The Neural Basis of Multisensory Spatial and Feature-Based Attention in Vision and Somatosensation

PhD Thesis

Veldri Kurniawan

Supervised by:
Dr. Christopher D. Chambers
Dr. Jane Klemen

School of Psychology
Cardiff University
2012

Summary

Attention refers to the cognitive processes that prioritise a subset of available sensory information for enhanced processing, and which can be directed towards spatial locations, object features, time, or other aspects of the environment. While the majority of research has focused on studying attention within sensory modalities, a growing body of evidence has demonstrated that attention interact with multisensory processes. Several neuroimaging studies have shown that higher cortical regions activated during attention to multiple sensory modalities overlap significantly with the dorsal and ventral frontoparietal regions activated during visual attention tasks. This evidence has led some researchers to propose the existence of *supramodal* frontoparietal system that controls the deployment of attention across various sensory modalities. Although influential, this hypothesis has been challenged by other studies that discovered evidence for modality-specific regions in the parietal cortex. In this thesis, I investigated the generality and specificity of the frontoparietal network associated with multisensory spatial and feature-based attention, in vision and touch, by applying multivoxel pattern analysis (MVPA) to fMRI data. Recent studies have successfully demonstrated that MVPA methods could be used to discriminate various experimental conditions from weak distributed patterns of activity within overlapping cortical regions found by univariate fMRI analysis. Here, I applied similar logic to examine overlapping frontoparietal regions activated during multisensory attention. Contrary to the supramodal hypothesis, the results supported the existence of modality-specific systems in the posterior parietal cortex during both attention to spatial locations and stimulus features. Additional evidence for modality-specific processes was also indicated in the patterns of top-down modulatory activity in visual cortex. Overall, the current findings supported the view that both modality-specific and potentially supramodal frontoparietal regions work in concert to selectively bias activity in sensory cortical regions during various states of attention.

Acknowledgements

First, I would like to express my sincere gratitude to my primary supervisor, Chris Chambers, and secondary supervisor, Jane Klemen, for their guidance, advice, and help throughout my PhD. I am particularly grateful to Chris for the knowledge on how to design and implement good cognitive neuroscience experiments, for his constant support and encouragement, and for his endless inspiration on how to write better and communicate scientific ideas more effectively. Jane has been very instrumental in helping me to design and analyse the fMRI experiments, and to solve various problems related to the eyetracking in the MR-scanner. I am also grateful for her constant support, and for long hours of discussions concerning various aspects the project.

I would like to acknowledge the School of Psychology and Wales Institute of Cognitive Neuroscience (WICN) for their financial support. I also want to thank the support staff of the School of Psychology for their help concerning various technical apparatus used in this research, in particular to Martin Stuart, Rik Nash, Dennis Simmonds, and the late Denis Price.

I want to thank our research collaborators, Mark Williams and Christian Ruff for their inputs and suggestions concerning the design of the multisensory spatial attention experiment. I am also very grateful to Andreas Bungert for his help in technical, conceptual and practical aspects concerning the TMS/fMRI experiment, and to Chris Allen and Leah Maizey for their help in data collection during the TMS/fMRI experiment. I also want to thank John Evans for his assistance in solving various technical problems associated with running multisensory apparatus inside the MR-scanner, Krish Singh and Sian Robson for sharing their knowledge about retinotopic mapping, and Nick Puts and Dave McGonigle for discussion about somatosensory processing.

I am also grateful to others whom I have known while I was living in Cardiff, in particular to Marcel, Rushda, Martynas, and Rizwan for friendship and lively discussions concerning various philosophical topics. I also want to thank all my friends back home for friendship. Finally, I would like to extend my gratitude to my parents and family for their support and understanding.

Table of Contents

Chapter 1 - General Introduction

In our daily experience, we are constantly bombarded with streams of stimuli in multiple senses and from multiple locations. Due to the limited processing capacity of our nervous system, it is important to selectively attend to portions of our total sensory input that are most relevant to our current behaviour (Desimone and Duncan, 1995a). Attention helps to prioritize significant sensory signals across modalities, spatial locations, time, and object properties.

While most studies have focused on studying attention within a sensory modality, in the last two decades increasing evidence has also demonstrated close coupling between attention and multisensory processes (Mozolic et al., 2008a; Koelewijn et al., 2010; Talsma et al., 2010). Many cross-modal attention experiments have demonstrated that strategically orienting attention to one location in one modality can enhance processing of stimuli presented in another modality within the same attended location (Driver and Spence, 1998; McDonald et al., 2000; Spence et al., 2000). These findings have led several authors to postulate the hypothesis of a '*supramodal'* attentional control system that operates across wide range of sensory modalities (Farah et al., 1989; Macaluso and Driver, 2001; Macaluso, 2010; Green et al., 2011). Evidence for the existence of this supramodal system has emerged from several neuroimaging studies, which revealed that higher cortical regions commonly associated with attentional processing in a single modality (frontoparietal attention network; Corbetta et al., 2008) are also activated during deployment of attention to multiple sensory modalities (Macaluso and Driver, 2001; Eimer et al., 2002b; Macaluso, 2010; Smith et al., 2010; Green et al., 2011).

Although influential, interpreting overlapping activations found in neuroimaging experiments as evidence for a supramodal attention system is controversial and has been debated in the literature (Chambers et al., 2004b; Klemen and Chambers, 2012). Recent evidence from TMS studies has indicated the presence of both modality-specific and potentially supramodal systems in the frontoparietal regions (Chambers et al., 2004b, 2007), implicating multifaceted interrelationships between various attentional sub-regions in regulating top-down attentional control to multiple sensory modalities.

Recent advances in multivoxel pattern analysis (MVPA) methods have enabled neuroscientists to exploit fine-grained distributed patterns of activity within the fMRI voxels for discriminating perceptual or cognitive states (Haynes and Rees, 2006; Tong and Pratte, 2012). MVPA methods have been successfully applied to distinguish various experimental conditions within overlapping cortical regions (Peelen and Downing, 2007), as demonstrated in various studies of object and face recognition (Haxby et al., 2001; Spiridon and Kanwisher, 2002; Peelen and Downing, 2007), and in decoding top-down control signals in frontoparietal regions (Esterman et al., 2009; Greenberg et al., 2010).

In this thesis we combined fMRI and MVPA to investigate the modality-specificity of frontoparietal attention networks during deployment of endogenous spatial and feature-based attention in the visual and somatosensory modalities. Additionally, we also examined top-down modulatory effects of multisensory attention on visual and primary somatosensory cortex using both conventional ROI-analysis and ROI-based MVPA classification. To solve the challenges of displaying reliable visual stimuli during multisensory visuo-tactile experiments, we have also designed and constructed a novel MR-compatible visual presentation system that fibre-optically transmits LED light points controlled by programmable microcontroller circuits. Lastly, a pilot concurrent TMS/fMRI study was conducted to probe attention-dependent modulatory effects associated with TMS over the frontal cortex during sustained feature-based attention in vision.

This chapter begins with a brief introduction to the theories of attention relevant to the present studies, followed by a discussion of the neural basis of spatial and feature-based attention. Subsequently, the neural basis of multisensory attention and the supramodal debate will be discussed. Finally, the chapter conclude with a summary of the aims and outline of this project.

1.1 Attention

Attention refers to the neural process by which organisms select a portion of incoming sensory stimuli for temporary enhancement or integration with other stimuli (Pashler, 1998). Behaviourally, it has been shown that attention enhances perceptual sensitivity of stimuli and shortens the reaction time needed for responding to targets (Müller and Humphreys, 1991; Shepherd and Müller, 1989; Wright and Ward, 2008). Many decades of research probing different characteristics of attention have demonstrated that attention can be directed to various aspects, dimensions, and modalities of the stimuli, including spatial location (Posner et al., 1982; Moran and Desimone, 1985), time (Coull et al., 2000; Nobre et al., 2007), features (Treue and Martínez Trujillo, 1999; Saenz et al., 2002; Martinez-Trujillo, 2011), objects (Egly et al., 1994; Serences et al., 2004a; Shomstein and Behrmann, 2006), sensory modalities (Driver and Spence, 1998; Driver and Noesselt, 2008; Spence, 2010) and even internal mental processes (Chun et al., 2011; Lewis-Peacock and Postle, 2012).

One influential framework of attention proposed by Posner and Petersen (1990) has suggested that the attention system can be partitioned into at least three different processes that include alerting, orienting, and executive control. *Alerting* is defined as sustaining a state of high vigilance to incoming stimuli, and is related to the arousal system controlled by the brain stem. *Orienting* refers to the ability to prioritize information from sensory inputs by selecting the relevant modality or location. Finally, the *executive control* system is related to the process of target detection and conflict resolution among possible responses. Recently, Petersen and Posner (2012) have elaborated and extended their framework to include new components that were thought to be important for future attention research such as self-regulation, network efficiency, attentional training, and evolution. Other researchers have also recommended a similar framework for attention, including the one proposed by Wright and Ward (2008) which also consists of three main aspects: *orienting*, which refers to the process of aligning sensory organs towards relevant stimulus and away from the other; *filtering*, which is related to selective enhancement of attended stimuli and suppression of the unattended inputs; and *searching*, which describes the role of attention in the process of finding preferred objects among competitors.

A related and equally influential theory of attention developed by Desimone and Duncan (1995) has proposed an alternative model for attentional selection based on the '*biased competition*' account. According to this model, selective attention and behavioural inhibition are seen as two aspects of the same process. Any effects of attentional enhancement could be understood in the context of biasing competition in favour of task relevant information and simultaneous inhibition among conflicting task-irrelevant representations (Desimone, 1998; Kastner and Ungerleider, 2001; Beck and Kastner, 2009). There are five main principles in this model that apply to visual processing. The first is that stimuli in the visual fields compete for the representations in visual cortical neurons. The second is that strongest competition happen in a cortical region when competing stimuli fall within the same receptive fields of the neurons in that local region. The third is that these competitive interactions are mediated by several mechanisms including bottom-up bias and top-down feedback mechanisms. The fourth principle is that the feedback bias not only affects spatial processing but also other dimensions of the stimuli such as shape, colour, texture, motion, etc. Lastly, the fifth is that the source of top-down bias to visual cortex is postulated to originate from areas involved in working memory like the prefrontal cortex.

Attention can also be oriented either in an endogenous (goal-driven) or exogenous (involuntary) way. We orient our attention endogenously when we want to voluntarily attend to a particular location or to some objects with certain properties. For example, if we know that our friend is wearing a blue t-shirt, we can find her more easily in the midst of the crowd by focusing our attention on those people who are wearing blue colours. In contrast, abruptly appearing or intense stimuli can cause reflexive orienting of attention in an exogenous stimulus-driven manner, such as when a fire alarm suddenly goes off or when a traffic light suddenly changes from green to red. Exogenous attention enhances stimulus processing at the same location of the cue from about 100ms after the onset of the cue stimulus (Müller and Humphreys, 1991), whereas endogenous attention usually takes about 300ms to benefit processing after cue (Shepherd and Müller, 1989). Recent psychophysical evidence, however, suggests that strategic orienting on the basis of location and colour may accrue faster than previously realised, beginning to show perceptual benefits from ~100ms after cue onset (Adams and Chambers, 2012).

Contemporary theories of attention draw a key distinction between mechanisms of covert and overt orienting (Posner, 1980; Rorden et al., 2002; Wright and Ward, 2008). Attention is oriented overtly when it is accompanied by the movements of the eyes, head or body to enhance stimulus processing (i.e. to centre a visual stimulus in the fovea), whereas during covert orienting we shift our attention ‘silently’ without making any overt movements. In real life, covert orienting of attention usually occurs together with overt orienting, but it is possible to dissociate these processes experimentally. In fact, most research considers covert attention orienting separately from its overt manifestation (Wright and Ward, 2008), with the exception of some theories such as the premotor theory of attention (Rizzolatti et al., 1987; Corbetta et al., 1998a; Craighero and Rizzolatti, 2010), which proposed that both processes might actually share common neural mechanism. However, more recent behavioural and neuroimaging evidence indicates that although covert and overt attention share some neural substrates, the underlying processes are not identical (Corbetta and Shulman, 2002; Smith and Schenk, 2012).

1.2 Spatial and Feature-based Attention

Objects can be selected for enhanced processing on the basis of their position in the visual field (spatial attention; Posner and Petersen, 1990; Desimone and Duncan, 1995; Spence, 2010) or according to the intrinsic attributes of the objects such as colour or direction of motion (feature-based attention; Martinez-Trujillo & Treue, 2004; Saenz et al., 2002; Treue & Martínez Trujillo, 1999). It is also possible to direct attention to complex objects composed of ensembles of features, a process known as object-based attention (Egly et al., 1994; Serences et al., 2004a; Shomstein and Behrmann, 2006). Furthermore, attention can also be selectively focused toward a particular sensory modality at the cost of supressing information coming from the other modalities (Ashkenazi and Marks, 2004; Turatto et al., 2004; Spence, 2010). All of these aspects of attention are required to work together in the ecologically valid situations.

1.2.1 Spatial Attention

Spatial attention is perhaps the most widely studied variety of attentional selection. The way attention prioritizes specific locations and filters out distracting sensory inputs has been likened to a spotlight (Posner, 1980) or zoom lens (Eriksen and St James, 1986). This metaphorical spotlight can be moved across the visual field covertly, and objects falling within the spotlight will be enhanced regardless of their relevance to the task. Covert attention thus enhances visual spatial resolution, improving performance in most behavioural contexts, but critically also impairing performance when optimum performance on a visual task requires sub-maximal resolution (as in texture segregation; see Yeshurun and Carrasco, 1998). Many behavioural studies have also shown that spreading attention over a large region results in loss of spatial resolution and processing efficiency compared to focused attention on one location (Eriksen and Yeh, 1985; Castiello, 1990). Theories of spatial attention have suggested that space may be the prototypical unit of attentional selection, although this argument is controversial and has been challenged by other ideas that highlight the importance of features (Corbetta et al., 1990; Maunsell and Treue, 2006) or objects (O'Craven et al., 1999).

Over the last 30 years, the neural basis of spatial attention has been studied using various electrophysiology and neuroimaging techniques. A pioneering single-cell neurophysiological study by Moran and Desimone (1985) showed that single V4 neurons in the monkey responded more strongly when a stimulus appeared in an attended vs. unattended location. Further neurophysiological recordings in primates have demonstrated similar modulatory effects in multiple extrastriate regions including retinotopic area V2, V3A, V4, and MT (Desimone and Duncan, 1995a; Desimone, 1998). Under certain conditions, neural activity in the primary visual cortex (V1) can also be affected by selective attention (Ito and Gilbert, 1999; Noesselt et al., 2002). In some of these studies, attentional modulation was observed much later (80-250ms) than the initial sensory evoked response in V1, suggesting the possibility of delayed feedback coming higher visual regions as the mechanism for attention (Vidyasagar, 1998; Noesselt et al., 2002). The magnitude of attentional modulation steadily increases as we ascend the hierarchy of visual areas, possibly reflecting gradually increasing feedback effects from parietal to visual cortex (Tootell et al., 1998; Liu et al., 2005).

Spatial attention can also modulate synchrony between groups of neurons. In a multi-electrode study in the monkeys, when clusters of V4 neurons were activated by the attended stimulus there was an increase in gamma frequency (35-90Hz) synchronization, but not when the same neurons were activated by distracter stimulus (Fries et al., 2001). This findings demonstrates that attention not only modulates single-neuron responses but also affects oscillatory dynamics operating between populations of neurons (Saalmann et al., 2007).

Much evidence from neuroimaging studies in humans has shown that spatial attention enhances the magnitude of the BOLD response in retinotopic regions of visual cortex corresponding to the attended location (Sengpiel and Hübener, 1999; Somers et al., 1999), while reducing the activity in cortical regions that represent unattended locations (Smith et al., 2000). Selective enhancement of neural activity has been observed in the striate (V1) and extrastriate cortex (V2, V3, V4, V5/hMT+) even before presentation of the target stimulus, suggesting preparatory priming at the attended location for subsequent target processing (Kastner et al., 1999; Serences et al., 2004b; Silver et al., 2007). Moreover, fMRI studies have revealed that spatial attention can modulate activity in subcortical regions, including lateral geniculate nucleus (LGN) and thalamus, by enhancing neural responses to attended stimuli, suppressing unattended stimuli, and inducing a preparatory baseline increase in the absence of stimulation (O'Connor et al., 2002).

Neuroimaging methods have also been proven to be valuable for investigating the *source* of spatial attentional control signals that lead to selective modulation in the target sensory regions (Corbetta and Shulman, 2002; Corbetta et al., 2008). In one of the earliest studies of spatial attention using PET, Corbetta et al. (1993) found that regions in the parietal cortex were activated during cued shifts of spatial attention whereas frontal areas were discernibly active only during subsequent target detection. Subsequent studies using fMRI have also distinguished between different cognitive processes involved in spatial attention, suggesting that alerting, orienting, and executive control recruit anatomically and functionally distinct networks (Coull and Nobre, 1998; Thiel et al., 2004; Fan et al., 2005; Petersen and Posner, 2012).

As noted above, the alerting system is thought to maintain vigilance throughout the task via brain stem mechanisms and the right parietal cortex (Posner and Petersen, 1990; Sturm and Willmes, 2001), whereas the orienting system is related to the shifting of attention to various dimensions and modalities. Based on a concordance of evidence from fMRI experiments, Corbetta and Shulman (2002) proposed an influential theory in which two brain networks coordinate the orienting system of spatial attention (Figure 1.1a). In particular, they suggested that a dorsal frontoparietal network consisting of the posterior parietal cortex near the intra parietal sulcus (IPS) and the frontal eye fields (FEF) is strongly evoked following cue presentation beyond fixation, and is thought to embody a top-down endogenous control mechanism that maintains the current focus of attention and biases processing in lower sensory regions. Meanwhile, a second system, the ventral frontoparietal network includes alternative regions in the temporoparietal junction (TPJ), middle frontal gyrus (MFG), inferior frontal gyrus (IFG), frontal operculum, and anterior insula. This ventral network was suggested to serve as a 'circuit breaker', activated not only when a behaviourally relevant stimulus is detected in the cued location, but crucially also during 'invalid' cueing conditions when subjects are cued to one location but a target appears in another unpredicted location (contingent capture).

It has been postulated that interactions between brain areas of the dorsal and ventral frontoparietal networks are facilitated by synchronization of their activities in the alpha (8-14 Hz) and gamma (30-70 Hz) frequency ranges (Doesburg et al., 2008). Converging evidence for the existence of these networks has emerged from studies of resting state functional connectivity, which report that when their subjects are resting inside the scanner without performing any task, the brain still exhibits spontaneous activity, manifesting as two anti-correlated networks that overlap with the dorsal and ventral attention networks (Fox et al., 2005).

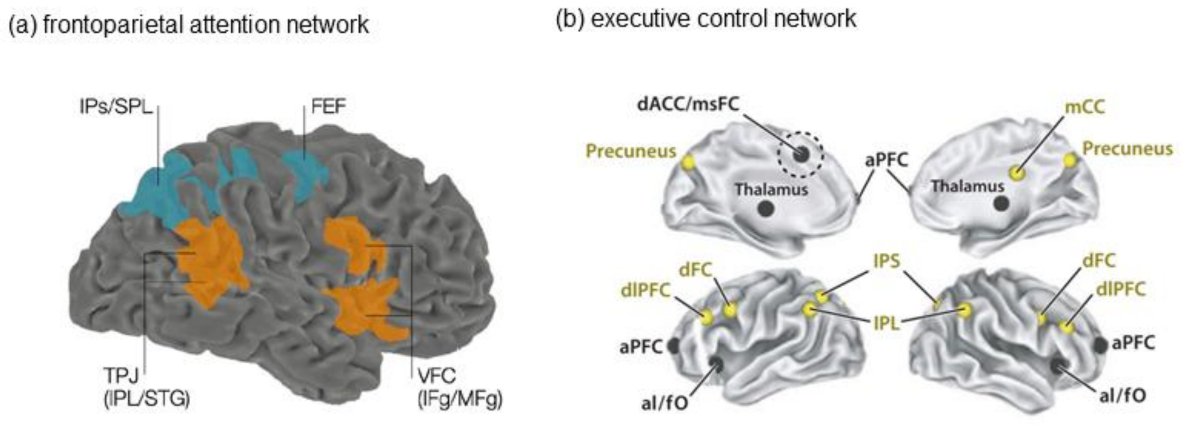


Figure 1.1. (a) Illustration of the dorsal and ventral attention network (adapted from Corbetta and Shulman, 2002). The regions highlighted in blue are part of the dorsal attention network, which includes the frontal eye fields (FEF) and the intraparietal sulcus/superior parietal lobe (IPS/SPL). The regions highlighted in orange are part of the ventral attention network which includes the temporoparietal junction (TPJ) and the ventral frontal cortex (VFC). **(b)** Illustration of the two networks of the executive control system. Areas in yellow indicate the frontoparietal control system for maintaining moment-to-moment task and areas in black indicate the cingulo-opercular system for task set maintenance (adapted from Petersen and Posner, 2012).

The third separate system associated with attentional processing is the executive control network, which involves the mechanism for resolving conflict among possible responses. This mechanism is associated with activity in the middle frontal cortex and anterior cingulate cortex (ACC; Cohen et al., 2000; Botvinick et al., 2004). Two well-known but competing theories have been proposed to explain the function of the executive control network. The first theory highlights the role of the ACC for conflict monitoring and the frontal area for conflict resolution (Botvinick et al., 2001, 2004). An alternative theory has argued for the existence of two separate executive control systems, consisting of a cingulo-opercular network for maintaining sustained background activity throughout task performance, and a fronto-parietal system that is related to task switching and moment-to-moment adjustment within trials (Dosenbach et al., 2006, 2007). This fronto-parietal system has been argued to be distinct from networks that mediate attentional orienting (Figure 1.1b).

1.2.2 Feature-based Attention

Although thematic focus of attention research has focused on orienting to spatial location, other studies have shown that attention can also operate globally across the visual field to enhance processing of objects with certain features, independently of the current focus of spatial attention (Treue and Martínez Trujillo, 1999; Saenz et al., 2002; Liu and Hou, 2011). Laboratory studies have shown that feature-selective attention can be directed strategically towards stimulus colour, orientation, shape, or direction of motion (Maunsell and Treue, 2006; Martinez-Trujillo, 2011). In practical situations, feature-based attention is useful when we know the defining feature of the object that we are looking for but have no knowledge of its location, such as when searching for an object with a particular colour among distracting objects.

Various neuroimaging studies have demonstrated that orienting of attention to stimulus features also engages similar fronto-parietal networks recruited during orienting to a spatial location (Shulman et al., 1999; Liu, 2003; Luks and Simpson, 2004; Stoppel et al., 2007), indicating a possible common or linked mechanism supporting both forms of attention (Wojciulik and Kanwisher, 1999). Several fMRI studies that compared spatial and feature attention within a single task, however, reported that despite large overlapping fronto-parietal activity, some regions are specifically activated by one type of attention, suggesting the presence of both generalized and specialized control networks for orienting of attention across different domains (Giesbrecht et al., 2003; Slagter et al., 2007). This dimension-specific hypothesis is also supported by the finding of a TMS study which showed that TMS to the right supramarginal gyrus (SMG) during cue presentation only disrupted strategic orienting of attention on the basis of stimulus location but not stimulus colour (Schenkluhn et al., 2008).

Attending to a feature dimension also modulates activity in the cortical region specialized for processing those specific dimensions. Initial evidence for this selective modulation within the visual cortex was reported in single-cell neurophysiological studies in monkeys, which observed an increased firing rate of V5/MT neurons when attention was directed towards the preferred direction of motion (Maunsell et al., 1991; Treue and Martínez Trujillo, 1999; Martinez-Trujillo and Treue, 2004). With the advent of fMRI, these findings were also replicated in various human studies that reported selective BOLD modulations of feature-based attention in several retinotopic visual regions including V5/hMT+ when motion was attended (Shulman et al., 1999; Saenz et al., 2002) and V4 when colour was attended (Liu, 2003). Furthermore, converging evidence from electrophysiological (Martinez-Trujillo and Treue, 2004; Bichot et al., 2005), psychophysical (Liu and Hou, 2011; Liu and Mance, 2011), and neuroimaging (Boynton et al., 2006; Serences and Boynton, 2007) studies has revealed that feature-based attention can operate not only within the current locus of spatial attention but also spreads globally throughout the entire visual field to locations that are unstimulated and/or irrelevant to the current task. Treue and Martínez Trujillo (1999) has proposed a 'Feature-Similarity Gain' hypothesis to explain these selective modulatory processes, in which responses of neurons that are tuned to the task-relevant features were amplified through multiplicative gain mechanism, whereas those neurons tuned to the other task-irrelevant features were suppressed (Martinez-Trujillo and Treue, 2004; Maunsell and Treue, 2006). The authors have also suggested the possibility that both spatial and feature attention might be driven by the same neural mechanisms, based on the evidence that both types of attention could equally strongly modulate the gain of the visual neurons that falls within the same receptive fields.

1.3 Multisensory Attention

While the majority of research has focused on studying attention within sensory modalities (primarily vision and audition), a growing number of studies have also demonstrated intermodal and cross-modal effects of attention in different sensory channels. Behavioural evidence has shown that responses to target stimuli presented in the voluntarily (endogenously) attended modalities are faster and more accurate than targets in the unattended modalities (Spence et al., 2001; Ashkenazi and Marks, 2004). These facilitatory effects cannot be explained simply by possible confounds such as response priming, criterion shifts, stimulus repetition, or spatial location (Spence and Driver, 1997b), and instead reflect the consequences of attentional facilitation of stimuli coming from a particular sensory modality at the expense of processing of stimuli presented in the other modalities. This modality specific enhancement has also been demonstrated using exogenous cuing paradigms, where the presentation of an abrupt cue in a particular sensory modality can facilitate processing of subsequently presented stimuli within the same modality (Turatto et al., 2002, 2004).

In addition to selective enhancement within attended modalities, many studies have also demonstrated cross-modal links of spatial attention across various modalities (Driver and Spence, 1998). Orienting attention to one location in one sensory modality can enhance processing of targets presented at the same location but in a different modality, and this cross-modal effect has been shown using both endogenous paradigms (with central predictive cues; Spence and Driver, 1996; Spence et al., 2000; Lloyd et al., 2003) and exogenous paradigms (with peripheral non-predictive cues; Spence and Driver, 1997a; Spence et al., 1998; McDonald et al., 2000).

In typical endogenous cross-modal studies, subjects are cued to orient attention toward one side within one modality, and asked to make a speeded discrimination of the targets presented in the non-predictive target modality and target side. As anticipated, accuracy and speed of response tend to be faster when the targets appear within the cued modality (i.e. vision) and cued side (i.e. right) as opposed to targets presented in the cued modality at the unattended side (i.e. left), implicating the effect of within-modal spatial attention. Importantly, faster and more accurate discriminations were also observed when the targets were presented in the cued location in the unattended modality (i.e. audition or somatosensation), indicating the spread of spatial attention resources across various modalities (Driver and Spence, 1998; Spence, 2010). To avoid confounding factors of automatic response priming, these studies typically employed an orthogonal cueing paradigm (Spence and Driver, 1996) in which the spatial cue (i.e. left or right side) is presented in an orthogonal spatial axis to the target location (i.e. up or down; See Figure 1.2 for an example of orthogonal cueing task in vision).

In general, with respect to sensory modality, attentional processes can be classified into three different categories: intramodal or unimodal, intermodal, and cross-modal. Intramodal or unimodal attention refers to attentional processes within a single sensory modality across various stimuli dimensions such as space, feature, object, or time. Attention can also be directed to enhance stimuli processing in one sensory modality at the cost of impairment of processing in the other ignored modalities (intermodal attention), especially in the condition where there is concurrent signals coming into various modalities. Finally, in the spatial attention paradigm, selective enhancement of attention to a particular location can spread to various unattended modalities, signifying the presence of cross-modal effects of spatial attention selection.

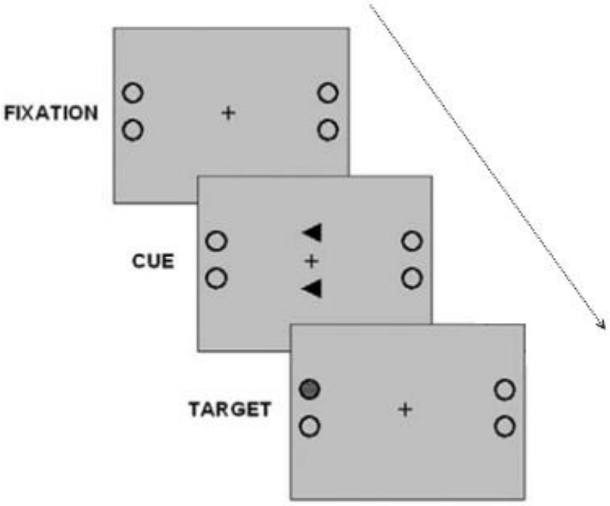


Figure 1.1. Typical example of a covert spatial attention task with orthogonal cueing paradigm (adapted from Chambers and Mattingley, 2005). An informative and strategic cue (central arrow) is presented to attract attention to one side of the visual field. Following the cue, the participants discriminate the elevation of the target stimulus (upper vs. lower) which is orthogonal to the cued location (left vs. right), avoiding possible confounds of automatic motor priming of the response induced by the cue. Improved performance is usually observed when the cue predicts the target location (valid trials) as opposed to when the cue incorrectly predicts the target location (invalid trials).

1.3.1 The Neural Basis of Multisensory Attention

The neural basis of multisensory processing has been actively investigated over the last three decades using various animal models, single-cellular recordings, tracing studies, and human neuroimaging studies (Bruce et al., 1981; Meredith and Stein, 1983; Macaluso and Driver, 2001; Driver and Noesselt, 2008; Beauchamp et al., 2008; Stein and Stanford, 2008; Klemen and Chambers, 2012). In some of these earliest studies, various cortical and subcortical structures that received inputs from multiple senses such as the superior colliculus (SC), basal ganglia, superior temporal sulcus (STS), ventral premotor cortex, and part of the parietal cortex were first identified in non-human primates (Bruce et al., 1981; Meredith and Stein, 1983; Schmahmann and Pandya, 1991; Duhamel et al., 1998). By comparing the response properties of these multisensory neurons during unisensory and multisensory inputs, it can be identified whether the neurons exhibit subadditive, additive, or superadditive mechanisms of combining multisensory information. Neuroimaging technologies such as PET and fMRI have enabled neuroscientific studies of multisensory processing in humans, providing further evidence in support of multisensory convergence zones (Beauchamp et al., 2008; Klemen and Chambers, 2012). Surprisingly, increasing evidence from recent monkey electrophysiology and neuroimaging studies have revealed that multisensory processes not only affect commonly regarded higher-level ‘multimodal’ regions but can also influence lower level cortical regions that are traditionally considered ‘sensory specific’ (Macaluso, 2006; Driver and Noesselt, 2008).

Multisensory processes are also known to interact strongly with attentional processing (Talsma and Woldorff, 2005; Mozolic et al., 2008a; Koelewijn et al., 2010; Talsma et al., 2010). Several studies have now investigated the neural basis of modality-specific attentional modulations in the sensory cortices using multimodal tasks that requires the subjects to select the targets from one sensory modality while ignoring stimuli in the other modalities. A pioneering multichannel electrophysiology study in the macaque visual system revealed that attending to visual stimuli while ignoring simultaneously presented auditory streams strongly modulated activity in visual area V1, V2, and V4 (Mehta et al., 2000a). The most robust and earliest effect of attentional modulation occurred in V4 during the 100-300ms post-stimulus period, followed by smaller effects in V2 around the same interval, and then followed much later by smaller modulation in V1. This temporal profile suggests that attentional modulations were mediated by feedback projections from higher to lower visual regions (Mehta et al., 2000b).

Similar evidence for modulation of sensory specific regions was also provided by neuroimaging studies using PET and fMRI (Macaluso et al., 2002a; Shomstein and Yantis, 2004; Johnson and Zatorre, 2005; Ciaramitaro et al., 2007). In an early PET study reported by Macaluso et al. (2002a), subjects were presented with bimodal and bilateral visuo-tactile stimuli, and asked to sustain their attention to a particular side (i.e. left or right side), and in one modality, while performing a target discrimination task. They found that attention to one modality selectively enhanced activity in the sensory regions of the attended modality (i.e. areas near visual cortex were enhanced during visual attention and somatosensory areas were enhanced during tactile attention). Moreover, location-specific attentional modulation was also found in the occipital cortex during sustained attention within touch, suggesting crossmodal effects of tactile attention on visual cortex. Another key fMRI study of attentional shifts between modalities (Shomstein and Yantis, 2004) revealed that shifting attention from audition to vision selectively enhanced activity in the visual cortex while supressing activity in the auditory cortex, and vice versa. Deactivations of sensory regions that represent the unattended modality are consistent with the influence of cross-modal links on areas that are traditionally regarded as sensory-specific (Driver and Noesselt, 2008). Evidence for cross-modal modulations of sensory regions have also been observed in many event-related potential (ERP) studies (Karns and Knight, 2009; Saupe et al., 2009; Green et al., 2011). In several experiments conducted by Eimer and colleagues (Eimer and Schröger, 1998; Eimer et al., 2002a; Macaluso et al., 2003b), strategically orienting attention to a certain modality and location was found to not only modulate the task-relevant sensory modality but also modulates the ERP components of task-irrelevant modalities in specific sensory cortical regions (visual, auditory, or somatosensory).

In order to isolate pure multisensory attentional effects in sensory regions, above and beyond interactions between bimodal or multimodal stimuli, several studies have also investigated preparatory attention in the absence of actual stimulus presentation, generally in the baseline activity following cue presentation (Macaluso et al., 2003b; Mozolic et al., 2008b; Trenner et al., 2008; Langner et al., 2011). A previous fMRI study of auditory-visual attention conducted by Mozolic and colleagues (2008b) reported deactivations in the unattended sensory modality but did not discover baseline activity increase in the attended modality. However, in a more recent study using similar cue-only trials, Langner et al. (2011) found that preparatory attention to visual, auditory, and tactile stimulus selectively increased baseline activity in the attended sensory regions and at the same time decreased activity in the irrelevant sensory regions. These results imply that top-down effects of modality-specific attentional enhancement and deactivation are independent from processing of multimodal stimuli.

1.3.2 Sources of Multisensory Attentional Control and the Supramodal Hypothesis

In addition to modulatory effects on sensory cortical regions, neuroimaging studies of multisensory attention have also revealed that higher cortical regions are activated during strategic orienting of attention to various modalities (Macaluso and Driver, 2001; Macaluso, 2010; Smith et al., 2010). For example, an early fMRI study investigating the link between spatial attention in vision and touch reported equally robust activations in the anterior IPS, FEF, and TPJ elicited by stimulation to both sensory modalities and attended sides (Macaluso and Driver, 2001). The authors interpreted these findings as evidence for feed-forward convergence of sensory inputs from early unimodal regions within higher multimodal brain regions. Additional evidence for the involvement of frontoparietal network emerged from a subsequent neuroimaging study using a cross-modal spatial cueing paradigm (Macaluso et al., 2002b). In this study, participants covertly shifted their attention to one side (left or right) after presentation of a symbolic auditory cue that indicated the most likely stimulated side (80% valid cue), and then discriminated the elevation of subsequently delivered target in the visual or tactile modality on one side. Compared to valid trials, invalidly cued trials triggered more activation in the TPJ and inferior frontal regions, irrespective of target modality, whereas the IPS and FEF were equally enhanced by both valid and invalid trials presented in any modality. This result was further corroborated in an fMRI study that used cue-only trials to isolate preparatory activity associated with endogenous attention to visual or tactile stimuli (Macaluso et al., 2003b). Here the authors presented bimodal and bilateral stimuli and participants were instructed to discriminate targets in the cued modality and location. Cue-related preparatory activity was observed in the dorsal premotor cortex (around FEF) and IPS regardless of whether attention was oriented towards vision or touch.

