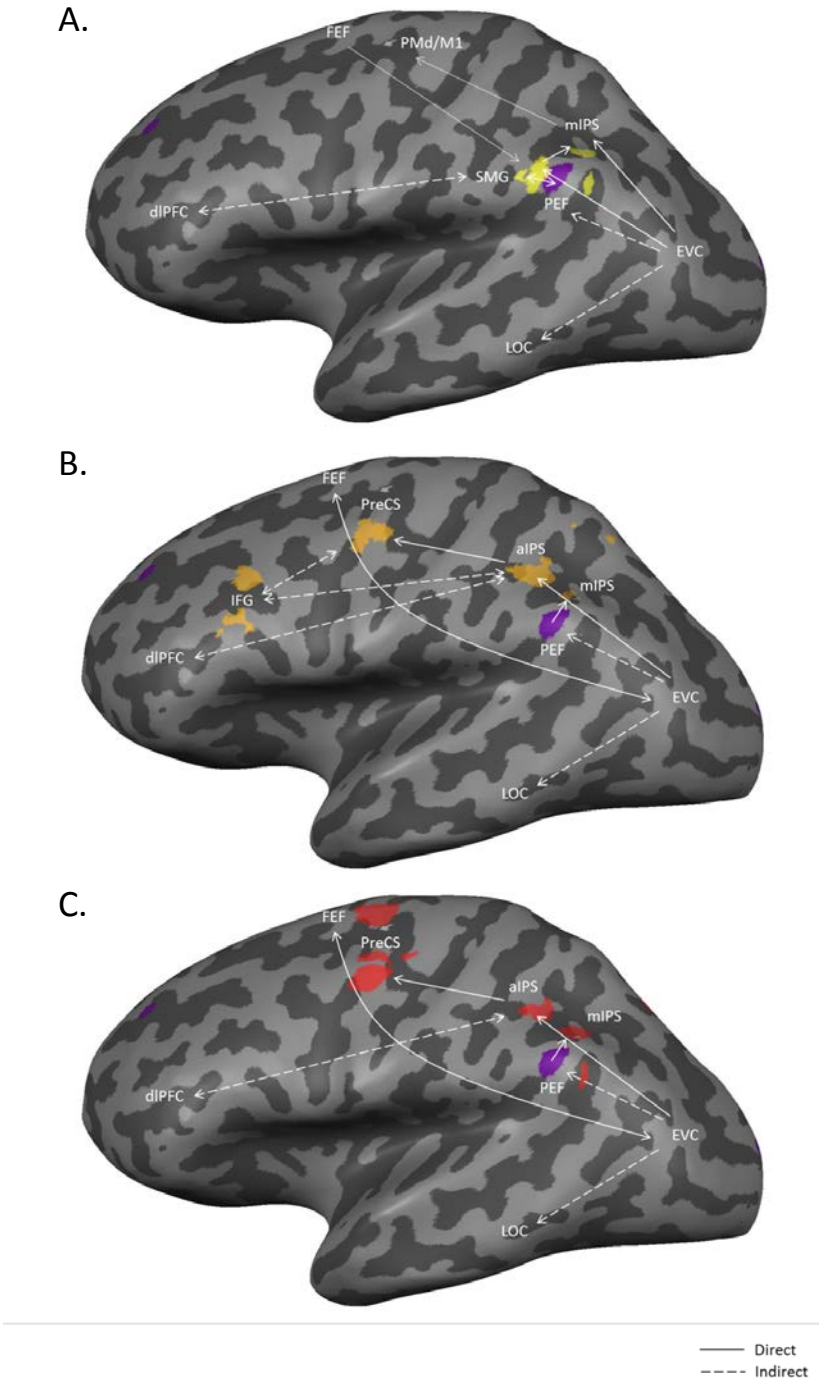

Figure 12. Inflated brain summary diagram of three spatial conditions and possible networks within each condition. ***A.*** *Space-fixed TSI system*. Mapped onto an inflated brain of the left hemisphere of an exemplary participant is the activation during the Space-fixed condition, as well as the parietal eye field (PEF; shown in purple) and possible direct and indirect networks, involving the dorsolateral prefrontal cortex (dlPFC), lateral occipitotemporal cortex (LOC, and adjacent occipital and temporal areas) and early visual cortex (EVC). ***B.*** *Retina-fixed TSI system*. Shown onto an inflated brain rendering of the left hemisphere of an exemplary participant is the activation during the Retina-fixed condition, and possible direct and indirect networks involving the PEF, EVC and dlPFC. (Motor output areas have been left out for the sake of clarity, but are assumed to also be part of this system.) ***C.*** *Frame-independent TSI system*. Onto an inflated brain rendering of an exemplary participant is shown activation during the Frame-independent condition and potential direct and indirect network connections between the activation and the PEF, EVC and dlPFC. (Motor output areas have been left out for the sake of clarity, but are assumed to also be part of this system.)

Colby, 2003; Nakamura & Colby, 2002) and then, transformed both stimuli into some other coordinate frame to perform the task. Thus, a rather diverse network of excitatory and inhibitory signals may have been required to deal with the complex and arbitrary spatial transformations involved in this task.

2.5e Integration of our 3 networks within the general transsaccadic network.

Figure 8A, B, C provides a schematic of the three networks that we observed in this study and their hypothetical relationships to other brain areas that have been implicated in transsaccadic memory and integration. Dorsolateral prefrontal cortex has been implicated in task switching between fixation and transsaccadic memory (Tanaka et al., 2014), so we speculate that it might play a similar role here, helping to select between these networks. Early visual cortex not only provides input to the visual system in general, it has been shown to be modulated by saccade signals (McFarland, Bondy, Saunders, Cumming, & Butts, 2015; Sylvester, Haynes & Rees, 2005; Ross et al., 2001) and play a role in transsaccadic spatial updating of features (Malik et al., 2015). The parietal eye fields (located amongst our 3 networks) and frontal eye fields (modulated in our Frame-independent task) may provide the saccade efference copy inputs for spatial updating, so again these signals might have been suppressed or gated differently in our non-Space-fixed tasks. The implication is that the solution to seemingly small changes in the spatial nature of a visual task may require rather sweeping cortical network changes.

2.5f Conclusion: overall comparison of results from the three spatial conditions

We set out to test if different cortical networks are employed for trans-saccadic comparisons of stimuli paired in Space-fixed, Retina-fixed, or Frame-independent coordinates. Clearly, this was the case. This is consistent with a recent finding that the cortical mechanisms

for visually-guided reach depend on the reference frame employed in the task (Chen et al., 2014). A general trend that we observed was the increased recruitment of parietofrontal areas as we went from the most natural (Space-fixed) to the most arbitrary (Frame-independent) task. Although we did not observe any significant differences in behavioral performance in these tasks, it seems likely that the more natural versions of the task were able to rely on well-trained normal mechanisms, whereas subjects had to recruit additional cortical areas for more arbitrary tasks. It is noteworthy therefore that SMG, which was the most prominent unique area for the Space-fixed task, was no longer modulated in the other tasks, re-enforcing a special purpose for this area in real life.

CHAPTER 3

GENERAL DISCUSSION

3.1 Discussion

In this chapter, I will discuss how the results from our transsaccadic integration of object orientation in multiple spatial configurations have contributed to the transsaccadic integration field. I will also discuss some questions that remain from our study, potential applications of our work, and future directions in this line of research.

3.2 Contributions to transsaccadic integration literature

Previously, research on transsaccadic processes focused predominantly on identifying the type of information that we are able to retain within a fixation and how that information is stored and carried across multiple fixations (through saccades, for example). To probe the ability to store information in what has been found to be a visual short-term memory-like buffer (i.e., transsaccadic memory), experiments that utilize a line-intersection task, for example, have demonstrated our ability to integrate pre- and post-saccadic information in order to act upon the transferred information (Prime et al., 2006). The ability to retain object feature information has also been investigated, with respect to specific features (i.e., colour, luminance, spatial frequency, orientation), as well as to how this information is maintained and integrated relative to spatial location (Luck & Vogel, 1997; Prime et al., 2011). Other aspects of our visual world have been investigated, such as our ability to read and how this is influenced or how this process occurs across saccades (McConkie & Zola, 1979). These studies have found that we are able to identify object identity and then integrate across saccades, regardless of the change in letter case (Henderson, 1997; McConkie & Zola, 1979). Features such as motion have also been studied (Ross et al., 2001), however, within a specific reference frame. Thus, it seems that the visual system is able to integrate multiple features of an object across saccades and in a manner that relates it to the spatial position within its surroundings. The way in which this information is

stored and utilized may be dependent upon the task, which may ultimately influence transsaccadic integration as well as transsaccadic memory.

Although the link between object features and spatial encoding may have been investigated psychophysically, neurophysiologically, as well as using non-invasive human techniques (i.e., TMS), no study had previously looked specifically at identifying this relationship and the neural network that is involved therein. However, a recent fMRI-adaptation (fMRIa) study explored the relationship between maintaining and integrating object feature information (i.e., object orientation) across saccades and the spatial frame in which this information was presented (Dunkley et al., submitted). Dunkley et al. (submitted) found that an area within the posterior parietal cortex is involved in integrating orientation information in a space-fixed task, as well as an extrastriate area (consistent with V4).