The brain regions activated in studies of multimodal attention overlap closely with the dorsal and ventral frontoparietal networks in visual attention studies (Corbetta et al., 2008), leading some researchers to postulate the existence of '*supramodal'* circuits for controlling attention across various modalities (Eimer et al., 2002b; Macaluso et al., 2002b; Macaluso, 2010; Green et al., 2011). Evidence for a supramodal attentional network was also reported in a study that investigated preparatory activity during orienting of auditory spatial attention (Wu et al., 2007) as well as in a more recent study using orthogonal cuing paradigm in an audio-visual spatial attention task (Smith et al., 2010). Furthermore, the supramodal hypothesis was also supported by a recent study using electrical neuroimaging technique of electroencephalogram (EEG) recording (Green et al., 2011). They found that the timing and sequence of activity within the localized fronto-parietal regions were almost identical during the shifts of attention to visual and auditory stimuli, pointing to the possibility that the same neural system mediates endogenous spatial attention control across various sensory modalities.

Most neuroimaging studies define multisensory areas by studying overlapping activations in response to stimuli or attentional demands in different modalities. Cortical regions that respond to more than one modality (usually in frontoparietal regions) have thus been attributed as supramodal processors that control deployment of attention independently of the modality in which information is received (Macaluso et al., 2002b; Macaluso, 2010).

Although appealing, the interpretation of common fMRI activations as supramodal control regions has been challenged, partly due to the spatial limitation of the neuroimaging methods used (Figure 1.3). In particular, it is possible that a commonly activated fMRI voxel might contain spatially overlapping but anatomically distinct sub-voxel neuronal populations that are modality-specific and arranged in a topographic manner (Klemen and Chambers, 2012), similar to the organization of orientation preference map in the primary visual cortex. Another logical conundrum that might arise when interpreting common activations in anatomically separate cortical regions is the problem of inferring causality in fMRI data. Activation of a certain brain region found using fMRI does not automatically imply that the region is causally involved in bringing about a certain cognitive state (Chambers et al., 2004b). Instead, the region may have been activated due to epiphenomenal processes that accompany the core cognitive processes. Moreover, because of the limited temporal resolution of the fMRI BOLD response, it is difficult to distinguish the flow of information within these potentially supramodal regions. For example, areas A, B, and C might be all recruited in orienting within vision and touch, but it is possible that the sub-second temporal sequence of information transmission between these regions differs during visual vs. tactile attention. Visual attention might involve signals transmission following the pathways such as: A → B → C, whereas tactile attention might follow a different route such as: B → A → C.

Experimental evidence for modality-specific control of spatial attention in vision and touch has been demonstrated in two reversible neurodisruption studies using transcranial magnetic stimulation (TMS). These studies stimulated regions in the parietal cortex during both endogenous (Chambers et al., 2004b) and exogenous cueing tasks (Chambers et al., 2007) using similar orthogonal cueing paradigm reported in (Macaluso et al., 2002b). The participants were presented with a central endogenous cue that predicted the most likely location (left or right side) of the upcoming target stimulus (75% valid cue) and then performed a speeded discrimination task to identify the elevation (upper or lower) of the target presented randomly in the visual or somatosensory modality on either side. TMS trains were applied for 300ms following the cue or target onset to four different sites (Angular

Gyrus/AG, Supramarginal Gyrus/SMG, Superior Temporal Gyrus/TPJ, and Superior Parietal Lobe/SPL). They found that TMS to the right SMG during cue presentation only impaired strategic orienting to visual targets but not to somatosensory targets, providing evidence for modality specificity of this posterior parietal region.

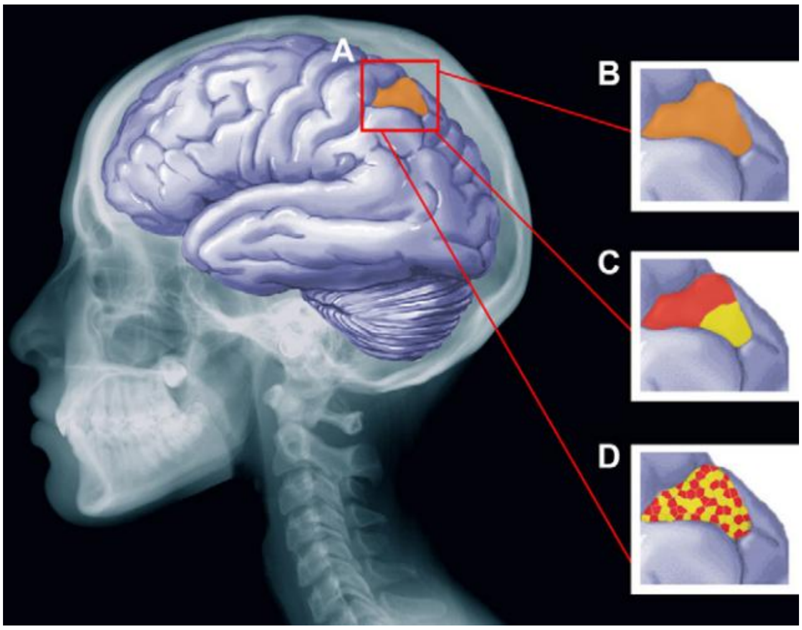


Figure 1.3. (A) Hypothetical common brain activations found using fMRI during attention to sensory modality X and sensory modality Y. (B) The observed overlapping activations could be caused by a truly supramodal area recruited during attention to both sensory modalities. (C) Alternatively, there could be two functionally distinct but spatially adjacent areas for controlling attention to modality X and Y. Both areas co-activate each other but only one of the areas is functionally necessary for attention to each sensory modality. (D) Another alternative is that the region consisted of topographically arranged and functionally distinct neuronal subpopulations for attention to different modalities (adapted from Klemen and Chambers, 2012)

In a follow-up study reported in Chambers et al. (2007), a similar cueing paradigm was used but this time with a non-informative exogenous spatial cue, presented in the visual or somatosensory modality on either side shortly before target presentation. This time TMS was delivered for 100ms in synchrony with the cue onset. Reflexive orienting in both modalities was not impaired when TMS was applied during visual cues. During tactile cues, however, the same TMS applied to the right AG significantly impaired reflexive orienting to both visual and tactile targets presented contralateral to the TMS site, whereas TMS to the right SMG disrupted orienting to visual events only. These results further point to the existence of complex and nontrivial interrelationships between various parietal sub-regions in regulating top-down attentional control to various modalities and dimensions.

Consistent with these TMS results, a recent functional connectivity study using resting state fMRI to investigate connectivity between IPS and other dorsal attention and cingulo-insular networks revealed that points of maximal connectivity between IPS and these other attentional regions are topographically organized (Anderson et al., 2010). They have identified at least seven different connectivity clusters of the IPS region in both hemispheres, and each of the cluster displayed distinct patterns of connectivity involving visual, auditory, somatosensory, and default mode networks. This result reflects the possibility that IPS might contain modality-specific topographic maps that enables neuronal populations in IPS to specifically modulate the relevant sensory modality and location during various multisensory attention conditions.

1.4 Aims and Thesis Outline

1.4.1 Aims of the thesis

This thesis presented four different studies, including five fMRI experiments and one combined TMS/fMRI pilot experiment. The first three fMRI experiments were conducted to test the feasibility of the fibre-optic visual presentation system designed and constructed in the first study. In the fourth experiment, we investigated the neural basis of spatial attention in vision and touch, and in the fifth experiment, the neural basis of feature-based attention in vision and touch was examined. The final pilot experiment was conducted to investigate the coupling between remote influences of TMS and top-down attentional factors during sustained feature-based attention in vision.

Presenting visual stimuli within close proximity to the tactile stimuli inside the MR-scanner carries significant technical challenges. To solve this problem, we designed and constructed a fibre-optic visual presentation system and several supporting structures that enable delivery of the multisensory stimuli in peripersonal space surrounding both hands. We then conducted a study consisting of three fMRI experiments to test and validate the feasibility of this device to deliver reliable visual stimulus in the scanner. In the first experiment, we tested whether presentation of visual stimuli in the left and right hemifield could elicit contralateral responses in the striate and extrastriate cortex. The second experiment was performed to test the reliability of the device for displaying coloured stimuli in a colour discrimination task. Finally, in the third experiment, we conducted a simple multisensory interaction experiment involving frequency discrimination task to compare brain activations elicited by unimodal vs. bimodal visuo-tactile stimuli. Visual stimulus was displayed using a fibre-optic prism located on the left visual field, presented in synchrony with tactile stimulus delivered to the glabrous tip of the left index finger using a QuaeroSys^{TM} tactile stimulator.

In the second study, we used fMRI to investigate the role of frontoparietal networks in controlling strategic spatial attention to visual and somatosensory modality. Specifically, we asked whether such top-down processes are modality specific or supramodal by applying multivoxel pattern analysis (MVPA) to the imaging data (Haynes and Rees, 2006; Haxby, 2012; Tong and Pratte, 2012). The behavioural paradigm used in this experiment involved a sustained spatial attention task during presentation of bimodal and bilateral stimuli, similar to the methods adopted by Macaluso et al. (2002a). We first analysed half of the fMRI data using a classical univariate analysis to identify overlapping regions activated during attention to both sensory modalities. Then, using the second half of the data, we applied MVPA to classify the attended modality within the frontoparietal ROIs found by the univariate analysis. We reasoned that if the cortical regions identified by univariate analysis were truly supramodal, then MVPA should not be able to distinguish attended modality from the distributed patterns of activity within these regions. Additionally, we further applied an exploratory searchlight MVPA method (Kriegeskorte et al., 2006) and a cross-generalization procedure (Stokes et al., 2009a) to produce whole-brain cortical maps of modality and location specificity of attention.

The third study focused on investigating the neural basis of intermodal feature-based attention in vision and touch. To my knowledge this is the first time that neural correlates of feature-based attention in vision and touch have been investigated using fMRI. Two main questions were examined in this study, the first whether feature-based attention to somatosensory events recruits similar frontoparietal regions during attention to visual events; and the second to characterise the top-down modulatory effects of feature-based attention on sensory cortical regions using both univariate and multivariate analyses. In accordance with the second study, we also applied an MVPA searchlight analysis to test the supramodal hypothesis on the overlapping cortical regions found by the univariate analysis. Furthermore, we performed several classical ROI analyses and ROI-based MVPA analyses to investigate intermodal and cross-modal modulatory effect of feature-based attention in the visual and somatosensory cortex.

In the fourth study, we aimed to investigate top-down modulatory effects of feature-based attention in retinotopic visual regions using combination of fMRI, simultaneous TMS/fMRI, and MVPA analysis. The study consisted of two pilot experiments, the first using fMRI to investigate top-down modulatory effect of feature-based attention to visual motion or colour, and the second using simultaneous TMS/fMRI to investigate task dependent functional coupling of the frontal eye fields and visual cortex. In both experiments, we applied MVPA to decode target-specific information in retinotopic visual regions, and we hypothesized that classification accuracy would be higher for the attended vs. unattended feature in feature-specific visual regions (V4 and hMT+/V5).

1.4.2 Thesis Structure

The theoretical background that motivates the studies conducted in this thesis has been described in this chapter.

Chapter 2 will introduce the Multivoxel Pattern Analysis (MVPA) technique for analysing fMRI data and describes the details of MVPA classification method and MVPA searchlight analysis used in the subsequent experiments described in chapter 4 and 5. A brief review of previous applications of MVPA for investigating various aspects of visual attention will be presented, followed by a discussion of conceptual issues in interpreting the result of MVPA classifications.

The design and implementation of an MRI compatible LED fibre-optic system will be presented in Chapter 3. The logic behind the design of the apparatus will be discussed and the electronic circuit diagrams of the microcontroller device for controlling the LEDs will be explained in detail. Subsequently, detailed methods of three fMRI experiments for validating the feasibility of the device will be described, followed by a discussion of the results of this first study.

Chapter 4 will discuss an fMRI study investigating specificity and generality of frontoparietal attention networks during sustained spatial attention in vision and touch. The chapter includes an introduction to the current state of debates regarding the ‘supramodal hypothesis’ that motivated the current study. Detailed experimental paradigm and analysis methods will then be described, followed by presentation and discussion of the results.

Chapter 5 will discuss an fMRI study that investigates multisensory feature-based attention in vision and touch. Relevant background concerning the neural basis of feature-based attention will be reviewed in the introductory section, followed by description of experimental paradigm and the analysis methods used. Experimental results are presented subsequently and their significance is discussed.

Chapter 6 will describe a study investigating feature-based attention to visual motion and colour. Two experiments will be reported in this chapter, the first using fMRI and the second using simultaneous TMS/fMRI. The introduction section will provide relevant background about feature-based attention task used in this study and a brief review of previous TMS/fMRI studies. Methods and results of the experiments will then be presented, together with discussions of the findings.

Chapter 7 presents summary, general discussion, and conclusion of the studies discussed in this thesis.

Chapter 2 - Multivoxel Pattern Analysis (MVPA)

Multivoxel Pattern Analysis (MVPA) is a powerful fMRI analysis method that has gained increasing popularity over the last decade owing to its sensitivity in detecting fine-grained distributed patterns of information that correlate with experimental conditions (Haynes and Rees, 2006; Norman et al., 2006; Wagner and Rissman, 2010; Tong and Pratte, 2012). Many fMRI studies that applied this method have demonstrated its power and elegance to tackle questions that were previously unanswerable by classical univariate analysis. In contrast with classical voxel-based inferential statistics, which identify correlations between each independent voxel with experimental conditions, MVPA considers correlations between activation patterns of neighbouring voxels with the experimental conditions, considering subtle variations in the voxel populations as important information that can discriminate different conditions (O'Toole et al., 2007).

This chapter gives an overview of the MVPA methods and the relevant applications for decoding attentional processes in the brain. We begin by reviewing early developments of the methods, followed by discussion of the basic principles of MVPA classifications and MVPA searchlight analysis. We then briefly reviewed recent applications of MVPA in studying modulatory effects of attention in visual cortex and decoding information in the frontoparietal regions. Finally, several conceptual issues in relation to the interpretation of MVPA classification results will be discussed.

2.1 Early Developments

The idea of applying multivariate statistics or machine learning classifiers to analyze multidimensional data obtained from various neuroscience experiments is not new. In an early PET imaging study, Kippenhan et al. (1992) applied a neural-network classifier for discriminating normal and abnormal scans in relation to Alzheimer disease. They found that despite the low resolution of PET images, the performance of the classifier was nearly comparable to the opinions of human experts. Similar application of a neural-network classifier combined with various dimensionality reduction methods (PCA, SVD) on PET scans was also reported by Lautrup et al. (1994). Another multivariate method which has been successfully applied in early functional neuroimaging research to correlate brain activity with experimental design was Partial Least Squares (PLS), a statistical technique originally developed for econometrics and chemometrics (McIntosh et al., 1996). Although this method is not as prevalent as other multivariate techniques that were more commonly used in neuroimaging, such as correlation or SVM, various studies have demonstrated its power to tackle various problems in cognitive and clinical neuroimaging (see Krishnan et al., 2011 for review).

Within the neuroimaging community, an interest in multivariate classification methods was renewed in the early 21st century by a pivotal work of Haxby et al. (2001). In their study, they showed that the pattern of brain activity in the ventral temporal (VT) cortex could reliably discriminate multiple object categories viewed by subjects (Figure 2.1). This categorical discrimination cannot be simply explained by differences in the intensities of voxels that responded strongly to one category relative to the other, because when these voxels were removed, discrimination performance remained well above chance. This combination of multivariate classification and 'virtual lesion' type of analysis suggests that neural representations of objects and faces were probably overlapping and distributed throughout the VT region. Although the conclusion of this finding has been challenged by subsequent studies which also utilized multivariate methods (Spiridon and Kanwisher, 2002; Peelen and Downing, 2007), nonetheless it has opened up a new vista to creatively apply multivariate classification methods to tackle difficult and controversial problems in neuroscience.

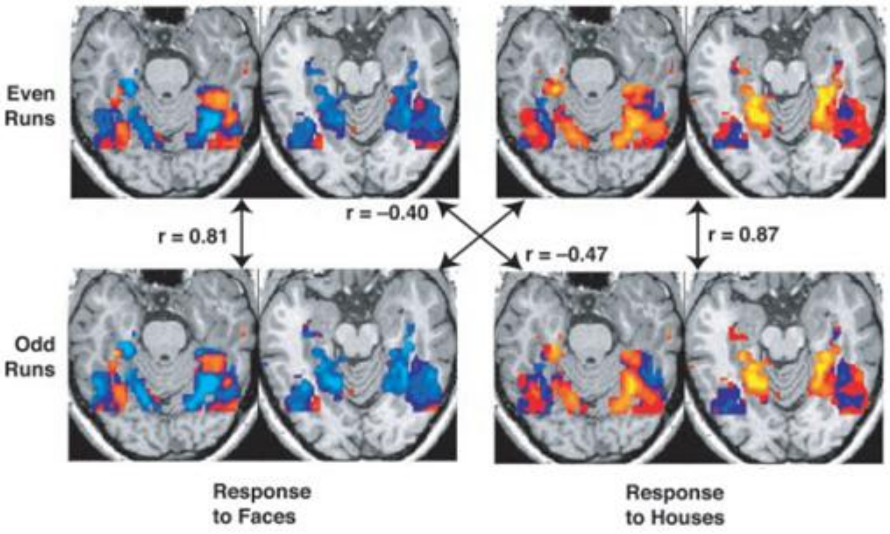


Figure 2.1. Example of correlation approach in brain activity decoding (adapted from Haxby et al., 2001). Overlaid on top of the brain images are normalized patterns of response for faces and houses in the ventral temporal cortex, measured separately for even and odd runs. Pairwise correlations within an object category and between two object categories were calculated between even and odd runs. Decoding was considered successful if the within-category correlations ($r = 0.81$ for faces, and $r = 0.87$ for houses) were larger than the between-category correlations ($r = -0.4$ and $r = -0.47$).

Another pioneering study that pushed forward the application of multivariate analysis methods was conducted by Kamitani and Tong (2005). In their study, they trained an ensemble of eight linear support vector machines to classify eight different orientation of grating based on the activity of visual cortex. After being trained, the classifiers were employed to predict the orientation of newly viewed gratings by choosing the orientation that corresponded to the classifier with the maximal output. They found that it was possible to decode orientation of the observed stimulus in visual cortex with surprisingly high accuracy (Figure 2.2b), even though orientation- and direction-selective neurons in visual cortex were topographically organized at the scale of sub-millimeter columns (Bartfeld and Grinvald, 1992; Obermayer and Blasdel, 1993), much smaller than the resolution of the voxel itself (3mm).

Boynton (2005) performed a simulation to explain that random irregularities in the distribution of orientation selective neurons could give rise to small orientation bias in each voxel; thus by aggregating information across multiple neighbouring voxels, the pattern classifier was able to robustly decode orientation of the grating from the activity of visual cortex (Figure 2.2a). A subsequent study using high resolution fMRI by Swisher et al. (2010) also supported this voxel bias hypothesis (Figure 2.2c). In a replication and extension of Kamitani and Tong (2005), Haynes and Rees (2005) reported above-chance decoding accuracy in visual cortex, despite the fact that the subjects were rendered unaware of the orientation of the gratings through backward masking. This finding provides initial evidence of the presence of unconscious information in the primary visual cortex.

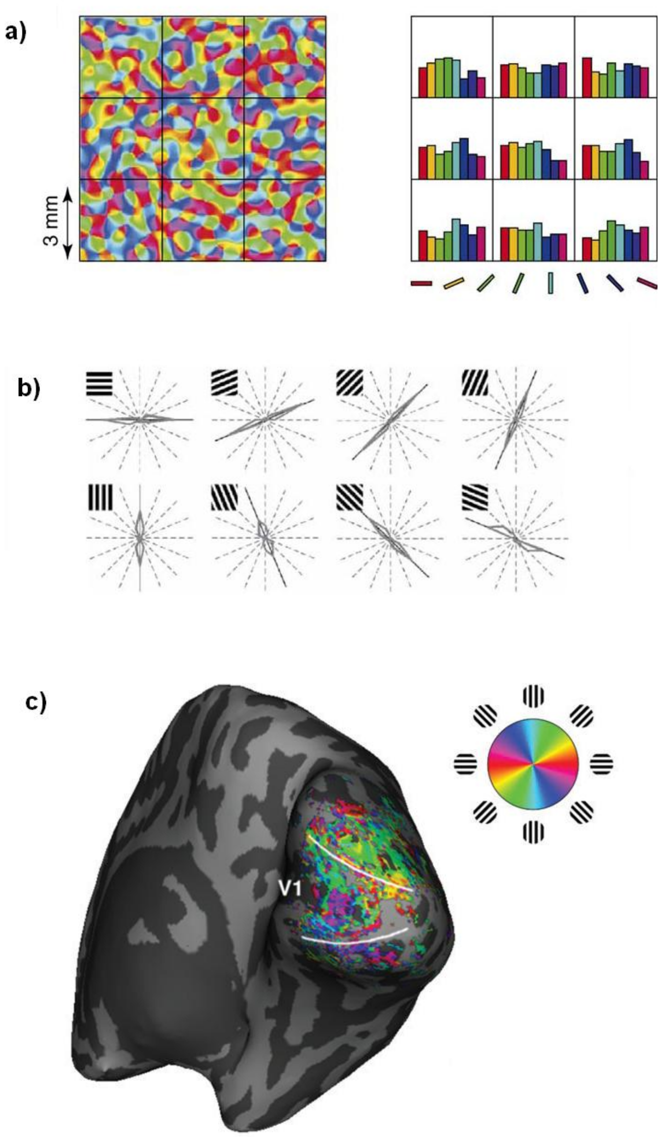


Figure 2.2. (a) Illustration of how organization of the visual cortex gave rise to slight orientation bias in the voxels activity (adapted from Boynton, 2005). The panel on the left shows a simulated orientation tuning map with a voxel size of 3 mm, with each colour represent different orientation. The histogram on the right panel shows the distribution of orientation selectivity values for each of the voxels shown in the left panel. Eight different orientations were indicated by different coloured line, shown below the panel. The shape of the distribution is slightly different for each voxel and thus biases the response of each voxel differently from the others. The learning algorithm is able to exploit this random variability to decode line orientations from patterns of activity in multiple voxels. **(b)** MVPA decoding of the oriented gratings from activity patterns in V1/V2 (adapted from Kamitani and Tong, 2005). The polar plots indicate the distribution of the predicted orientations for each of the eight orientations. Solid black lines indicate the true orientation. **(c)** Orientation preference map in the visual cortex measured using high-resolution fMRI with 1 mm voxel resolution and rendered on an inflated cortical surface (adapted from Swisher et al., 2010).

The interest in applying multivariate analyses of neuroimaging data has grown exponentially during the last decade partly due to the realization that fMRI data analysis can be framed as a pattern classification problem; a type of problem which is also actively studied in statistics, machine learning, and data mining fields (Bishop, 2006; Mitchell, 2006; Hastie et al., 2009; Pereira et al., 2009). This approach enables neuroscientists to apply various classification algorithms that have been well developed and extensively used in other domains to analyze functional imaging data (Norman et al., 2006). Many commonly used pattern classification algorithms have been successfully applied, including linear Support Vector Machines (SVM) (Cox and Savoy, 2003; Kamitani and Tong, 2005; Esterman et al., 2009; Greenberg et al., 2010; Kalberlah et al., 2011), Fisher's Linear Discriminant Analysis (LDA) (Carlson et al., 2003; O'Toole et al., 2005; Haynes and Rees, 2005), Neural Network (Polyn et al., 2005), and Gaussian Naïve Bayes classifiers (Mitchell et al., 2004). More recently, several labs have also published open source software libraries for analyzing multivariate neuroimaging data, such as MVPA toolbox released by Princeton lab (Detre et al., 2006) and a Python based library, PyMVPA (Hanke et al., 2009). These libraries greatly simplify the complexity of applying various sophisticated machine learning algorithms to process neuroimaging data, thus enabling neuroscientists to save time and focus more on the analysis rather than technical details of implementation.

2.2 MVPA Classification Methods

Multivoxel pattern analysis considers information contained in the distributed patterns of activity across multiple voxels, so that relative differences in voxel activity can provide relevant information that could be used to distinguish perceptual, cognitive or behavioural states. Instead of testing whether an individual voxel responds more strongly in one condition compared to the other, as in traditional univariate analysis, multivariate analysis analyses are designed to test whether experimental conditions correlate with distributed patterns of activation across multiple voxels. Multivariate methods might therefore be able to decode fine-grained patterns that differentiate task conditions even when the average level of activity in those voxels is the same (Figure 2.3).

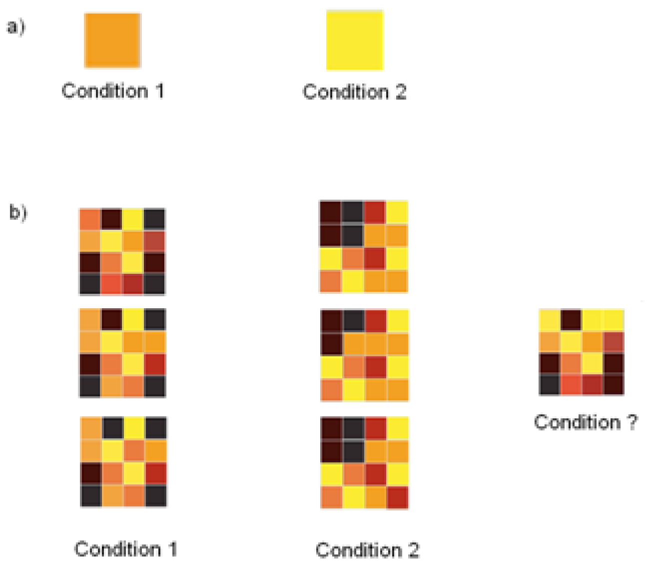


Figure 2.3. (a) Illustration of a response of a single voxel for two experimental conditions. In classical univariate analysis, differences of brain activations between one experimental condition with the other was computed by comparing the response of each voxel independently from the other voxels. **(b)** Hypothetical patterns of activity in a cortical region correlated with two different conditions. Three sample data representing activation patterns elicited by three different trials were shown for each condition. A new sample pattern shown on the right would be classified as condition 1 because its pattern of activity is more similar to patterns of activity of condition 1 than condition 2.

The basic principles of multivariate classification of neuroimaging data can be explained using a simple example comprising two voxels as shown in Figure 2.4. In this figure, each dot represents a data sample obtained from the scan and their colour signifies the experimental condition. The horizontal and vertical axis represents the strength of activation for the first and second voxel, respectively. As we can observe from the Gaussian density plot shown on the border of each axis, univariate analysis will not be able to dissociate experimental conditions only by considering activation of the first or second voxel alone since both voxels were equally activated in both conditions. However, if we look at the two dimensional scatter plots of the dots, it is obvious that the data can be separated into two classes by tracing a diagonal line that intersects the boundary between the two conditions. This diagonal line represents the model or decision boundary of the classifier. All points that lie above the line will be classified as belonging to the red condition and all points that lie below the line as belonging to the blue condition. In typical multivariate analysis of neuroimaging data, each data sample will be represented as a dot in N-dimensional space (where N is the number of voxels). Given the training data (pattern of activity) and labels (experimental conditions), a linear classifier will find a separating hyperplane (a model) that divides the data into two conditions. It is also possible to use a non-linear classifier that produces non-linear decision boundaries, although its application for neuroimaging data has been criticized due to the absence of additional benefits compared with simpler linear classifiers (Cox and Savoy, 2003) and difficulties in interpreting the outcome (Kamitani and Tong, 2005).

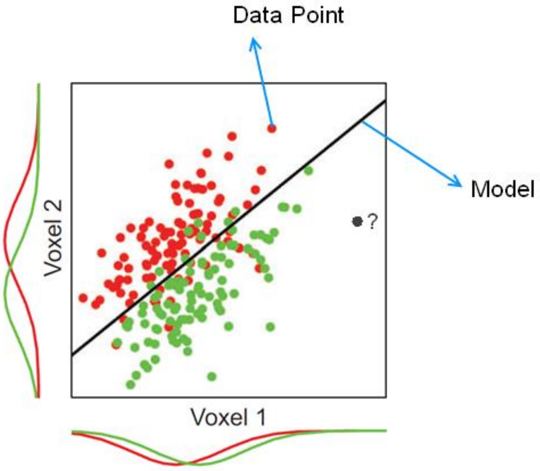


Figure 2.4. Hypothetical example of multivariate classification of two experimental conditions using activity of two voxels (adapted from Tong and Pratte, 2012). Each dot represents a data sample and their colour signifies the experimental condition. The Gaussian density plots shown on the border of each axis indicate the response distribution of each condition for the first and second voxel in isolation. This diagonal line represents the model or a decision boundary that separates the two conditions. The black dot shown with a question mark indicates a testing data that would be classified as green as it lies below the dividing line.

Typical multivariate analysis of neuroimaging data requires several stages of processing (Pereira et al., 2009). The first step is to select which voxels are going to be included in the analysis (feature selection). This step is important because typical neuroimaging data consists of tens of thousands of voxels and not all of them are activated during the cognitive task. Selecting uninformative voxels might seriously hinder the performance of the classifier due to noise and increased dimensionality of the data. One of the main challenges in applying machine learning techniques to neuroimaging data is the problem of how to manage the ‘curse of dimensionality’. This problem arises because the dimension of the input data (i.e. the number of voxels in the brain) is much larger than the number of samples or images obtained from the scan. In machine learning research, these difficulties are categorized as ill-posed learning problems, which make it difficult for the classifier to learn the underlying patterns of the data because the number of parameters that needs to be estimated (like the weights) far exceeds the quantity of example data. In some early studies, such as reported by (Lautrup et al., 1994), researchers have tried various dimensionality reduction procedures including PCA (Principal Component Analysis) or SVD (Singular Value Decomposition) to the initial imaging data so that the dimension of the input data to the classifier is more manageable. There are other ways to define features and limit the number of voxels included in the analysis, such as using predefined anatomical ROIs or ROIs from functional localizer, selecting voxels that are significantly activated using simple t-test or GLM, selecting voxels with reliable difference in the mean activation across conditions using ANOVA, or using more sophisticated feature selection methods like searchlight (Kriegeskorte et al., 2006) and recursive feature elimination (De Martino et al., 2008).

The next step after selecting features is to label each pattern of brain activity within a specific time point in the experiment in relation to the actual experimental condition. Depending on the research question, various conditions can be used as the label, including perceptual input, state of perception, cognitive states, affective states, or memory. The labelling procedure also needs to take into account the time lag of the haemodynamic response function (Huettel et al., 2004), usually by shifting the label forward by several timepoints, depending on the actual TR (repetition time) of the scans (usually about 6s).

After obtaining the labelled data set, in the third step we need to choose a classifier and then run a cross-validation procedure to train and validate the classifier. There are several commonly used cross-validation methods, including K-fold cross-validation, odd-even cross validation, and leave-one-out cross-validation (Kohavi, 1995). In a K-fold cross-validation, the data set is partitioned into K subsamples. K minus 1 subsamples are then used to train the classifier and the remaining independent subsample is used for testing the trained classifier. This process is repeated K-times (K-fold), each time using a unique subsample as the validation set. Overall classification performance is then evaluated by averaging K classification results. Figure 2.5 graphically illustrates this procedure for K=3.

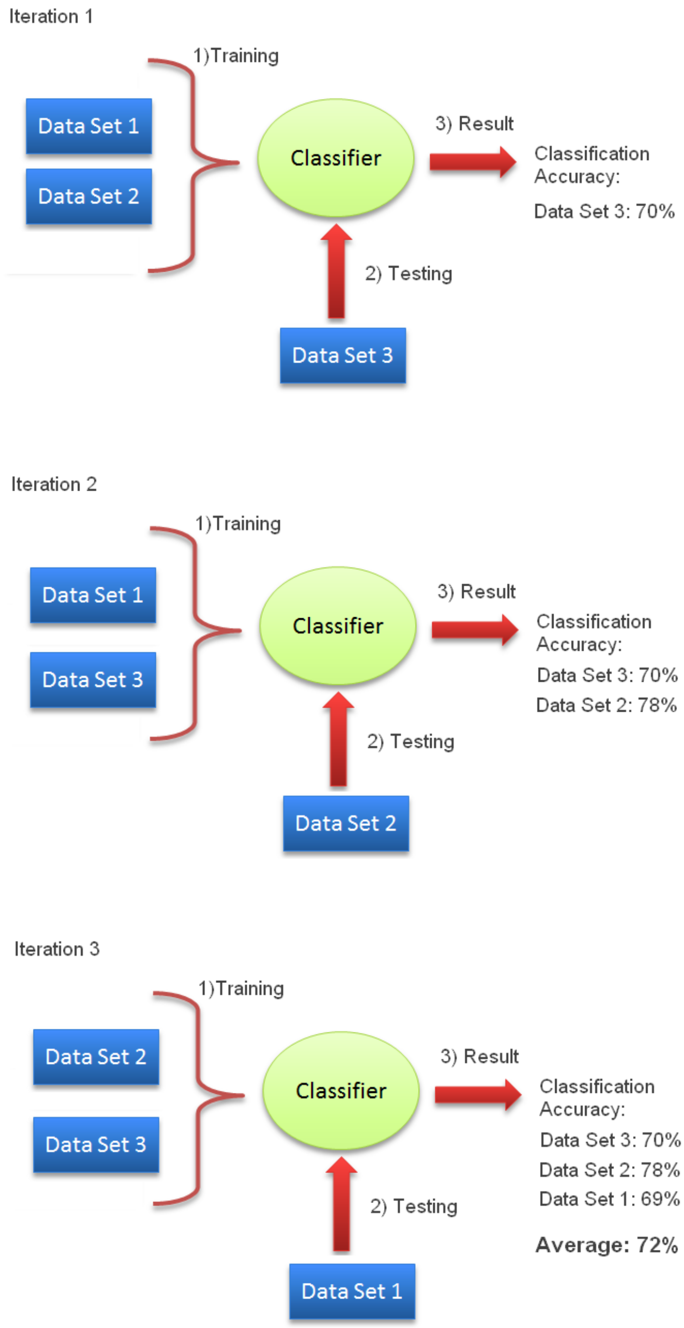


Figure 2.5. Illustration of three-fold cross-validation procedure (K=3). In the first iteration, dataset-1 and dataset-2 were used to train the classifier (step 1). Next, the performance of the classifier was tested using dataset-3 (step 2) yielding classification accuracy value for the first iteration (step-3). These steps were repeated in the second and third iterations using unique training and testing dataset, resulting in three different classification value, which then averaged to produce an overall classification performance.

Odd-Even cross-validation is a simple version of K-fold cross-validation in which the dataset is partitioned into two subsamples; the first half contains all odd numbered data point and the second half contains all even numbered data point. In leave-one-out cross-validation, all data samples, except one, is used as the training set. The remaining single data sample is then used to validate the classifier. This process is repeated as many times as the number of data points in the sample, therefore it is computationally very expensive. Computer simulations on various real-world data sets have demonstrated that ten-fold cross-validation may be better than expensive leave-one-out cross validation (Kohavi, 1995).

After obtaining classification performance for individual subjects, the next step is to perform additional computation to estimate the statistical significance of the result, deciding whether or not we can reject the null hypothesis that the dataset contains significant information about the condition of interest. One way to achieve this is by running permutation testing (Golland and Fischl, 2003; Al-Rawi and Silva Cunha, 2012), training the classifier using randomly permuted label of the training set and then test it on the testing set, repeated several hundred times (usually 1000 times is sufficient) to estimate the null-distribution of classification performance. The p-value is then computed as the probability of the random classification having the result higher than or equal to the result of the original classification (by dividing the number of random classification results that are higher or equal to the original classification result with the number of permutations). Although this non-parametric method is statistically robust, it is computationally expensive and usually not feasible to be applied for neuroimaging experiment with large datasets (Pereira and Botvinick, 2011). Alternatively, instead of permuting the label of the input data set, it is also possible to estimate the null-distribution non-parametrically by randomly permuting the coefficients of a wavelet decomposition of the classifier output, such as demonstrated by (Polyn et al., 2005). The other way to compute the p-value is to estimate the null-distribution using various parametric statistics estimations (Pereira and Botvinick, 2011).

2.3 Searchlight Analysis

In the classical univariate analysis of fMRI data, we typically seek to localise significant activations that distinguish our experimental conditions. To answer this question, the activation statistic is computed for each voxel in the brain volume using various methods such as GLM (General Linear Model), resulting in a whole-brain activation map (Friston et al., 1995b, 2006). Spatial smoothing is usually performed before the analysis to remove fine-grained structure of the activity pattern and to increase statistical likelihood of finding significant activations in the group analysis. The core assumption in this approach is that neighbouring voxels in a region are always activated as a whole, so that any fine-grained spatial patterns are treated as noise that should be removed (Hopfinger et al., 2000; Mikl et al., 2008). Although this assumption is useful to reduce the spatial complexity of the data, and to simplify the problem of multiple comparisons, we might also miss relevant distributed information that is present within the fine-grained pattern of activity.

How can we combine the idea of functional brain mapping with multivariate analysis? Kriegeskorte et al. (2006) proposed an approach that substitutes the idea of activation with a more abstract idea of information that is contained in a local neighbourhood. Rather than asking where in the brain activations changes across conditions, they asked which local brain regions contain relevant information about the experimental condition. This information can be either a change in the average level of activity or a change in the fine-grained activity pattern. They showed that it is possible to continuously map distributed information across the entire brain volume and visualize the result analogously to univariate brain maps.

In their approach, Kriegeskorte et al. (2006) utilized an abstraction of a small spherical searchlight with a typical radius ranging from two to five voxels. To obtain the information map of the whole volume, this searchlight is moved throughout the brain, centred on each voxel in turn. Multivariate classification is then performed on each searchlight position, resulting in a whole brain information map showing the regions that can distinguish the experimental conditions. After that, a p-value can be obtained for each searchlight location using either permutation tests or inferential parametric statistics. From these p-values we can then apply corrections for multiple comparisons using False Discovery Rate (FDR) or Family-Wise Error rate (FWE) to find significant voxels that contain task-relevant information. It is also possible to combine individual searchlight maps into a group level information maps using a two-level approach of information-based mapping (Kriegeskorte et al., 2006).

2.4 Decoding Attentional Processes

Several studies in recent years have demonstrated the advantages of applying multivariate analysis methods for the study of visual attention. Kamitani and Tong (2005) are among the first to show the effectiveness of multivariate analysis in decoding attended feature among overlapping features in visual cortical regions. In their experiment, they initially trained a multivariate decoder to discriminate activities in the visual cortex evoked by perception of 45^{o} oriented gratings versus 135^{o} oriented gratings. The trained decoder was then used to predict which of the two overlapping gratings was attended by the subject when they were presented simultaneously. They found that fMRI activity patterns in V1-V4 could reliably predict which orientation was currently being attended with almost 80% accuracy level, on a trial-by-trial basis. This result provides human neuroimaging evidence for endogenous attentional modulation of feature-selective neuronal populations in the early visual cortex, corroborating previous studies of the feature-based attention mechanism in non-human primates (Martinez-Trujillo and Treue, 2004).

Similar experiments using overlapping motion stimuli also revealed successful decoding of attended direction of motion in V1-V4 and V5/MT+ (Kamitani and Tong, 2006). A replication and extension of this study by Serences and Boynton (2007) further demonstrated that this feature-selective attentional modulation spreads to stimuli in unattended visual fields, even when these regions contain no stimulus, corroborating previous results of single-cell recordings (Treue and Martínez Trujillo, 1999; Bichot et al., 2005). A more recent study by Jehee et al. (2011) showed that feature-based attentional modulation enhanced neuronal responses to task-relevant features only, and can have distinct effect in different visual regions. In their first experiment, they found improved orientation decoding of attended stimuli only during an orientation discrimination task but not during a contrast discrimination task. In a similar second experiment using orientation and colour as the features, colour-selective responses were increased only when colour was behaviourally relevant. They also observed a spread of feature-selective bias to locations outside the focus of spatial attention, consistent with previous observations (Saenz et al., 2002; Serences and Boynton, 2007). MVPA classification has also been successfully applied to decode target-specific preparatory activity in a higher visual area (Stokes et al., 2009b). In their study, a searchlight classifier was initially trained to discriminate patterns of activity elicited while viewing ‘O’ vs. ‘X’ shape. Subsequently, the trained pattern classifier was applied to decode shape-specific preparatory activity following the cue presentation, but crucially before the onset of the target. Searchlight classifier was able to identify target-specific information in the lateral occipital complex (LOC), providing evidence for top-down attentional modulation that selectively activated task-relevant representations in visual cortex.

Multivariate analysis has also been applied to study potential top-down sources of attentional control in the brain. Previous univariate analyses have demonstrated widespread activations in the frontal and parietal regions during the shift of attention to various domains and sensory modalities (Eimer et al., 2002a; Smith et al., 2010; Green et al., 2011). However, this analysis method was not sensitive enough to pick up subtle changes in the cortical activations correlated with attention to different domains or modalities (i.e. between spatial vs. feature or between vision vs. audition), and therefore led researchers to conclude that such activations are domain and modality-nonspecific.

Recent MVPA studies have begun to shed more light into the nature of information contained in these fronto-parietal regions. A key study by Greenberg et al. (2010) found that it was possible to decode whether the subject was shifting their attention to location or colour using a distributed pattern of activity in the posterior parietal cortex. This result indicates that although this region is commonly involved in shifting attention to various domains, it still contains neuronal subpopulations that are tuned to domain-specific information. Similar success in decoding sources of attentional control was reported by Kalberlah et al. (2011). In their experiment, they applied surface based searchlight analysis in combination with classical activation-based mapping to map the topographic locus of spatial attention in the fronto-parietal regions. A topographic spatial attention map was found in the occipital and parietal regions but not in frontal regions, although some frontal regions still contain specific information about the locus of spatial attention, suggesting that spatial-preference and laterality information become less and less topographic as we move forward from occipital to frontal areas. Another similar study by Liu et al. (2011) also demonstrated successful decoding of attended direction of motion and attended colour in the fronto-parietal regions.

2.5 Conceptual Issues

One of the main issues in interpreting the result of MVPA classification is the relation between successful decoding and the cognitive functions performed in the brain. In many studies that aimed to identify brain regions that could reliably discriminate between various task conditions, successful classifications were usually interpreted as evidence for cognitive processing in that particular location (Haxby et al., 2001). However, this type of inference is logically unsound because successful discrimination of a particular condition from a brain region does not necessarily imply that the region is truly selective for that condition. It might be possible that a pattern of discriminative information about certain conditions exists in a particular region but not actually processed *by* that brain region. For example, a study by (Cox and Savoy, 2003) revealed that early visual areas can outperform higher-level object areas in discriminating object categories because there were multiple differences in the low-level properties of images in different categories (i.e. spatial frequency, orientation, etc) that can be decoded from early visual regions.

A related MVPA study demonstrated successful use of the classifier to decode orientation of the grating in V1 even though it was not consciously perceived by the subjects due to the use of backward masking (Haynes & Rees, 2005), implying that information decoded by MVPA does not always reliably indicate the mental state of the subject. In fact, more recently it has been shown that it was possible to predict and partially reconstruct natural images that were shown to the subjects using patterns of activations in V1 (Kay et al., 2008; Miyawaki et al., 2008; Naselaris et al., 2009). In one such study, the subjects were presented with approximately one thousand different natural images while being scanned. Afterwards, the response preference of each voxel in V1 for retinotopic position, spatial frequency, and orientation was estimated from these training images. The subjects were then shown 120 new pictures and the trained model was able to predict which of these new images was being shown with high accuracy (Kay et al., 2008). The latest development of this type of work has recently reported successful reconstruction of seen movie clips from activations in early visual regions (Nishimoto et al., 2011). Although all of these feats are impressive, it would be a mistake to conclude such an achievement as an instance of mind reading, because reading information received by sensory regions like V1 does not automatically imply reading the content of the subject’s mind; it simply means successful reading of information encoded in the subject’s brain (Tong and Pratte, 2012). Decoding internally generated thoughts or imaginations are closer to the idea of mind reading (Stokes et al., 2009a; Reddy et al., 2010), since the information that is being decoded from the brain is private and subjective.

One way to determine cognitive relevance of a particular brain region is to correlate decoding performance with behavioural performance. An example of this approach was reported by

Williams et al. (2007) where they showed that decoding accuracy of object category information in the human lateral occipital cortex (LOC) was much higher on correct trials than on incorrect trials, but that no differences in decoding were observed in the retinotopic cortex during task performance. This suggests that although information was present in both visual regions, only in LOC was the information ‘read out’ for the actual cognitive task. Similar result was reported in a study that compared decoding performance of correct and incorrect trials in an orientation discrimination task where they found that successful discrimination of orientation in primary visual cortex correlated with task performance (Scolari and Serences, 2010). Another way to investigate the nature of discriminative patterns in the brain is by correlating classifier performance with properties of the input stimulus such as similarities in visual orientation (Kamitani and Tong, 2005), colour (Brouwer and Heeger, 2009), objects (O’Toole et al., 2005), or odours (Howard et al., 2009). The more similar the input stimulus, the more the classifier performance was impaired, implicating relevant functional role of the region in processing stimulus features.

Chapter 3 – Microcontroller-Based MR-compatible Fibre-Optic Visual Presentation System for Multisensory Neuroimaging

Presenting visual stimuli in physical 3D space during fMRI experiments carries significant technical challenges. Certain types of multisensory visuo-tactile experiments and visuo-motor tasks require presentation of visual stimuli in peripersonal space, which cannot be accommodated by ordinary projection screens or binocular goggles. However, light points produced by a group of LEDs can be transmitted through fibre-optic cables and positioned anywhere inside the MRI scanner. Here we describe the design and implementation of a microcontroller-based programmable digital device for controlling fibre-optically transmitted LED lights from a PC. The feasibility of this device to deliver reliable visual stimulus in the scanner was demonstrated in three different fMRI experiments.

This chapter begins with an introduction to various methods of presenting visual stimuli inside the MR-scanner. We then discuss the design and implementation of a microcontroller-based electronic circuit for controlling multiple coloured LEDs. Finally, three fMRI experiments will be described, followed by a discussion of the results of the analysis.

This chapter has been published as the following article:

Kurniawan, V., Klemen, J. & Chambers, C.D. (2011). Microcontroller based fibre-optic visual presentation system for multisensory neuroimaging. *Journal of Neuroscience Methods, 202,* 28-37.

3.1 Introduction

Functional MRI is one of the most widely used non-invasive research tools for investigating brain activity correlated with human behaviour. Most fMRI experiments utilize a projected LCD screen for presenting high-resolution visual stimuli. Although this standard visual presentation system is sufficient for most experiments, there are still many challenges in delivering visual stimuli for certain types of experiments such as visuo-motor reaching tasks (Filimon et al., 2007; Culham JC et al., 2008) and multisensory visuo-tactile tasks (Macaluso and Driver, 2005; Macaluso, 2010; Spence, 2010). In some visuo-motor reaching tasks there is a need to display visual stimuli at different depths in various locations near the subject's body or face, which is difficult to accomplish using an ordinary video projector (Huang and Sereno, 2008). Presenting visual stimuli in close proximity with the source of tactile stimuli is also important for multisensory visuo-tactile experiments, especially when investigating spatial aspects of intersensory interactions (Spence and McDonald, 2004; Macaluso et al., 2005). Besides this limitation, there are several reasons that serve to discourage the use of LCD video projectors for some applications of fMRI, including the impossibility of obtaining complete darkness (except with special filters, such as described in Kimmig et al., 2008), restricted field of view, and limited refresh rate (60Hz for typical LCD projector).

An alternative method of displaying visual stimuli is using real objects inside the scanner, which sometimes need to be moved manually by a trained operator standing next to the scanner bore (Makin et al., 2007; Menz et al., 2009). Although practical and straightforward, the timing and the precision of positioning can become problematic in this case. As an alternative, several studies have also managed to use a group of light emitting diodes (LEDs) positioned at various locations inside the scanner (Marx et al., 2004; Culham JC et al., 2008). These LEDs were powered directly by electrical wires connected to a computer or an electronic control apparatus in the scanner control room. Using this approach, extra care must be taken to ensure that these wires are properly shielded (Gallivan et al., 2009), or they can cause unwanted heating or image artefacts produced by interaction of electricity flowing inside the cable with the scanner RF (radio-frequency) pulses and switching gradients. Moreover, this approach is feasible only for experiments that use small numbers of LEDs.

Several factors must be considered when constructing MRI compatible equipment, most importantly: the participant's safety, RF (radio frequency) interference leading to image artefacts and heating hazard, interactions between the equipment and the static magnetic field, spatial restriction of the scanner bore, and leakage currents (Keeler et al., 1998). The problems associated with bringing conductive electrical wires that power LEDs into the scanner can be overcome by transmitting light emitted by these LEDs via fibre-optics instead (Huang and Sereno, 2008). Fibre-optics are completely safe in the MRI environment and do not lead to heating or RF interference. In some experiments, optical fibres have been used to relay high-resolution video images from CRT displays in a control room to a participant lying inside the scanner, operating as binocular fibrescope (Cornelissen et al., 1997; Hoffman et al., 2003). However, instead of using fibrescopes to transmit entire visual images, for multisensory experiments, in particular, it can be more desirable to transmit point light sources emitted by the LEDs into various positions near subject's body in 3D space. Additionally, LED light sources have wider contrast ranges compared to CRT or LCD screens and superior temporal resolution.

In most visual experiments, visual stimuli need to be dynamically updated in the spatio-temporal domain. Unlike ordinary video displays, this problem becomes challenging when LEDs are used to present stimuli. If only a few LEDs are required, usually they can be connected directly to a PC parallel port (which can control up to 8 LEDs) and then each LED can be turned ON/OFF by sending 0/1 to a corresponding pin of the parallel port. Another approach that efficiently accommodates more LEDs using a single parallel port has been demonstrated by Huang and Sereno (2008). The authors connected a parallel port to a custom made circuit that performs translation (demultiplexing) of 8-bit binary codes of the parallel port into a signal that activates one of 256 LEDs at once. There are, however, several limitations to this approach. First, the device can either activate one LED, or a prewired group of LEDs at the same time. More complex patterns can possibly be simulated by blinking several LEDs ON and OFF in rapid succession, however this increases the complexity of the required software. Second, slightly different wiring in the hardware circuitry is required for displaying stimuli in different experimental paradigms. Third, the control of brightness of each LED is very limited.

The challenge here, therefore, is to develop a general-purpose programmable digital device for controlling LEDs that can be utilized for various experimental paradigms. The device should be flexible enough to display various stimulus patterns simply by changing the software, without the need to modify the underlying hardware circuitry. In this paper we describe the design of a microcontroller-based fibre-optic LED stimulus presentation system that can be controlled from a PC via a USB port. The device was designed in a modular and extensible way so that it can drive up to several hundred LEDs, depending on the requirements of the experiment. Tri-colour RGB LEDs were used in this device to enable the display of various colours by specifying the brightness level of each red, green, and blue component (4096 gradation levels per colour). Additionally, colour, brightness, and timing of each LED can be controlled independently, which enables greater flexibility for displaying various visual stimulus patterns, analogous to manipulating pixels on an LCD screen. Any popular programming language with an access to USB port (such as Matlab® or C++) can be used to command the device, and we provide example Matlab® code.

3.2 Materials and Methods

3.2.1 Design Concepts

The fibre-optic system consisted of several components, including a microcontroller-based digital hardware, software for programming the microcontroller, software for interfacing between the microcontroller and a PC, and some supporting structures for holding the optical fibres. In this paper, we describe the design and implementation of the hardware and software for controlling 80 LED fibre-optic point lights.

One aim of constructing this fibre-optic visual presentation device is to complement the tactile stimulator system that we currently utilize for multisensory visuo-tactile fMRI experiments. The tactile stimulator was manufactured by Quaerosys^{TM} and consists of several stimulator modules driven by MRI-safe piezoelectric components. Each module contains 20 small plastic pins (1mm in diameter) arranged into a 4×5 grid as shown in Figure 3.1a. The position and timing of each pin can be controlled independently from a PC, forming Braille-like patterns needed for particular somatosensory experiments. In order to visually match pin arrangements of the tactile stimulator module, we constructed a custom-made prism from Perspex material to reflect light points transmitted by 20 strands of optical fibres (2 mm in diameter). This formed an arrangement of 4×5 light dots on the surface of the prism, resembling the grid of the tactile stimulator pins (shown in Figure 3.1b). The other end of the optical fibres was connected to the LEDs, in such a way that the end of each optical fibre coincided perpendicularly with the top surface of each LED (Figure 3.1c). These LEDs were controlled by a dedicated LED controller module shown in Figure 3.1d.

For supporting structures, we constructed two opaque plastic compartments (also made from Perspex material) for holding the subject’s hands, tactile stimulator, and fibre-optic prisms in place. Throughout the experiment, subjects rested their hands inside this plastic compartment on the corresponding side, positioning their index fingers on top of each tactile stimulator module. At the same time, they were also able to see the visual stimuli (with help of mirrors) coming from fibre-optic prisms mounted on top of the compartments directly above their hands, on both sides of the visual field (Figure 3.1e). The plastic compartments were held together on corresponding sides by a transparent plastic board made from Perspex material, and positioned on the subject’s lap while they lay supine on the scanner bed. In the middle of the board, in between the left and right plastic compartments, a single fibre-optic light point served as a fixation point. A mirror setup, consisting of two mirrors at approximately 45^{o} right angle positioned on top of the RF-coil, enabled subjects to see fibre-optic point lights and both hands without any reversal, as if they were looking down directly towards their hands.

3.2.2 Hardware Design and Implementation

The principal challenge in constructing the hardware for controlling LEDs is to design an electronic circuit that is modular, programmable, and sufficiently flexible to be used in different experimental applications – without the need to change the underlying hardware. Considering this problem, we designed a digital circuit based on a microcontroller as the main component. A microcontroller is a miniaturized computer on a single integrated circuit (IC) consisting of a CPU (central processing unit), memory, oscillators, timers, and input/output (I/O) ports (Predko M, 2002). Microcontrollers have been used in almost every modern digital electronic product ranging from toys, washing machines and mobile phones to automobile control systems and medical implants. A microcontroller can be programmed by writing the software on a PC and then uploading the binary code into the chip using a programmer circuit. Various behaviours of the hardware can be achieved by simply changing the software without the need to rewire any of the circuit. Several types and vendors of microcontrollers are available on the market today, and one of the most popular, low cost, and easy to use is the Microchip PICmicro® microcontroller. Currently, there are several hundred variations of the PICmicro® microcontroller, each differing in processor speed, memory capacity, I/O pins, packaging, and supported peripheral functions. Among these options, we chose two PIC microcontrollers: PIC18F2553 and PIC18F4455 which suited our needs.

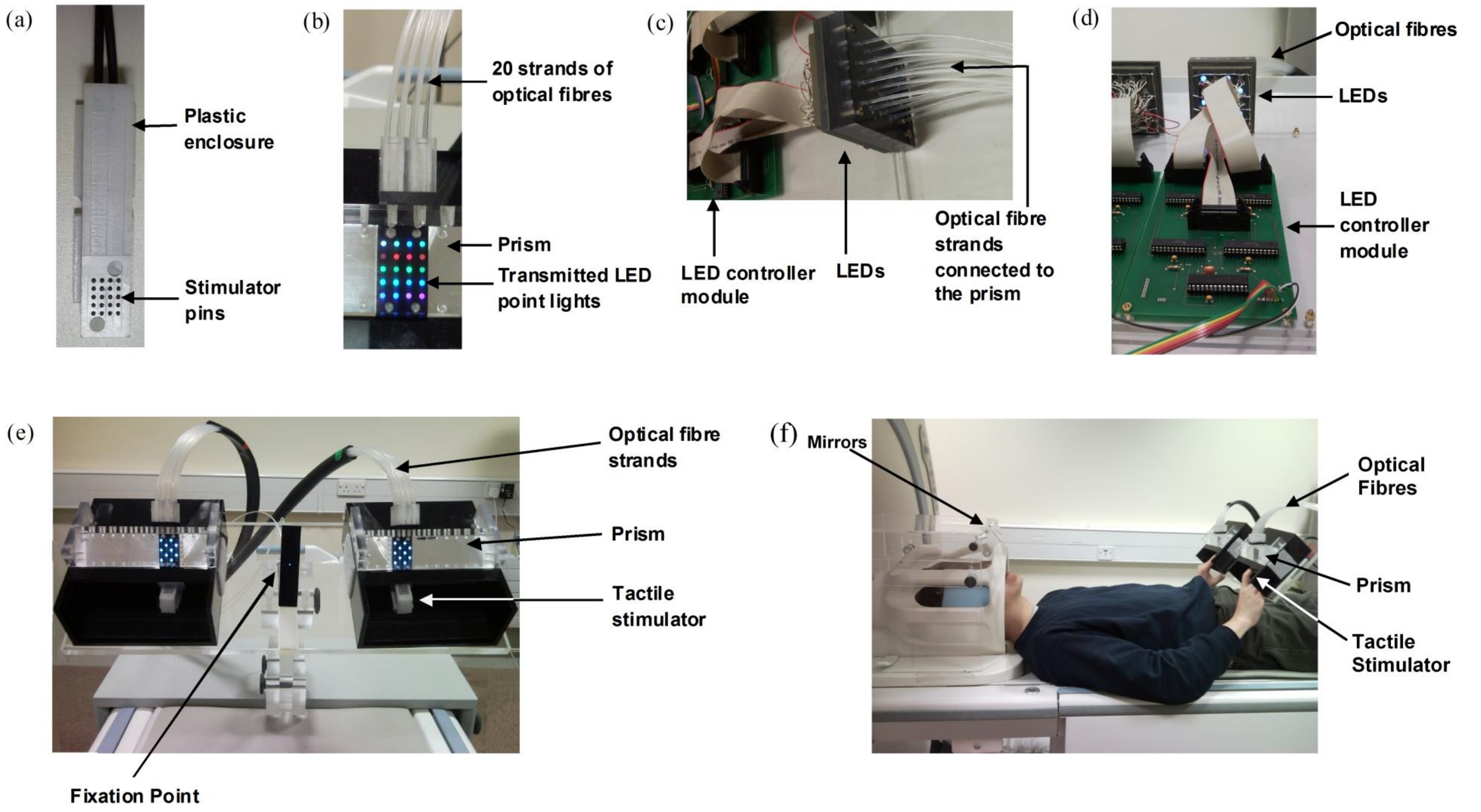


Figure 3.1. (a) An fMRI compatible tactile stimulator module (Quaerosys^{TM}) with a 4×5 grid of plastic pins. **(b)** A single fibre-optic prism displaying 20 LED light points, arranged into a 4×5 grid. **(c)** In the MR control room, 20 strands of optical fibres were connected to 20 LEDs. **(d)** Close-up view of the LED controller module. **(e)** Supporting structures made from Perspex material for mounting both tactile stimulators and fibre-optic prisms in place. (f) Example of multisensory experimental setup with subject, two fibre-optic prisms and two tactile stimulators.

Figure 3.2a illustrates the conceptual diagram of the controller hardware. Instead of using a single circuit to control all LEDs, we designed the hardware in a modular way, separating the circuits that control the LEDs (the 'LED controller module') from the circuit that communicates with a PC and coordinates all LED controller modules (the 'coordinator module'). This design accommodates for the possibility of using greater or fewer LED arrays depending on the need of the experiment. In this application, each LED controller module was responsible for controlling colour, brightness, and timing of an array of 20 RGB LEDs, which were transmitted by fibre-optic cables into a single prism. As the overseer of the entire circuitry, the coordinator module is responsible for receiving information about stimulus parameters and triggers from a PC via a USB port, distributing this information to each LED controller module concurrently. Any programming language that supports USB communication can be used to control this device, and Matlab® was our choice for this experiment. The PIC18F2553 microcontroller was used as the main component for LED controller module, and the PIC18F4455 microcontroller was used in the coordinator module.

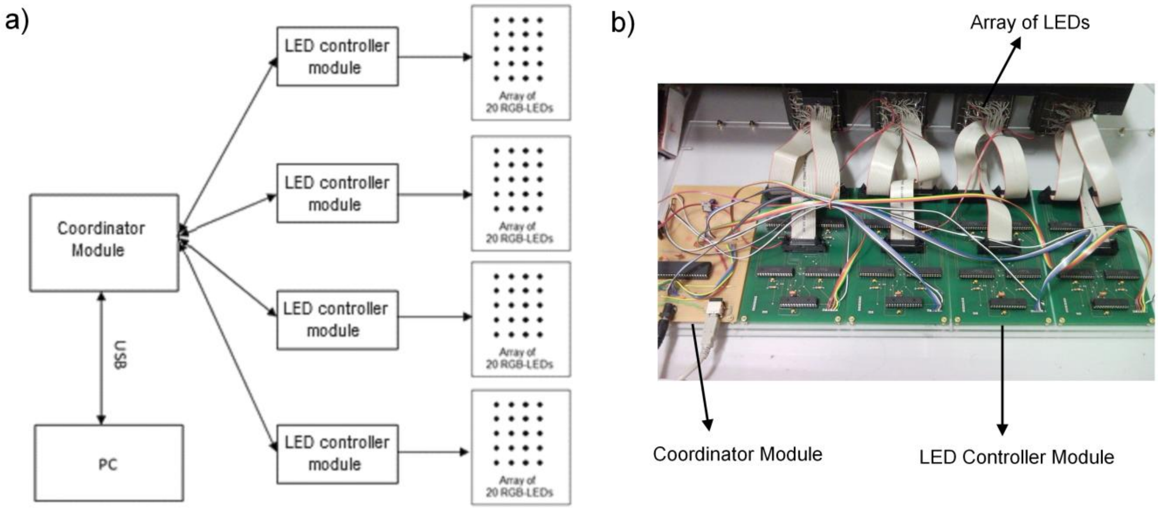


Figure 3.2. (a) Conceptual diagram of the LED controller hardware. The *coordinator module* was connected to a PC through a USB port for receiving information about the stimulus to be presented. This information is then distributed to each *LED controller module*, which in turn activates specific LEDs. Fibre-optic cables (not shown) then transmit light into the scanner. **(b)** Photo showing the coordinator module and the LED controller module circuit boards.

The schematic circuit of the LED controller module is presented in Figure 3.3. The main components used in this circuit are the PIC18F2553 microcontroller and several TI TLC5940 PWM LED-drivers (Texas Instruments, Inc.). The TLC5940 chip is necessary for controlling the brightness level of each LED by varying the current that passes through that LED using PWM (Pulse Width Modulation) control. PWM provides an intermediate amount of electrical power by switching quickly between fully ON and fully OFF states. Various power levels can be attained by using different switching frequencies, for example if a 500Hz PWM produced maximum output power, then a 250Hz PWM will produce 50% of the maximum power. This method of gradual power adjustment is efficient and well suited for digital circuits, because of their ON/OFF nature. Although it is possible to implement PWM in software using the PIC microcontroller alone, it would be challenging to write fast and efficient PWM software for controlling the brightness level of 20 RGB LEDs simultaneously. Moreover, the PWM software would consume considerable microcontroller processing time, introducing timing inaccuracies and impairing its function for controlling stimulus presentation. For this reason, it is more effective to combine both a microcontroller and several dedicated PWM chips such as TI TLC5940.

Four TI TLC5940 chips (T1, T2, T3, T4) and one PIC18F2553 microcontroller were used in each LED controller module. Each TLC5940 chip can drive up to 16 output channels, providing each channel with 4096 levels of brightness control through the PWM. Each RGB LED has four pins, one pin for each primary colour (red, green, blue) and one pin for the common ground. Various colour combinations can be produced by mixing different brightness levels of red, green, and blue colour, as with standard colour production in computer monitors. Four TI TLC5940 chips can drive 64 output channels, which are sufficient for controlling 20 RGB LEDs (60 individual pins). More than one TI TLC5940 chips can be cascaded and controlled as a single chip, simplifying control. The role of the PIC18F2553 microcontroller is to coordinate the operation of the TI TLC5940 by providing a constantly oscillating clock source and sending information about the brightness of each LED to each TI TLC5940 chip. The PIC18F2553 is an 8-bit microcontroller, capable of operating with speeds of up to 48Mhz. It has 32KB of program memory plus 2KB random access memory (RAM), which is enough for our purpose of displaying patterns of visual stimuli with 20 RGB LEDs.

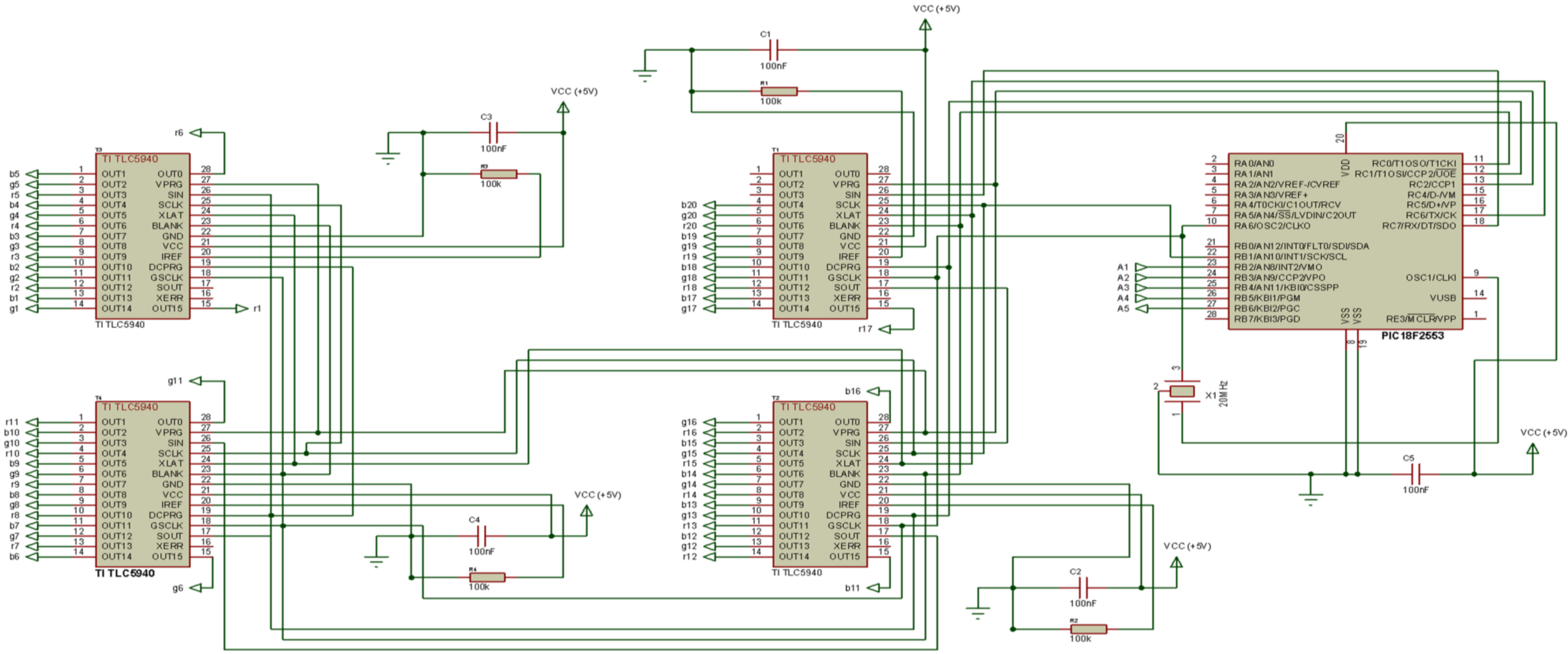


Figure 3.3. Circuit diagram of the LED controller module. This circuit was designed to control the colour, brightness level, and timing of an array of 20 RGB-colour LEDs. Four TI TLC5940 LED drivers were used to regulate PWM (Pulse Width Modulated) currents that flow through each LED. Varying the PWM signals enables control of the luminance and colours of each LED. Each RGB LED has three pins that are connected to three light bulbs (red, green and blue bulb) inside its plastic case. The intensity of each light bulb can vary depending on current strength. Each bulb can emit only one primary colour but various colours can be produced by mixing different intensities of the primary colour, analogous to colour RGB pixels on a monitor screen. From the diagram, it can be seen that output channels of the TI TLC5940 chips were connected to each pin of the RGB LEDs. The pins of each RGB LED are indicated by triplet of symbols [(r1, g1, b1), (r2, g2, b2), …, (r20, g20, b20)], representing the red, green, and blue pins, respectively. A 100KΩ resistor was used in each TI TLC5940 chip to limit the maximum current of all 16 channels. For controlling and coordinating the entire circuitry, a PIC18F2553 microcontroller (shown on the right) was connected to each TI TLC5940 chips. These connections were required for clock synchronization and serial communication, sending information about colour and brightness of each LED to the TI TLC5940 chips. A 20MHz external crystal resonator was used as a clock source for both the microcontroller and the LED driver chips.

Communication between the PIC 18F2553 and the TI TLC5940 was accomplished through hardware SPI (Serial Peripheral Interface) data transfer protocol, as described in the TI TLC5940 datasheet. A 20 MHz external crystal resonator (X1) was used in the circuit for providing an oscillating clock source for both the microcontroller and the TI TLC5940 LED-driver chips. The microcontroller itself runs at 48MHz, achieved by multiplying this external clock frequency with its internal PLL (Phase-Locked Loop) circuitry. Each TI TLC5940 was connected to a current limiting resistor (R1, R2, R3, R4) that limits the maximum amount of current that can flow through the LEDs, which in effect limits the maximum brightness of each LED. Several decoupling capacitors (C1, C2, C3, C4, C5) were used to stabilize the circuit by filtering the voltage inside and outside of the microchips.

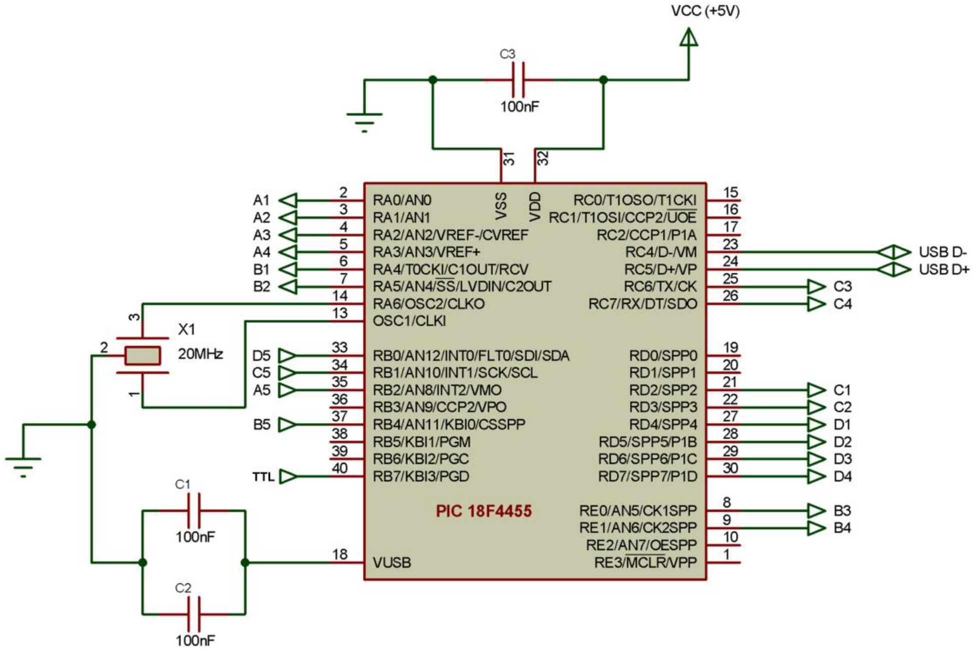


Figure 3.4. Circuit diagram of the *coordinator module*. The major component in this circuit is a PIC18F4455 microcontroller, responsible for interfacing with a PC through a USB connection and also for coordinating several *LED controller modules* for timely stimulus presentation. The sequence of alphanumeric symbols beginning with A (A1, A2, .., A5) denotes pins that are connected to the first *LED controller module*, the sequence beginning with B (B1, B2, …, B5) denotes pins for connection to the second *LED controller module*, and so on, until the fourth LED Controller (D1, D2, …, D5). USB D- and USB D+ denote pins that are connected to the USB port.