This study has delved deeper into understanding how the spatial configuration can change the way in which object orientation information is processed and integrated across saccades, as well as which neural networks are involved. I was able to carry out this task by utilizing multiple spatial configurations to present object orientation information. I asked participants to make a judgment about whether the orientation was repeated or if it was novel. The results indicate that a space-fixed configuration activates the posterior parietal cortex (specifically, the supramarginal gyrus), as well as a small area within the intraparietal sulcus (pmIPS). These areas are activated in response to novel conditions (when the orientations within a trial are different). Within this same spatial configuration, I also observed occipitotemporal activation. This separation in networks (dorsal vs. ventral, for example) may indicate that it may not be just one network that is working to process object feature information, even low-level object features such as orientation. I also found parietal-frontal network activity during the integration of orientation information in

a retina-fixed configuration. Lastly, I observed different parietal-frontal network activation (for the repetition suppression effect) and occipitotemporal activation (for the repetition enhancement effects) in response to a frame-independent configuration. The results show that there are distinct constellations of cortical regions at play in integrating low-level object features in spatial configurations such as the ones tested here. Interestingly, I observed that the more unusual spatial configurations (retina-fixed and frame-independent) recruited the more cortical regions. Also, the dissociation between the dorsal and ventral streams was observed in multiple spatial configurations tested here. Overall, I identified the cortical regions involved in object orientation information integration across saccades, and within multiple spatial configurations.

3.3 Unresolved questions

Although I have now identified the areas that may be involved in integration low-level object features, such as object orientation, across eye movements within multiple spatial configurations, there are several questions that remain from this study, as well as in the domain of transsaccadic integration.

Within the realm of this study, one aspect of the experimental design that must be considered is the experimental technique that I used to probe transsaccadic integration of object orientation (i.e., fMRIa). Functional imaging has a specific temporal scale (usually based on a two-gamma haemodynamic response function) that may encompass only a certain amount of what the brain is doing within such a task (Grill-Spector et al., 2006). This begs the question, what is happening in the brain during transsaccadic integration of an object feature like orientation, temporally-speaking? Although several of the studies have looked to identify the qualitative aspects of what is taking place within transsaccadic integration and its sister-component, transsaccadic memory (see section 1.6), none have tried to identify the implications

of what is occurring through time. Does this mean that other regions of activation are being missed because of the time-scale upon which fMRI works?

In a related vein, what about receptive fields throughout transsaccadic integration? This task is a little longer (on the order of seconds) than the most related neurophysiological study (Subramanian & Colby, 2014) and neuroimaging does not allow us to probe how receptive fields change or respond to the task. Are receptive fields modulated based on the spatial configuration in which the object orientation is presented? Do they encode the information in one reference frame in one spatial configuration initially and transition into another coding frame throughout the task? Although Mullette-Gillman et al. (2005, 2009) investigated how receptive fields encode visual and auditory information and found that information is encoded in receptive fields that demonstrate multisensory properties, how does this finding complement or explain the results that we have here?

Additionally, I tested only one object feature here and its integration relative to space. Would other object features engage the same cortical networks? (This question can also be answered using fMRIa studies in similar spatial configurations.) Although, it can be expected that some features such as colour may activate a slightly different network (Allison, McCarthy, Nobre, Puce, Belger, 1994; Chao & Martin, 1999; Hadjikhani, Liu, Dale, Cavanagh & Tootell, 1998) than the one used for motion perception (Ross et al., 2001) for example. Also, I used a single-step task here and along the horizontal plane. How would a more realistic task (i.e., double-step task; Colby, Duhamel & Goldberg, 1995; Heide et al., 1995) affect our results or those of other transsaccadic integration tasks?

To my knowledge, this is the first attempt at trying to identify the neural mechanisms and networks that are involved in transsaccadic integration of object features, especially of object

orientation, in multiple frames of reference using fMRI adaptation techniques. The knowledge that we have obtained about the possible neural mechanisms is an excellent starting point at trying to uncover the components of the networks involved in this, as well as other feature integration tasks. Understanding how these networks at a larger scale interact with and/or affect the neurophysiological (receptive field) mechanisms remains to be investigated. Also, what is the underlying process or phenomenon that is responsible for producing these results and others? Is it a top-down modulated process, such as attention? Would a 'simple,' bottom-up process affect our results? Presumably, the results obtained here would not change drastically if it was transsaccadic integration of orientation that was being calculated in the brain. How would these results hold up for other eye movement tasks, such as smooth pursuit eye movements, etc.? These are just a few of the possible questions that remain to be answered within this field that may be pursued to help us obtain a better understanding of transsaccadic integration (of object features).

3.4 Possible applications (medical, industrial, transportation safety)

Eye movement research has been investigated with respect to clinical populations, such as those individuals with schizophrenia, since the early 1900s (Diefendorf & Dodge, 1908; Klein & Ettinger, 2008; Levy, Holzman, Matthysse, & Mendell, 1993). It has been indicated that individuals with schizophrenia have a different pattern of eye movement during visual search (Gold, Fuller, Robinson, Braun, & Luck, 2007; Lubow, Kaplan, Abramovich, Rudnick, & Laor, 2000). These individuals have also been shown to have impairments on cognitive tasks, such as those tapping into memory for example (Weickert et al., 2000). Thus, our results could be applied in more causally-linked tasks that explore transsaccadic integration in a clinical population such as the aforementioned. Could the networks that we have identified here,

especially the one involved in a space-fixed spatial configuration which is often encountered in everyday life, be affected or modulated in an alternative manner that leads to or impacts the symptoms that these individuals experience? Another group of individuals that may have altered or impacted transsaccadic neural networks may be individuals who suffer from post-traumatic stress disorder (PTSD). These individuals have been shown to have impaired memory and their attention also appears to be easily disrupted (Brandes et al., 2002). Thus, understanding how neural networks are impacted within PTSD populations and if our results are related to same attention or memory networks found here is important. These findings may allow us to develop better treatment opportunities.

Not only are eye movements important in studying and helping to treat clinical populations, but they are also relevant in other fields. Individuals in industry have to be able to produce reliable eye movements to key or salient aspects of the visual scene to perform something like a search task and utilize that information to apply it, be it to the assembly of car parts or to ensuring correct manufacturing of a food product. Perhaps, strengthening some innate aspect of the neural mechanisms involved in transsaccadic integration will better assist companies to optimize production of products and employee performance.

Lastly, because public and private transportation plays such an important role in our lives, it is important to understand how eye movements and integrating information from one fixation to the next can impact our ability to perform a task such as driving well, as well as what happens when it does not work as smoothly. Individuals who have been involved in car accidents may have had a particular modulation of their neural networks that prevented them from identifying all of the important components of the visual scene and ended up in a car accident, perhaps hurting themselves and others in the process. Could we know beforehand if a particular

change in the network may result in such a devastating event? On a related note, could we study saccades and the information that drivers obtain from each fixation, how they integrate that information, to allow transportation rules to adjust how they design roads? Our primary visual cortex is subdivided into columns that respond optimally to certain line orientations (Hubel & Wiesel, 1968); other parts of our brain have been implicated in scene assessment (Epstein et al., 1999), in facial recognition (Kanwisher et al., 1997), etc. How can our transportation regulations make use of this information to create more efficient ways of constructing roads, to conform architecture to ensure that there are fewer tragedies, and to improve access to and within cities? The research stemming from transsaccadic integration of such object features and complex scenes may help greatly in advancing our ability to achieve all of the tasks mentioned above.

3.5 Future directions

Given the many possible questions that remain from our study, in addition to the possible applications that the results of the study may have, there some immediate questions that I hope to answer in my doctoral studies. One research goal with the field of transsaccadic integration that I would like to pursue specifically is to establish a causal link between the activation in the supramarginal gyrus and transsaccadic integration of object orientation in the space-fixed spatial configuration. I would like to do this using transcranial magnetic stimulation. TMS has been used previously to disrupt the neural activity during a transsaccadic integration task of other object features (Ruter, Kammer & Herzog, 2010; Scharnowski et al., 2009), and I would like to make use of this effect to probe the brain directly in a transsaccadic task.

Within this vein, I would like to analyze the diffusion tensor imaging (DTI) data that Dunkley et al. (submitted) and I collected in our studies. Specifically, I would like to identify the anatomical connectivity between the areas that Dunkley et al. (submitted) and I found. This will

help in linking anatomy to the differential functional patterns of activity that we have seen in response to transsaccadic integration of object orientation, as well as of spatial frequency.

Additionally, I would like to explore object features and how they are integrated across saccades. Features such as spatial frequency and, perhaps, colour would be of interest, as these two features in addition to orientation comprise a large component of the visual surroundings that we encounter on a daily basis. They have a distinct importance in that spatial frequency and colour can be found in all of the applications that were mentioned earlier- making sure that the right pieces are put together, or that the food prepared/packaged looks to be the right colour and consistency, or that the driver is not entering a 'Do Not Enter' area, etc.

Lastly, obtaining information about how multiple features may be integrated, as well as their temporal scale may be of future interest. How these networks interact on a temporal scale, as well as within clinical populations (i.e., individuals with schizophrenia) are also among future endeavours in the field of transsaccadic integration. Being able to identify anomalies or alterations in the neural networks that we can identify, probe and establish a causal relationship between cortical regions and transsaccadic integration, and then apply that to the symptoms that we see in clinical populations is among the first steps to identifying better or plausible treatment options.