The schematic diagram of the coordinator module circuit is shown in Figure 3.4. The circuit core component is the PIC18F4455 microcontroller, which handles communication and coordination between a PC and multiple LED controller modules. In the application described here, the coordinator module was connected to four LED controller modules. Each connection to one LED controller module was accomplished by connecting five I/O pins of the PIC18F445 with five I/O pins of the PIC18F2553. Data transfer between the PIC18F4455 and the PIC18F2553 was achieved using software emulation of SPI (Serial Peripheral Interface) protocol. A 20 MHz crystal resonator was also used in this circuit for driving the microcontroller to run at 48MHz speed using PLL.

The coordinator module also handles incoming triggers from a PC as the signal to start presenting the visual stimulus. The incoming trigger can either be sent by a TTL signal into pin number 40 of the PIC18F4455 or by sending a one-byte trigger instruction through the USB connection. Simultaneous visuo-tactile presentation can be achieved by concurrently sending a TTL signal from the PC parallel port to both the fibre-optic device and the tactile stimulator. The timing latency of each device should also be considered in order to achieve synchronized multisensory presentation.

3.2.3 Software Implementation

Three different programs are needed for controlling the entire device, including one program for controlling the LED controller module (uploaded to the PIC18F2553), one program for controlling the coordinator module (uploaded to the PIC18F4455), and one program that sends triggers and information about stimulus parameters from a PC to the device via a USB port. These programs were written in the MikroC^{TM} language (mikroElektronika$^{®}$), a variant of the C programming language for microcontroller applications. After being compiled into binary code using the MikroC^{TM} compiler, this code was then uploaded into each microcontroller using the PICkit^{TM} Programmer (Microchip Technology, Inc.).

Borrowing an idea from other visual stimulus presentation programs, stimulus patterns were organized into individual frames, with each frame consisting of a brightness and colour value for 20 LEDs, organized into 4-rows × 5-columns. In the current design, basic stimulus patterns that will be used in the experiment should be uploaded or programmed into each PIC18F2553 microcontroller beforehand (inside the LED controller module) and about 10 unique stimulus patterns can be stored inside the PIC18F2553 memory (2KB RAM). An alternative approach which is straightforward to implement is to use the PIC18F4455 memory as a cache, so that stimuli for a particular block can be sent from the PC before the beginning of each block. The PIC18F4455 has 2KB of RAM, so only approximately 10 unique stimulus patterns can be stored in the cache at one time. In the current implementation, USB communication is handled by the USB-HID protocol, which limits the communication speed to 64KB/s. With this speed, sending 10 frames from the PC takes about 30ms, and owing to the fact that there is usually a considerable amount of delay in between blocks, this amount of time should not be problematic to handle. Sending stimulus patterns in real-time is also possible with the current hardware design. This approach will be limited by the bandwidth of the USB connection and the communication speed between the microchips. In the current implementation, it takes about 1.5ms to send one stimulus pattern from the PC to the coordinator module (PIC18F4455) and about 12ms to send the pattern from the coordinator module to the LED controller module (PIC18F2553). Therefore, the minimum achievable inter-stimulus interval time is about 13.5ms, which would not present a problem for the majority of psychological experiments. In addition, the USB communication speed can be improved by using a faster USB communication protocol such as USB 2.0, and the data transfer speed between microcontrollers can also be improved by using hardware SPI instead of software emulation of SPI protocol.

Before the start of an experiment, the sequence of stimuli that are going to be presented is sent from a PC through the USB connection into the buffer of the PIC18F4455 in the coordinator module. This sequence contains information about the order of frames to be presented, the duration of each frame, and the interval between frames. Depending on the requirements of a particular experiment, other types of information (such as colour, frequency, etc) can also be included in this sequence. Thereafter, the coordinator module will wait until it receives a trigger from the PC (through TTL signal or USB connection) and then broadcast information from its sequence buffer to each individual LED controller module as a signal to present a particular stimulus frame. A second program that manages this sequence buffer and triggering was implemented in MikroC^{TM} programming language and uploaded into the PIC18F4455. The third program was written in MATLAB® and runs on a PC. This program is responsible for overseeing the experiment and for sending information about the sequence of stimuli and triggers to the coordinator module. USB communication in the MATLAB$^{®}$ program was achieved via the external USB-HID (Human Interface Device) library. In the current software implementation, it is not yet possible to adjust the stimulus parameters dynamically in the course of the experiment. However, if desired it is straightforward to modify the software so that it can be used for certain types of experiments that require dynamic stimulus adjustment on each trial, such as adaptive staircase procedures.

3.2.4 Neuroimaging Experiments

In order to test the feasibility of using the LED fibre-optic system for stimulus presentation in the MRI environment, three fMRI experiments were conducted.

3.2.4.1 Experiment 1

The first experiment tested whether the visual stimulus produced by the fibre-optic system can elicit activation in the primary visual cortex. In this experiment, the participants were asked to fixate on a central fixation dot while passively viewing an alternating visual stimulus presented in either the left or right visual field. Four fibre-optic prisms were mounted on a flat surface near the top of each participant's lap, with two prisms each on the left and right visual fields, respectively, with a central fixation dot in between. Visual stimuli were positioned in the peripheral visual field, 8^o horizontally from the central fixation point and 1^o above the fixation, stimulus dimensions were 1^o (W) × 0.8^o (H). Stimuli were presented in white color at 25% maximum brightness level. Participants viewed the visual stimuli through the mirrors mounted on top of the head coil, directly above their eyes. They were instructed to keep their eyes open and to maintain central fixation throughout the experiment. Stimuli were presented in a block design with 15s block duration of alternating 'stimulus' and 'rest' periods (see Figure 3.5).

With the aim of distinguishing lateralized visual cortex activation, 'stimulus' periods were further divided into two distinct 'left stimulus' and 'right stimulus' conditions. In the 'left stimulus' condition, a 4Hz contrast-reversing checkerboard-like stimulus was presented on the left side of the visual field. Similarly, in the 'right stimulus' condition, the same type of stimulus was presented on the right hand side. Flickering checkerboard-like stimuli were chosen because it has been shown in many visual retinotopic mapping studies that this kind of stimulus elicits a strong and reliable haemodynamic response in the occipital cortex (Engel et al., 1997). Three right-handed participants (two males, one female, aged 29-32, with normal or corrected-to-normal vision) were recruited for the first experiment and gave written informed consent according to the guidelines approved by Cardiff University's School of Psychology Ethics Committee. Each participant was scanned in one 25-minutes session, consisting of five individual runs, which lasted for 300s each. Overall, 25 blocks were obtained for each condition.

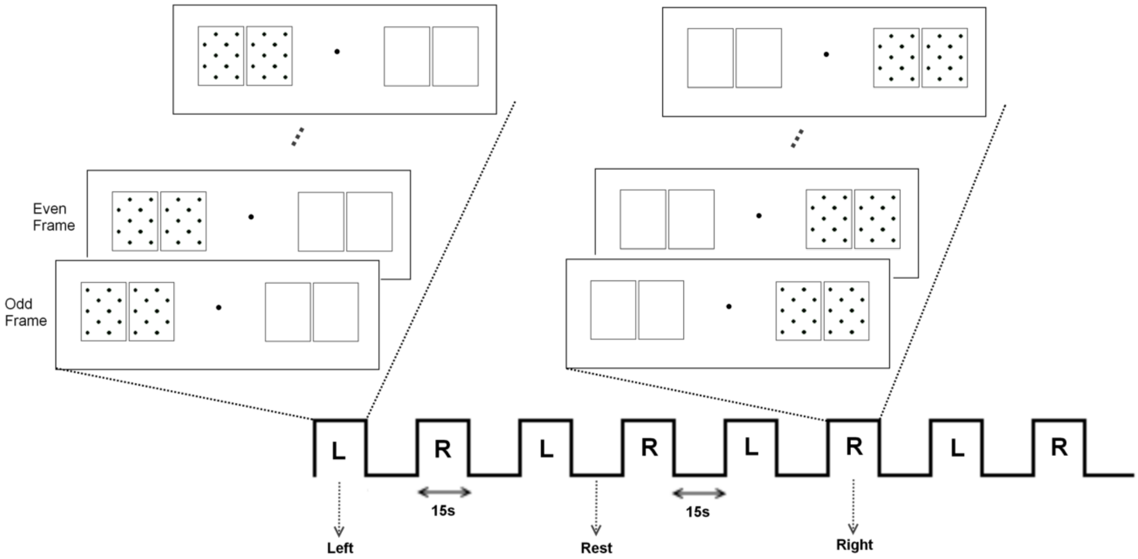


Figure 3.5. Diagram of the experimental procedure of Experiment 1. For each stimulus block, odd and even frames were continuously alternated at 4Hz for a period of 15s. A 15s rest period followed, during which no stimulus was presented. Following the rest period, another alternating pattern was displayed for 15s, this time in the opposite visual field.

3.2.4.1 Experiment 2

The second fMRI experiment was conducted to test the feasibility of the fibre-optic system for presenting coloured visual stimuli. Several human neuroimaging studies have demonstrated that ventral occipital regions (V2/3 and V4) respond strongly to chromatic stimuli in both passive viewing (Beauchamp et al., 1999; Wade et al., 2002) and colour discrimination tasks (Barrett et al., 2001; Ting Siok et al., 2009). In this experiment, the participant was asked to perform a simple colour discrimination task by judging whether the colour of the stimulus presented on the left hand side was the same or different to the stimulus colour presented on the right hand side. Visual stimuli were presented using two fibre-optic prisms, with each prism in the left and right visual field surrounding a central fixation dot. Stimuli were positioned in the peripheral visual field, 6.5° horizontally from the central fixation dot and 1° vertically above fixation. The dimension of each stimulus was 0.5° (W) x 0.8° (H). Consistent with the first experiment, the participant was instructed to view the stimulus through the mirror and maintain central fixation throughout the experiment.

A simple block design was used in the fMRI task with 15s block duration alternating between ‘stimulus’ and ‘rest’ (see Figure 3.6). Each block consisted of 5 individual trials. For each trial, 2Hz flickering checkerboard-like stimulus was presented in both left and right visual fields for 1s, followed by response collection for another 1s, and a 1s ISI. The ‘stimulus’ blocks were further divided into blocks containing either coloured-stimuli or achromatic gray-stimuli. In the coloured stimuli condition, the stimulus on the left hand side was displayed with either the same or different hue value as that of the stimulus on the right hand side. During the response period, the participant was instructed to press one out of two response buttons that signified whether the colours in each visual field were the same or different, using a LumiTouch™ MRI optical keypad (Photon Control, Inc.). Three different hue values were used for the stimuli, including pure red, pure green and pure blue. Prior to the experiment, the brightness level of each colour was matched subjectively by the participant. Equal numbers of ‘same’ and ‘different’ coloured stimuli were presented, with the order of stimuli randomized. Gray-stimuli blocks were introduced as the control condition. In this condition, instead of comparing the colour of the stimuli, the participant was asked to compare the brightness level between the left and the right stimuli. All stimuli in this block were presented in white colour with three different levels of brightness (10%, 15%, and 25%). One right-handed male participant (aged 28, with normal vision) was recruited for the second experiment and gave written informed consent according to the guidelines approved by Cardiff University’s School of Psychology Ethics Committee. The participant was scanned in a short 24-minutes session, consisting of three individual runs, each lasting 8 minutes. Overall, 24 blocks were obtained for each condition.

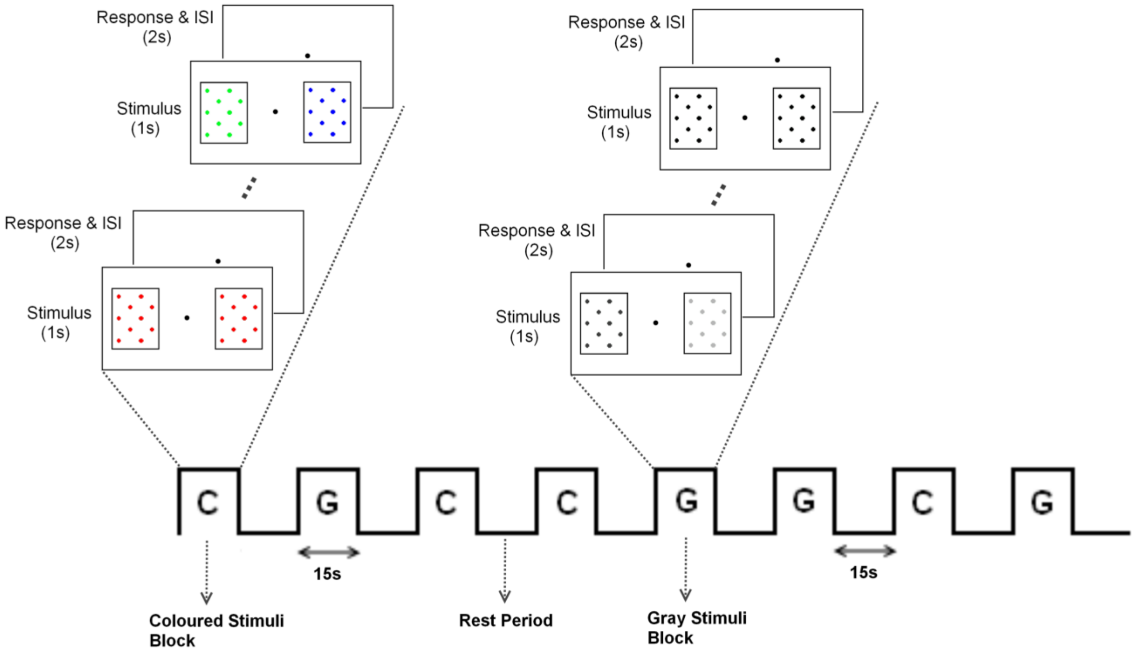


Figure 3.6. Diagram of the experimental procedure for Experiment 2. In the coloured-stimuli blocks, the participant performed a simple colour discrimination task by comparing the hue of the left and right stimulus (same or different), whereas in the grey stimuli block, the participant compared the brightness of the left and right stimulus.

3.2.4.3 Experiment 3

In the third and final experiment, a simple multisensory fMRI experiment was conducted to establish the feasibility of combining the fibre-optic system with the Quaerosys^{TM} tactile stimulator. The aim of the experiment was to visualize brain regions involved in bimodal visuo-tactile processing. Several neuroimaging studies of multisensory interactions in the human brain have shown that multimodal stimuli strongly activated cortical multisensory regions including the lateral occipital region, MT, the superior temporal region, the ventral intraparietal region, premotor cortex, and others (Macaluso and Driver, 2005; Beauchamp, 2005).

A simple blocked fMRI design (Figure 3.7) was employed, which allowed us to compute the contrast of activations correlated with bimodal visio-tactile processing against activations correlated with unisensory processing (visual or tactile). Each block consisted of 5 individual trials. On each trial, a low-frequency (6Hz) or high-frequency (12Hz) stimulus was presented for 500ms, and the participant performed a frequency discrimination task by pressing the appropriate response button. Visual stimuli were presented using one fibre-optic prism positioned 6.5^{o} to the left of the fixation dot. The subject rested the tip of their left index finger on top of the tactile stimulator positioned directly below the prism, inside the black Perspex box (Figure 3.1f). Similar checkerboard-like patterns were used for both visual and tactile stimuli. The colour of the visual stimuli was white at 25% maximum brightness level and the intensity of the tactile stimulation was at 30% maximum level. In the multisensory condition, both visual and tactile stimuli were delivered simultaneously at the same frequency. The participant who was recruited for the second experiment also participated in the third experiment and was scanned again in a 30-minute session, consisting of four individual runs, each lasting 7.5 minutes. Overall, 20 blocks were obtained for each condition.

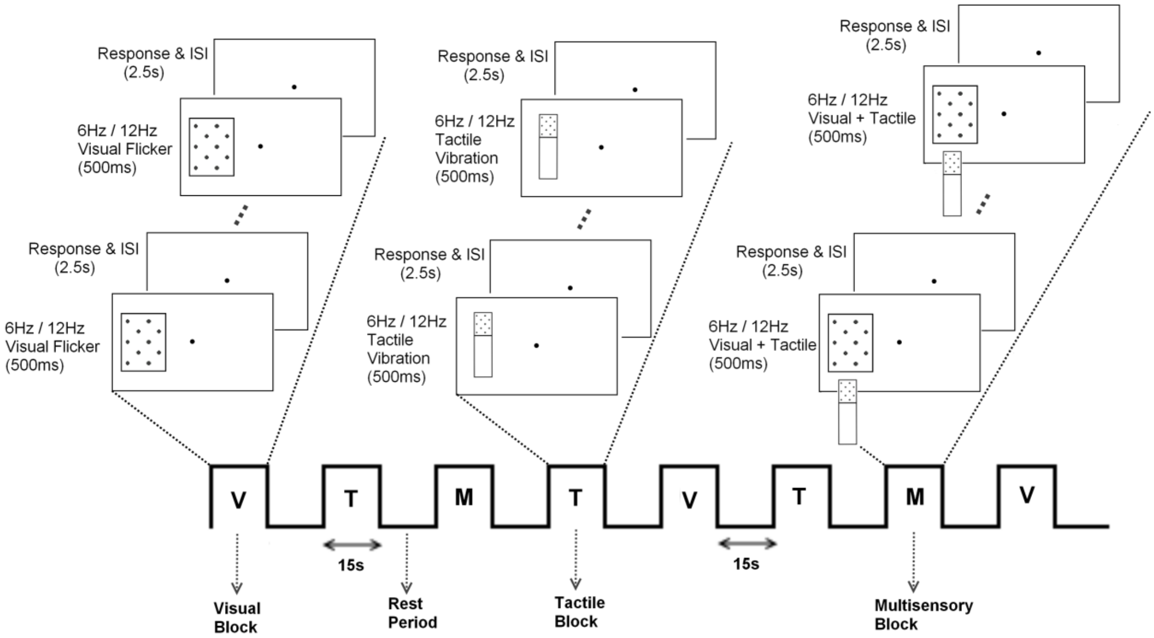


Figure 3.7. Diagram of the experimental procedure of Experiment 3. In all conditions, the participant performed a simple frequency discrimination task by deciding whether the frequency of the visual flicker and/or tactile vibration was high (12Hz) or low (6Hz). The stimulus was presented for 500ms and the response was collected up to 1s after the stimulus offset.

3.2.5 Image Acquisition and Analysis

Functional MRI was used to measure the blood-oxygenation level dependent (BOLD) signal changes in the brain during stimulus presentation via a gradient echo-planar imaging sequence (EPI). All scans were acquired on a 3T GE scanner with 53 contiguous 3.4mm thick axial slices covering the whole-brain. In-plane resolution was 3.4mm × 3.4mm, with a matrix size of 64 × 64 × 53, 90^o flip angle, 35ms echo time (TE), and 3000ms repetition time (TR). The obtained brain activation maps were aligned on previously acquired T1-weighted anatomical images having 1.0 x 1.0 x 1.0 mm voxel resolution.

Statistical Parametric Mapping (Friston et al., 1995a) (SPM8b) software was used for data pre-processing and analysis. BOLD images were realigned within and between scans to correct for asynchronous slice acquisition and head movement, and then spatially smoothed with a 5 × 5 × 5 mm Gaussian filter. Thereafter, a 128s temporal high-pass filter was applied to remove low-frequency artefacts. Analysis was carried out via the general linear model (GLM) in SPM. For the first experiment, all five runs (for a total period of 25 minutes) were analyzed to detect significant activations in the occipital region (whole-brain, $p < 0.001$, *uncorrected*). Two contrasts were evaluated: left stimulation minus right stimulation (left > right), and right stimulation minus left stimulation (right > left). For the second experiment, all three runs were analyzed together and a whole brain activation contrasting the colour condition and the grey condition (colour > grey) was evaluated with the threshold set at $p < 0.001$, *uncorrected*. In the third experiment, four runs were analyzed to visualize a whole brain contrast of the multisensory condition vs. the unisensory conditions (multisensory > unisensory), also evaluated with the threshold set at $p < 0.001$, *uncorrected*.

3.3. Results

The response of primary occipital areas to visual stimuli produced by the fibre-optic system was tested in the first experiment (Figure 3.8). Red and green voxels denote significant activations elicited by stimulation in the left and right visual fields, respectively. Significant lateralized activations in the visual cortex can be observed in all participants, indicating that visual stimuli produced by the fibre-optic system are suitable for applications in visual neuroimaging experiments.

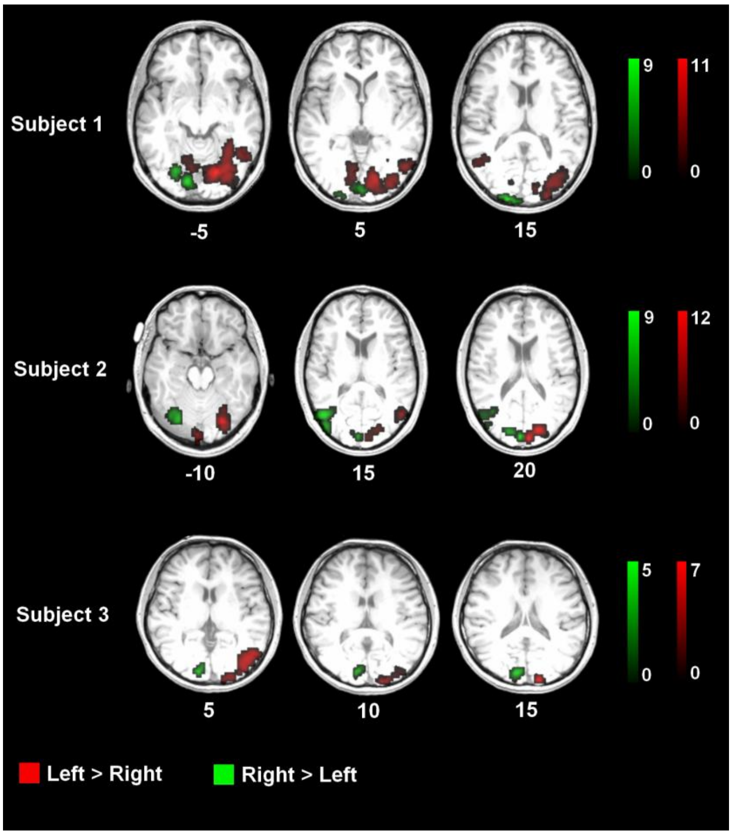


Figure 3.8. Brain areas that were activated during visual stimulus presentation with the fibre-optic LED system (*p < 0.001*, *uncorrected*, shown with a 30 voxels-cluster threshold). It can be seen clearly that the visual stimuli reliably activated the visual cortex of all participants.

Participant	Hemisphere	Coordinates (mm)			T-value
		X	Y	Z	
Subject 1	Right	18	-77	-6	11.34
		27	-72	-2	9.54
		18	-81	5	8.60
	Left	-18	-100	16	9.46
		-22	-98	19	8.43
		-11	-103	13	6.80
Subject 2	Right	7	-92	20	11.80
		24	-72	-11	10.47
		41	-79	5	7.93

	Left	-24	-69	-3	9.22
		-3	-92	17	9.18
		-41	-65	14	8.34
Subject 3	Right	16	-80	16	7.17
		41	-62	2	5.98
		48	-55	5	5.44
	Left	-11	-76	17	5.75
		-11	-74	6	4.82
		-8	-70	9	4.13

Table 3.1. Coordinates of peak activations for clusters in the left and right occipital cortex (Experiment 1). All values are whole-brain, uncorrected with $p < 0.001$.

The result of the second experiment is shown in Figure 3.9. It can be observed that some of the right ventral occipital regions (V4) were activated, consistent with previous neuroimaging studies of colour discrimination (Barrett et al., 2001; Ting Siok et al., 2009). The pattern of activation in the fronto-parietal area is also similar to the findings reported by Ting Siok et al. (2009). This test demonstrates that chromatic stimuli delivered via the fibre-optic system reliably activate the expected cortical brain regions.

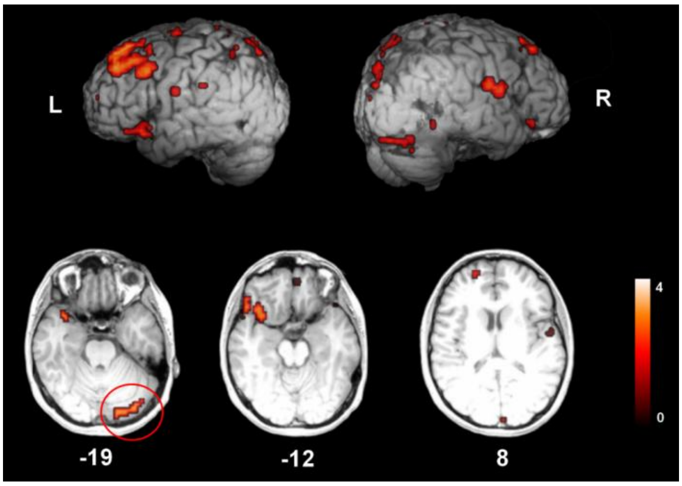


Figure 3.9. A single subject activation map during simple colour discrimination task with colour > grey as the contrast at a threshold of $p < 0.001$, *uncorrected*. Red circle denotes activated voxels around the ventral occipital regions.

Region	Coordinates (mm)			T-value
	X	Y	Z	
V1	4	-92	14	3.36
V4	41	-78	-19	3.35
	34	-81	-21	3.37
	15	-87	-20	3.26

Table 3.2. Coordinates of peak activations for clusters in V1 and V4 regions (Experiment 2)

Figure 3.10 shows the brain regions activated in the simple multisensory interaction experiment (the third experiment). The image was obtained by contrasting the activations in the multisensory condition with the activations during the unisensory conditions. Strong activations can be observed in both left and right superior temporal sulcus (STS), consistent with previous studies of visuo-tactile interactions (Macaluso and Driver, 2005; Beauchamp et al., 2008).

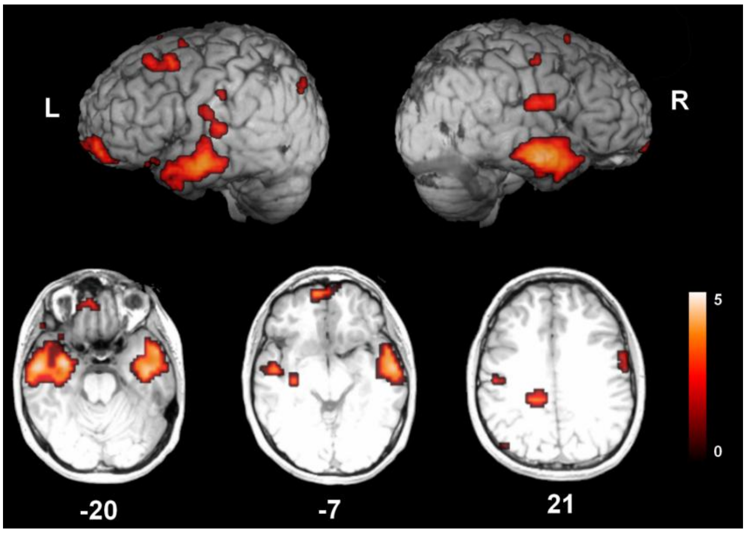


Figure 3.10. Activation map of a single subject while performing a simple multisensory task, obtained using multisensory condition minus unisensory condition as the contrast ($p < 0.001$, *uncorrected*).

Region	Coordinates (mm)			T-value
	X	Y	Z	
Left Temporal	-31	-1	-22	3.71
	-53	-3	-17	3.70
Right Temporal	57	-7	-12	3.71
	50	-3	-15	3.66

Table 3.3. Coordinates of peak activations for clusters in the left and right temporal regions (Experiment 3).

3.4 Discussion

Our primary aim in developing the fibre-optic LED presentation system was to present visual stimuli in close proximity with the tactile stimuli for applications in multisensory fMRI experiments. Additionally, it is also possible to employ this system for other fMRI experiments that require visual stimuli presentation in various locations near the participants' body or face. The current design establishes the feasibility of designing microcontroller based fibre-optic visual presentation systems together with the implementation of required hardware, software, and supporting structures. Using simple visual stimuli, we have shown that visual stimuli produced by the device can elicit reliable BOLD responses in visual cortical areas. The second experiment demonstrates the feasibility of the device for neuroimaging experiments that require coloured stimuli. In the last experiment we have shown that in combination with the Quaerosys^{TM} tactile stimulator, the fibre-optic device can deliver reliable visual stimuli required for typical studies of multisensory interactions.

Our system complement similar MRI compatible fibre-optic LED system described in Huang and Sereno (2008), and offers additional features and flexibilities, including independent control of each LED, support up to several hundreds of LEDs, the ability to display coloured stimuli, and fully adjustable brightness levels. Moreover, the modular design of the hardware and software enables this device to be adapted more readily for many different fMRI applications. The use of a programmable microcontroller also provides additional flexibility: Instead of modifying the hardware for every different experimental paradigm, we need only change the stimulus presentation software and perhaps the supporting structures.

Although the hardware described in this paper was designed to accommodate 4 fibre-optic prisms, with each prism displaying 20 LED lights arranged in 4×5 arrays, it is technically straightforward to extend the circuit to support more prisms or more light points within each prism. The LED controller modules can support more LEDs simply by adding more TLC5940 LED-drivers into the circuit, without the need to change or add new microcontroller; this is due to the cascading feature of the TLC5940 chip, which makes it possible to control dozens of TLC5940 chips using a single microcontroller. If more fibre-optic prisms were required, the PIC18F4455 microcontroller could be replaced by a similar microcontroller with more I/O pins. Since both the PIC18F2553 and the PIC18F4455 have very limited storage memory, more complex experiments with complex visual stimulus patterns might also need to consider using PIC microcontrollers with larger memory capacity. In the current implementation, the PIC18F2553 can only hold approximately 10 unique frames. However, it is straightforward to upgrade the system to support more frames if needed. One possible option is to replace the PIC18F2553 with a more powerful microcontroller such as dsPIC33FJ64MC802, a 16-bit microcontroller with 16KB memory, which theoretically can store up to about 80 unique frames. This alternative microchip has the same number of pins as the existing one (28-pins) but its pin arrangements are different, so slight rewiring of the circuit is required to match the pin numbering. Moreover, on the software side there will be a small difference in programming a 16-bit microcontroller compared to the 8-bit microcontroller. Another option, which will completely eliminate the problem of limited memory, is to replace the microcontroller with much more powerful embedded computer modules, such as those developed by GumStix® (www.gumstix.com).

3.5 Summary

In order to solve the technical challenges of presenting simultaneous visuo-tactile stimuli inside the MR-scanner, we have designed and implemented a fibre-optic LED visual presentation system and supporting structures that enable delivery of the multisensory stimuli in peripersonal space surrounding both hands. The main feature of this device is the ability to independently control the colour, brightness, and timing of each LED. Moreover, the device was designed in a modular and extensible way, which enables easy adaptation for various experimental paradigms. The device was tested and validated in three fMRI experiments involving basic visual perception, a simple colour discrimination task, and a blocked multisensory visuo-tactile task. The results revealed significant lateralized activation in occipital cortex of all participants, a reliable response in ventral occipital areas to colour stimuli elicited by the device, and strong activations in multisensory brain regions in the multisensory task. Overall, these findings confirm the suitability of this device for presenting complex fibre-optic visual and cross-modal stimuli inside the MR scanner.

Chapter 4 - Neural Basis of Spatial Attention in Vision and Touch

Neurobiological theories of attention emphasize a critical role for frontoparietal networks in the selection of sensory representations, but whether such top-down operations are modality-specific or supramodal is contentious. Here we probed the modality-specificity of attentional control by combining a visuo-tactile spatial attentional task with MVPA classification of fMRI data. Consistent with previous neuroimaging studies of attention in various sensory modalities, classical univariate analysis discovered widespread overlapping activity in the frontoparietal regions associated with attention to vision and touch. We further investigated the nature of distributed patterns of activity within these overlapping regions using MVPA classification and searchlight analysis, and discovered evidence for modality-specific information in the parietal cortex and the posterior part of the frontal cortex.

This chapter begins with a general introduction, followed by detailed descriptions of the apparatus and methods used in the present study. The results of both univariate analysis and MVPA classifications are then presented in the subsequent section, followed by discussions of the implications of the findings.

4.1 Introduction

In everyday life, it is vital for neural systems to select and integrate incoming signals from multiple sensory modalities. An influential theory has proposed that attention emerges from integrated activity of multiple brain systems to resolve competition for sensory processing and control of behaviour (Desimone and Duncan, 1995b; Duncan, 1998). This account suggests that attention is both top-down (goal-directed) and bottom-up (stimulus driven). Top-down endogenous control is believed to enhance signals of behaviourally relevant stimuli while suppressing irrelevant inputs (Desimone and Duncan, 1995b; Kastner and Ungerleider, 2000). An increasing body of evidence from electrophysiology and human neuroimaging studies suggests that this control mechanism is mediated by brain regions distributed across a dorsal frontoparietal (dFP) network for goal-directed top-down selection and binding of stimuli and responses, and a ventral frontoparietal (vFP) network for identifying salient and relevant stimuli as well as filtering irrelevant distractors (Corbetta and Shulman, 2002; Corbetta et al., 2008; Beck and Kastner, 2009).

Although most behavioural and neuroimaging studies on attention usually consider only one modality at a time, the last two decades have witnessed increasing evidence of close coupling between orienting of spatial attention and multisensory integration (see Driver and Noesselt, 2008; Spence, 2010 for reviews). Many behavioural experiments on crossmodal cueing have shown that spatially orienting attention to one location in one modality can enhance processing of stimuli presented in another modality within the same attended location (Driver and Spence, 1998; McDonald et al., 2000; Spence et al., 2000). Based on this finding, several researchers have proposed the hypothesis of generalized supramodal attentional system that operates across wide range of sensory modalities (Farah et al., 1989; Macaluso and Driver, 2001; Green et al., 2011). The nature and interpretation of this supramodal attention network is controversial and has been debated in the literature (Chambers et al., 2004b). Several neuroimaging and ERP studies have provided evidence for supramodal regions based on the common activations within dorsal and ventral frontoparietal regions in crossmodal attention tasks (Eimer et al., 2002a; Macaluso et al., 2002a, 2002b; Smith et al., 2010; Green et al., 2011). For example, in an event-related fMRI study, Macaluso et al. (2003b) reported common activations in dorsal premotor cortex and intraparietal sulcus during cue-related preparatory attention in vision and touch. Contrary to the hypothesis, other neuroimaging studies on audiovisual spatial attention task have reported distinct regions in parietal cortex recruited during attending to different modalities (Bushara et al., 1999; Salmi et al., 2007). In a reversible neurodisruption study using TMS in visuotactile attention task, (Chambers et al., 2004b) demonstrated that disruption of a region in the parietal cortex (right-SMG) only impaired endogenous visual orienting, but had no effect on tactile orienting, providing evidence of modality-specific attentional control.

Inferring overlapping patterns of neuroimaging data as supramodal system has been criticized because observing common activations in multiple regions does not implies that all of these regions are *necessary* for orienting attention to each modality. It might be possible that only a certain subset of the regions are actually *crucial* for orienting attention to specific modality (Chambers et al., 2004b). Furthermore, each fMRI voxel contains an average of activity of several millions of neurons (Logothetis, 2008). Any sub-voxel population coding that might contain modality or location specific information might not be able to be distinguished by mass-univariate analysis since it only considers information within a single voxel, independently from all other voxels. Recently, multivoxel pattern analysis (MVPA) methods have been utilized to decode weak distributed pattern across neighbouring voxels that correlated with task conditions (Norman et al., 2006; Wagner and Rissman, 2010). Several fMRI studies have applied MVPA to address the question of whether overlapping regions involved in visual attention and cognitive control contains specific information about the experimental conditions and successfully found reliable domain specific population coding in the parietal cortex (Esterman et al., 2009; Greenberg et al., 2010).

In this study, we applied MVPA to investigate whether there was any modality specific information in overlapping frontoparietal voxels recruited during sustained spatial attention to vision and touch. We used conventional mass-univariate analysis (conjunction analysis) to look for commonly activated voxels in both attentional conditions and then applied MVPA analysis to decode attended modality in these overlapping regions, using independent data. Furthermore, we also tested the specificity and generality of frontoparietal regions in encoding information about the attended modality and attended location, using a combination of searchlight MVPA (Kriegeskorte et al., 2006) and cross-generalization procedures (Stokes et al., 2009a). Specifically, in the first searchlight analysis, we tested whether there was any modality-nonspecific but location-specific information that contain common codes for attended location across modalities (Macaluso, 2010) by training a statistical model to discriminate the attended location in one modality and then tested how well this model could predict the attended location in the other modality. In the second searchlight analysis, we applied similar logic to test whether there was any spatially-nonspecific but modality-specific information by training a statistical model to discriminate attended modality in one location and tested the model to predict attended modality in the other location. In the third searchlight analysis, we trained and tested the pattern classifier to distinguish four attentional conditions (vision-left, vision-right, touch-left, touch-right) to look for modality-specific and location-specific information.