REFERENCES

1. Abel, L.A., Troost, B.T., & Dell'Osso, L.F. (1983). The effects of age on normal saccadic characteristics and their variability. *Vision Res, 23*, 33-37.
2. Allison, T., McCarthy, G., Nobre, A., Puce, A., & Belger, A. (1994). Human extrastriate visual cortex and the perception of faces, words, numbers, and colors. *Cereb Cor, 5*:544-554.
3. Andersen, R.A., Asanuma, C., & Cowan, W.M. (1985). Callosal and prefrontal associational projecting cell populations in area 7a of the macaque monkey: a study using retrogradely transported fluorescent dyes. *J Comp Neurol, 232*, 443-455.
4. Andersen, R.A., Brotchie, P.R., & Mazzoni, P. (1992). Evidence for the lateral intraparietal area as the parietal eye field. *Curr Opin Neurobiol, 2*, 840-846.
5. Andrews, D.P. (1967). Perception of contour orientation in the central fovea part II: spatial integration. *Vision Res, 7*, 999-1013.
6. Averbach, E., & Coriell, A.S. (1961). Short-term memory in vision. *Bell Sys Tech J, 40*, 309-328.
7. Avidan, G., Hasson, U., Hendler, T., Zohary, E., & Malach, R. (2002). Analaysis of the neuronal selectivity underlying low fMRI signals. *Curr Biol, 12*, 964-972.
8. Baddeley, A. (2003). Working memory: looking back and looking forward. *Nat Rev Neurosci, 4*, 829-839.
9. Bahill, A.T., Clark, M.R., & Stark, L. (1975). The main sequence: a tool for studying human eye movements. *Math Biosci, 24*, 191–204.
10. Baumann, M.A., Fluet, M.-C., & Scherberger, H. (2009). Context-specific grasp movement representation in the macaque anterior intraparietal area. *J Neurosci, 29*, 6346-6448.

11. Becker, W., & Fuchs, A.F. (1969). Further properties of the human saccadic system: eye movements and correction saccades with and without visual fixation points. *Vis Res, 9,* 1247–1258.
12. Binofski, F., Buccino, G., Posse, S., Seitz, R.J., Rizzolatti, G., & Freund, H.-J. (1999). A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *Eur J Neurosci, 11,* 3276-3286.
13. Brainard, D. (1997). The psychophysics toolbox. *Spat Vis, 10,* 443-446.
14. Brandes, D., Ben-Schachar, G., Gilboa, A., Bonne, O., Freedman, S., & Shalev, A.Y. (2002). PTSD symptoms and cognitive performance in recent trauma survivors. *Psychiatry Res, 110,* 231-238.
15. Bridgeman, B. (1981). Cognitive factors in subjective stabilization of the visual world. *Acta Psychol (Amst), 48,* 111-121.
16. Bridgeman, B., & Mayer, M. (1983). Failure to integrate visual information from successive fixations. *Bull Psychonom Soc, 21,* 285-286.
17. Brown, M.W., & Xiang, J.Z. (1998). Recognition memory: neuronal substrates if the judgement of prior occurrence. *Prog Neurobiol, 55,* 149-189.
18. Buneo, C.A., & Andersen, R.A. (2006). The posterior parietal cortex: sensorimotor interface for the planning and online control of visually guided movements. *Neuropsychologia (Oxford), 44,* 2594-2606.
19. Buttner, U., Buttner-Ennever, J.A., & Henn, V. (1977). Vertical eye movement related unit activity in the rostral mesencephalic reticular formation of the alert monkey. *Brain Res, 130,* 239–252.

20. Buttner-Ennever, J.A., & Buttner, U. (1978). A cell group associated with vertical eye movements in the rostral mesencephalic reticular formation of the monkey. *Brain Res, 151*, 31–47.
21. Buttner-Ennever, J.A., Cohen, B., Pause, M., & Fries, W. (1988). Raphe nucleus of the pons containing omnipause neurons of the oculomotor system in the monkey and its homologue in man. *J Comp Neurol, 267*, 307–321.
22. Byrne, P., & Becker, S. (2007). Remembering the past and imagining the future: a neural model of spatial memory and imagery. *Psychol Rev, 114*, 340-375.
23. Carlson-Radvansky, L. (1999). Memory for relational information across eye movements. *Percept Psychophys, 61*, 919-934.
24. Carpenter, R.H. (2004). Contrast, probability and saccadic latency; evidence for independence of detection and decision. *Curr Biol, 14*, 1576-1580.
25. Carrasco, M., & McElree, B. (2001). Covert attention accelerates the rate of visual information processing. *Proc Natl Acad Sci, 98*, 5363-5367.
26. Chaffee, M.V., & Goldman-Rakic, P.S. (1998). Matching patterns of activity in primate prefrontal area 8a and parietal area 7ip neurons during a spatial working memory task. *J Neurophysiol, 79*, 2919-2940.
27. Chao, L.L., & Martin, A. (1999). Cortical regions associated with perceiving, naming, and knowing about colors. *J Cogn Neurosci, 11*, 25-35.
28. Chen, Y., Monaco, S., Byrne, P., Yan, X., Henriques, D.Y.P., & Crawford, J.D. (2014). Allocentric versus egocentric representation of remembered reach targets in human cortex. *J Neurosci, 34*, 12515-12526.

29. Cheyne, D., Kristeva, R., & Deecke, L. (1991). Homuncular organization of human motor cortex as indicated by neuromagnetic recordings. *Neurosci Lett, 122*, 17-20.

30. Colby, C.L., Duhamel, J.R., & Goldberg, M.E. (1995). Oculocentric spatial representation in parietal cortex. *Cereb Cor, 5*, 470-481.

31. Collewijn, H., Erkelens, C.J., & Steinman, R.M. (1988). Binocular co-ordination of human vertical saccadic eye movements. *J Physiol (Lond), 404*, 183-197.

32. Compte, A., Brunel, N., Goldman-Rakic, P.S., & Wang, X.-J. (2000). Synaptic mechanisms and network dynamics underlying spatial working memory in a cortical network model. *Cereb Cortex, 10*, 910-923.

33. Connolly, J.D., Andersen, R.A., & Goodale, M.A. (2003). FMRI evidence for a 'parietal reach region' in the human brain. *Exp Brain Res, 153*, 140-145.

34. Corballis, M.C., & Cullen, S. (1986). Decisions about the axes of disoriented shapes. *Mem Cognition, 14*, 27-38.

35. Corballis, M.C., Zbrodoff, N.J., Shetzer, L.I., & Butler, P.B. (1978). Decision about identity and orientation of rotated letters and digits. *Mem Cognition, 6*, 98-107.

36. Courtney, S.M., Ungerleider, L.G., Keil, K., & Haxby, J.V. (1996). Object and spatial visual working memory activate separate neural systems in human cortex. *Cereb Cortex, 6*, 39-49.

37. Crane, J., & Milner, B. (2005). What went where? Impaired object-location learning in patients with right hippocampal lesions. *Hippocampus, 15*, 216-231.

38. Crawford, J.D., Henriques, D.Y.P., & Medendorp, W.P. (2011). Three-dimensional transformations for goal-directed action. *Annu Rev Neurosci, 34*, 309-331.

39. Crawford, J.D., & Vilis, T. (1993). Modularity and parallel processing in the oculomotor integrator. *Exp Brain Res, 96*, 443-456.

40. Culham, J.C., Danckert, S.L., DeSouza, J.F.X., Gati, J.S., Menon, R.S., & Goodale, M.A. (2003). Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Exp Brain Res, 153*, 180-189.

41. Culham, J.C., & Kanwisher, N.G. (2001). Neuroimaging of cognitive functions in human parietal cortex. *Curr Opin Neurobiol*, *11*, 157-163.

42. D'Avossa, G., Tosetti, M., Crespi, S., Biagi, L., Burr, D.C., & Morrone, M.C. (2007) Spatiotopic selectivity of BOLD responses to visual motion in human area MT. *Nat Neurosci*, *10*, 249-255.

43. D'Esposito, M., Aguirre, G.K., Zarahn, E., Ballard, D., Shin, R.K., & Lease, J. (1998) Functional MRI studies of spatial and nonspatial working memory. *Cognitive Brain Res, 7*, 1-13.

44. DeValois, R.L., Abrecht, D.G., & Thorell, L.G. (1982). Spatial frequency selectivity of cells in macaque visual cortex. *Vision Res*, *22*, 545-559.

45. Decety, J., Grezes, J., Costes, N., Perani, D., Jeannerod, M., Procyk, E., Grassi, F., & Fazio, F. (1997). Brain activity during observation of actions-influence of action content and subject's strategy. *Brain, 120*, 1763-1777.

46. Dechent, P., & Frahm, J. (2003). Functional somatotopy of finger representations in human primary motor cortex. *Hum Brain Mapp, 18,* 272-283.

47. Desimone, R. (1996). Neural mechanisms for visual memory and their role in attention. *Proc Natl Acad Sci*, *93*, 13494-13499.

48. Desimone, R., & Ungerieider, L.G. (1989). Neural mechanisms of visual processing in monkeys. In: Handbook of neuropsychology (Goodglass H, Damasio AR, cds), pp 267-300. Amsterdam: Elsevier.

49. Deubel, H. (1989). Sensory and motor aspects of saccade control. *Eur Arch Psychiatr Neurol Sc, 239*, 17-22.

50. Dias, E.C., & Segraves, M.A. (1999). Muscimol-induced inactivation of monkey frontal eye field: effects on visually and memory-guided saccades. *J Neurophysiol*, *81*, 2191-2214.

51. Diefendorf, A.R., & Dodge, R. (1908). An experimental study of the ocular reactions of the insane from photographic records. *Brain, 31*, 451-489.

52. Dodge, R. (1919). Five types of eye movement in the horizontal meridian plane of the field of regard. *Am J Physiol*, *8*, 307-329.

53. Doma, H., & Hallett, P.E. (1988). Dependence of saccadic eye-movements on stimulus luminance and an effect of task. *Vision Res, 28*, 915-924.

54. Duann, J.-R., Ide, J.S., Luo, X., & Li, C.-S. R. (2009). Functional connectivity delineates distinct roles of the inferior frontal cortex and presupplementary motor area in stop signal inhibition. *J Neurosci, 29*, 10171-10179.

55. Duhamel, J., Colby, C., & Goldberg, M. (1992a). The updating of the representation of visual space in parietal cortex by intended eye movements. *Science, 255*, 90–92.

56. Duhamel, J.R., Goldberg, M.E., Fitzgibbon, E.J., Sirigu, A., & Grafman, J. (1992b). Saccadic dysmetria in a patient with a right frontoparietal lesion. The importance of corollary discharge for accurate spatial behaviour. *Brain, 115*, 1387-1402.

57. Duhamel, J.R., Colby, C.L., & Goldberg, M.E. (1998). Ventral intraparietal area of the macaque: congruent visual and somatic response properties. *J Neurophysiol, 79*, 126-136.

58. Dunkley, B.T., Baltaretu, B.R., & Crawford, J.D. (submitted). Trans-saccadic interactions in human parietal and occipital cortex during the retention and comparison of object orientation. *Neuroimage*.

59. Epstein, R., Graham, K.S., & Downing, P.E. (2003). Viewpoint-specific scene representations in human parahippocampal cortex. *Neuro, 37*, 865-876.

60. Epstein, R., Harris, A., Stanley, D., & Kanwisher, N. (1999). The parahippocampal place area: recognition, navigation, or encoding? *Neuron, 23*, 115-125.

61. Fecteau, J.H., & Munoz, D.P. (2005). Correlates of capture of attention and inhibition of return across stages of visual processing. *J Cog Neurosci, 17*, 1714-1727.

62. Fernandez-Ruiz, J., Goltz, H.C., DeSouza, J.F.X., Vilis, T., & Crawford, J.D. (2007). Human parietal "reach region" primarily encodes intrinsic visual direction, not extrinsic movement direction, in a visual-motor dissociation task. *Cereb Cortex, 17*, 2283-2292.

63. Fletcher, W.A., & Sharpe, J.A. (1986). Saccadic eye movement dysfunction in Alzheimer's disease. *Ann Neurol, 20*, 464–471.

64. Forman, S.D., Cohen, J.D., Fitzgerald, M., Eddy, W.F., Mintun, M.A., & Noll, D.C. (1995). Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a cluster-size threshold. *Magn Reson Med, 33*, 636–647.

65. Friston, K. (2005). A theory of cortical responses. *Philos Trans R Soc Lond 360*:815-836.

66. Funahashi, S. (2013). Thalamic mediodorsal nucleus and its participation in spatial working memory processes: comparison with the prefrontal cortex. *Front Syst Neurosci, 7*, 1-13.

67. Gagnepain, P., Chetelat, G., Landeau, B., Dayan, J., Eustache, F., & Lebreton, K. (2008). Spoken word memory traces within the human auditory cortex revealed by repetition priming and functional magnetic resonance imaging and electroencephalography. *J Neurosci, 25*, 5281-5289.

68. Gallivan, J.P., & Culham, J.C. (2015). Neural coding within human brain areas involved in actions. *Curr Opin Neurobiol, 33*, 141-149.

69. Garbutt, S., Han, Y., Kumar, A.N., Harwood, M., Harris, C.M., & Leigh, R.J. (2003). Vertical optokinetic nystagmus and saccades in normal human subjects. *Invest Ophthalmol Vis Sci*, *44*, 3833-3841.

70. Gaymard, B., Ploner, C.J., Rivaud, S., Vermersch, A.I., & Pierrot-Deseillginy, C. (1998). Cortical control of saccades. *Exp Brain Res*, *123*, 159-163.

71. Gaymard, B., Ploner, C.J., Rivaud-Pechoux, S., & Pierrot-Deseilligny, C. (1999). The frontal eye field is involved in spatial short-term memory but not in reflexive saccade inhibition. *Exp Brain Res*, *129*, 288-301.

72. Gertz, H., & Fiehler, K. (2015). Human posterior parietal cortex encodes the movement goal in a pro-/anti-reach task. *J Neurophysiol*, *114*, 170-183.

73. Gilinsky, A.S. (1968). Orientation-specific effects of patterns of adapting light on visual acuity. *J Opt Soc America*, *58*, 13-18.

74. Glezer, L.S., Jiang, X., & Riesenhuber, M. (2009). Evidence for highly selective neuronal tuning to whole words in the 'visual word form area.' *Neuron*, *62*, 199-204.

75. Gnadt, J.W., & Andersen, R.A. (1988). Memory related motor planning activity in posterior parietal cortex of macaque. *Exp Brain Res*, *70*, 216-220.

76. Gold, J.M., Fuller, R.L., Robinson, B.M., Braun, E.L., & Luck, S.J. (2007). Impaired top-down control of visual search in schizophrenia. *Schizophr Res*, *94*, 148-155.

77. Goldberg, M.E., & Bruce, C.J. (1990). Primate frontal eye fields. III. Maintenance of a spatially accurate saccade signal. *J Neurophysiol*, *64*, 489-508.

78. Goldberg, M.E., & Colby, C.L. (1992). Oculomotor control and spatial processing. *Curr Opin Neurobiol*, *2*, 198-202.

79. Golomb, J.D., Chun, M.M., & Mazer, J.A. (2008). The native coordinate system of spatial attention is retinotopic. *J Neurosci, 28,* 10654-10662.

80. Golomb, J.D., Pulido, V.Z., Albrecht, A.R., Chun, M.M., & Mazer, J.A. (2010). Robustness of the retinotopic attentional trace after eye movements. *J Vis, 10,* 1-12.

81. Golomb, J.D., & Kanwisher, N. (2011). Higher level visual cortex represents retinotopic, not spatiotopic, object location. *Cereb Cortex* doi: 10.1093/cercor/bhr357.

82. Golomb, J.D., & Kanwisher, N. (2012). Retinotopic memory is more precise than spatiotopic memory. *Proc Natl Acad Sci, 109,* 1796-1801.

83. Goodale, M.A., Meenan, J.P., Bulthoff, H.H., Nicolle, D.A., Murphy, K.J., & Racicot, C.I. (1994). Separate neural pathways for the visual analysis of objet shape in perception and prehension. *Curr Biol, 4,* 604-610.

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

85. Goodale, M.A., & Milner, A.D. (1992). Separate visual pathways for perception and action. *Trends Neurosci, 15,* 20-25.

86. Goodale, M.A., & Westwood, D.A. (2004). An evolving view of duplex vision: separate but interacting cortical pathways for perception and action. *Curr Opin Neurobiol, 13,* 203-211.

87. Gotts, S.J., Chow, C.C., & Martin, A. (2012). Repetition priming and repetition suppression: A case for enhanced efficiency through neural synchronization. *Cognitive Neurosci, 3,* 227-237.

88. Grafton, S.T., Hazeltine, E., & Ivry, R.B. (1998). Abstract and effector-specific representations of motor sequences identified with PET. *J Neurosci, 18,* 9420-9428.

89. Grill-Spector, K., Henson, R., & Martin, A. (2006). Repetition and the brain: neural models of stimulus-specific effects. *Trends Cogn Sci, 10*, 14-23.

90. Grill-Spector, K., Kushnit, T., Edelman, S., Aidan, G., Itzchak, Y., & Malach, R. (1999). Differential processing of objects under various viewing conditions in the human lateral occipital complex. *Neuron, 24*, 187-203.

91. Grill-Spector, K., Kushnir, T., Hendler, T., & Malach, R. (2003). The dynamics of object-selective activation coreralte with recognition performance in humans. *Nat Neurosci, 3*, 837-843.

92. Grill-Spector, K., & Malach, R. (2001). fMR-adaptation: a tool for studying the functional properties of human cortical neurons. *Acta Psychol (Amst), 107*, 293-321.

93. Groner, R., & Groner, M.T. (1989). Attention and eye movement control: an overview. *Eur Arch Psychiatr Neurol Sci, 239*, 9-16.

94. Guerard, K., Tremblay, S., & Saint-Aubin, J. (2009). Similarity and binding in memory: bound to be detrimental. *Q J Exp Psychol, 62*, 26-32.

95. Hadjikhani, N., Liu, A.K., Dale, A.M., Cavanagh, P., & Tootell, R.B.H. (1998). Retinotopy and color sensitivity in human visual cortical area V8. *Nat Neurosci, 1*, 235-241.

96. Hallett, P.E., & Lightstone, A.D. (1976a). Saccadic eye movements towards stimuli triggered by prior saccades. *Vision Res, 16*, 99-106.

97. Hallett, P.E., & Lightstone, A.D. (1976b). Saccadic eye movements to flashed targets. *Vision Res, 16*, 107-114.

98. Hamker, F.H., Zirnksak, M., Ziesche, A., & Lappe, M. (2011). Computation models of spatial updating in peri-saccadic perception. *Philos Trans R Soc Lond B Sci, 366*, 554-571.

99. Hampshire, A., Chamberlain, S.R., Monti, M.M., Duncan, J., & Owen, A.M. (2010). The role of the right inferior frontal gyrus: inhibition and attentional control. *Neuroimage*, *50*, 1313-1319.

100. Harris, I.M., & Miniussi, C. (2003). Parietal lobe contribution to mental rotation demonstrated with rTMS. *J Cognitive Neurosci*, *15*, 315-323.

101. Harrison, S.A., & Tong, F. (2009). Decoding reveals the contents of visual working memory in early visual areas. *Nature*, *458*, 632-635.

102. Hayhoe, M., Lachter, J., & Feldman, J. (1991). Integration of form across saccadic eye movements. *Perception (London)*, *20*, 393-402.