For the behavioural paradigm, we used a multisensory spatial attention task. Participants were instructed to sustain their attention to one modality (visual or tactile) and one location (left or right) throughout each block. In each trial, after concurrent bimodal and bilateral visuo-tactile stimuli were presented, participants were asked to identify the elevation of the target (upper or lower) within the attended modality and location, in a non-speeded way. The location of the target was chosen to be orthogonal to the attended location to avoid possible confounds of automatic motor priming (Driver and Spence, 1998). Targets were always presented in both modalities and locations, so that overall the sensory input was held constant and only participants' attentional condition was manipulated throughout the experiment. There was no informative relationship between tactile and visual stimuli (i.e. every possible stimuli combination in both modalities at both sides was presented with equal probability).

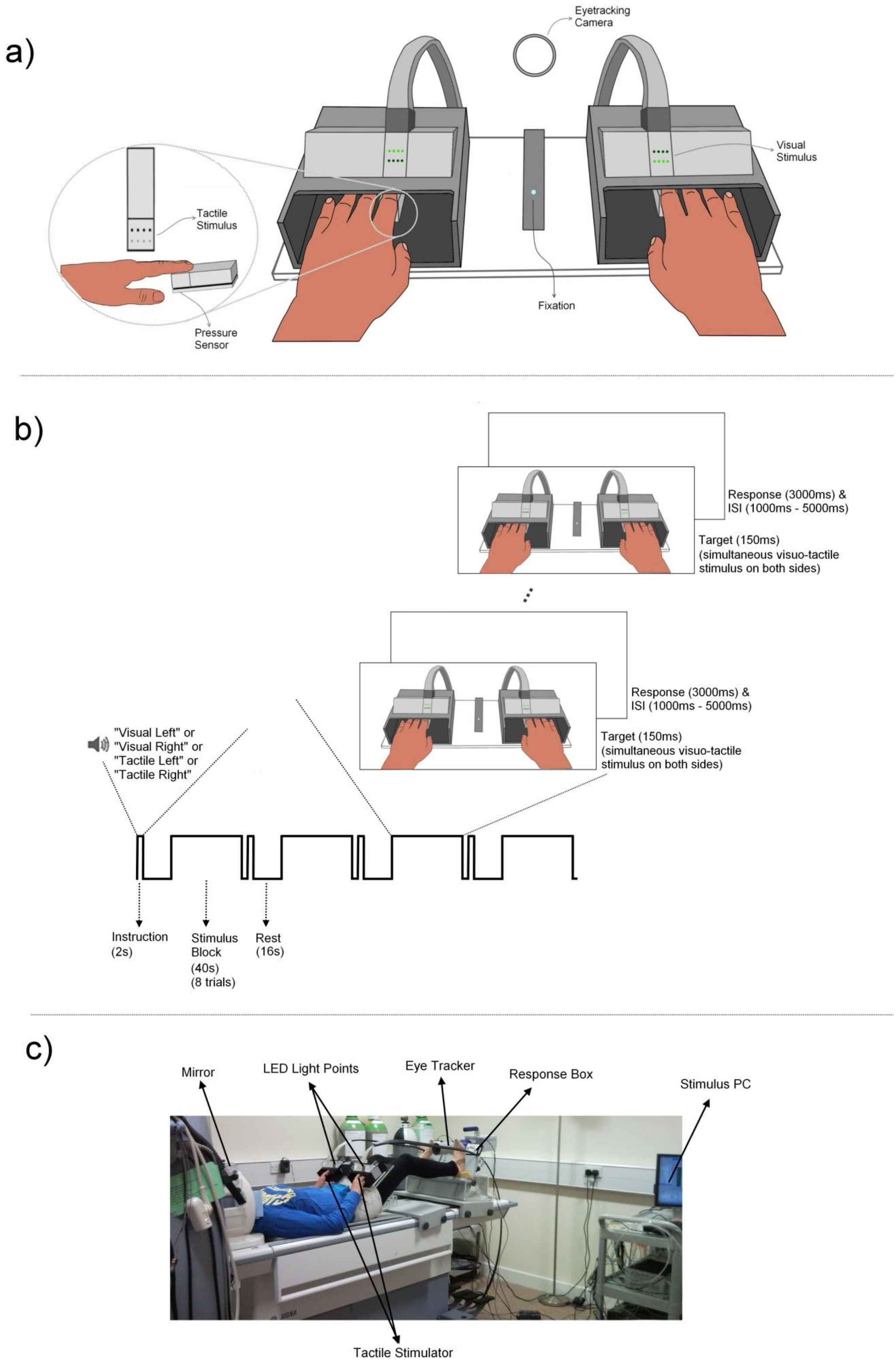


Figure 4.1. (a) Schematic illustration of the apparatus setup for the multisensory experiment, as seen from participant’s perspective while lying supine on the scanner bed (through a mirror positioned on

top of the head coil). The shape of visual stimulus presented in each hemifield resembled a stacked pair of horizontal lines, comprised of LED light points transmitted through a fibre optic cable onto a prism. The location of the brighter line (upper or lower position) was the target. Participant's index fingers were rested on top of Quaerosys^{TM} tactile stimulator, directly beneath the location of visual stimulus on each side. The shape of tactile stimulus was identical with the visual stimulus and the target was the location of the horizontal line with higher amplitude. In each trial, four targets were presented simultaneously in their respective modality and side. Remote eyetracker (SMI iView X™) were positioned at the end of the scanner bed for monitoring eye movements. The amount of downward pressure on the tactile stimulator was also monitored in real-time using an in-house built pressure sensor located beneath each stimulator. **(b)** The experimental design. In the beginning of each block, auditory instruction was delivered for 2s, cuing participant to sustain attention to one out of four possible combinations of modalities and hemifields. After 16s rest period, 8 trials were presented within each block. In each trial, simultaneous visuo-tactile stimulus were presented on both sides for 150ms. Participants were asked to report the location of the target (upper or lower location) in the attended modality and side within 3000ms response period. **(c)** Photo illustrating the actual experimental condition in the mock scanner.

4.2 Materials and Methods

4.2.1 Participants

Fourteen healthy right-handed participants (ages 19 - 32, mean 23, 9 females) with normal or corrected-to-normal vision were recruited for the study. Written informed consent was obtained in accordance to the approval of Ethics Committee of the School of Psychology, Cardiff University.

4.2.2 Apparatus

Tactile stimuli were delivered via two fMRI compatible piezoelectric tactile stimulator modules manufactured by Quaerosys^{TM} (Figure 4.1a), each positioned beneath participants' left and right index finger on either side of the sagittal midline. Each tactile module contained 20 pins (1mm pin diameter) arranged in 4 × 5 grid. Amplitude, frequency, and timing of these pins were controlled independently using MATLAB to produce various patterns needed for the experiment. Visual stimuli were presented using a custom-made fibre-optic visual presentation system (see Chapter 3 for details), which transmits a group of LED light points into two prisms. The prism was constructed in a similar configuration to the tactile stimulator module, consisting of a grid of 4 × 5 LED light points (Figure 4.1a). Control of LED patterns, intensity, and timing was accomplished through a digital microcontroller-based circuit, receiving commands from a PC running a custom MATLAB script.

Throughout the experiment, participant rested their hand inside a custom-built plastic box on the corresponding side, positioning their index finger on top of a tactile stimulator housed inside each box. A prism receiving fibre-optically transmitted LED lights was mounted on top of each box, directly on top of participant's index finger, so that visual and tactile stimuli were presented in a close spatial proximity to each other (similar to Macaluso et al., 2002, 2003; Spence et al., 2004). Both plastic boxes were held together by a transparent Perspex board, positioned above the participant's lap while lying supine on the scanner bed. A fibre-optic LED light point was positioned in the middle of the board, in between the left and right plastic box to serve as a central fixation (1^o below the location of the visual stimulus). In each trial, participant responded by pressing a button with their left or right toe. A custom-made supporting structure was mounted on the end of the scanner bed to hold Lumitouch^{TM} fMRI compatible response boxes directly beneath participant's feet.

A front-projection mirror was used to enable the participants to see both the LED lights and their hands without any image reversal. The mirror setup consisted of two mirrors angled at 45^o, mounted on top of the RF-coil directly above participant's eye. An MRI-compatible remote eye-tracking camera (SMI iView X™, SensoMotoric Instruments) was mounted on the far end of the scanner bed, in-between participants' feet, pointing directly towards the reflection of the right eye in the mirror. Horizontal eye movements, pupil diameter and blinks were recorded at a sampling rate of 60Hz. Downward pressure of the left and right index finger was also monitored using custom-made force transducers that were positioned underneath each tactile stimulator module. The sensor sent out an analog value of instantaneous pressure on both sides to a dedicated analog-to-digital circuit which then transmitted digital time series data at 100 Hz sampling rate to a MATLAB script.

4.2.3 Stimuli

On each trial, participants were presented with concurrent bimodal and bilateral visuo-tactile stimuli as illustrated in Figure 4.1a (four stimuli comprising four targets were simultaneously presented). The shape of the stimulus presented in each modality and each side resembles a stacked pair of horizontal lines. One line of this pair was always brighter (in the visual modality) or had higher elevation (in the tactile modality) then the other line. The location of this line was the target stimulus (upper or lower). Targets were always present in both modalities, at both sides. Participant was instructed to ignore all irrelevant targets and only report the location of the target in the attended modality on the attended side. The location of the targets was randomized so that every possible combinations of the target were presented with equal frequency and probability. There was no informative relationship between the location of the target in the visual and tactile modality, or the location of the target on the left and right side. Therefore, overall sensory input was held constant and only participants' attention was manipulated by instruction throughout the experiment. Both visual and tactile stimuli were presented briefly for 150ms with the same frequency of 3.3Hz. The stimulus was positioned on the peripheral visual field, 8^o horizontally from the central fixation point, and 1^o above fixation. The size of the visual stimulus was ~0.5^o (width) x ~0.4^o (height), and it was displayed in green colour.

4.2.4 Procedure

The multisensory spatial attention task followed a 2×2 factorial design, including factors of attended modality (touch or vision), and the location of covert spatial attention (left or right hemifield). The experiment was divided into blocks of 8 individual trials. In the beginning of each block, participants were cued via recorded auditory speech to attend to one modality and one hemifield only and to maintain sustained attention to that condition throughout entire block (Figure 4.1b). A 16s rest period was included between the end of the block instruction and the onset of the first trial of each block. The interval between trial onsets was fixed at 4s. Two null events (empty trials) lasting for 4s each were randomly interspersed within each block.

Each trial began with the presentation of concurrent bimodal and bilateral targets (150ms). Participants were instructed to identify the location of the target (upper or lower) within the instructed modality and location, and then respond accordingly using their left or right foot. In this task, we employed a non-speeded variant of the orthogonal cueing paradigm (Spence and Driver, 1994, 1998). We asked the participant to judge the elevation of the target (upper or lower) which was orthogonal to the attended location (left or right), avoiding possible confounds of automatic motor priming of the response. Following target presentation, participants were permitted up to 3s to respond in a non-speeded manner. In the first half of the experiment, participants were told to assign the left foot response with the upper target and the right foot response with the lower target. This instruction was reversed in the second half of the experiment to avoid confounding influences of the motor responses for the MVPA analysis.

Before the scanning, participants were trained to practice the multisensory attention task in a mock scanner for two sessions (2 hours each) using the same apparatus setup used during actual scanning. Performance was calibrated individually to 80% correct, with task difficulty adjusted throughout the training by increasing or decreasing the contrast difference between the target and the baseline within each modality. EPI volumes of the main task were collected in a single 2-hour scanning session, consisting of 8 experimental runs, 8 blocks per run (64 trials), and a total of 512 trials. A separate scanning session was undertaken to acquire a high-resolution whole-brain anatomical scan, two runs of an index-finger somatotopy localizer (300s each), and two runs of retinotopic mapping scans (300s each).

4.2.5 MRI Data Acquisition

Imaging data were acquired with a General Electric 3T scanner at the Cardiff University Brain Research Imaging Centre (CUBRIC). Functional images for the main task were obtained using a T2-weighted echo-planar imaging (EPI) pulse sequence, with a repetition time (TR) of 3000ms, echo time (TE) of 35ms, flip angle of 90^o, matrix size of 64 × 64, 46 contiguous slices, and a voxel resolution of 3.2 × 3.2 × 3.2 mm. Each experimental run was acquired with 160 volumes and lasted for 8 min. Whole brain structural images were acquired using T1-weighted images with 1 × 1 × 1 mm voxel resolution, repetition time (TR) of 8ms, echo time (TE) of 3ms, flip angle of 20^o, matrix size of 256 × 256, and 172 slices. Functional images for the retinotopic mapping analysis were obtained using a T2-weighted EPI pulse sequence, with a TR of 3000ms, TE of 35ms, flip angle of 90^o, matrix size of 128 × 128, 37 slices, and a voxel resolution of 2 × 2 × 2 mm. Two runs of retinotopic data were acquired, each consisting of 100 volumes, lasting 5 min. Images for the index-finger somatotopy localizer were obtained using a T2-weighted EPI pulse sequence, with a TR of 3000ms, TE of 35ms, flip angle of 90^o, matrix size of 64 × 64, 46 contiguous slices, and an isotropic voxel resolution of 3.2 mm. Two runs were obtained for the localizer, consisting of 100 volumes each.

4.2.6 Retinotopic Mapping

Standard retinotopic mapping procedure was used to define the borders of lower visual areas in the occipital cortex. Participants were scanned while viewing a rotating stimulus with different visual angles and eccentricities that allows responses at different retinotopic locations to be mapped. This map was then projected on a flattened representation of the visual cortex and the boundaries between visual regions were identified (Sereno et al., 1995; DeYoe et al., 1996).

The stimuli used for retinotopic mapping comprised of small yellow dots moving in a 3D flow pattern, subtending a 70^o wedge. The wedge was rotating around the fixation point with a period of one rotation per minute (1 rpm) for five minutes. Two runs were obtained in the scanning session, the first run with a wedge rotating in clockwise direction and the second run in anticlockwise direction. Analysis of retinotopic data was performed using an in-house software (developed by Krish Singh) that computed phase angle estimates (Φ) with correction for haemodynamic lag for each voxel and estimated the strength of retinotopy (r) using the power of the variance in the time-series at 1 rpm frequency. The phase angles were plotted as a coloured map on the flattened occipital cortex using mri3dX software (http://www.cubric.cf.ac.uk/Documentation/mri3dX/). Regions of interests (ROIs) representing visual area V1, V2, V3, V4, V5, V7, and V8 were defined from these maps.

4.2.7 Eye Tracking and Finger Pressure Analysis

Throughout the scanning, horizontal positions of the eye, pupil diameter, and pressure data for both index fingers were recorded. These time series were averaged within the time window of 100ms prior to the trial onset and 500ms after the onset, yielding four measurements (a four-dimensional vector) for each trial. To examine whether there was any differences in the pattern of eye fixations and finger pressures in each attention condition, we analysed the data using the same linear-SVM classification algorithm that was used to analyse the fMRI data. Specifically, we ran a leave-one-run-out cross-validation test, in which we trained the classifier to distinguish the attended modality (irrespective of attended side) using the eye and pressure data from 7 runs and then tested the classifier using the remaining run. The classification procedure was repeated 8 times, each with different set of training and testing runs. Classifier accuracy across 8 testing runs was averaged to produce a single classification performance for each subject.

4.2.8 fMRI Data Analysis

Stage 1: ROI analysis of sensory cortices

To investigate top-down modulatory effect of multisensory attention on respective sensory regions, we conducted a ROI-based analysis (Poldrack, 2007) using retinotopically defined visual ROIs and functionally defined primary somatosensory ROIs. We used all EPI data from all runs, and calculated mean activity in each ROI individually for each subject. The EPI volumes were initially realigned to correct for head movements artefacts, and then smoothed using 8mm isotropic Gaussian kernel. Afterwards, a high-pass filter at 128s was applied to remove slow drifts in the time series. Using SPM8, we first estimated two beta-contrasts for two attentional conditions, attention to vision and attention to touch, collapsed across attended sides. Mean activation for each ROI and condition was then calculated using a custom MATLAB script, by averaging beta-contrast value of that condition for all voxels in that ROI, producing single value for each ROI and subject. The result was then summarized on a group-level by averaging the mean activity of each ROI across all subjects, yielding a single activation value for each ROI and attentional condition.

Stage 2: univariate conjunction analysis

We conducted a GLM conjunction analysis to examine commonly activated voxels in the visual and tactile attention conditions. Neuroimaging data were analysed using SPM8 (Friston et al., 1995b, 2006). Before the analysis, all EPI runs were first realigned to correct for head movements. In this analysis, we used EPI data from all odd numbered runs (the first data set), and reserved all even numbered runs (the second data set) for subsequent ROI-based MVPA analysis. Independent datasets were used to avoid circularity that could bias the analysis results (Kriegeskorte et al., 2009).

The first dataset was spatially smoothed with an 8mm isotropic full-width half-maximum Gaussian kernel. A high-pass filter at 128s was then applied to the dataset together with pre-whitening by AR(1) autoregressive model. Analysis was performed in individual native space (first level analysis) to find whole-brain activations correlated with each attentional condition. Four regressors corresponding to each attention condition (visual-left, visual-right, tactile-left, and tactile-right) were modelled by convolving a canonical hemodynamic response function with box-car models that represent the onset and duration of individual sustained attention blocks. The contrast of interest in this analysis was conjunction between the visual attention condition and tactile attention condition in the respective location: (visual-left AND tactile-left) and (visual-right AND tactile-right). GLM conjunction analysis with the global-null hypothesis (Friston et al., 2005) was computed on the whole-brain volume to produce the contrasts ($p < 0.001$, uncorrected). These conjunction maps were then converted into a binary mask to produce ROIs for ROI-based MVPA analysis described in the 3rd analysis.

Whole-brain statistical maps shown in Figure 4.4a and 4.4c were produced using similar steps of analysis described above. Individual structural images were co-registered with the EPI volumes and normalized into SPM-MNI coordinates. The normalization was then applied to all EPI volumes in the first dataset. After smoothing, high-pass filtering and modelling of the four regressors, first level GLM analysis was performed to produce four contrasts ([visual-left], [tactile-left], [visual-right], [tactile-right]) for each subject ($p < 0.001$, uncorrected). The resulting contrasts of all participants were entered into a second-level random effects analysis for computing conjunction between [visual-left AND tactile-left] contrast and [visual-right and tactile-right] contrast (threshold set at $p < 0.05$, FDR).

Stage 3: ROI-based MVPA analysis

The second dataset, consisting of EPI data from all even numbered runs, was subjected to multivoxel pattern analysis (MVPA) to test whether groups of commonly activated voxels found in the previous analysis contained distributed information that could distinguish currently attended modality. For each participant, whole-brain conjunction map ROI obtained from the previous analysis were parcellated into different sections according to their individual brain's anatomical structures, resulting in several ROIs corresponding to different brain regions. We used Mindboggle software (Klein et al., 2005) for parcellating and labelling brain structural volumes into commonly recognized regions.

Multivariate pattern classification of the second dataset was undertaken using the Princeton MVPA Toolbox for MATLAB (Detre et al., 2006) and a linear support vector machine (SVM) as the learning algorithm (Cortes and Vapnik, 1995). Pattern analysis was performed in individual native space using raw, unsmoothed EPI data. MVPA for each participant and each ROI was conducted in several steps: First, raw EPI data of the second dataset were loaded together with the ROI mask (voxels outside the mask were discarded). Second, the BOLD time series was normalized using a z-score transform. Third, a binary regressor matrix specifying task condition blocks (visual or tactile) was loaded as category labels for each sample volume. The regressor was shifted by 6 seconds (2 TRs) to account for haemodynamic lag in the BOLD signal. Fourth, cross-validation indices were prepared for a leave-one-run-out training procedure. In this procedure, N-1 runs were used to train the classifier and the last remaining independent run was used for the testing set. Each different run was used in turn as a testing set, so with N runs the classifier was tested and trained exactly N times. Fifth, classification accuracy was computed as the average of N times of training and testing in the cross-validation procedure. Sixth, group-level classification accuracy was then computed by averaging classification result of all participants for each ROI. Finally, to assess statistical significance of the classification result, we undertook nonparametric permutation testing to estimate the null distribution (Golland and Fischl, 2003; Pereira and Botvinick, 2011). The category labels within each training set were randomly permuted 1000 times, and for each random permutation cross-validation classification was conducted, resulting in 1000 samples of accuracy under the null-hypothesis (null-samples) for each subject. On a group-level, mean classification accuracy under the null-hypothesis was computed by randomly selecting one sample from the null-samples of each subject, and then averaged the accuracy values across all subjects. This was repeated 100,000 times and the final group-level p-value for each ROI was estimated by computing the proportion of these random mean classification accuracies that were greater than or equal to the actual mean classification accuracy (i.e. p = [# of random mean classification accuracies >= actual mean classification accuracy] / 100,000).

Stage 4: whole-brain MVPA searchlight analysis

Searchlight analysis was conducted using Princeton MVPA Toolbox for MATLAB (Detre et al., 2006) with linear-SVM (Cortes and Vapnik, 1995) as the learning algorithm. Before analysis, the EPI images were motion corrected and normalized using a z-score transformation. Raw, unsmoothed EPI volumes from all experimental runs were used in this analysis. We next prepared a binary regressors matrix specifying which experimental condition was represented by each sample volume, and the regressors was then shifted by 2 TRs (6s) to account for haemodynamic lag in the BOLD signals. Sample volumes from 8 trials within each experimental block were then averaged in order to increase statistical power for classification (Preston and Eckstein, 2010; Etzel et al., 2011).

To extract local activity pattern, we moved a 3D spherical searchlight of 8mm radius through the whole brain volume, centred on each voxel in turn. Classification accuracy at each voxel was then computed by running a statistical classifier using signals from all voxels within the searchlight volume. Eightfold cross-validation with leave-one-run-out procedure was performed for each searchlight sphere, resulting in a map representing how well local multivariate signals on each voxel can discriminate the experimental conditions. The searchlight map was initially obtained for each subject in their individual brain space and then combined on a group-level by normalizing each map into standard MNI template and averaging the classification accuracy values at each voxel across all subjects. Statistical significance map was then produced for the group-level map using random-effect analysis by computing an independent one-sample t-test against chance (Haynes et al., 2007; Soon et al., 2008; Stokes et al., 2009a). Accuracy maps of voxels that survived correction for multiple comparisons were superimposed on a normal brain template and visualized as the final result of the analysis.

4.3 Results

4.3.1 Behavioural Results

Before the scanning, participants were trained in the mock scanner to perform the task at about 80% correct accuracy level in all attended modalities and sides. Average behavioural performance of each attentional condition during the scanning was shown in Figure 4.2. Mean accuracy across all conditions and participants was 78% (+/- 0.07 SE).

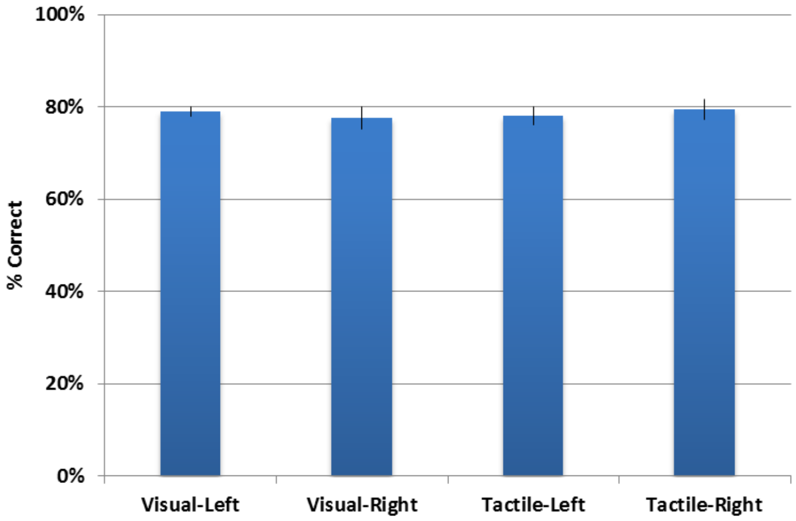


Figure 4.2. Average behavioural performance for each attentional condition. There were no significant differences of task performance across attended modalities and sides.

4.3.2 Effects of Modality Specific Sustained Attention

Previous neuroimaging studies of multimodal attention have shown that focusing attention to a particular sensory modality enhanced neural activity in the sensory cortex associated with the attended modality while at the same time suppressed neural activations in the sensory regions associated with the ignored modality (Macaluso and Driver, 2001; Mozolic et al., 2008b; Fairhall and Macaluso, 2009). To replicate this finding and verify the validity of the attention task, we conducted ROI-analysis in the visual and somatosensory cortical regions, comparing the BOLD response induced by sustained attention to vision with the response induced by sustained attention to touch, irrespective of attended side. The ROIs were independently identified using a retinotopic mapping procedure and a tactile functional localizer. As expected, significant increase in neural activations was observed in the extrastriate visual cortex (V3A, V4, V5, V8) during sustained visual attention, whereas activity in the same regions was suppressed when attention was sustained towards the tactile modality (Figure 4.3a). On the other hand, enhanced neural activations was observed in bilateral finger somatotopy region in SI when attention was directed to touch compared to when attention was directed to vision (Figure 4.3b).

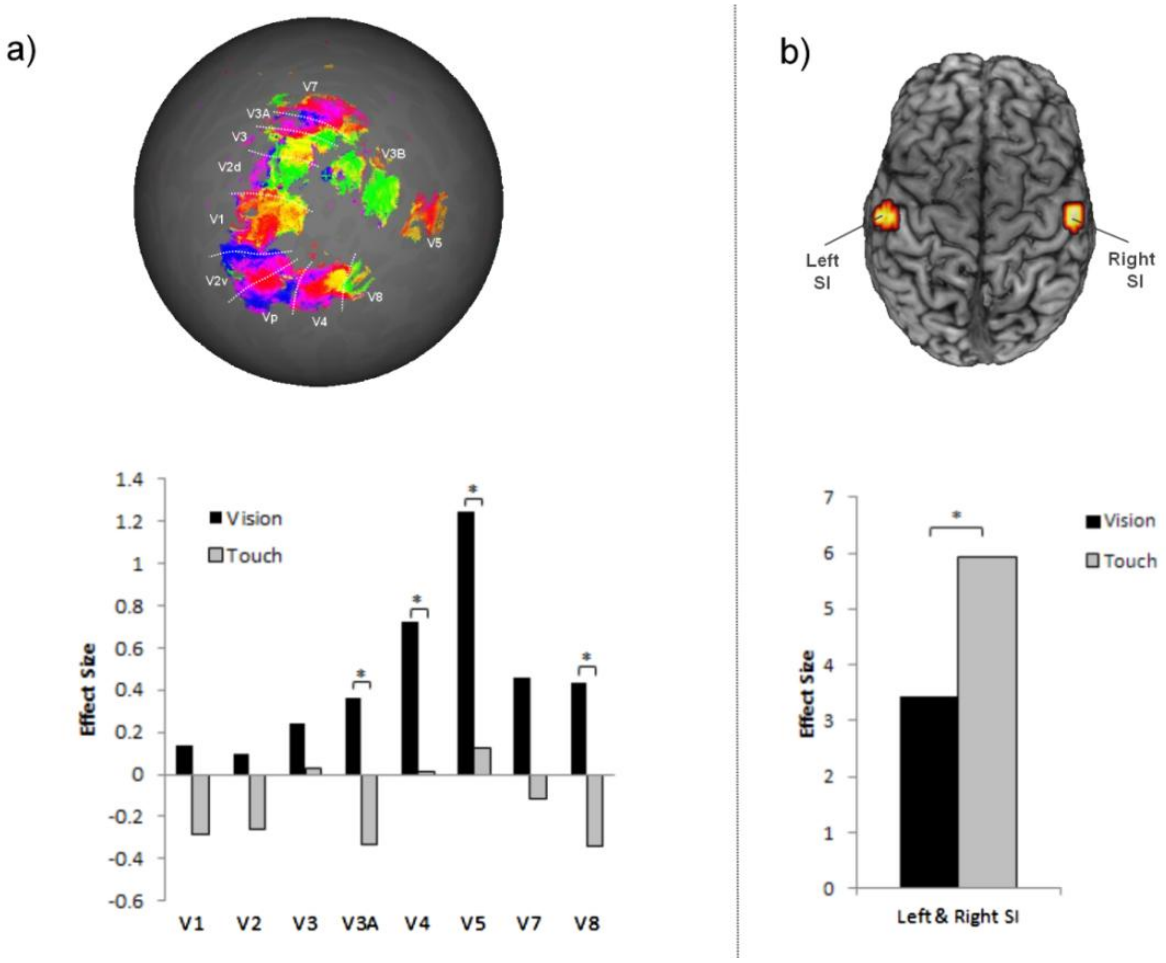
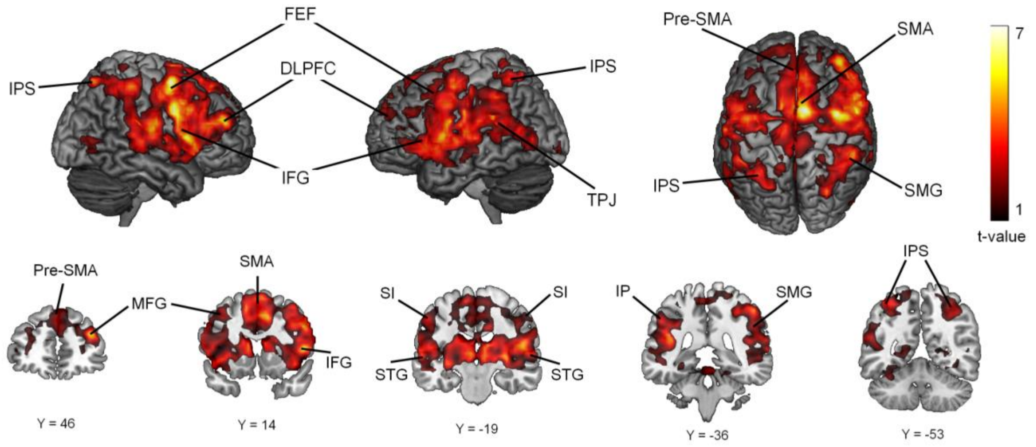


Figure 4.3. (a) BOLD response induced in retinotopically defined visual regions while attending to visual and tactile stimuli, collapsed across attended hemifield and brain hemisphere. In all visual regions, activations were higher when attention was direction to vision than to touch and the difference was significant ($p < 0.05$) in several extrastriate regions (V3A, V4, V5, V8). **(b)** In contrast, BOLD response induced in bilateral SI region defined by finger somatotopy functional localizer revealed stronger activations when attention was directed to touch than to vision ($p = 0.04$).

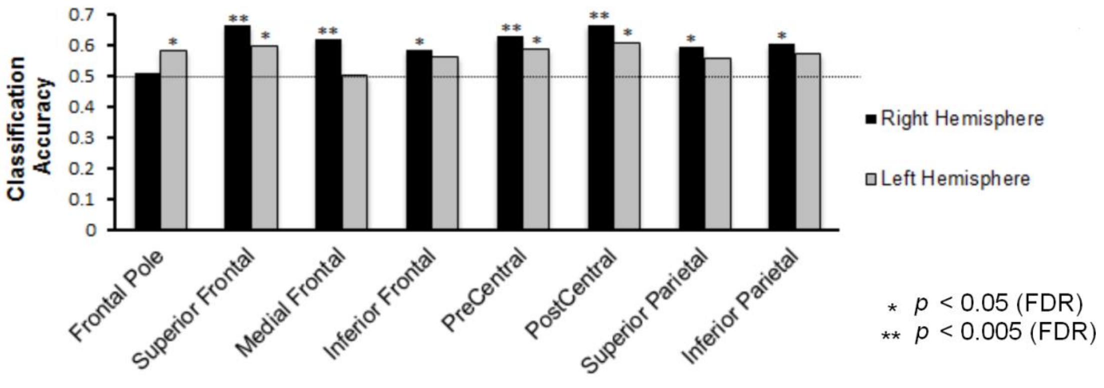
4.3.3 Whole-Brain Univariate Conjunction analysis

To visualize voxels that were commonly activated during both sustained attention to vision and touch, we conducted a conjunction analysis at a group level over two orthogonal contrasts using SPMs (Friston et al., 2005), and the null distribution was computed based on two statistics. During sustained attention on the left hemifield, conjunction analysis revealed widespread bilateral activations in the frontal (FEF, IFG) and parietal regions (IPS, SMG) common to both visual and tactile attention condition (Figure 4.4a), in agreement with previously reported overlapping regions found in other multimodal attention studies in vision and touch (Macaluso and Driver, 2005; Driver and Noesselt, 2008; Macaluso, 2010). Significant activations were also observed in the supplementary motor area (SMA, pre-SMA), indicating motor demands associated with the attention task. Comparatively weaker but similar pattern of activations was observed when attention was directed towards stimulus on the right hemifield (Figure 4.4c).

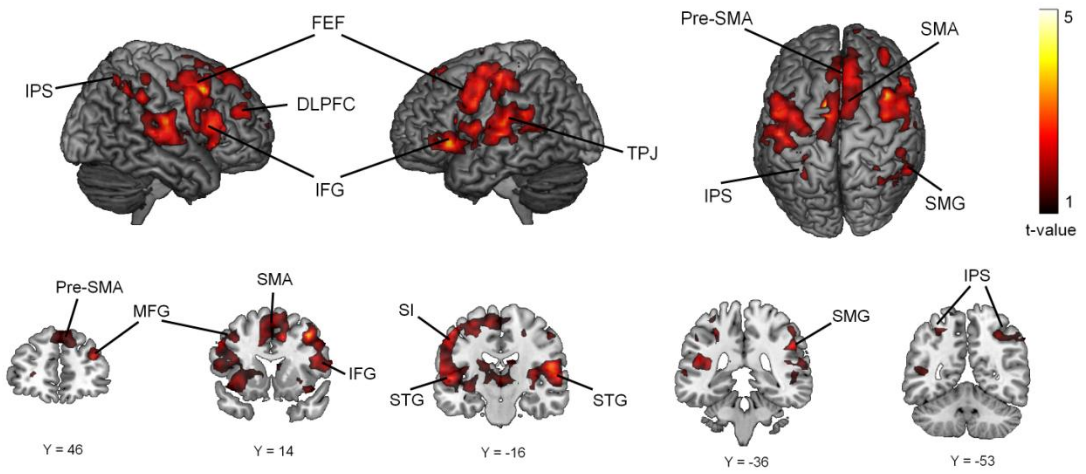
a) Univariate Conjunction of Attend Visual-Left and Attend Tactile-Left



b) MVPA Decoding of Visual-Left vs. Tactile-Left Within Overlapping ROIs



c) Univariate Conjunction of Attend Visual-Right and Attend Tactile-Right



d) MVPA Decoding of Visual-Right vs. Tactile-Right Within Overlapping ROIs

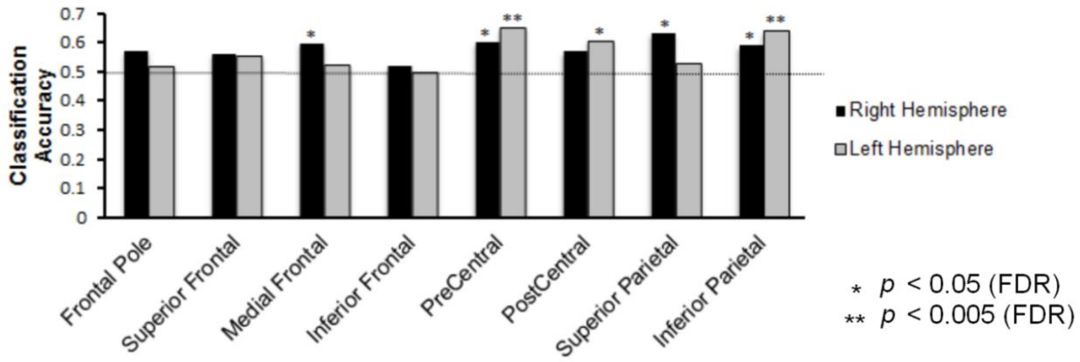


Figure 4.4. (a) Activation maps obtained from group univariate conjunction analysis of attend left-visual contrast and attend left-tactile contrast. Above baseline activations spread across bilateral frontal-parietal network commonly associated with deployment of attention (DLPFC, FEF, IFG, IPS, SMG) as well as motor and premotor regions (SMA and pre-SMA). Maps were corrected for multiple comparisons with $p < 0.05$, FDR. **(b)** Average classification accuracy for decoding currently attended modality in functionally defined ROIs obtained from conjunction analysis on attend-left conditions. Significantly above chance discrimination (>0.5) were observed in several frontal-parietal ROIs, indicating that these overlapping regions contained distributed information of attended modality. **(c)** Activation maps obtained from group univariate conjunction analysis of attend right-visual contrast and attend right-tactile contrast (corrected for multiple comparisons with $p < 0.05$, FDR). Similar but slightly weaker activations were observed in bilateral frontal-parietal regions as well as premotor regions. **(d)** Average classification accuracy for decoding currently attended modality in functionally defined ROIs obtained from conjunction analysis on attend-right conditions.