103. Hayhoe, M., Moeller, P., Ballard, D., & Albano, J.E. (1990). Guidance of saccades to remembered targets and the perception of spatial position. *Invest Ophthalmol Vis Sci*, *13*, 603.

104. Haxby, J.V., Grady, C.L., Horwitz, B., Ungerleider, L.G., Mishkin, M., Carson, R.E., Herscovitch, P., Schapiro, M.B., & Rapoport, S.I. (1991). Dissociation of spatial and object visual processing pathways in human extrastriate cortex. *Proc Nad Acad Sci USA*, *88*, 1621-1625.

105. Haxby, J.V., Horwitz, B., Ungerleider, L.G., Maisog, J.M., Pietrini, P., & Grady, C.L. (1994). The functional organization of human extrastriate cortex: a PET-rCBF study of selective attention to faces and locations. *J Neurosci*, *14*, 6336-6353.

106. Heide, W., Blankenburg, M., Zimmermann, E., & Kompf, D. (1995). Cortical control of double-step saccades: implications for spatial orientation. *Ann Neurol*, *38*, 739-748.

107. Heiser, L.M., & Colby, C.L. (2006). Spatial updating in area LIP is independent of saccade direction. *J Neurophysiol*, *95*, 2751-2767.

108. Helmholtz,, H. von (1963). Hanbuch der Physiologischen Optik [Handbook of physiological optics]. In JPC Southall (Ed. 2nd Trans). Helmholtz's treatise on physiological optics (Vol 3, pp.247-270). New York: Dover. (Original published 1866; English translation originally published 1925)

109. Henderson, J.M. (1997). Transsaccadic memory and integration during real-world object perception. *Psychol Sci*, *8*, 51-55.

110. Henderson, J.M., Pollatsek, A., & Rayner, K. (1987). Effects of foveal priming and extrafoveal preview on object identification. *J Exp Psychol*, *13*, 449-463.

111. Henson, R., & Rugg, M.D. (2003). Neural response suppression, haemodynamic repetition effects, and behavioural priming. *Neuropsychologia (Oxford)*, *41*, 263-270.

112. Henson, R., Shallice, T., & Dolan, R. (2000). Neuroimaging evidence for dissociable forms of repetition priming. *Science*, *287*, 1269-1272.

113. Hepp, K., & Henn, V. (1979). Neuronal activity preceding rapid eye movements in the brain stem of the alert monkey. *Progr Brain Res*, *50*, 645–652.

114. Hikosaka, O., Igusa, Y., Nakao, S., & Shimazu, H. (1978). Direct inhibitory synaptic linkage of pontomedullary reticular burst neurons with abducens motoneurons in the cat. *Exp Brain Res*, *33*, 337–352.

115. Horn, A.K.E., Buttner-Ennever, J.A., Wahle, P., & Reichenberger, I. (1994). Neurotransmitter profile of saccadic omnipause neurons in nucleus raphe interpositus. *J Neurosci*, *14*, 2032–2046.

116. Horn, A.K.E., Buttner-Ennever, J.A., Suzuki, Y., & Henn, V. (1995). Histological identification of premotor neurons for horizontal saccades in monkey and man by parvalbumin immunostaining. *J Comp Neurol*, *359*, 350–363.

117. Horn, A.K.E., & Buttner-Ennever, J.A. (1998). Premotor neurons for vertical eye movements in the rostral mesencephalon of monkey and human: histologic identification by parvalbumin immunostaining. *J Comp Neurol*, *392*, 413–427.

118. Huaman, A., & Sharpe, J.A. (1993). Vertical saccades in senescence. *Invest Ophthalmol Vis Sci*, *34*, 2588–2595.

119. Hubel, D.H., & Wiesel, T.N. (1961). Integrative action in the cat's lateral geniculate body. *J Physiol*, *155*, 385-398.

120. Hubel, D.H., & Wiesel, T.N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J Physiol*, *160*, 106-154.

121. Hubel, D.J., & Wiesel, T.N. (1968). Receptive fields and functional architecture of monkey striate cortex. *J Physiol*, *195*, 215-243.

122. Irwin, D.E. (1991). Information integration across saccadic eye movements. *Cog Psychol*, *23*, 420-456.

123. Irwin, D.E. (1992). Memory for position and identity across eye movements. *J Exp Psychol Learn Mem Cogn*, *18*, 307-317.

124. Irwin, D.E. (1993). Perceiving an integrated visual world. In DE Meyer & S Kornblum (Eds.), *Attention and Performance XIV: Synergies in experimental psychology, artificial intelligence, and cognitive neuroscience- A silver jubilee* (pp. 121-142). Cambridge, M.A.: MIT press.

125. Irwin, D.E. (1996). Integrating information across saccadic eye movements. *Curr Dir Psychol Sci*, *5*, 94-100.

126. Irwin, D.E., Brown, J.S., & Sun, J.S. (1988). Visual masking and visual integration across saccadic eye movements. *J Exp Psychol: Gen*, *117*, 276-287.

127. Irwin, D.E., & Gordon, R.D. (1998). Eye movements, attention and trans-saccadic memory. *Vis Cog, 5,* 127-155.

128. Irwin, D.E., Yantis, S., & Jonides, J. (1983). Evidence against visual integration across saccadic eye movements. *Percept Psychophys, 34,* 49-57.

129. Irwin, D.E., Zacks, J.L., & Brown, J.S. (1990). Visual memory and the perception of a stable visual environment. *Percept Psychophys, 47,* 35-46.

130. Irwin, D.E., & Zelinsky, G.J. (2002). Eye movements and scene perception: memory for things observed. *Percept Pscyhophys, 64,* 882-895.

131. James, T.W., & Gauthier, I. (2006). Repetition-induced changes in BOLD response reflect accumulation of neural activity. *Hum Brain Mapp, 27,* 37-46.

132. James, T.W., Humphrey, G.K., Gati, J.S., Menon, R.S., & Goodale, M.A. (2002). Differential effects of viewpoint on object-driven activation in dorsal and ventral streams. *Neuron, 35,* 79-801.

133. Javal, E. (1879). Essai sur la physiologie de la lecture. *Annales d'Oculometrie, 82,* 242-253.

134. Johnson, J.S., Hollingworth, A., & Luck, S.J. (2008). The role of attention in the maintenance of feature bindings in visual short-term memory. *J Exp Psychol Hum Percept Perform, 34,* 41-55.

135. Jonides, J., Smith, E.E., Koeppe, R.A., Awh, E., Minoshima, S., & Mintun, M.A. (1993). Spatial working memory in humans as revealed by PET. *Nature, 363,* 623-625.

136. Kalesnykas, R.P., & Hallett, P.E. (1987). The differentiation of visually guided and anticipatory saccades in gap and overlap paradigms. *Exp Brain Res, 68,* 115-121.

137. Kanwisher, N., McDermott, J., & Chun, M.M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J Neurosci, 17*, 4302-4311.

138. Kanwisher, N., Woods, R.P., Iacoboni, M., & Mazziotta, J.C. (1997). A locus in human extrastriate cortex for visual shape analysis. *J Cognit Neurosci, 9*, 133-142.

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

140. Keller, E.L. (1974). Participation of the medial pontine reticular formation in eye movement generation in monkey. *J Neurophysiol, 37*, 316–332.

141. Kheradmand, A., Lasker, A., & Zee, D.S. (2013). Transcranial magnetic stimulation (TMS) of the supramarginal gyrus: a window to perception of upright. *Cereb Cortex* doi:10.1093/cercor/bht267.

142. Klein, C., & Ettinger, U. (2008). A hundred years of eye movement research in psychiatry. *Brain Cogn,, 68*, 215-218.

143. Klier, E., & Angelaki, D. (2008). Spatial updating and the maintenance of visual constancy. *Neuroscience, 156*, 801-818.

144. Knauff, M., Mulack, T., Kassubek, J., Salih, H.R., & Greenlee, M.W. (2002). Spatial imagery in deductive reasoning: a functional MRI study. *Cognitive Brain Res, 13*, 203-212.

145. Koriat, A., & Norman, J. (1985). Mental rotation and visual familiarity. *Percept Psychophys, 37*, 429-439.

146. Krekelberg, B., Boynton, G.M., & van Wezel, R.J.A. (2006). Adaptation: from single cells to BOLD signals. *Trends Neurosci, 29*, 250-256.

147. Lawrence, B.M., Myerson, J., & Abrams, R.A. (2004). Interference with spatial working memory: an eye movement is more than a shift of attention. *Psychon Bull Rev, 11*, 488-494.

148. Lebedev, S., Van Gelder, P., & Tsui, W.H. (1996). Square-root relations between main sequence parameters. *Invest Ophthalmol Vis Sci, 37,* 2750-2758.

149. Lee, D., & Chun, M.M. (2001). What are the units of visual short-term memory: objects or spatial locations? *Percept Psychophys, 63*, 253-257.

150. Leigh, R.J., & Kennard, C. (2004). Using saccades as a research tool in the clinical neurosciences. *Brain, 127*, 460-477.

151. Leoné, F., Monaco, S., Henriques, Y.P.D., Toni, I., & Medendorp, P.W. (2015). Flexible reference frames for grasp planning in human parieto-frontal cortex. eNeuro. DOI: 10.1523/eneuro.0008-15.2015.

152. Levy, R., & Goldman-Rakic, P.S. (2000). Segregation of working memory functions within the dorsolateral prefrontal cortex. *Exp Brain Res, 133,* 23-32.

153. Levy, D.L., Holzman, P.S., Matthysse, S., & Mendell, N.R. (1993.) Eye tracking dysfunction and schizophrenia: a critical perspective. *Schizophr Bull, 19,* 461-536.

154. Li, L., Miller, E.K., & Desimone, R. (1993). The representation of stimulus familiarity in anterior inferior temporal cortex. *J Neurophysiol, 69,* 1918-1929.

155. Logothetis, N.K. (2002). The neural basis of the blood-oxygen-level-dependent functional magnetic resonance imaging signal. *Phil. Trans. R. Soc. Lond. B.* DOI: 10.1098/rstb.2002.1114

156. Logothetis, N.K., Paul,s J., & Poggio, T. (1995). Shape representation in the inferior temporal cortex of monkeys. *Curr Biol, 5*, 552-563.

157. Lubow, R.E., Kaplan, O., Abramovich, R., Rudnick, A., & Laor, N. (2000). Visual search in schizophrenia: latent inhibition and novel pop-out effects. *Schizophr Res, 45*, 145-156.

158. Luck, S.J., & Vogel, E.K. (1997). The capacity of visual working memory for features and conjunctions. *Nature, 390,* 279-281.

159. Maccotta, L., & Buckner, R.L. (2004). Evidence for neural effects of repetition that directly correlate with behavioral priming. *J Cogn Neurosci*, *16*, 1625-1632.

160. Malach, R., Levy, I., & Hasson, U. (2002). The topography of high-order human object areas. *Trends Cog Sci, 6,* 176-184.

161. Malach, R., Reppas, J.B., Kwong, K.K., Jiang, H., Kennedy, W.A., Ledden, P.J., Brady, J., Rosen, B.R., & Tootell, R.B. (1995). Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proc Natl Acad Sci USA, 92*, 8135-8138.

162. Malik, P., Dessing, J.C., & Crawford, J.D. (2015). Role of early visual cortex in trans-saccadic memory of object features. *J Vis, 15,* 1-7.

163. Matsuzaka, Y., Aizawa, H., & Tanji, J. (1992). A motor area rostral to the supplementary motor area (presupplementary motor area) in the monkey: neuronal activity during a learned motor task. *J Neurophysiol, 68,* 653-662.

164. McConkie, G.W., & Zola, D. (1979). Is visual information integrated across successive fixations in reading? *Percept Psychophys, 25,* 221-224.

165. McFarland, J.M., Bondy, A.G., Saunders, R.C., Cumming, B.G., & Butts, D.A. (2015). Saccadic modulation of stimulus processing in primary visual cortex. *Nat Commun 6*: doi:10.1038/ncomms9110.

166. Mecklinger, A., & Pfeifer, E. (1996). Event-related potentials reveal topographical and temporal distinct neuronal activation patterns for spatial and object working memory. *Cognitive Brain Res, 4*, 211-224.

167. Medendorp, W.P., Goltz, H.C., Vilis, T., & Crawford, J.D. (2003). Gaze-centered updating of visual space in human parietal cortex. *J Neurosci, 23*, 6209-6214.

168. Melcher, D. (2007). Predictive remapping of visual features precedes saccadic eye movements. *Nature, 10*, 903-907.

169. Melcher, D. (2009). Selective attention and the active remapping of object features in trans-saccadic perception. *Vision Res, 49*, 1249-1255.

170. Melcher, D., & Colby, C.L. (2008). Spatiotopic transfer of visual-form adaptation across saccadic eye movements. *Curr Biol, 15*, 1745-1748.

171. Merriam, E.P., Genovese, C.R., & Colby, C.L. (2003). Spatial updating in human parietal cortex. *Neuron, 39*, 361-373.

172. Merriam, E.P., Genovese, C.R., & Colby, C.L. (2007). Remapping in human visual cortex. *J Neurophysiol, 97*, 1738-1755.

173. Miller, E.K., & Desimone, R. (1994). Parallel neuronal mechanisms for short-term memory. *Science, 263*, 520-522.

174. Miller, E.K., Li, L., & Desimone, R. (1993). Activity of neurons in anterior inferior temporal cortex during a short-term memory task. *J Neurosci, 13*, 1460-1478.

175. Milner, A.D., & Goodale, M.A. (2008). Two visual systems re-viewed. *Neuropsychologia (Oxford), 46*, 774-785.

176. Milner, A.D., Paulignan, Y., Dijkerman, H.C., Michel, F., & Jeannerod, M. (1999). A paradoxical improvement of misreaching in optic ataxia: new evidence for two separate neural systems for visual localization. *Proc R Soc Lond B, 266*, 2225-2229.

177. Mishkin, M., Ungerleider, L.G., & Macko, K.A. (1983). Object vision and spatial vision: two cortical pathways. *Trends Neurosci, 6*, 414-417.

178. Monaco, S., Chen, Y., Medendorp, W.P., Crawford, J.D., Fiehler, K., & Henriques, D.Y.P. (2014). Functional magnetic resonance imaging adaptation reveals the cortical networks for processing grasp-relevant object properties. *Cereb Cortex* doi:10.1093/cercor/bht006.

179. Moschovakis, A.K. (1997). The neural integrator of the mammalian saccadic system. *Front Biosci, 2*, 552-577.

180. Moschovakis, A.K., Scudder, C.A., & Highstein, S.M. (1991a). Structure of the primate oculomotor burst generator. I. Medium-lead burst neurons with upward on-directions. *J Neurophysiol, 65*, 203–217.

181. Moschovakis, A.K., Scudder, C.A., & Highstein, S.M. (1991b). Structure of the primate oculomotor burst generator. II. Medium-lead burst neurons with downward on-directions. *J Neurophysiol, 65*, 218–229.

182. Moschovakis, A.K., & Highstein, S.M. (1994). The anatomy and physiology of primate neurons that control rapid eye movements. *Ann Rev Neurosci, 17*, 465–488.

183. Motter, B.C. (1994). Neural correlates of feature selective memory and pop-out in extrastriate area V4. *J Neurosci, 14*, 2190-2199.

184. Mullette-Gillman, O.A., Cohen, Y.E., & Groh, J.M. (2005). Eye-centered, head-centered, and complex coding of visual and auditory targets in the intraparietal sulcus. *J Neurophysiol, 94*, 2331-2352.

185. Mullette-Gillman, O.A., Cohen, Y.E., & Groh, J.M. (2009). Motor-related signals in the intraparietal cortex encode locations in a hybrid, rather than eye-centered reference frame. *Cereb Cortex, 19*, 1761-1775.

186. Munoz, D.P. (2002). Commentary: saccadic eye movements: overview of neural circuitry. *Prog Brain Res, 40*, 89-96.

187. Munoz, D.P. (2006). Stabilizing the visual world. *Nat Neurosci, 9*, 1467-1468.

188. Murata, A., Gallese, V., Luppino, G., Kaseda, M., & Sakata, H. (2000). Selectivity for the shape, size, and orientation of objects for grasping in neurons of monkey parietal area AIP. *J Neurophysiol, 83*, 2580-2601.

189. Muri, R.M., Iba-Zizen, M.T., Derosier, C., Cabanis, E.A., & Pierrot-Desseiligny, C. (1996). Location of the human posterior eye field with functional magnetic resonance imaging. *J Neurol Neurosurg Psychiatry, 60*, 445-448.

190. Muri, R.M., Roesler, K.M., & Hess, C.W. (1994). Influence of transcranial magnetic stimulation on the execution of memorised sequences of saccades in man. *Exp Brain Res, 101*, 521-524.

191. Nakamura, K., & Colby, C.L. (2002). Updating of the visual representation in monkey striate and extrastriate cortex during saccades. *Proc Natl Acad Sci, 99*, 4026-4031.

192. O'Regan, J.K. (1992). Solving the 'real' mysteries of visual perception: the world as an outside memory. *Can J Psychol, 46*:461-488.

193. O'Regan, J.K., Deubel, H., Clark, J.J., & Rensink, R.A. (2000). Picture changes during blinks: looking without seeing and seeing without looking. *Vis Cog, 7*, 191-211.

194. O'Sullivan, E.P., Jenkins, I.H., Henderson, L., Kennard, C., & Brooks, D.J. (1995). The functional anatomy of remembered saccades: a PET study. *Neuroreport (Oxford), 6*, 2141-2144.

195. Opris, I., Barborica, A., & Ferrera, V.P. (2003). Comparison of performance on memory-guided saccade and delayed spatial match-to-sample task in monkeys. *Vision Res, 43*, 321-332.

196. Peigneux, P., Salmon, E., van der Linden, M., Garraux, G., Aerts, J., Delfiore, G., Degueldre, C., Luxen, A., Orban, G., & Franck, G. (2000). The role of the lateral occipitotemporal junction and area MT/V5 in the visual analysis of upper-limb postures. *NeuroImage, 11*, 644-655.

197. Perry, R.J., & Zeki, S. (2000). The neurology of saccades and covert shifts in spatial attention. *Brain, 123*, 2273-2288.

198. Pierrot-Deseilligny, C., Israel, I., Berthoz, A., Rivaud, S., & Gaymard, B. (1993). Role of the different frontal lobe areas in the control of the horizontal component of memory-guided saccades in man. *Exp Brain Res, 95*, 166-171.

199. Pierrot-Deseilligny, C., Milea, D., & Muri, R.M. (2004). Eye movement control by the cerebral cortex. *Curr Opin Neurobiol, 17*, 17-25.

200. Pierrot-Deseilligny, C., Muri, R.M., Nyffeler, T., & Milea, D. (2005). The role of the human dorsolateral prerontal cortex in ocular motor behavior. *Ann NY Acad Sci, 1039*, 239-251.