4.3.4 ROI-based MVPA analysis

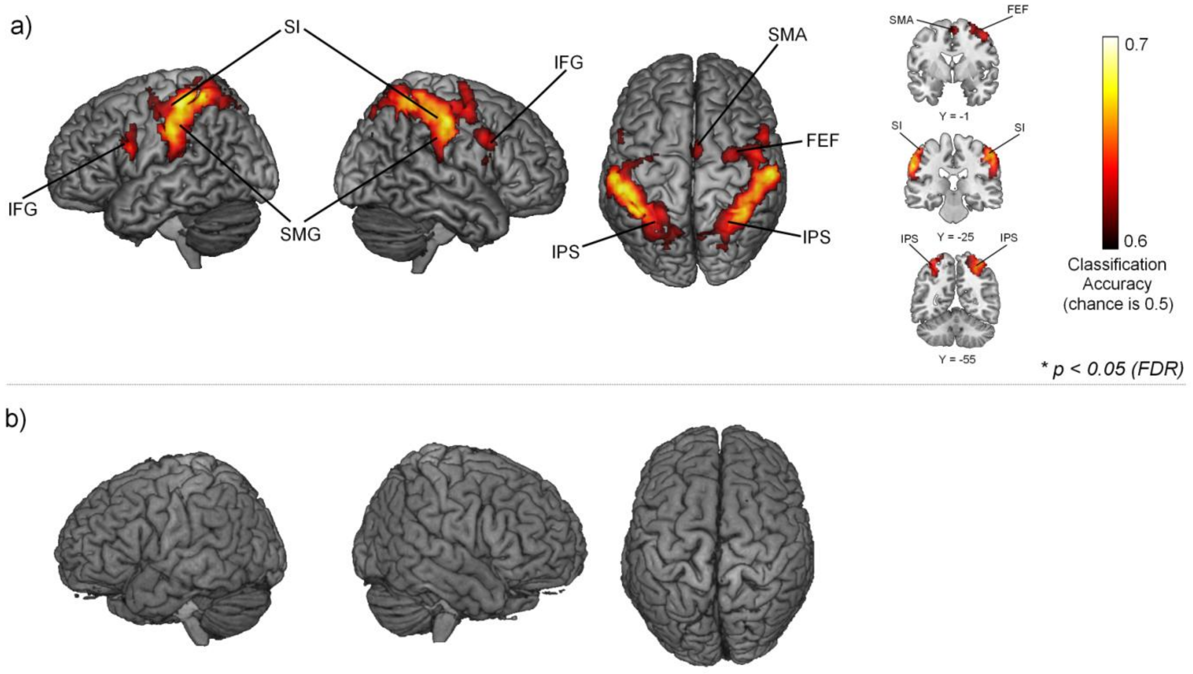
We tested the supramodal region hypothesis by applying region of interests (ROIs) pattern classification analysis (Etzel et al., 2009) on the overlapping brain regions found by univariate conjunction analysis. Functionally-defined ROIs were obtained by running single-subject conjunction analysis on the first half of the data set (odd runs) over two orthogonal contrasts (vision and touch on respective side) for each subject. The resulting conjunction map was then thresholded ($p < 0.001$, uncorrected) and parcellated into several ROIs based on their anatomical locations. Classification analysis was undertaken on these ROIs using independent second half of the data set (even runs) to prevent selection bias (Kriegeskorte et al., 2009) (see Section 2.2 for more details of the MVPA classification methods).

The result of MVPA classification of attend-left condition was shown in Figure 4.4b. Significantly above chance (>0.5) classification accuracy was observed in several overlapping ROIs in frontal and parietal areas (right superior-frontal: 0.66, $p = 0.0001$; right medial-frontal: 0.62, $p = 0.0056$; right inferior-frontal: 0.58, $p = 0.0367$; right pre-central: 0.63, $p = 0.0013$; right post-central: 0.66, $p = 0.0001$; right superior-parietal: 0.59, $p = 0.0341$; right inferior-parietal: 0.60, $p = 0.0137$; left superior-frontal: 0.60, $p = 0.0181$; left pre-central:0.59, $p = 0.0288$; left post-central: 0.61, $p = 0.014$). In attend-right condition (Figure 4.4d), similar classification performance was observed, although there was fewer significantly above chance classification in the frontal areas (right medial-frontal: 0.60, p = 0.026; right pre-central: 0.60, p = 0.0151; right superior-parietal: 0.63, p = 0.0146; right inferior-parietal: 0.59, p = 0.031; left pre-central: 0.65, p = 0.0009; left post-central: 0.61, p = 0.0165; left inferior-parietal: 0.64, p = 0.0021). This result indicates that although all of these regions were activated in both attention to vision and touch, nevertheless they contain unique population coding that reliably distinguished currently attention modality.

4.3.5 MVPA Searchlight Analysis

In this exploratory analysis, we aimed to investigate generality and specificity of information about attended modality and attended location that might exist in various cortical regions. For this purpose, we analysed the EPI data in three separate MVPA searchlight analysis (Kriegeskorte et al., 2006). In the first analysis, we asked a question of whether any brain regions contained distributed patterns of activity that could distinguish attended modality (visual vs. tactile) irrespective of currently attended sides (i.e. modality specific but location-nonspecific information). To test this relationship, we conducted a cross-generalization procedure (Stokes et al., 2009a) by training a searchlight classifier to discriminate patterns of activity elicited by attention to vision and touch in one location (i.e. left side) and then tested whether this classifier could predict attended modality from patterns of activity during attention to the opposite location (i.e. right side). This procedure was repeated for the second time, so that both attended location was used as the training and testing data in turn, and the results was then averaged to produce the final result.

Group-level classification accuracy map was overlaid on the surface of the normal brain and visualized in Figure 4.5a. Only voxels that survived corrections for multiple comparisons ($p < 0.05$, FDR) and having cross-generalization accuracy higher than 60% were reported in this result. The informative cortical regions containing modality-specific but location-nonspecific activity was found to span across the known dorsal-ventral frontoparietal network (Corbetta et al., 2008). In the dorsal frontal region, significant information was found near the right FEF, a region important for saccadic eye movements (Berman et al., 1999; Corbetta et al., 1998a; Amiez and Petrides, 2009). We also observed modality specific information in bilateral prefrontal cortex near the region commonly classified as IFG. In the parietal cortex, large clusters of informative voxels were found around the IPS extending to the SMG of both hemispheres.



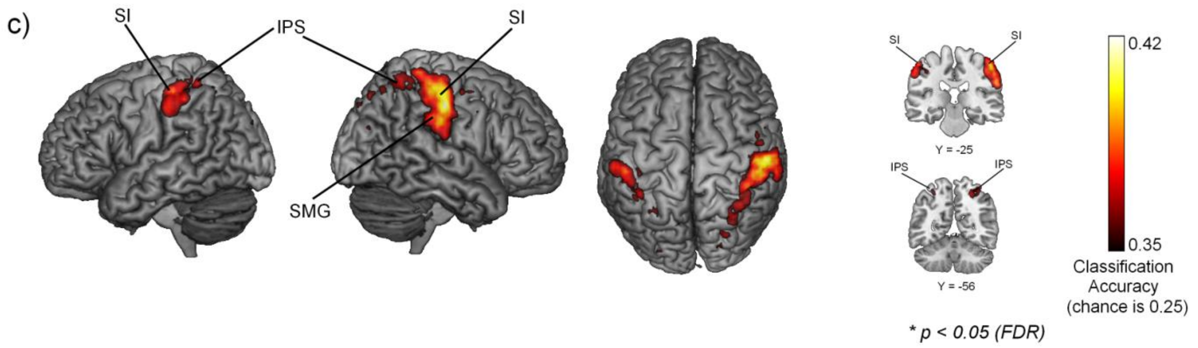


Figure 4.5. (a) Whole brain maps of modality-specific but location-nonspecific information identified by cross-generalization searchlight analysis, overlaid on the MNI template brain. Clusters of significant information were found primarily along the parietal cortex, on both hemispheres, with peaks in the IPS and SMG. Only small clusters of activity were observed in the frontal regions, including areas in the IFG and right FEF. Classification accuracy maps are shown for voxels that survived correction for multiple comparisons ($p < 0.05$, *FDR*) and having accuracy greater than 0.6. **(b)** No statistically significant voxel that contains location-specific but modality-nonspecific information was found (after corrections for multiple comparisons, $p < 0.05$, FDR) **(c)** Results of searchlight analysis classifying four main attentional conditions. Peak of significant information were found in the right SI and the right SMG, extending posteriorly to the IPS. The maps were corrected for multiple comparisons ($p < 0.05$, *FDR*).

We next inquired about cortical regions that contained information about attended locations (left vs. right) regardless of attended modality (i.e. location specific but modality-nonspecific) by running cross-generalization procedure with a searchlight classifier trained to distinguish location in one modality (i.e. visual) and then tested in the other modality (i.e. tactile). Similar with previous analysis, we performed the analysis twice with different order of modalities for training and testing the classifier, and then averaged the classification result. Interestingly, this time we did not find any significant regions with common population codes for attended location across modalities (Figure 4.5b), suggesting the possibility that information about attended location was unique between different modality or it might be the case that regions that contained location information was different between attention to vision and touch. To test this hypothesis further, we ran another searchlight analysis classifying attended location within each modality (see Appendix A, Figure A.4). Close to significant informative regions were found around postcentral gyrus, bordering anterior parietal cortex for the tactile condition, whereas during visual condition we found location specific regions distributed throughout the occipital lobe, slightly extending to the posterior parietal cortex. This result revealed that location specific information during spatial attention task was present primarily in the respective sensory cortical regions and not in the frontal-parietal regions, suggesting the effect of top-down modulatory activity in these sensory regions. Nevertheless, this does not rule out the possibility that neuronal populations in the fronto-parietal regions might actually contain information about currently attended location but our experimental and analysis method were not sensitive enough to pick up these faint patterns of activity.

Lastly, we conducted another MVPA searchlight analysis to map brain regions that could distinguish four different attentional conditions (attend visual-left, visual-right, tactile-left, and tactile-right), looking for pattern of information that was modality specific and location specific (Figure 4.5c). Peak of significant information was found around primary somatosensory cortex (SI) of the right hemisphere, extending to right SII and right SMG. Lesser degree of activation was also observed in the left SI and around IPS of both hemispheres.

4.3.6 Eyetracking and Pressure Sensor Data Analysis

During the experiment, horizontal eye positions, pupil diameter, and downward pressures of both index fingers were recorded in real time. These data were then analysed using linear-SVM algorithm, the same statistical classifier used in the MVPA analysis of the neuroimaging data. Specifically, we examined whether attended modality could be decoded from multivariate patterns of eye movements and downward pressures. The results of the analysis revealed that there were no significant differences in the patterns of eye movements and downward pressures that could be used to distinguish attended modality (Figure 4.6).

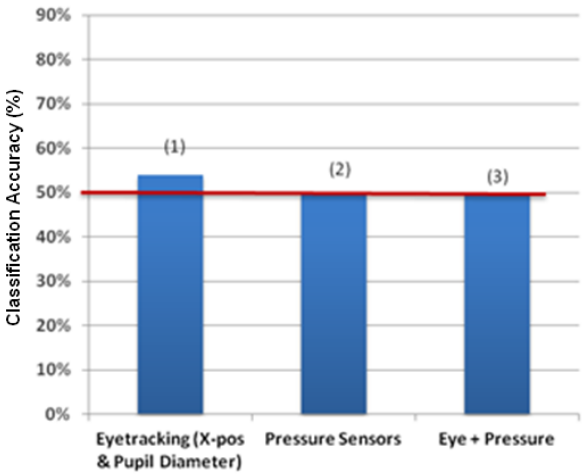


Figure 4.6. Results of linear-SVM classification of the currently attended modality using multivariate data comprising of (1) eye tracking data (horizontal positions and pupil diameters), (2) pressure

sensors data of both left and right index finger, and (3) horizontal eye positions, pupil diameters and pressure sensors data of both left and right index fingers. No significantly above chance classification was observed (permutation tests: 1: $p = 0.099$, 2: $p = 0.95$, 3: $p = 0.7$).

4.4 Discussion

The aim of the present study was to investigate the role of dorsal and ventral frontoparietal networks in controlling endogenous spatial attention in visual and touch. Specifically, we asked whether these top-down sources of attentional modulation were supramodal or modality-specific by applying multivoxel pattern analysis (MVPA) techniques to find modality specific information within these regions. Overall, the results support the view that spatial attention is coordinated by integrated, modality-specific processes rather than a supramodal network.

Previous neuroimaging studies of visuo-tactile spatial attention using PET (Macaluso et al., 2002a) and fMRI (Macaluso and Driver, 2001; Macaluso et al., 2003b) have discovered that directing endogenous spatial attention to both modalities activated similar frontoparietal regions, leading these researchers to propose the existence of '*supramodal*' network for controlling attention in multiple modalities (Farah et al., 1989; Macaluso and Driver, 2001; Macaluso, 2010). Additional evidence for the recruitment of similar frontoparietal networks was also reported in several studies involving voluntary shifts of attention within the visual and auditory modalities (Shomstein and Yantis, 2004; Smith et al., 2010). Although influential, interpreting overlapping activations as supramodal regions is logically challenging, partly due to limited spatial and temporal resolution of the neuroimaging techniques. It is possible, if not probable, that commonly activated voxels contain anatomically distinct and topographically arranged neuronal populations that codes for specific modalities (Klemen and Chambers, 2012). Another concern is that, like all neuroimaging methods, fMRI can only reveal correlational relationships between brain activity and behaviour. Thus, activation of a certain region in all task conditions does not imply that the region is *necessary* for all conditions (Chambers et al., 2004b).

The behavioural paradigm used in this study was similar to the task adopted in Macaluso et al. (2002a). Participants were instructed to sustain covert attention to one sensory modality and one hemifield only. On each trial, bimodal and bilateral targets were presented concurrently and the participants had to discriminate the location of the target presented in the attended modality and on the attended side, while ignoring all distractors presented in the unattended modality and on the unattended side. Orthogonal targets (i.e. judging upper vs. lower elevation rather than left vs. right side) were used to avoid automatic priming of the motor responses (Spence and Driver, 1994, 1998).

We tested the existence of a supramodal attention network by applying an MVPA classifier to decode the attended modality from distributed patterns of activity in frontoparietal cortex. We reasoned that if a region is truly supramodal, the classifier should not be able to distinguish distinct patterns of activity that code for different attentional conditions. Overall, our results indicated that although spatial attention to vision and touch elicited widespread common activations in frontoparietal areas, most of these overlapping regions actually contained modality-specific information.

Furthermore, the supramodal hypothesis also proposes that dorsal fronto parietal (dFP) networks biased currently attended spatial locations in a modality-independent manner (Macaluso, 2010), which would imply the existence of common population coding for attended locations across modalities. To test this hypothesis, we also performed exploratory searchlight analyses searching for informative regions that code for attended modality and/or attended location. We looked for common encoding of attended location irrespective of the attended modality (i.e. location-specific but modality-nonspecific information) by training a statistical model to discriminate the attended location within one modality and then testing whether this model could predict the attended location in the other modality. No statistically significant voxels were found in this analysis, reflecting the likelihood that information about attended location is essentially encoded in a modality-specific manner.

To confirm this result, we ran another searchlight analysis decoding all 4 attentional conditions to find both modality-specific and location-specific information in the brain. Significant information was found in the IPS and SMG, suggesting the existence of population coding that is sensitive to attended modality and topographic location at the same time within the posterior parietal cortex. Finally, we also conducted another searchlight analysis to test whether modality-specific encoding was commonly shared across attended locations (i.e. modality-specific but location-nonspecific information), and found informative voxels across the frontoparietal regions, including the IPS, SMG, and IFG.

4.4.1 Intermodal Top-Down Modulatory Effect of Spatial Attention on Visual and Somatosensory Cortex

Recent neuroimaging studies have demonstrated that attention to sensory modalities can influence not only higher-level multimodal regions but can also selectively modulate activities in the lower level ‘unisensory’ regions (Macaluso, 2006; Driver and Noesselt, 2008). Selective modulations on sensory cortices have been shown during intermodal attention using bimodal stimuli presentation (Roland, 1982; Macaluso et al., 2002a; Shomstein and Yantis, 2004; Saupe et al., 2009) as well as in the preparatory baseline activity after presentation of attentional cue to a particular modality, in the absence of actual target presentation (Langner et al., 2011). In general, these studies found that directing attention to a particular sensory modality could selectively enhance activity in the sensory cortex of the attended modality while simultaneously suppressing activity in the sensory regions that process stimuli from the unattended modalities. In this study, we replicated this finding of intermodal selective modulations in visual and somatosensory cortices (described in Section 4.3.2) and thus verified that the multisensory attention task used in this experiment could selectively modulate sensory regions. Critically, our findings could neither be explained by variations in the sensory inputs nor difference in motor responses. Overall, the stimuli presented on each trial were identical, with the exception of slight contrast differences signifying target locations. The locations of the targets were randomized and equally balanced throughout all attentional conditions so that overall inputs and motor outputs within each condition were matched. Other possible confounding factors such as potential eye movements, variation in pupil size, or variable amount of finger pressure during the task (discussed in Section 4.3.6) were also ruled out as the potential explanation for modality specific modulations.

The results of our study showed that intermodal attention can selectively modulate neural activity in both visual and somatosensory cortex, irrespective of attended sides. Sustained covert attention to visual events strongly up-regulated responses of both striate and extrastriate cortex, while directing attention to tactile events suppressed the activity in all visual regions, consistent with previous multimodal attention studies (Macaluso et al., 2002a; Shomstein and Yantis, 2004; Langner et al., 2011). When visual modality was attended, we observed much smaller signal amplification in the early visual areas (V1 - V3) compared to the late visual areas (V3A, V4, V5, V7, V8). This gradual decrease in attentional modulation down the hierarchy of visual regions might be caused by gradually diminishing feedback from parietal to visual cortex (Liu et al., 2005). Larger attentional modulations in the higher visual regions have also been reported in sustained attention studies in vision (Tootell et al., 1998; Kastner et al., 1999; Maunsell and Cook, 2002) as well as in studies using cued trials (Liu et al., 2005). On the other hand, most of the visual regions were deactivated during attention to tactile targets, implying inhibitory processes to minimise the influence of task-irrelevant targets (Slotnick et al., 2003; Mozolic et al., 2008b; Langner et al., 2011).

In the primary somatosensory cortex (SI), opposite effects were observed. Neural responses in SI were significantly stronger during sustained attention to touch than to vision, reflecting amplification of tactile signals to enhance processing of relevant targets. Modulatory effects of tactile attention were more often observed in higher order somatosensory regions, near the parietal operculum and inferior lateral parietal cortex, including area SII (Mima et al., 1998; Backes et al., 2000; Hamada et al., 2003). Nevertheless, a number of studies have also found evidence for selective modulation in contralateral primary somatosensory cortex when attending to tactile targets (Johansen-Berg et al., 2000; Meador et al., 2002; Van De Winckel et al., 2005; Wacker, 2011), indicating that although much smaller than modulatory effects in SII, top-down attention can nevertheless shape activity in SI.

4.4.2 Frontoparietal Network Recruited in Multisensory Spatial Attention to Vision and Touch

For the main analysis conducted in this study, we tested the existence of a supramodal control system in the dorsal frontoparietal network by testing whether commonly activated regions found by classical univariate analysis contained distinct patterns of activity that code for the currently attended modality. We first performed univariate conjunction analysis to map brain regions commonly activated in both sustained attention to visual and tactile events. Widespread activation in frontoparietal attentional regions was found during attention to either modality, consistent with previously reported studies of unimodal and multimodal spatial attention (Kastner and Ungerleider, 2000; Macaluso, 2010; Szczepanski et al., 2010). Along the dFP network, common activations were observed in the dorsal frontal cortex along the precentral sulcus, near the FEF, and in the boundary between superior and inferior parietal lobe that contains the IPS. The dFP network has been suggested as the potential source of top-down endogenous signals for maintaining the current focus of attention and for biasing processes in the sensory cortex (Corbetta and Shulman, 2002; Corbetta et al., 2008).

We also observed common activations within the ventral frontoparietal (vFP) network, including the TPJ, the ventral part of the SMG, and the IFG. The vFP network is not activated by preparatory attention but is instead believed to function as a ‘circuit breaker’ that interrupts ongoing attentional biases in the dFP network when behaviourally relevant stimuli were detected (Corbetta and Shulman, 2002; Corbetta et al., 2008). Activation of both dFP and vFP networks was expected in this task because in this multisensory attention paradigm both elements of endogenous attentional orienting (i.e. sustained attention to one modality and side) and bottom-up stimulus driven inputs (i.e. bimodal and bilateral stimuli) were present.

Additionally, we also noticed more robust activity during attention to the left side compared to attention to right side, but qualitatively, the overall patterns of activity were very similar in both conditions. Although we have carefully matched the behavioural performance and there were no significant differences in response accuracy between different attended sides, there was still a possibility that this asymmetry might be due to the more demanding efforts for attending to left vs. right targets. Previous studies have also shown that greater task difficulty during attention is associated with more increased activation in right frontal regions (e.g. Sunaert et al., 2000).

In line with our findings, previous neuroimaging studies have also discovered that similar frontoparietal networks are involved in orienting of spatial attention to different modalities. In a pioneering PET study of multimodal spatial attention, Macaluso et al. (2002a) reported common multimodal effects in the anterior IPS, dorsal premotor cortex (FEF), and superior temporal sulcus during attention to visual and tactile events. Similar to our study, they employed presentation of bimodal and bilateral stimuli and asked their participants to sustain attention to one side and one modality only while performing a target discrimination task. In a related fMRI study using a cross-modal spatial cueing paradigm, Macaluso et al. (2002b) reported enhancement of the TPJ and IFG regions elicited by invalid vs. valid cues presented in either modality. In contrast, activity in dorsal frontoparietal regions (IPS and FEF) was equally enhanced by both types of cues irrespective of target modality, implying a common role of the dFP regions in sending top-down bias signals across various modalities. These findings were extended in a subsequent fMRI study that incorporated cue-only trials to isolate preparatory signals associated with strategic spatial attention to vision and touch (Macaluso et al., 2003b). Again, modality nonspecific cue-related enhancements were observed in the FEF and IPS regions, suggesting dFP as the possible ‘*source*’ of modality-independent (supramodal) attentional bias signals. Additional evidence for the involvement of a common frontoparietal network for orienting of attention to various modalities were reported in an fMRI study that investigate cue-related activity during spatial attention to auditory targets (Wu et al., 2007), and in a more recent fMRI study investigating audiovisual interactions using orthogonal cueing paradigm (Smith et al., 2010).

4.4.3 MVPA Analysis

The discovery of similar frontoparietal networks recruited during strategic spatial orienting to various modalities have led several researchers to postulate the existence of supramodal circuits in the dFP regions that biases relevant spatial location in a modality-independent way (Macaluso et al., 2002b; Macaluso, 2010; Smith et al., 2010; Green et al., 2011). We examined this hypothesis by exploiting novel MVPA techniques to discriminate attended modality from the distributed patterns of activity in the overlapping frontoparietal ROIs found by mass univariate analysis. The multivariate classification results revealed that information about attended modality were present in the majority of overlapping frontoparietal ROIs. When participants attended to the left hemifield, modality-specific information could be decoded in the right parietal cortex (that includes IPS), and most of the frontal regions including superior frontal cortex (location of FEF), right middle frontal cortex (DLPFC), and right inferior frontal cortex (IFG). Similarly, when participants attended to the right hemifield, modality-specific information was discovered in the bilateral inferior parietal and right superior parietal cortex, but comparatively less informative regions were found in the frontal cortex, and only the right middle frontal region could significantly classify above chance.

These findings cannot be explained by the selection bias in the analysis (Kriegeskorte et al., 2009; Vul et al., 2009; Vul and Kanwisher, 2010), because independent datasets for defining the ROIs and MVPA analysis were used. In particular, the first half of the dataset were used to functionally define the frontoparietal ROIs using univariate conjunction analysis, while the second half was later used for MVPA classification. Moreover, the functional ROIs were defined in individual brain space rather than normalised space to preserve subject-specific variance in the anatomical locations of the overlapping activations.

In addition to ROI-based MVPA classification, we also independently analysed the imaging data using searchlight analyses to map cortical regions that contain information about the attended modality and/or attended location. In the first searchlight analysis, we looked for modality-specific but location-nonspecific information, and found widespread activity spanning across bilateral posterior parietal cortex (PPC), including IPS and SMG/TPJ, extending to superior premotor areas (SMA, FEF) and the IFG. By contrast, searchlight analysis found no evidence for location-specific but modality-nonspecific information in the brain, suggesting the existence of distinct location-specific coding for different modalities.

These findings are inconsistent with the hypothesis of supramodal dFP networks that control the deployment of spatial attention in a modality independent manner (Macaluso, 2010). However, the results of our study are in line with several fMRI and TMS studies that reported domain- and modality- specificity of the PPC regions. Reversible disruptions of right SMG using TMS has been shown to impair strategic orienting of spatial attention in the visual modality but not in the somatosensory modality (Chambers et al., 2004b). Related evidence was reported in an MVPA study investigating the role of frontoparietal networks in controlling shifts of spatial and feature-based attention in vision (Greenberg et al., 2010). They discovered that despite the observation of overlapping activations in the frontoparietal regions, the classifier could still decode domain-specific transient signals in the PPC region. Furthermore, a recent multisensory integration study reported that functional connectivity between IPS and the lower-level sensory regions were weighted by the reliability of the sensory modality (Beauchamp et al., 2010). Using structural equation modelling, they found that connection weights between IPS and somatosensory cortex were significantly increased when tactile stimuli was more informative than visual stimuli, whereas the connection weight between IPS and visual cortex increased when visual stimuli was more informative than tactile stimuli. The findings of the present study further corroborate and complement the previous findings by providing evidence for modality-specific coding in the PPC region during multisensory spatial attention task.

In addition to the PPC region, modality-specific information was also found in the IFG. A growing number of evidence from previous neuroimaging studies have highlighted the involvement of the IFG in various domains, including cognitive control (Duncan and Owen, 2000; Derrfuss et al., 2005), response inhibition (Logan and Cowan, 1984; Aron et al., 2004), and natural language comprehension (Constable et al., 2004; Jung-Beeman, 2005). The findings of modality-specific information in the IFG complements these previous findings and provides additional evidence for the existence of adaptive coding in prefrontal cortex that integrates various cognitive functions like memory, attention, language, and control (Duncan and Owen, 2000; Duncan, 2001; Woolgar et al., 2011a).

4.4.4 Summary

In the present study, we applied fMRI and MVPA classification to probe the generality and specificity of the frontoparietal attention networks during sustained spatial attention to visual and somatosensory modality. Consistent with previous studies, we found that visual and somatosensory attention elicited widespread overlapping neural activation, consistent with a supramodal selection mechanism. On closer inspection, however, most of these bimodal conjunctions contained fine-grained modality-specific information that cannot be explained by changes in sensory inputs, motor output, or eye position. Searchlight analyses further confirmed that strategic spatial attention can be accounted for by integrated modality-specific processes in the parietal cortex. We still, however, observed some commonly activated regions that contained no modality-specific information in the frontal cortex, implying the existence of potentially supramodal regions. Overall, our findings revealed evidence for modality-specific top-down selection in the parietal cortex, and support the view that spatial attention is driven by modality-specific systems that are anatomically intermingled yet functionally distinct.

Chapter 5 - Multisensory Feature-based Attention in Vision and Touch

Investigation of neural correlates of multisensory feature-based attention in vision and touch is relatively unexplored. In this study, we applied univariate fMRI analysis and MVPA classification algorithm to investigate the role of the frontoparietal attention network in maintaining feature-based attention in vision and touch. Specifically, we probed whether feature-based attention to somatosensory events recruits similar frontoparietal regions activated during attention to visual events. Additionally, we also examined feature-selective attentional modulatory effects in the visual and somatosensory cortex using ROI-analysis and ROI-based MVPA classification.

In this chapter, relevant background concerning feature-based attention will be discussed, followed by description of the experimental paradigm and the analysis methods used. The findings of the experiments will be presented subsequently and their significance discussed.

5.1 Introduction

The majority of attention research has investigated processes related to the orienting of attention to different spatial locations (Desimone and Duncan, 1995b; Wright and Ward, 2008). However, as discussed in Section 1.2.2, attention can also be allocated to a particular feature of an object, such as orientation, colour, frequency, or direction of motion (Treue and Martínez Trujillo, 1999; Saenz et al., 2002; Martinez-Trujillo and Treue, 2004). The ability to selectively attend to relevant features is important in various tasks that require active target selection among distractors, such as during visual search. In typical visual search tasks, subjects are presented with a set of items and asked to search for a particular target with a specific feature or combination of features, such as colour or orientation (Wolfe and Horowitz, 2004; Wolfe, 2010). Feature-based attention can improve target detection by enhancing visual information that matches the feature(s) currently held in working memory, and by supressing distracting components.

5.1.1 Top-Down Modulatory Effect of Feature-based Attention

Psychophysical studies have provided evidence that feature-based attention can improve reaction time and heighten detection sensitivity across visual fields (Rossi and Paradiso, 1995; Sàenz et al., 2003; Liu and Hou, 2011). Single-unit electrophysiological studies have demonstrated that searching for a particular stimulus feature enhanced baseline activity of inferior-temporal cortex neurons that preferred the stimulus, even before the actual stimulus presentation (Chelazzi et al., 1993, 1998). Similar findings were also reported in visual area V4 that responds differentially depending on the grating orientation of the pursued target (Haenny and Schiller, 1988; Maunsell et al., 1991). Other research in non-human primates has shown that this feature-based modulation in visual cortex could also spread beyond the current locus of spatial attention, extending to distant unattended locations (McAdams and Maunsell, 2000; Martinez-Trujillo and Treue, 2004; Bichot et al., 2005). This indicates that feature-specific enhancements might actually have a more global effect across the entire visual-field (Saenz et al., 2002; Liu and Hou, 2011), unconstrained by the limited spotlight of spatial attention (Boynton et al., 2006; Liu and Mance, 2011).

Similar observations have been reported in the dorsal visual area V5/MT, in which attention to the preferred direction of motion caused selective response enhancement in MT neurons (Treue and Martínez Trujillo, 1999; Martinez-Trujillo and Treue, 2004). A multiplicative gain mechanism is thought to play a key role in these selective modulation processes, causing an amplified response of neurons that are tuned to the chosen features and suppression of those that are tuned to the other irrelevant features (Maunsell and Treue, 2006). The 'feature-similarity gain' hypothesis (Treue and Martínez Trujillo, 1999) further proposed that both feature and spatial attention might be driven by the same neural mechanisms, owing to the evidence that both types of attention could equally strongly modulate the gain of the visual neurons that falls within the receptive fields.

On a more macroscopic level, many neuroimaging studies have also investigated the neural basis of feature-based attention. A pioneering study using positron emission tomography (PET) revealed differential activations in extrastriate visual cortex correlated with the deployment of attention to various stimulus attributes including shape, colour, and velocity (Corbetta et al., 1990). Subsequent studies using functional magnetic resonance imaging (fMRI) further enriched evidence of top-down modulation by showing that the differential modulatory effect of feature-based attention could also be reliably measured using BOLD signals in the visual cortex. Attentional modulation of visual area V5/hMT+ was consistently reported in various fMRI tasks that asked the observer to pay attention to motion stimuli (Beauchamp et al., 1997; O'Craven et al., 1997; Shulman et al., 1999; Saenz et al., 2002), corroborating previous findings gained from electrophysiology experiments. The BOLD modulatory effect of feature-based attention was also reported when attention was directed towards other feature dimensions such as colour (Saenz et al., 2002; Liu, 2003). In an fMRI experiment using a Stroop task, Polk et al. (2008) found that selective attention to colour enhances activation in a functionally defined colour area while at the same time suppressing responses in functionally defined word areas in visual cortex. These findings provide evidence supporting the biased competition model of feature-based attention (Desimone and Duncan, 1995a; Desimone, 1998; Kastner and Ungerleider, 2000).

To closely investigate the temporal nature of this feature-based modulatory effect, electroencephalography (EEG) and magnetoencephalography (MEG) recordings have also been applied (Nobre et al., 2006). Many of these studies have highlighted the differences in event-related potentials (ERPs) evoked by attention to a spatial location vs. attention to a specific feature of the stimuli. Directing attention to a specific location was known to correlate with an amplitude enhancement of the early positive (P1 at 80-120ms) and negative (N1 at 140-190ms) components of the visual evoked potentials (Martínez et al., 1999; Noesselt et al., 2002). In contrast, feature-based attention modulates selection negativity (SN) components between 150 and 300ms post-stimulus, which possibly reflects feedback signals to visual cortex (Anllo-Vento and Hillyard, 1996; Beer and Röder, 2004). However, a more recent study using simultaneous presentation of competing features found an evidence of earlier modulation of P1 component at ~100ms post-stimulus, suggesting that an early-selection mechanism can also operate in feature-based selection, especially under conditions of direct competition (Zhang and Luck, 2009). Complementary to this result, feature-specific pre-stimulus modulations within visual regions have also been shown previously by Shibata et al. (2008), using a combination of MEG, fMRI and hierarchical Bayesian analysis.

5.1.2 Frontoparietal Sources of Feature-based Attentional Control

In addition to investigating the top-down modulatory effect of feature-based attention on sensory cortical regions, several fMRI studies have also focused their inquiry on elucidating the source of feature-specific attentional control signals in the brain (Shulman et al., 1999;

Stoppel et al., 2007). Activity in the dorsal and ventral frontoparietal networks (Corbetta and Shulman, 2002) that are recruited during spatial attention has also been observed in most of these studies of feature attention, suggesting the possibility that both types of attention actually share a common neural mechanism (Wojciulik and Kanwisher, 1999). Specifically, orienting attention to the features of objects has been found to strongly activate the dorsal network that includes the bilateral IPS and FEF, as well as a ventral network consisting of the right TPJ and right IFG (Shulman et al., 1999; Liu, 2003; Luks and Simpson, 2004).

Other more detailed studies, however, have also reported the existence of subregions within this fronto-parietal network that are more specialized for controlling attention to specific dimensions (spatial location or feature), supporting the hypothesis of a combined generalized and specialized attentional control network for shifting attention within various domains (Shulman et al., 2002; Giesbrecht et al., 2003; Slagter et al., 2007). This evidence was further supported by a recent TMS study reported by Schenkluhn et al. (2008). Using a covert visual search paradigm, they cued the subject to either the location or colour of a target item, and TMS was applied during the cue presentation to the right parietal cortex. Significant behavioural impairment in both spatial and feature attention was observed when anterior IPS was stimulated, whereas stimulation of the right SMG only disrupted the deployment of spatial attention.