201. Pierrot-Deseilligny, C., Muri, R.M., Ploner, C.J., Gaymard, B., Demeret, S., & Rivaud-Pechoux, S. (2003). Decisional role of the dorsolateral prefrontal cortex in ocular motor behavior. *Brain, 126*, 1460-1473.

202. Pierrot-Deseilligny, C., Ploner, C.J., Muri, R.M., Gaymard, B., & Rivaud-Pechoux, S. (2002). Effects of cortical lesions on saccadic eye movements in humans. *Ann NY Acad Sci, 956*, 216-229.

203. Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., & Agid, Y. (1991). Cortical control of reflexive visually-guided saccades. *Brain, 114,* 1473-1485.

204. Pigott, S., & Milner, B. (1993). Memory for different aspects of complex visual scenes after unilateral temporal- or frontal-lobe resection. *Neuropsychologia (Oxford), 31,* 1-15.

205. Pouget, P., Emeric, E.E., Stuphorn, V., Reis, K., & Schall, J.D. (2005). Chronometry of visual responses in frontal eye field, supplementary eye field, and anterior cingulate cortex. *J Neurophysiol, 94,* 2086-2092.

206. Pratte, M.S., & Tong, F. (2014). Spatial specificity of working memory representations in the early visual cortex. *J Vis, 14,* 1-12.

207. Prime, S.L., Niemeier, M., & Crawford, J.D. (2006). Transsaccadic integration of visual features in a line intersection task. *Exp Brain Res, 169,* 532-548.

208. Prime, S.L., Tsotsos, L., Keith, G.P., & Crawford, J.D. (2007). Visual memory capacity in transsaccadic integration. *Exp Brain Res, 180,* 609-628.

209. Prime, S.L., Vesia, M., & Crawford, J.D. (2008). Transcranial magnetic stimulation over posterior parietal cortex disrupts transsaccadic memory of multiple objects. *J Neurosci, 28,* 6938-6949.

210. Prime, S.L., Vesia, M., & Crawford, J.D. (2009). TMS over frontal eye fields disrupts trans-saccadic memory of multiple objects. *Cereb Cortex, 18,* 2410-2415.

211. Prime, S.L., Vesia, M., & Crawford, J.D. (2010). TMS over human frontal eye fields disrupts trans-saccadic memory of multiple objects. *Cereb Cortex, 20,* 759-772.

212. Prime, S.L., Vesia, M., & Crawford, J.D. (2011). Cortical mechanisms for trans-saccadic memory and integration of multiple object features. *Phil Trans R Soc B, 366,* 540-553.

213. Race, E.A., Shanker, S., & Wagner, A.D. (2009). Neural priming in human frontal cortex: multiple forms of learning reduce demands on the prefrontal executive system. *J Cogn Neurosci, 21,* 1766-1781.

214. Rayner, K. (1998). Eye movements in reading and information processing: 20 years of research. *Psychol Bull, 124*, 372-422.

215. Rayner, K., McConkie, G.W., & Zola, D. (1980). Integrating information across eye movements. *Cogn Pyschol*, *12*, 206-226.

216. Reddi, B.A., Asrress, K.N., & Carpenter, R.H. (2003). Accuracy, information, and response time in asaccadic decision task. *J Neurophysiol*, *90*, 3538-3546.

217. Regan, D., & Beverley, K.I. (1985). Postadaptation orientation discrimination. *J Opt Soc America*, *2*, 147-155.

218. Rensink, R.A., O'Regan, J.K., & Clark, J.J. (1997). To see or not to see: the need for attention to perceive changes in scenes. *Psychol Sci*, *8*, 368-373.

219. Ringo, J.L. (1996). Stimulus specific adaptation in inferior temporal and medial temporal cortex of the monkey. *Behav Brain Res*, *76*, 191-197.

220. Robinson, D.A. (1978). The purpose of eye movements. *Invest Ophtalmol Vis Sci*, *17*, 835-837.

221. Robinson, D.A. (1981). The control of eye movements. In: Brooks VB, ed. Handbook of physiology, vol 2, part 2. Bethesda, MD: American Physiology Society, p1275–1320.

222. Rosano, C., Krisky, C.M., Welling, J.S., Eddy, W.F., Luna, B., Thulborn, K.R., & Sweeney, J.A. (2002). Pursuit and saccadic eye movement subregions in human frontal eye field: a high-resolution fMRI investigation. *Cereb Cortex*, *12*, 107-115.

223. Ross, J., Morrone, M.C., Goldberg, M.W., & Burr, D.C. (2001). Changes in visual perception at the time of saccades. *Trends Neurosci, 24*, 113-121.

224. Russ, M.O., Mack, W., Grama, C.-R., Lanfermann, H., & Knopf, M. (2003). Enactment effect in memory: evidence concerning the function of the supramarginal gyrus. *Exp Brain Res, 149*, 497-504.

225. Ruter, J., Kammer, T., & Herzog, M.H. (2010). When transcranial magnetic stimulation (TMS) modulates feature integration. *Eur J Neurosci, 32*, 1951-1958.

226. Sajad, A., Sadeh, M., Keith, G.P., Yan, X., Wang, H., & Crawford, J.D. (2014), Visual-motor transformation within frontal eye fields during head-unrestrained gaze shifts in the monkey. *Cereb Cortex* doi: 10.1093/cercor/bhu279.

227. Sakata, H., Taira, M., Murata, A., & Mine, S. (1995). Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cereb Cortex, 5*, 429-438.

228. Sakata, H., Taira, M., Kusunoki, M., Murata, A., & Tanaka, Y. (1997). The parietal association cortex in depth perception and visual control of hand action. *Trends Neurosci, 20*, 350-357.

229. Schacter, D.L., & Buckner, R.L. (1998). Priming and the brain. *Neuron, 20*, 185-195.

230. Scharnowski, F., Ruter, J., Jolij, J., Hermens, F., Kammer, T., & Herzog, M.H. (2009). Long-lasting modulation of feature integration by transcranial magnetic stimulation. *J Vis, 9*, 1-10.

231. Schall, J.D. (2002). The neural selection and control of saccades by the frontal eye field. *Phil Trans R Soc Lond B, 357*, 1073-1082.

232. Schlag, J., & Schlag-Rey, M. (1987). Evidence for supplementary eye field. *J Neurophysiol, 57*, 179-200.

233. Schlag, J., Schlag-Rey, M., & Dassonville, P. (1990). Saccades can be aimed at the spatial location of targets flashed during pursuit. *J Neurophysiol, 64*, 575-581.

234. Schlag-Rey, M., Amador, N., Sanchez, H., & Schlag, J. (1997). Antisaccade performance predicted by neuronal activity in the supplementary eye field. *Nature*, *390*, 398-401.

235. Schnyder, H., Reisine, H., Hepp, K., & Henn, V. (1985). Frontal eye field projection to the paramedian pontine reticular formation traced with wheat germ agglutinin in the monkey. *Brain Res*, *329*, 151–160.

236. Scudder, C.A., Moschovakis, A.K., Karabelas, A.B., & Highstein, S.M. (1996). Anatomy and physiology of saccadic long-lead burst neurons recorded in the alert squirrel monkey. I. Descending projections from the mesencephalon. *J Neurophysiol*, *76*, 332–352.

237. Scudder C.A., Moschovakis, A.K., Karabelas, A.B., & Highstein, S.M. (1996). Anatomy and physiology of saccadic long-lead burst neurons recorded in the alert squirrel monkey. II. Pontine neurons. *J Neurophysiol*, *76*, 353–370.

238. Scudder, C.A, Kaneko, C.S., & Fuchs, A.F. (2002). The brainstem burst generator for saccadic eye movements: a modern synthesis. *Exp Brain Res*, *142*, 439–462.

239. Segaert, K., Weber, K., de Lange, F.P., Petersson, K.M., & Hagoort, P. (2013). The suppression of repetition enhancement: a review of fMRI studies. *Neuropsychologia (Oxford), 51*, 59-66.

240. Sereno, A.B., & Maunsell, J.H.R. (1998). Shape selectivity in primate lateral intraparietal cortex. *Nature, 395*, 500-503.

241. Sharpe, J., & Wong, A. M. (2005). Anatomy and physiology of ocular motor systems. *Walsh and Hoyt's Clinical Neuro-Ophthalmology*, 1, 809-885.

242. Sharpe, J.A., Troost, B.T., Dell'Osso, L.F., & Daroff, R.B. (1975). Comparative velocities of different types of fast eye movements in man. *Invest Ophthalmol 14*, 689–692.

243. Sharpe, J.A., & Zackon, D.H. (1987). Senescent saccades: effects of aging on their accuracy, latency and velocity. *Acta Otolaryngol*, *104*, 422–428.

244. Shelhamer, M., & Joiner, W.M. (2003). Saccades exhibit abrupt transition between reactive and precitive; predictive saccade sequences have long-term correlations. *J Neurophysiol*, *90*, 2763-2769

245. Shima, K., Mushiake, H., Saito, N., & Tanji, J. (1996). Role for cells in the presupplementary motor area in updating motor plans. *Proc Natl Acad Sci 93*, 8694-8698.

246. Shipley, T.F. (2003). The effect of object and event orientation on perception of biological motion. *Psychol Soc*, *14*, 377-380.

247. Shiraishi, Y., & Nakao, S. (1995). Differential locations in the midbrain of distinct groups of vertical eye movement-related neurones in cat: their projections and direct connections with oculomotor neurones. *Acta Physiol Scand*, *154*, 151–163.

248. Simion, F., Bagnara, S., Roncato, S., & Umilta, C. (1982). Transformation processes upon the visual code. *Percept Psychophys*, *31*, 13-25.