Neural correlates of feature-based attention in sensory modalities other than vision and audition are relatively unexplored. Analogous to the effect of top-down attentional modulation found within the visual cortex, we would also expect similar enhancement in the respective sensory regions when attention is directed in other modalities. A small number of neuroimaging studies in the last decade have indeed found that attending to a tactile stimulus can increase activity in the contralateral primary somatosensory cortex (Meyer et al., 1991; Johansen-Berg et al., 2000; Meador et al., 2002; Van De Winckel et al., 2005). However, modulatory effects of tactile attention are more often observed in higher order somatosensory areas located near the parietal operculum and inferior lateral parietal cortex, including area SII (Mima et al., 1998; Backes et al., 2000; Hämäläinen et al., 2002; Hamada et al., 2003).

Attention to somatosensory stimuli can also activate the fronto-parietal networks observed during visual attention (Corbetta and Shulman, 2002). A key study by Burton and colleagues (2008) examined the cortical network engaged during selective cueing to the temporal duration or frequency of a vibrotactile stimulus applied to the right fingertip. They reported increased responses in the FEF, dorsal premotor cortex, anterior and posterior IPS, superior temporal sulcus (STS), and supplementary motor area (SMA), consistent with commonly found regions in visual attention tasks. Similar findings were reported in a more recent study of feature-selective attention to a pattern or frequency of a vibrotactile stimulus presented to the left index fingertip (Wacker, 2011). However, in this study they did not observe any activations near the FEF, indicating the possibility that FEF might not be required for tactile attention that does not involve a spatial element or decision. Notably, in the study of Burton et al. (2008), the authors presented the visual cues (words) below the fixation cross during vibrotactile stimulations, which could have induced spatial shifts of covert visual attention that might explain their observed FEF activations.

5.1.3 Overlapping Activations and the Supramodal Hypothesis

The recruitment of task-dependent common fronto-parietal networks in both visual and tactile attention tasks have led to the hypothesis of a supramodal control network that is activated when performance is goal-directed (Fox et al., 2005), irrespective of the sensory modality or dimension of the target stimulus (Corbetta and Shulman, 2002; Corbetta et al., 2008). Several neuroimaging studies of multisensory spatial attention have provided supporting evidence for this supramodal network by demonstrating the existence of overlapping voxels in the fronto-parietal regions activated while attention was directed towards stimuli in various sensory modalities including vision, touch, and audition (Eimer et al., 2002a; Macaluso et al., 2002b; Krumbholz et al., 2009; Smith et al., 2010; Macaluso, 2010).

However, directly interpreting overlapping fMRI activations as an evidence for the existence of supramodal control mechanism has been criticized and challenged partly because it was not possible to decide whether or not common activation of a single voxel is caused by activity of the same neuronal populations. A typical fMRI voxel is estimated to contain about 5.5 million neurons, 22 km of dendrites, and 220 km of axons (Logothetis, 2008); therefore, within the volume of a single voxel there might be numerous topographically arranged neuronal microcircuits that are tuned to different properties of the inputs. Moreover, recruitment of common cortical regions in a multisensory task does not automatically imply that these regions function in the same way for different sensory modalities. Evidence for modality specific control has been reported in a number of TMS studies, showing that TMS to the right

SMG only disrupted strategic orienting of attention to vision but had no significant effect on attention to touch (Chambers et al., 2004; see also Chambers et al., 2007).

More recently, the application of multivoxel pattern analysis (MVPA) has provided another perspective to study the nature of distributed population coding underlying overlapping cortical regions found by classical univariate analysis. For example, the pattern of activity within the posterior parietal cortex (PPC) differed substantially between shifting attention to locations and colours, despite the fact that the voxels in these regions were equally strongly activated in both conditions (Greenberg et al., 2010). A related MVPA study has revealed that, within the PPC BOLD response, it is possible to reliably decode spatial shifts of attention versus rule shifts (Esterman et al., 2009), suggesting domain-specificity of parietal cortex in orienting of attention and task switching in multiple domains. In addition to decoding task specific information, recent MVPA studies have also demonstrated successful decoding of attended stimulus locations (Kalberlah et al., 2011) and target features (Liu et al., 2011) in frontoparietal regions, extending previous studies that demonstrated reliable classification of attended motion direction in retinotopic visual regions (Serences and Boynton, 2007).

5.1.4 Aims and Goals

During the last decade, the majority of visuo-tactile multisensory attention studies have been focusing on finding the neural basis of orienting to spatial location (Macaluso, 2010). To our knowledge no other studies have investigated the neural correlates of multisensory feature-based attention in vision and touch using fMRI. In the present study, functional magnetic resonance imaging (fMRI) and MVPA classification algorithms were used to investigate the generality and specificity of the frontoparietal attention network involved in maintaining feature-based attention in vision and touch. Additionally, we also aimed to examine feature-selective attentional modulation in the occipital and somatosensory cortex using both classical univariate region of interests (ROI) analysis and information-based ROI analysis. Moreover, we adopted a variant of a feature-based attention task that has so far received less scrutiny, where we asked the subject to attend to a specific feature of the stimulus (i.e. shape) and ignore another competing feature that was simultaneously present within the same stimulus (i.e. frequency). Most other feature-based attention studies utilized a task in which the subjects were given a cue to locate objects with a certain feature in the midst of other objects having different features, but did not require them to attend to a feature of an object while simultaneously supress other feature present in that object. Less is known about the effect of feature attention on the same object with competing features, although several electrophysiological studies in monkeys (Mirabella et al., 2007; Chen et al., 2012) and neuroimaging studies in humans (Nobre et al., 2006; McMains et al., 2007) have begun to probe this particular issue. Furthermore, using a single object with different features instead of multiple objects with multiple features might be advantageous to avoid possible confounds of mixing elements of spatial and feature attention in our task. Since attention was maintained within a single object throughout the entire task, there was no need to covertly shift attention to different locations or objects.

The apparatus and behavioural task used in this study is depicted in Figure 5.1a and 5.1c respectively. Participants maintained their gaze on a central fixation dot and attended covertly to multisensory stimuli presented on their left-hand side throughout entire session. In the beginning of each block, brief visual instructions were displayed on the right hand side, informing participants to sustain their attention either to the shape or to the frequency of the stimulus presented in a particular modality (vision or touch). Altogether, there were four different possible attentional instructions: attend visual-shape, attend visual-frequency, attend tactile-shape, and attend tactile-frequency. In each trial, following presentation of concurrent bimodal stimuli, participants pressed a button in a non-speeded way to indicate the shape or frequency of the target stimulus in the attended modality. There were four possible types of target within each modality, representing all possible combinations of the shapes (horizontal or vertical) and frequency (low or high), as illustrated in Figure 5.1b. Overall sensory input and motor responses were equally matched for each attentional condition by making sure that every possible target combinations across modalities were presented with equal probability, so that any neuronal differences found in fMRI analysis could be attributed to the changes in participants' internal cognitive states, and were not caused by confounding factors like statistical variation of the input targets or motor responses.

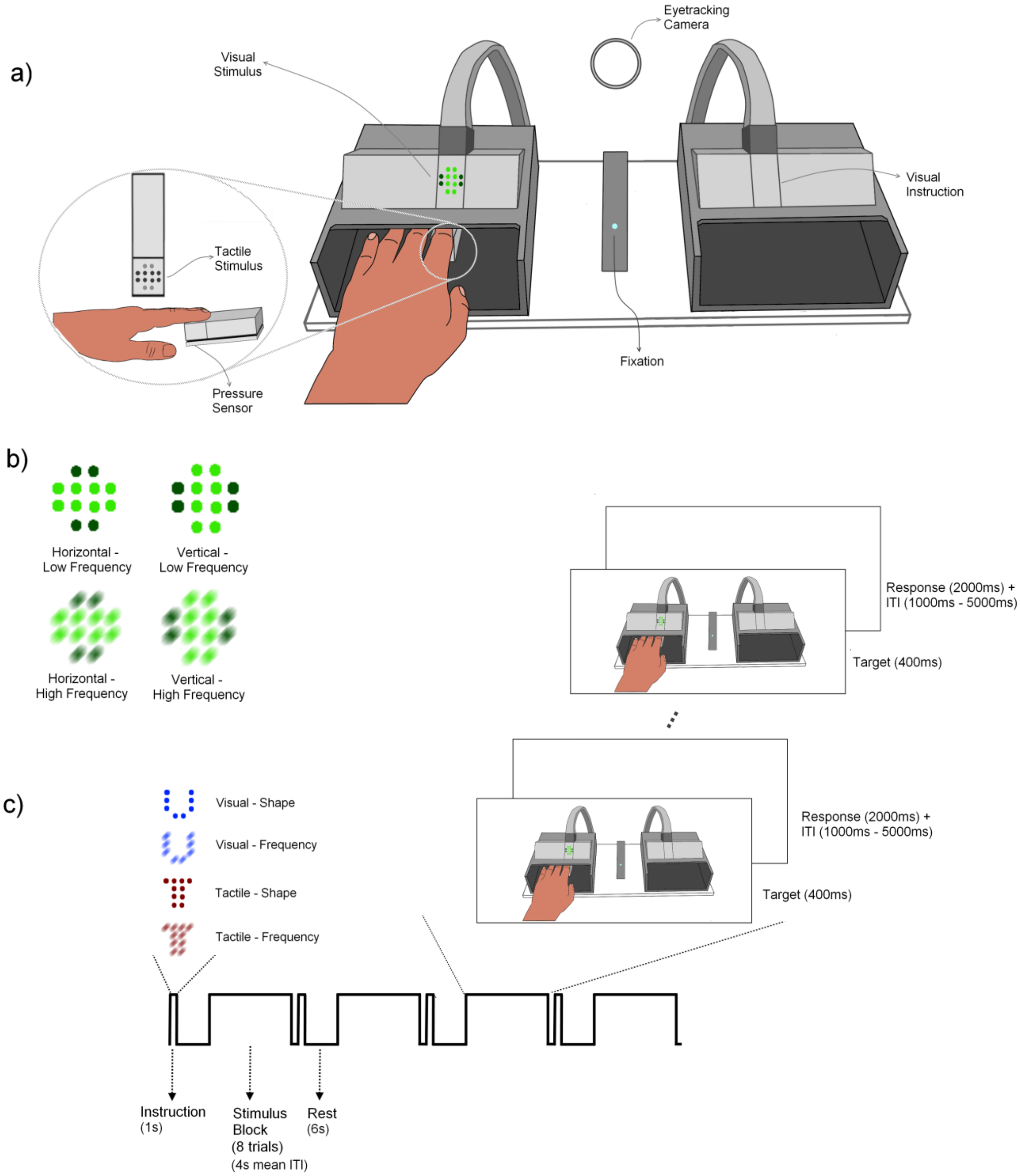


Figure 5.1 (a) Illustration of the experimental apparatus used in Experiment 5, from the observer viewpoint while lying supine on the scanner bed, looking up through a double mirror positioned on top of the MRI head coil. The visual stimulus was displayed on the left prism in synchrony with presentation of a tactile stimulus to the participant's left index finger. The prism on the right hand side was used to display task instruction in the beginning of each block. Horizontal eye position and pupil diameter were recorded continuously using an MRI compatible remote eye tracker (SMI iView X™) that was fixed at the end of the scanner bed and pointing directly to the image of the participant's eye reflected in the mirror. Downward pressure on the tactile stimulator was also monitored in real-time

using a pressure sensor located beneath the stimulator. **(b)** Schematic illustration of four possible types of target stimulus presented in both the visual and tactile modalities. For the tactile modality, bright green dots represent tactile stimulator pins with higher amplitude and the dark green dots represent the pins with lower amplitude. Each target consisted of two intrinsic features: shape and frequency. The shape could either be in horizontal or vertical orientation, and flickering in low or high frequency. **(c)** Diagram of the experimental design. Task instruction was given in the beginning of each block, informing participants to sustain their attention to a particular modality (i.e. visual or tactile) and specific feature (i.e. shape or frequency) of the target stimulus presented in that modality. Following a 6s rest period, 8 consecutive trials were presented in succession within each block. At the onset of each trial, 400ms targets were presented simultaneously in both sensory modalities. Responses were collected within a 2000ms window after target presentation, followed by a random inter trial interval (ITI) delay of 1000ms to 5000ms.

5.2 Materials and Methods

5.2.1 Participants

Thirteen healthy right-handed volunteers (ages 20 - 32, mean 24, 7 females) with normal or corrected-to-normal vision participated in this fMRI study and written informed consent was obtained before the scanning. The study was approved by the Ethics Committee of the School of Psychology, Cardiff University. Imaging data from one participant were excluded from the analysis due to excessive head movement artefacts and poor behavioural performance during the scanning (average response accuracy for one condition was below 60%).

5.2.2 Apparatus

The experiment utilized similar apparatus setup with the previous multisensory spatial attention study (Experiment 4, described in Chapter 4). Tactile stimulation was delivered to participants' glabrous tip of the left index finger using a 20-points (4-column × 5-rows matrix) piezoelectric tactile stimulator (QuaeroSys, St. Johann, Germany). Participants rested their left hand inside a plastic box and placed the tip of their index finger on top of the tactile stimulator housed inside the box. Two fibre optic prisms were used to deliver the visual stimulus, one on each side of the sagittal midline. The prism on the left hand side was positioned directly above the tactile stimulator, and this prism was used for presenting the target visual stimulus. Another prism positioned on the right hand side of the fixation was used to present task instructions at the beginning of each block. An LED for fixation was positioned centrally, 1^o below the location of the prisms. Presentation and coordination of visual and tactile stimuli was accomplished using a custom MATLAB script (MathWorks, Inc.). Participants responded using their right hand by pressing one of two assigned buttons on an MRI compatible response box.

To enable participants to view ecologically valid multisensory stimuli (i.e. to see the visual stimulus and their hands without any optical reversal), a front-projection mirror positioned above the RF-coil was built and employed. Throughout the experiment, horizontal eye movements, pupil diameter, and blinks were recorded in real-time using a remote eye-tracking camera (SMI iViewX™, SensoMotoric Instruments). The amount of downward pressure of the left index finger was also monitored using a custom built MRI compatible force transducer positioned beneath the tactile stimulator module.

5.2.3. Stimuli and Procedure

Concurrent bimodal visual and tactile stimuli were presented in the participant's left visual field and to the left index finger respectively (Figure 5.1). Each stimulus consisted of two intrinsic features: shape (horizontal or vertical) and frequency (low or high). The visual stimulus was displayed on a 4 × 5 array of LED light-points, geometrically analogous to the 4x5 array of pins of the tactile stimulator. The visual stimulus was located in the periphery visual field, ~8^o horizontally from the fixation point. The size of the visual stimulus was ~0.5^o (W) × ~0.5^o (H) and the target was displayed in pure green colour.

The multisensory feature attention task was conceived as a 2 × 2 factorial design, including two levels of *attended modality* (vision or touch) and two levels of *attended feature dimension* (shape or frequency). At the beginning of each block, participants were presented with a small visual cue that appeared in the right visual field, informing the combination of sensory modality and feature dimension that was task-relevant (and, thus, to be attended) during the upcoming block. Four possible cue instructions were presented using a static or flickering (4Hz) symbolic pattern resembling character 'T' or 'V', which denoted the tactile or visual modality, respectively. A non-flickering character denoted attention to the shape dimension whereas a flickering one denoted attention to the frequency dimension. In combination, therefore, a non-flickering character 'T' was displayed for the instruction to attend to tactile-shape, a flickering character ‘T’ for instruction to attend to tactile-frequency, a non-flickering character ‘V’ for attention to visual-shape, and a flickering ‘V’ for attention to visual-frequency. The cue was presented for 1s. After cue presentation, there was a 6s rest period before the onset of the first trial. Each sustained attention block consisted of 8 individual trials. The inter-trial intervals (ITI) were randomly jittered with the mean values of 4s (ranging from 3s to 7s).

On each trial, stimuli were delivered concurrently in both modalities for 400ms. Depending on the instruction given in the beginning of each block, after target presentation, participants were asked to identify either the shape (horizontal/vertical) or the frequency (low/high) of the stimulus in the attended modality. A non-speeded response was collected within 2s period after the target offset. The first response button was assigned to the horizontal or low frequency response and the second button for the vertical or high frequency one. This response mapping was reversed in the second half of the experiment to avoid correlating motor effectors with feature dimensions in the MVPA decoding of the attended modality.

Prior to the scanning, participants were familiarized with the multisensory feature attention task in a mock scanner for one session (two hours) using the same apparatus as the actual scanning. During this training session, the task difficulty was regulated either by adjusting the contrast of the shape or the difference in the frequency, so that the participant achieved ~80% correct performance on all four attentional conditions.

5.2.4 MRI Data Acquisition

Imaging data were acquired on a General Electric 3T scanner at the CUBRIC. Functional images were obtained using a T2-weighted echo-planar imaging (EPI) sequence with a repetition time (TR) of 3000ms, echo time (TE) of 35ms, flip angle of 90^o, matrix size of 64 × 64, 46 contiguous slices covering the entire brain, and a voxel resolution of 3.2 × 3.2 × 3.2 mm. For each experimental run, 116 volumes were acquired, lasting 5.8 min. The scanning was conducted in a single 2-hour scanning session, consisting of 8 experimental runs with 8 blocks per run (64 trials), and a total of 512 trials.

In a separate scanning session, a whole-brain structural image, a retinotopic mapping functional localizer, and a finger-somatotopy localizer were acquired. T1-weighted structural scans were obtained with 1 × 1 × 1 mm voxel resolution, repetition time (TR) of 8ms, echo time (TE) of 3ms, flip angle of 20^o, matrix size of 256 × 256, and 172 slices. Functional images for the retinotopic mapping analysis were obtained using a T2-weighted EPI sequence, with a TR of 3000ms, TE of 35ms, flip angle of 90^o, matrix size of 128 × 128, 37 slices, and a voxel resolution of 2 × 2 × 2 mm. Two runs of retinotopic data were acquired (one each in a clockwise and anticlockwise direction), each consisting of 100 volumes, lasting 5 min.

The finger somatotopy functional localizer was obtained using a T2-weighted EPI sequence, with a TR of 3000ms, TE of 35ms, flip angle of 90^o, matrix size of 64 × 64, 46 contiguous slices, and an isotropic voxel resolution of 3.2 mm. Two runs of a somatosensory functional localizer were acquired, each lasting 5 min (100 volumes). These localizers were used to define the ROIs in the primary somatosensory cortex for each participant.

5.2.5 Retinotopic Mapping

The same retinotopic mapping task and analysis procedure described in Section 4.2.6 was used to define the regions of interests (ROIs) of visual areas V1, V2, V3, V4, V5, V7, and V8 in each subject. The retinotopic mapping data from 2 subjects were excluded due to excessive head movements during the scanning, hence data from 11 subjects were analysed in the subsequent ROI-based analysis.

5.2.6 Eye Tracking and Finger Pressure Analysis

During the scanning session, fixations of the eye, pupil diameter, and downward pressure of the left index finger were recorded in real-time and saved as a time series data. For each trial, we summarized these time series by averaging the values within the window of 100ms before the onset and 500ms after stimulus presentation, resulting in three measurements per trial (a three-dimensional vector), consisting of average horizontal eye position, average pupil diameter, and average downward pressure. Similar to experiment 4 reported in chapter 4, we used linear-SVM classification to test whether there is any pattern of information in the eye movements and finger pressure that could distinguish the currently attended modality. Classification was performed using the same leave-one-run-out cross-validation test that was used to classify the imaging data, and the average classification accuracy was obtained by averaging 8 separate training and testing iterations. Statistical significance of the classification result (p-values) was estimated by running the same classifier with randomly permuted class labels for 1000 times. We then calculated the number of random samples that classified above the values of the original classification result, yielding the nonparametric null distribution of the sample.

5.2.7 Univariate Conjunction Analysis

Initially, we aimed to follow the same procedure that we used in the preceding experiment, in which we split imaging data for individual participants into two halves, with one half of the dataset for the univariate conjunction analysis and the other half for the ROI-based MVPA analysis applied on the ROIs found by the conjunction analysis. However, contrary to expectations, the individual subject conjunction analysis revealed little overlapping activity in the relevant fronto-parietal regions for more than half of the subjects (see Appendix B, Figure B.3 for examples of activation maps overlaid on top of individual subjects brain). This might indicate that overall there was less strong activity in these region for this feature attention task compared to the former spatial attention task, hence there was less statistical power to detect common activations within individual data.

As an alternative, we opted to run group-level conjunction analysis using the full dataset to examine potentially supramodal voxels activated during orienting of feature-based attention in both vision and touch. Separate MVPA and cross-generalization searchlight analyses were then conducted using the same dataset to look for modality specific information in the whole brain. By comparing the maps found by the searchlight analysis with the univariate conjunction maps we could effectively identify which of these overlapping regions was modality specific or potentially supramodal.

Univariate conjunction analysis was performed using SPM8 (Friston et al., 1995b, 2006). Individual EPI runs were first realigned to correct for head movement artefacts. Afterwards, both aligned EPI images and individual structural image were normalized into the SPM-MNI template. The EPI data was then spatially smoothed with an 8mm isotropic FWHM (full-width half-maximum) Gaussian kernel and high-pass filtered at 128s with pre-whitening using the AR(1) autoregressive model to remove low frequency artefacts. Whole-brain contrasts for each attentional condition (visual-shape, visual-freq, tactile-shape, tactile-freq) vs. baseline were first computed for individual subjects in the first level analysis. Four regressors corresponding to each condition were modelled by convolving a canonical haemodynamic response function with a box-car function indicating the sustained attention block. In the second level, individual contrasts were combined and analysed on a group level using conjunction analysis with the global-null hypothesis (Friston et al., 2005). Two conjunction maps were generated, one for conjunction between visual-shape AND tactile-shape and the other for conjunction between visual-freq AND tactile-freq. The result was thresholded at $p < 0.05$ with FDR correction for multiple comparisons.

5.2.8 ROI-based Activation Analysis

Univariate ROI-based analysis was conducted to examine top-down attentional modulation on activity in the retinotopic visual ROIs and somatosensory ROIs. Before analysis, the EPI data was realigned to correct for possible head movements during the scanning, and then smoothed using 8mm isotropic FWHM Gaussian kernel and high-pass filtered at 128s to remove low frequency drift in the fMRI time series. Whole-brain GLM contrasts for each attentional condition was estimated for individual subjects using SPM8 and the regressor was modelled using a box-car function convolved with a canonical haemodynamic response function, representing each trial block. Using a custom script written in MATLAB, average beta-values in each ROI was computed for each subject and task condition, and then averaged across subjects.

5.2.9 MVPA searchlight Analysis

In order to visualize the map of cortical regions that contains information about the attended modality (i.e. modality-specific areas) and attended feature dimension (i.e. dimension-specific areas), we conducted a whole-brain searchlight classification analysis (Kriegeskorte et al., 2006) using Princeton MVPA Toolbox for MATLAB (Detre et al., 2006) and linear-SVM learning algorithm. A spherical searchlight with 11.2mm radius was used in this analysis, centred in turn on each voxel in the brain. A searchlight map was initially computed for each subject within individual brain space using raw, unsmoothed EPI data. Before analysis, the EPI images were motion corrected and then normalized using a z-score transform. To increase statistical power, we also averaged the EPI volumes of 8 individual trials within each block into a single sample volume (Preston and Eckstein, 2010; Etzel et al., 2011). Additionally, the

EPI time series was also shifted by 2 TRs (6s) to account for haemodynamic delay. For each searchlight ROI, an eightfold cross-validation with leave-one-run-out procedure was performed, yielding classification accuracy values for each voxel in each individual brain. These individual classification accuracy maps were then normalized into the standard MNI template and combined on the group level by averaging the values of each voxel across all subjects. Statistical significance of this group-level map was assessed using random-effects analysis by performing an independent one-sample t-test versus chance (50% accuracy) (Haynes et al., 2007; Soon et al., 2008; Stokes et al., 2009a).

5.2.10 ROI-based MVPA analysis

To investigate the top-down modulatory effect of attention on population coding in visual and somatosensory cortex, we performed MVPA analysis in retinotopic visual ROIs and functionally defined ROIs in primary somatosensory cortex. Multivoxel pattern analysis was conducted using Princeton MVPA Toolbox for MATLAB (Detre et al., 2006) and a linear support vector machine (SVM ; Cortes and Vapnik, 1995). The analysis was undertaken in individual subject brain space using raw, unsmoothed EPI data. Initially, the EPI time series of voxels within the ROI mask was extracted and then normalized using a z-score transformation. Sample volumes corresponding to the onset of each trial were labelled according to categories corresponding to the task conditions of interest (i.e. visual-shape vs. tactile-shape condition), specifying the regressor matrix for this task. The regressor was then shifted by 6 seconds (2 TRs) to compensate for haemodynamic lag. N-folds cross-validation classification was then undertaken using a leave-one-run-out procedure and overall classification accuracy was calculated by averaging N accuracy values. Statistical significance of the classification result at the group level was estimated using a two-tailed single-sample t-test statistics against chance (50%).

5.3 Results

5.3.1 Behavioural

Mean behavioural performance during the fMRI sessions is depicted in Figure 5.2. The participants were able to reliably discriminate attended targets with an overall accuracy of 79% correct. There was no statistically significant difference in performance across attended modalities and feature dimensions.

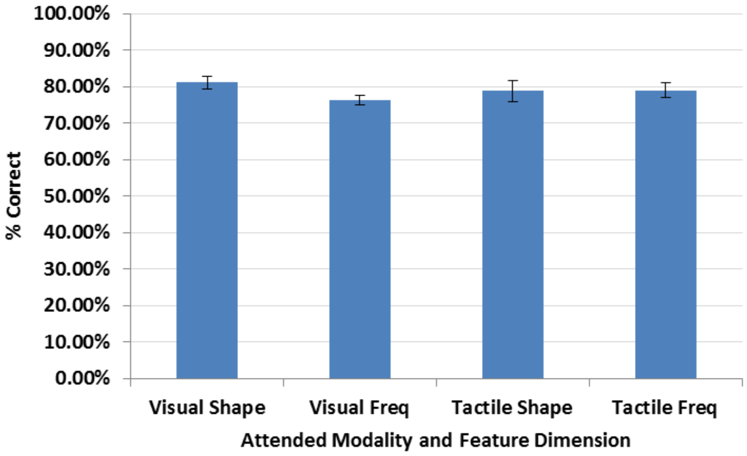


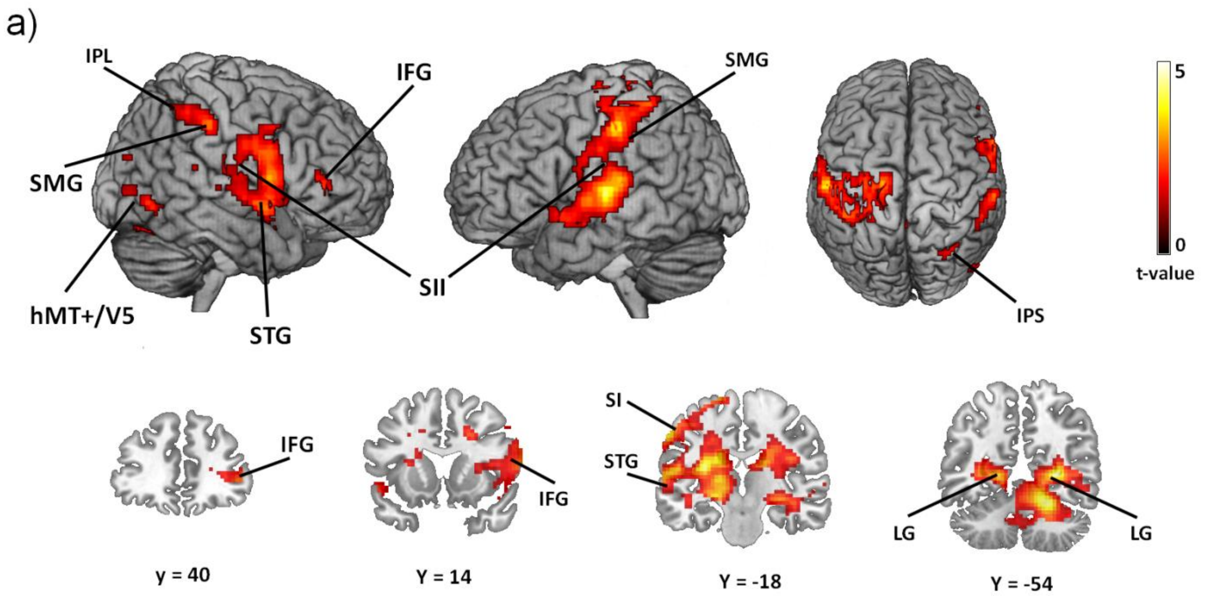
Figure 5.2. Mean behavioural performance for each attentional condition. No significant difference was observed when attending to different feature dimensions within each modality (paired sample t-test; visual-shape vs. visual-freq: $p = 0.066$; tactile-shape vs. tactile-freq: $p = 0.965$). Similarly, there was no significant difference in mean performance across modalities, but within the same attended feature dimension (paired sample t-test; visual-shape vs. tactile-shape: $p = 0.309$; visual-freq vs. tactile-freq: $p = 0.146$).

5.3.2 Modality Specific and Non-specific Activations

5.3.2.1 Common Top-Down Sources of Multisensory Feature-Based Attention

In the first stage of the analysis, we investigated the overall brain network involved in sustaining attention to a specific feature dimension (shape or frequency) across both modalities and to identify potential supramodal sources of feature-based attention. To test whether endogenous attention to visual-shape recruited similar fronto-parietal regions with attention to tactile-shape, we ran a conjunction analysis between the contrast of visual-shape vs. baseline and tactile-shape vs. baseline. Univariate conjunction analysis revealed several small but significant clusters of activations in the fronto-parietal network comprising the right IFG, right anterior IPS, and bilateral SMG (Figure 5.3a). We also observed significant responses in the relevant sensory regions, including bilateral secondary somatosensory cortex (SII) and right V5/hMT+. Superior temporal sulcus (STS), a region commonly associated with multisensory integration (Beauchamp et al., 2008), was also strongly activated by the concurrent visuo-tactile stimuli. An above-baseline response was also observed within bilateral lingual gyrus, possibly due to the task demand for shape recognition (Kanwisher et al., 1997; Saito et al., 2003). In agreement with previous findings on multisensory spatial attention in vision and touch (Macaluso et al., 2002a; Macaluso, 2010), we observed common activations in most of the dorsal and ventral frontoparietal network (Corbetta et al., 2008), with the exception of the FEF.

Conjunction analysis between the contrast of visual-frequency vs. baseline and tactile-frequency vs. baseline revealed a very similar pattern of activation (Figure 5.3b). The main noticeable difference compared to the attend-shape condition was more prominent spread of activations within frontal regions. Significant activations were observed in bilateral IFG, right middle frontal gyrus, bilateral inferior parietal lobe (IPL), right SII, and V5/hMT+, and bilateral lingual gyrus. In this condition, we also observed an elevated response of pre-SMA, a region that was not significantly activated in attend-shape condition.



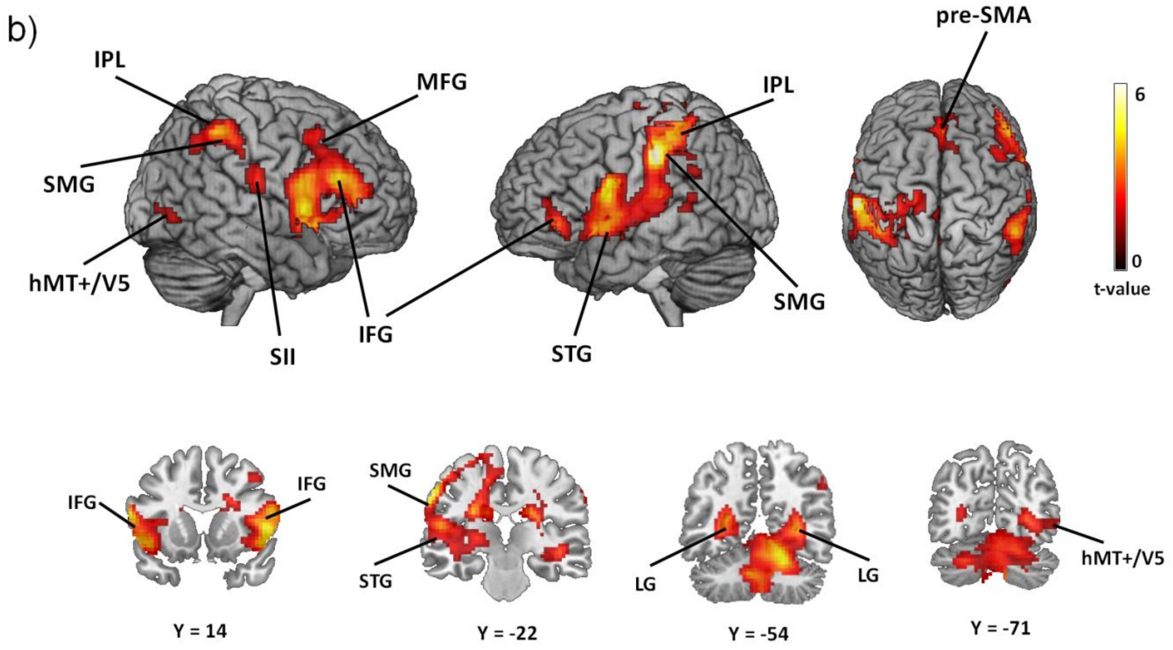
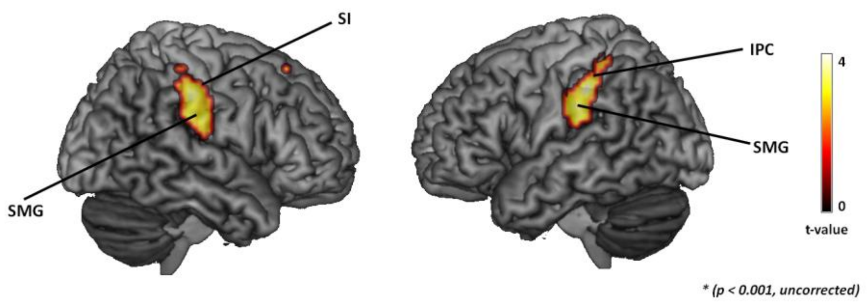


Figure 5.3. (a) Whole-brain activation maps obtained from conjunction analysis between the contrast of (visual-shape vs. baseline) and (tactile-shape vs. baseline). Peak activations were observed in the frontoparietal cortex, comprising the right IFG, right IPS, and bilateral SMG. Significant responses were also observed in the relevant sensory regions, including bilateral SII, right V5/hMT+, and the STS. Activation maps are thresholded at $p < 0.05$ (FDR-corrected). **(b)** Univariate conjunction maps between the contrast of (visual-frequency vs. baseline) and (tactile-frequency vs. baseline). Similarly, above baseline activities were observed in bilateral posterior parietal cortex comprising the SMG and IPL. In comparison to attend-shape conditions, more widespread activations were observed in the right frontal regions, including the IFG, MFG, and pre-SMA. Activation maps are thresholded at $p < 0.05$ (FDR-corrected).

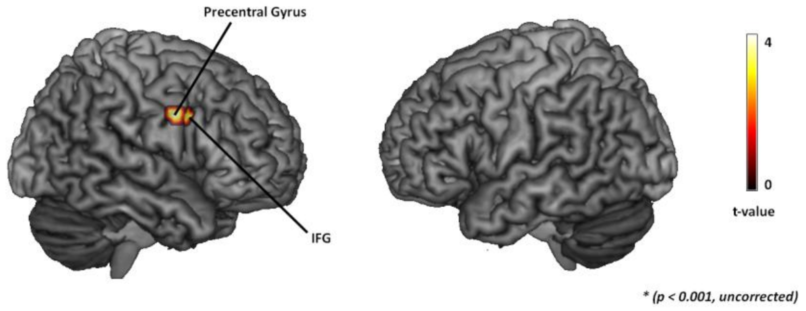
5.3.2.2 Modality Specific Activity (Univariate Analysis)

In the preceding analysis, univariate conjunction analyses revealed various brain regions that were commonly activated while sustaining attention to both visual and tactile features. In the next analysis, we asked the opposite question of whether any brain regions are differentially activated during feature-based attention in one sensory modality relative to the other modality (i.e. modality specific regions). Initially, we applied classical univariate analysis to test the contrast for the attend visual-shape vs. attend tactile-shape conditions. This contrast was computed by running a conjunction analysis of (visual-shape minus tactile-shape) with (tactile-shape minus visual-shape) to find regions that were strongly activated in visual-shape condition but not in tactile-shape condition and vice versa. No significant activation was found when multiple comparison was applied (*p < 0.05, FDR*). However, there was a trend towards significant activations in bilateral SMG, left inferior parietal cortex, and right somatosensory cortex, as shown in Figure 5.4a (*p < 0.001, uncorrected*).