249. Simons, D.J. (1996). In sight, out of mind: when object representations fail. *Psychol Sci*, *7*, 301-305.

250. Simons, D.J., & Levin, D.T. (1997). Change blindness. *Trends Neurosci*, *1*, 261-267.

251. Smeets, J.B., & Hooge, I.T. (2003). Nature of variability in saccades. *J Neurophysiol*, *90*, 12–20.

252. Smit, A.C., Van Gisbergen, J., & Cools, A.R. (1987). A parametric analysis of human saccades in different experimental paradigms. *Vision Res*, *27*, 1745–1762.

253. Smith, M.L., & Milner, B. (1989). Right hippocampal impairment in the recall of spatial location: encoding deficit or rapid forgetting. *Neuropsychologia (Oxford), 27*, 71-81.

254. Snyder, L.H., Grieve, K.L., Brotchie, P., & Andersen, R.A. (1998). Separate body- and world-referenced representations of visual space in parietal cortex. *Nature*, *394*, 887-891.

255. Sobotka, S., & Ringo, J.L. (1994). Stimulus specific adaptation in excited but not in inhibited cells in inferotemporal cortex of macaque. *Brain Res, 646*, 95-99.

256. Sobotka, S., & Ringo, J.L. (1996). Mnemonic responses of single units recorded from monkey inferotemporal cortex, accessed via transcommissural versus direct pathways: a dissociation between unit activity and behavior. *J Neurosci, 16*, 4222-4230.

257. Sommer, M.A., & Wurtz, R.H. (1998), Frontal eye field orthodromically activated from the superior colliculus. *J Neurophysiol*, *80*, 3331-3335.

258. Sommer, M.A., & Wurtz, R.H. (2004). What the brain stem tells the frontal cortex. I. Oculomotor signals sent from superior colliculus to frontal eye field via mediodorsal thalamus. *J Neurophysiol, 91*, 1381-1402.

259. Sparks, D.L. (2002). The brainstem control of saccadic eye movements. *Nat Neuro Rev, 3*, 952-964.

260. Sparks, D.L., & Mays, L.E. (1990). Signal transformations required for the generation of saccadic eye movements. *Annu Rev Neurosci, 13*, 309-336.

261. Stanton, G.B., Goldberg, M.E., & Bruce, C.J. (1988). Frontal eye field efferents in the macaque monkey. *J Comp Neurol, 27*, 473–506.

262. Stanton, G.B., Goldberg, M.E., & Bruce, C.J. (1988). Frontal eye field efferents in the macaque monkey: II Topography of terminal fields in midbrain and pons. *J Comp Neurol, 27*, 493–506.

263. Stoeckel, C., Gough, P.M., Watkins, K.E., & Devlin, J.T. (2009). Supramarginal gyrus involvement in visual world recognition. *Cortex, 45*, 1091-1096.

264. Strassman, A., Highstein, S.M., & McCrea, R.A. (1986). Anatomy and physiology of saccadic burst neurons in the alert squirrel monkey. II. Inhibitory burst neurons. *J Comp Neurol, 249*, 358–380.

265. Subramanian, J., & Colby, C.L. (2014). Shape selectivity and remapping in dorsal stream visual area LIP. *J Neurophysiol*, *111*, 613-627.

266. Suzuki, S., & Cavanagh, P. (1995). Facial organization blocks access to low-level features: an object inferiority effect. *J Exp Psychol Human*, *21*, 901-913.

267. Sylvestre, P.A., & Cullen, K.E. (1999). Quantitative analysis of abducens neuron discharge dynamics during saccadic and slow eye movements. *J Neurophysiol*, *82*, 2612–2632.

268. Sylvester, R., Haynes, J.-D., & Rees, G. (2005). Saccades differentially modulate human LGN and V1 responses in the presence and absence of visual stimulation. *Curr Biol*, *15*, 37-41.

269. Talairach, J., & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain. New York: Thieme Medical.

270. Talsma, D., White, B.J., Mathot, S., Munoz, D.P., & Theeuwes, J. (2013). A retinotopic attentional trace after saccadic eye movements: evidence from event-related potentials. *J Cog Neurosci, 25*, 1563-1577.

271. Tanaka, L.L., Dessing, J.C., Malik, P., Prime, S.L., & Crawford, J.D. (2014). The effects of TMS over dorsolateral prefrontal cortex on trans-saccadic memory of multiple objects. *Neuropsychologia (Oxford), 63*, 185-193.

272. Tarr, M.J., & Pinker, S. (1989). Mental rotation and orientation-dependence in shape recognition. *Cogn Psychol, 21*, 233-282.

273. Taylor, P.C.J., Muggleton, N.G., Kalla, R., Walsh, V., & Eimer, M. (2011). TMS of the right angular gyrus modulates priming of pop-out in visual search: combined TMS-ERP evidence. *J Neurophysiol*, *106*, 3001-3009.

274. Tong, F. (2003). Primary visual cortex and visual awareness. *Nat Neurosci 4*, 219-229.

275. Treisman, A.M., & Gelade, G. (1980). A feature-integration theory of attention. *Cogn Psychol*, *12*, 97-136.

276. Tremblay, S., Parmentier, F.B.R., Guerard, K., Nicholls, A.P., & Jones, D.M. (2006). A spatial modality effect in serial memory. *J Exp Psychol Learn Mem Cogn 32,* 1208-1215.

277. Troost, B.T., Weber, R.B., & Daroff, R.B. (1974). Hypometric saccades. *Am J Ophtalmol*, *78*, 1002-1005.

278. Turi, M., & Burr, D. (2012). Spatiotopic perceptual maps in humans: evidence from motion adaptation. *Proc R Soc B, 279,* 3091-3097.

279. Uchimara, M., Nakano, T., Morito, Y., Ando, H., & Kitazawa, S. (2015). Automatic representation of a visual stimulus relative to a background in the right precuneus. *Eur J Neurosci*, *42*, 1651-1659.

280. Ungerleider, L.G., & Haxby, J.V. (1994). 'What' and 'where' in the human brain. *Curr Opin Neurobiol*, *4*, 157-165.

281. Van Horn, M.R., Sylvestre, P.A., & Cullen, K.E. (2008). The brain stem saccadic burst generator encodes gaze in three-dimensional space. *J Neurophysiol*, *99*, 2602-2616.

282. Van Turennout, M., Ellmore, T., & Martin, A. (2000). Long-lasting cortical plasticity in the object naming system. *Nat Neurosci*, *2*, 1329-1334.

283. Valyear, K.F., Culham, J.C., Sharif, N., Westwood, D., & Goodale, M.A. (2006). A double dissociation between sensitivity to changes in object identity and object orientation in the ventral and dorsal visual streams: a human fMRI study. *Neuropsychologia (Oxford), 44*, 218-228.

284. Vesia, M., & Crawford, J.D. (2012). Specialization of reach function in human posterior parietal cortex. *Exp Brain Res, 221*, 1-18.

285. Vogel, E.K., Woodman, G.F., & Luck, S.J. (2001). Storage of features, conjunctions, and objects in visual working memory. *J Exp Pyschol Hum Percept Perform, 27*, 92-114.

286. Walker, P., & Cuthbert, L. (1998). Remembering visual feature conjunctions: visual memory for shape-colour associations is object-based. *Vis Cog, 5*, 409-455.

287. Wang, R.F., Crowell, J.A., Simons, D.J., Irwin, D.E., Kramer, A.F., Ambinder, M.S., Thomas, L.E., Gosney, J.L., Levinthal, B.R., & Hsieh, B.B. (2006). Spatial updating relies on an egocentric representation of space: effects of the number of objects. *Psychon Bull Rev, 13*, 281-286.

288. Wang, Y., Matsuzaka, Y., Shima, K., & Tanji, J. (2004). Cingulate cortical cells projecting to monkey frontal eye field and primary motor cortex. *NeuroReport, 15*, 1559-1563.

289. Watson, J.S. (1966). Perception of object orientation in infants. *Merrill Palmer Quart, 12*, 73-94.

290. Weber, R.B., & Daroff, R.B. (1971). The metrics of horizontal saccadic eye movements in normal humans. *Vision Res, 11*, 921–928.

291. Weickert, T.W., Goldberg, T.E., Gold, J.M., Bigelow, L.B., Egan, M.F., & Weinberger, D.R. (2000). Cognitive impairments in patients with schizophrenia displaying preserved and compromised intellect. *Arch Gen Psychiatry, 57*, 907-913.

292. Westheimer, G., Shimamura, K., & McKee, S.P. (1976). Interference with line-orientation sensitivity. *J Opt Soc America, 66*, 332-338.

293. Wiggs, C.L., & Martin, A. (1998). Properties and mechanisms of perceptual priming. *Curr Opin Neurobiol, 8*, 227-233.

294. Wolbers, T., Hegarty, M., Buchel, C., & Loomis, J.M. (2008). Spatial updating: how the brain keeps track of changing object locations during observer motion. *Nat Neurosci, 11*, 1223-1230.

295. Yarbus, A.L. (1967). Eye movements and vision. Plenum, New York.

296. Zacks, J.M., Gilliam, F., & Ojemann, J.G. (2003) Selective disturbance of mental rotation by cortical stimulation. *Neuropsychologia (Oxford), 41*, 1659-1667.

297. Zambieri, D. (2002). The latency of saccades toward auditory targets in humans. *Prog Brain Res, 140*, 51-59.

298. Zhou, W., & King, W.M. (1998). Premotor commands encode monocular eye movements. *Nature, 393*, 692–695.