A similar contrast was computed for the attend visual-frequency vs. attend tactile-frequency conditions. Likewise, we found no significant activation when the maps were corrected with multiple comparisons (*p < 0.05, FDR*). The trend towards significance (*p < 0.001, uncorrected*) was only observed in the right ventral precentral gyrus, bordering right IFG (Figure 5.4b).


a) Univariate Contrast for Visual-shape vs. Tactile-shape

Area	MNI Coordinates	t-value
R - SMG	51, -25, 40	5.3
R - SI	55, -20, 43	3.7
L - SMG	-51, -31, 40	5.7
L – inferior parietal	-45, -41, 56	3.9


b) Univariate Contrast for Visual-freq vs. Tactile-freq

Area	MNI Coordinates	t-value
R - Motor	45, 2, 31	4.5
R - IFG	42, 12, 32	1.6

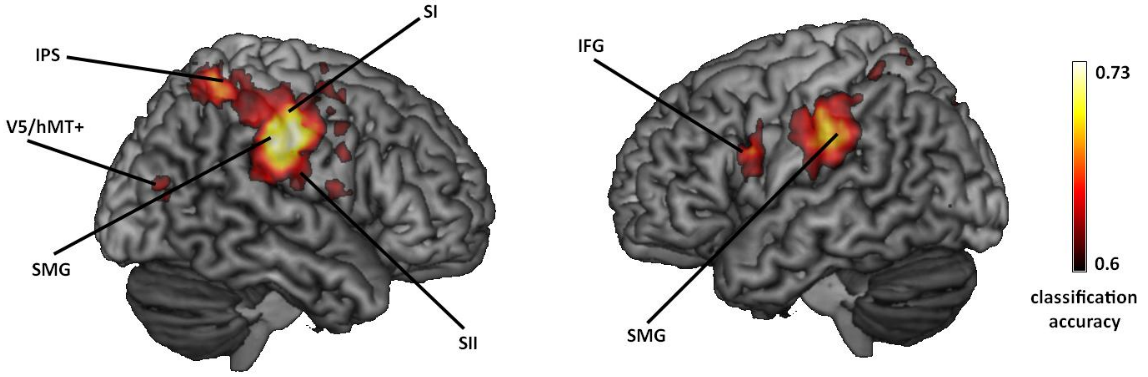
Figure 5.4. (a) Univariate contrast for attend visual-shape vs. attend tactile-shape condition, obtained using conjunction of (visual-shape > tactile-shape) contrast with (tactile-shape > visual-shape) contrast. A nearly significant response was found in bilateral SMG, left inferior parietal cortex, and right SI. **(b)** Univariate contrast for attend visual-frequency vs. attend tactile-frequency condition, obtained using conjunction of (visual-frequency > tactile-frequency) contrast with (tactile-frequency > visual-frequency) contrast. Almost no region was activated, except a small part of ventral precentral gyrus, neighboring pars opercularis IFG.

5.3.2.3 Modality Specific Activity (MVPA Analysis)

To increase the sensitivity of discovering modality specific regions and to examine whether there is any information that encodes the currently attended modality, we also analysed the fMRI data using the MVPA searchlight technique (Kriegeskorte et al., 2006). Initially, a whole-brain searchlight map was computed for each participant and then combined at the group level using random effect analysis in SPM (similar to Soon et al., 2008; Stokes et al., 2009). Significant above-chance classification of visual-shape vs. tactile-shape was observed in broader regions compared to earlier univariate analysis of the same contrast (Figure 5.5a). Peak discriminative voxels (greater than 70% classification accuracy) were identified in bilateral SMG and right SI, complementing the result of univariate analysis. Other significant clusters (above 60% accuracy) were also found in bilateral IPS and left IFG, suggesting the existence of modality specific population coding for top-down attentional selection in these common fronto-parietal regions.

Searchlight analysis also revealed clusters of informative voxels that could discriminate between the attend visual-frequency and attend tactile-frequency conditions (Figure 5.5b). Discriminative voxels were found in right IPS, right SII, right precentral gyrus, and left STS. Unlike the attend-shape condition, only a small cluster of informative voxels was observed in the right SMG and no significant voxels were found in the left SMG or left IFG.

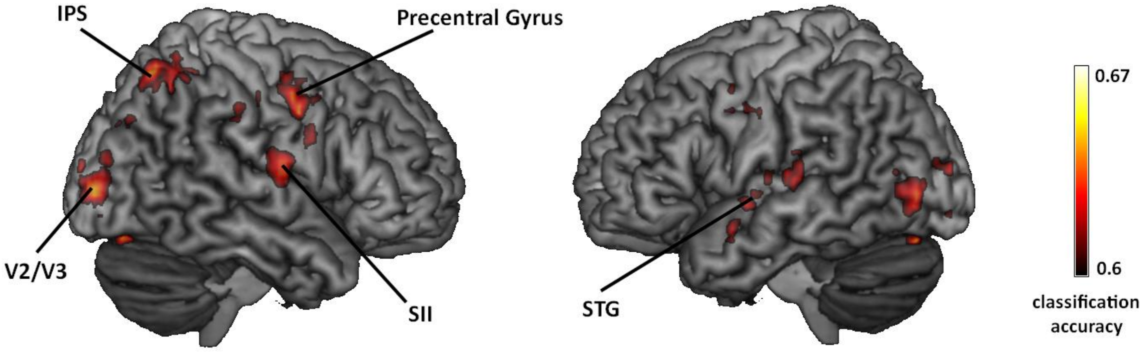
a) MVPA searchlight discriminating visual-shape vs. tactile-shape



* (p < 0.05, FDR)

Area	MNI Coordinate	Classification Accuracy
L – IFG	-55, 10, 25	.68
L – Postcentral (SI)	-59, -13, 31	.66
L – SMG	-58, -24, 33	.70
R – MT/V5	49, -76, 13	.66
R – IPS	33, -52, 64	.70
R – SMG	60, -25, 34	.73
R – Postcentral (SI)	60, -16, 38	.73

b) MVPA searchlight discriminating visual-frequency vs. tactile-frequency



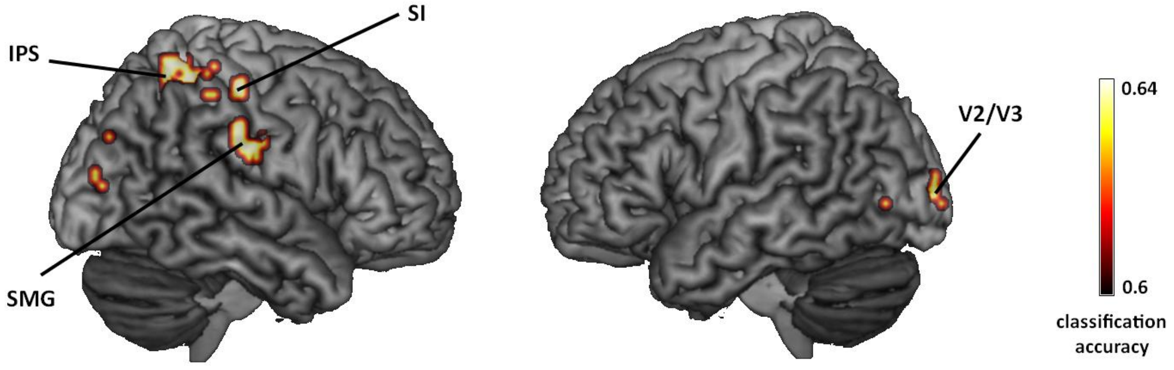
* (p < 0.05, FDR)

Area	MNI Coordinates	Classification Accuracy
L – STG	-65, -24, 7	.62
L – MT	-48, -77, 1	.64
R – V2/V3	33, -91, 3	.64
R – IPS	28, -64, 52	.63
R - SMG	62, -29, 38	.61
R – SII	61, -9, 16	.64
R – Motor Cortex	51, -1, 40	.64

Figure 5.5. (a) Multivariate searchlight analysis contrasting attend visual-shape vs. attend tactile-shape revealed several regions that contain informative population coding that can distinguish between these two attentional conditions. The most informative voxels (above 70% accuracy) were found in bilateral SMG and right SI. Highly informative voxels (above 60% accuracy) were also found in bilateral IPS, left IFG, right SII, and right visual area V5/hMT+. Classification accuracy maps are shown for voxels that survived correction for multiple comparisons ($p < 0.05$, *FDR*) and having accuracy greater than 60%. **(b)** MVPA searchlight maps of attend visual-frequency vs. attend tactile-frequency condition. Cluster of informative voxels (above 60% accuracy) were found in several regions including right IPS, right visual area V2/V3, right SII, right precentral gyrus, and left STS. Accuracy maps are shown for voxels surviving correction for multiple comparisons ($p < 0.05$, *FDR*).

5.3.2.4 Cross-generalization Searchlight Analysis

In the preceding MVPA searchlight analysis, we observed spatial overlap of modality specific regions for attend-shape and attend-frequency condition in right IPS, right SMG, and right SII (Figure 5.5). To further investigate whether these overlapping regions actually contained common population coding for the attended modality across different feature dimensions, we analysed the data using a cross-generalization searchlight procedure (Stokes et al., 2009a). In particular, we trained a classifier model to discriminate the attended modality (visual vs. tactile) in one feature dimension and then used it to predict the attended modality in the other dimension. Cross-generalization did not reveal any informative voxels that survived correction for multiple comparisons ($p < 0.05$, *FDR*). Nevertheless, there was a trend toward correct generalization in right IPS and right SMG, indicating the possibility that these regions host modality-specific but feature non-specific processes (Figure 5.6).



** (p < 0.001, uncorrected)*

Area	MNI Coordinates	Classification Accuracy
R - IPS	26, -55, 57	.61
R - SI	54, -25, 52	.61
R - SMG	66, -23, 31	.62
L – Visual (V2/V3)	-13, -97, 8	.60

Figure 5.6. The result of the cross-generalization searchlight discriminating attended modality across different feature dimensions. The classifier was trained to discriminate the attended modality (visual vs. tactile) in one feature dimension (i.e. shape) and then used to predict the attended modality in the other feature dimension (i.e. frequency). Each feature dimension was used as the training and testing set, in turn, and the final classification result was the average of the two classification results. No voxels survived correction for multiple comparisons. However, we observed a trend towards significant generalization in several regions including right IPS, right SMG, right SI, and left visual areas V2/V3 ($p < 0.001$, *uncorrected*), indicating the possibility of common functional roles of these regions in maintaining sustained attention to both visual and tactile modality, irrespective of feature dimensions.

5.3.3 Top-down Attentional Modulation of Sensory Cortices

Thus far, we have discussed the involvement of frontoparietal networks during strategic feature-based attention in vision and touch. In this section, we reported the results of the analyses that aimed to investigate the top-down modulatory effect of multisensory feature-based attention in visual and somatosensory cortex.

5.3.3.1 Attentional Modulation in Visual Cortex

Initially, we looked at the mean activity of the whole visual region (Figure 5.7), including both striate and extrastriate cortex. Directing attention to the visual stimulus significantly increased the evoked response in the contralateral visual cortex and at the same time suppressed neural activity on the ipsilateral side (paired t-test, collapsed across features, $p < 0.0001$). Similarly, when attention was directed towards the tactile stimulus, mean activity was significantly stronger in the right visual cortex than in the left visual cortex (paired t-test, collapsed across features, $p < 0.0001$). Contrary to expectations, attention to touch evoked slightly stronger mean responses in visual cortex than attention to vision, although the difference was not statistically significant (paired t-test, collapsed across features, $p = 0.682$

for the right hemisphere; and *p*=0.402 for the left hemisphere). This result might indicate the effect of crossmodal influence of tactile attention on visual cortex (Macaluso et al., 2000) or multisensory integration of visuo-tactile signals (Shams and Kim, 2010). Within each hemisphere, there was no significant difference between the different attentional conditions, as revealed by one-way ANOVA comparing the mean signals across all four attentional states (vis-shape, vis-freq, tac-shape, tac-freq) (*F*(3,40) = 0.43, *p* = 0.736 for left hemisphere; and *F*(3,40) = 0.13, *p* = 0.943 for right hemisphere), reflecting the possibility that attentional modulation in visual cortex was roughly equal in all of these conditions.

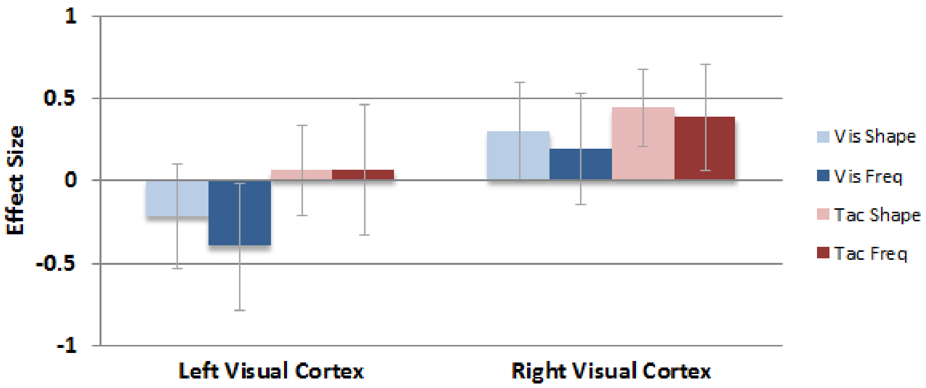


Figure 5.7. Mean BOLD signal changes in the left and right visual cortex during sustained attention to a specific modality and feature dimension, averaged across subjects. In general, attention to multisensory stimuli on the left hand side strongly up-regulated contralateral visual cortex, irrespective of the attended modality. Mean signal differences between left and right hemisphere collapsed across all four conditions were close to significance (two-way anova, *F*(1,80) = 3.86, *p* = 0.053). There were no significant differences among four attentional states in the right hemisphere (two-way anova, *F*(3,80) = 0.521, *p* = 0.67).

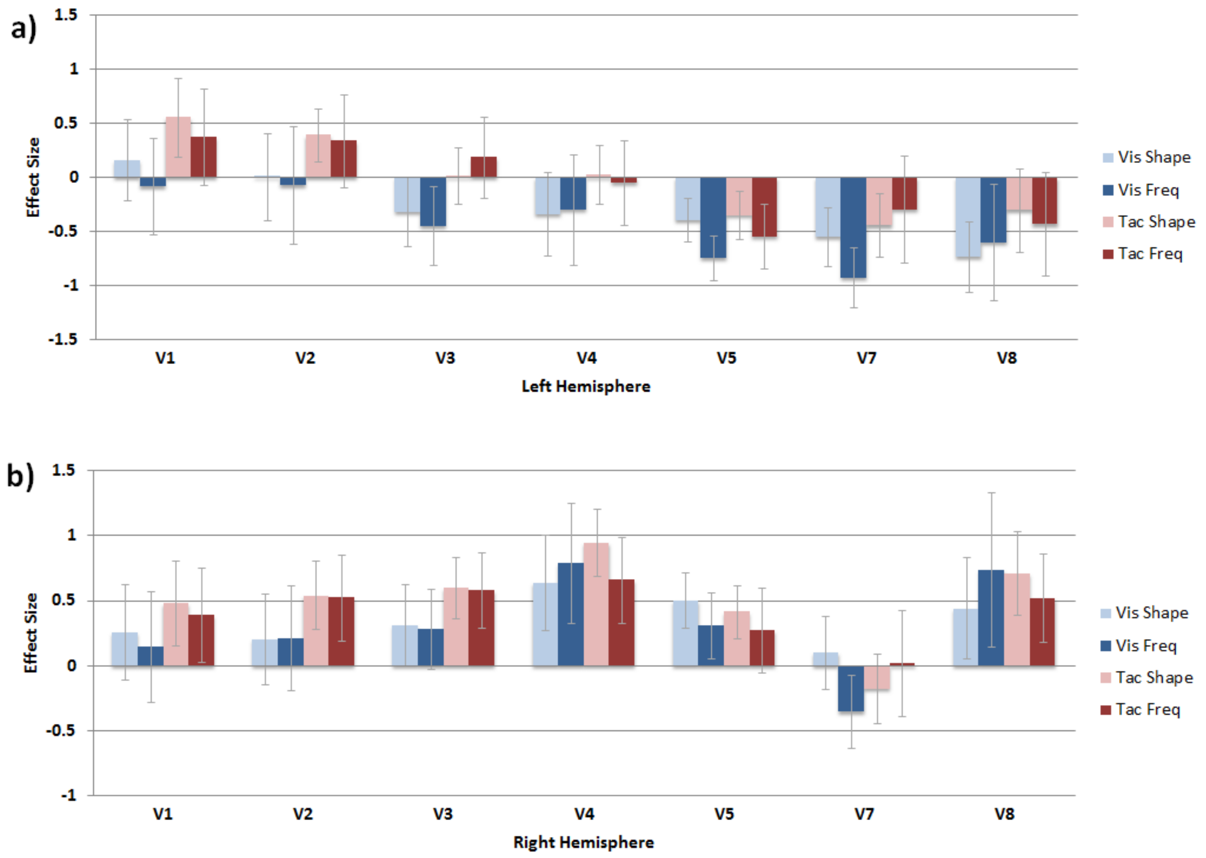


Figure 5.8. (a) Mean signal changes in the left retinotopic visual regions V1, V2, V3, V4, V5/MT, V7, and V8 for all four attentional states. Despite noticeable variance in the mean response across conditions within each ROI, no single region was found to elicit a statistically significant response. **(b)** Mean signal changes in the right retinotopic visual ROIs for all four attentional states. Likewise, no significant difference between attentional conditions was found in any of the ROIs.

We further investigated the effect of top-down attentional modulation in more details using retinotopically defined ROIs, asking whether mean signal differences in these areas could differentiate the attended modality and features. In the left hemisphere (Figure 5.8a), we can observe a trend of gradually increasing level of *deactivation* as we move from lower to higher visual regions. An opposite trend was observed in the right hemisphere (Figure 5.8b). The mean response increased gradually from V1 to V3, peaked at V4 and V8, but fell from V5 to V7. Although it seems that attention to touch evoked stronger responses in early visual regions (V1–V3) than attention to vision, the disparity was not statistically significant (paired t-test, collapsed across features; right-V1: p = 0.558; right-V2: p = 0.258, right-V3: p = 0.153). We also conducted a one-way ANOVA, independently for each retinotopic visual

ROIs in the right hemisphere, to test whether the difference in mean signal could be used to distinguish attended modality and features, and the results of analysis revealed that in spite of noticeable variance in mean response across conditions, there was not enough information to differentiate the different attentional states by looking at mean activations in these visual ROIs.

5.3.3.2 ROI-based MVPA Analysis in Visual Cortex

The preceding ROI analysis of visual cortical areas did not reveal any significant differences in mean BOLD signals between the attend-vision and attend-touch condition. However, we cannot conclude that both types of attention induced similar modulatory effects on visual cortex because it remains possible that, although the *mean* activity within the ROI is similar in both the visual and tactile conditions, the distributed pattern of activity within that ROI might be entirely different. Therefore, in this analysis, we applied ROI-based MVPA (Etzel et al., 2009) to further examine whether these visual ROIs contain distinct patterns of activity that could reliably discriminate between the attended modality and the attended feature dimension. Initially, we looked at the whole bilateral visual ROI, decoding the attended feature within each modality (visual-shape vs. visual-freq, tactile-shape vs. tactile-freq) and attended modality within each feature dimension (visual-shape vs. tactile-shape, visual-freq vs. tactile-freq).

Figure 5.9 shows the result of MVPA classification for the left and right visual cortex. Significant above-chance discrimination of the attended modality for both feature dimensions was observed in the right visual ROI, implying a distinct pattern of activity in visual cortex during sustained attention to visual and tactile targets. Interestingly, a modality-specific pattern of activity was also observed in the unstimulated region of left visual ROI, echoing the results of previous MVPA findings which reported spread of feature-selective attention in vision to regions that contained no stimulus (Serences and Boynton, 2007).

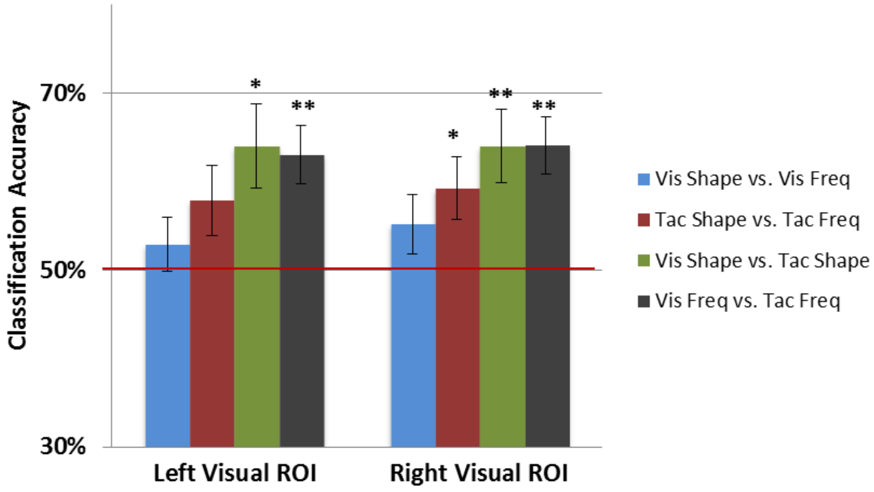


Figure 5.9. Results of ROI-based MVPA classification of attended modality and feature dimensions in the left and right visual ROI revealed significantly above chance classification of attended modality in both hemispheres and attended tactile feature in the right hemisphere. (* $p < 0.05$, ** $p < 0.01$, based on paired t-test against chance, 50%).

So far, the results of this classification analysis indicate that visual and tactile attention lead to distinguishable patterns of activity in visual cortex despite producing comparable changes in mean activity (Section 5.3.3.1). To identify possible differences in classification performance between early and late visual regions we repeated the same ROI-based MVPA classification using smaller retinotopically defined visual regions (Figure 5.10). Almost all visual regions (V1 – V8) in both hemispheres could reliably discriminate the attended modality (Figure 5.10b and 5.10d), indicating the presence of distributed modality-specific modulation throughout all visual regions. Moreover, this effect cannot be explained by differences in sensory input, because stimulus was always presented in both modalities and possible target combinations were equally balanced across all conditions. Information about the attended feature dimension in the visual modality could be decoded in the right visual region V5, V7, and V8, but not in the early visual regions (V1-V4) (Figure 5.10c, blue bars), suggesting that the effect of feature-selective modulation is greater in higher visual regions that are tuned to that specific feature. Similar trends was also observed in the unattended left hemisphere (Figure 5.10a, blue bars), although none were statistically significant. Interestingly, significantly above chance classification of feature dimension was also found in the right V4, right V7, and left V1 during attention in tactile modality (Figure 5.10c, red bars).

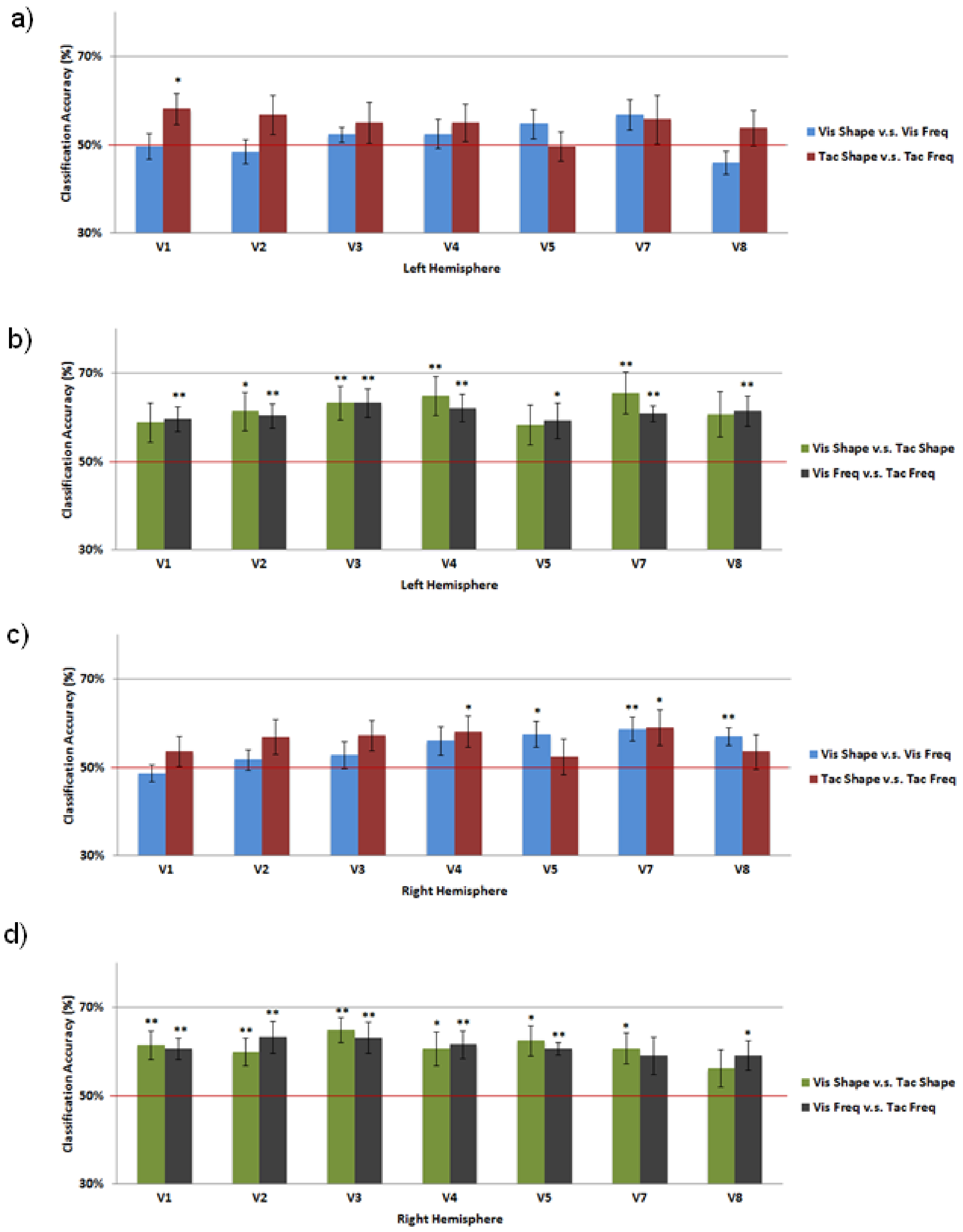
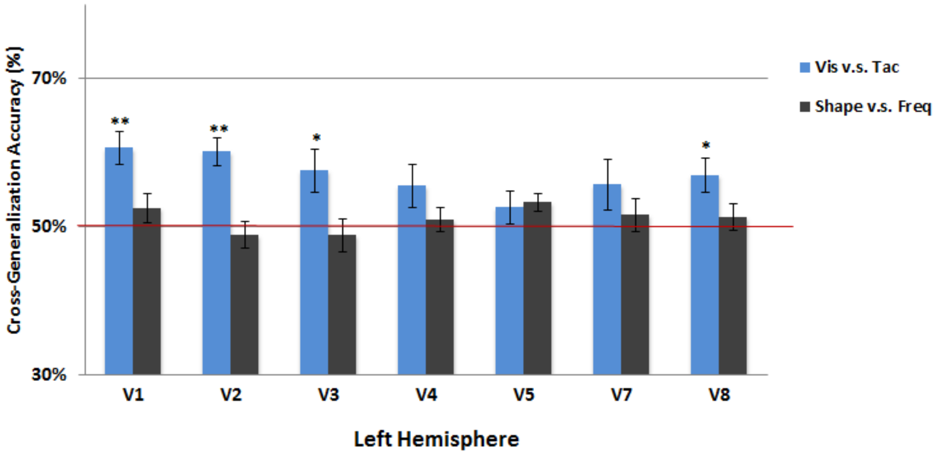


Figure 5.10. (a) ROI-based MVPA analysis classifying the attended feature dimension using retinotopic ROIs in the left hemisphere. **(b)** The corresponding MVPA classification results for the attended modality within the attended feature dimension in left visual cortex ROIs. **(c)** Result of MVPA analysis using retinotopic ROIs in the right hemisphere, discriminating the attended feature dimension within each modality. **(d)** Classification of attended modality within each attended feature dimension, using retinotopic ROIs in right hemisphere. (* $p < 0.05$, ** $p < 0.01$, based on paired t-test against chance (50%) and corrected for multiple comparisons).

To complete the analysis, we also performed cross-generalization MVPA analysis in these retinotopic regions (Figure 5.11). First, we tested whether a classifier trained to distinguish attended feature dimension in one modality (i.e. vision) could predict the attended feature in the other modality (i.e. touch). We reasoned that if modulatory activity in visual cortex during tactile attention was caused by spread of feature-selective effect to the visual distracter then the pattern of information that distinguishes between attention to shape from attention to frequency should be similar during attention to touch and attention to vision. The classifier trained to distinguish shape vs. frequency in one modality failed to discriminate attended feature dimension in the other modality (Figure 5.11, grey bars). These results provide further evidence for modality-specific modulation in these regions that cannot be simply explained by the spread of feature-selective attention to the unattended visual stimulus.

We next performed another cross-generalization analysis to test whether the distributed information of attended modality (visual vs. tactile) was similar between the attention to shape and attention to frequency conditions (Figure 5.11, blue bars). Significant cross-generalization performance was observed in area V1, V2 and V3 of both hemispheres, indicating that early visual regions contained modality specific but feature non-specific information, whereas some of the higher visual regions were modality specific and feature specific.

a)



b)

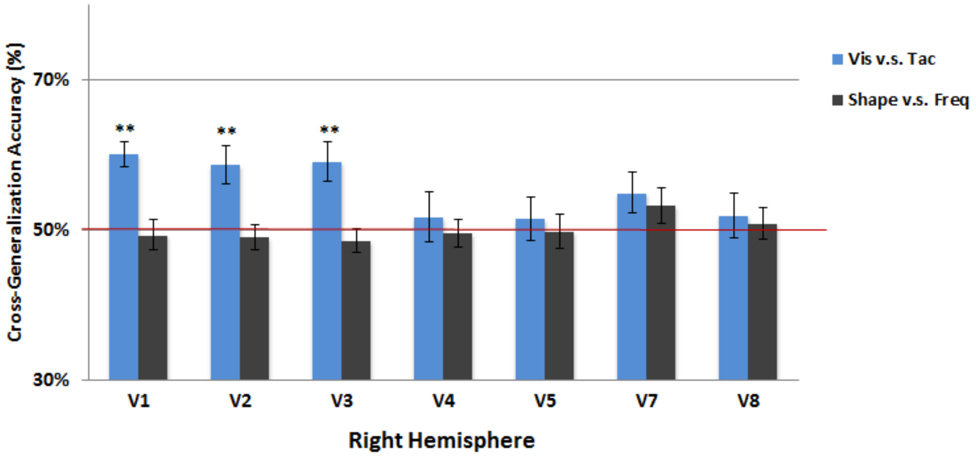


Figure 5.11. (a) Result of the cross-generalization MVPA analysis for retinotopic ROIs in the left visual hemisphere **(b)** Result of the same analysis in the right visual hemisphere. The blue bars denote the outcome of a classifier trained to distinguish the attended modality (visual vs. tactile) in one feature condition (i.e. shape) and then tested to discriminate the attended modality in the other feature condition (i.e. frequency). The grey bars denote the corresponding classification accuracy when the classifier was trained to discriminate the attended feature dimension (shape vs. frequency) in one modality (i.e. visual) and then used to classify the attended feature in the other modality (i.e. tactile). (* $p < 0.05$, ** $p < 0.01$, based on paired t-test against chance (50%) and corrected for multiple comparisons).

5.3.3.3 Attentional Modulation in SI

Analogous to previous ROI-analyses in retinotopic visual cortex described in Section 5.3.3.1, we have also conducted similar analysis to probe top-down modulatory effects of feature-based attention in primary somatosensory cortex (SI). Mean BOLD response in SI elicited by each of the attentional conditions were depicted in Figure 5.12. Directing attention to visual shape or visual frequency did not appear to enhance the baseline activity of either left or right SI, indicating the absence of cross-modal modulatory effects of vision on somatosensory cortex. In contrast, mean BOLD activities in bilateral SI were significantly increased during attention to tactile shape (single-sample t-test against 0, $p < 0.05$). Above baseline activity was also observed in the right SI during attention to tactile frequency, however, it was not statistically significant (single-sample t-test against 0, $p = 0.22$). These results point to the possibility that SI might be more important for discriminating the shape rather than the frequency of the tactile stimuli.

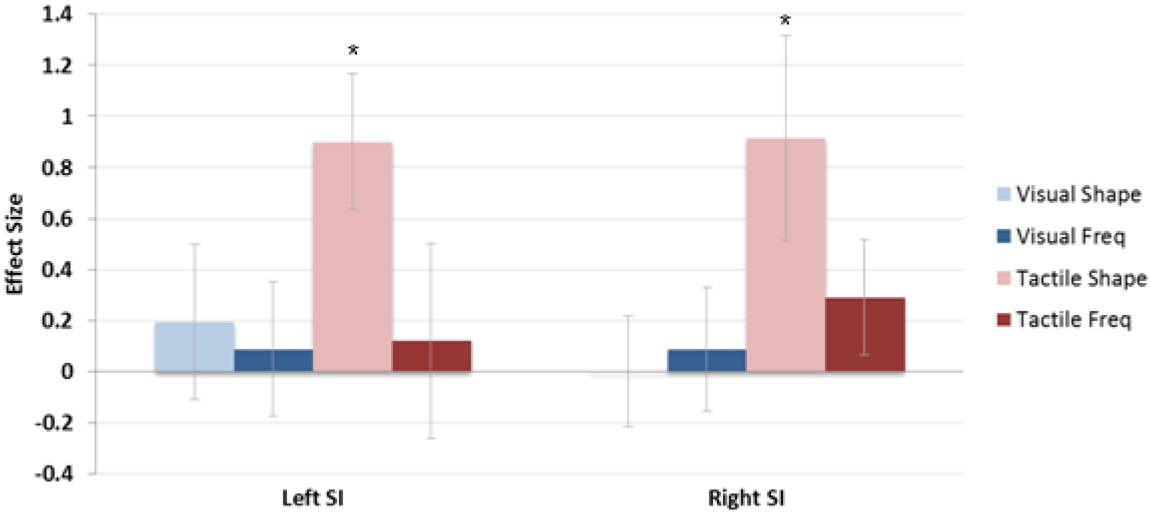


Figure 5.12. Mean BOLD signal changes in the left SI and right SI during four different attentional conditions, averaged across subjects. No significantly larger than baseline response was observed when visual stimuli were attended (left SI: visual-shape, *p* = 0.53; visual-freq, *p* = 0.74; right SI: visual-shape, *p* = 0.99; visual-freq, *p* = 0.71; single-sample t-test against 0). Similar null effects were observed during attention to tactile frequency, although mean response in right SI was closer to significance (left SI: *p* = 0.75; right SI: *p* = 0.22; single-sample t-test against 0). By contrast, significant increase in the baseline activity were observed bilaterally during attention to tactile shape (left SI: *p* = 0.006; right SI: *p* = 0.043; single-sample t-test against 0).

5.4 Discussion

In this study, we applied fMRI to investigate the neural activity associated with sustained feature-based attention within the modalities of vision and touch. The participants were instructed to sustain their attention either to the shape or frequency of the stimulus in one modality (i.e. visual or tactile), and to discriminate the target stimulus within that particular modality and dimension. To ensure constant sensory inputs throughout all attentional conditions, stimuli were always presented simultaneously in both modalities on each trial. Required motor responses were also matched across conditions by presenting randomized but balanced targets for each modality and feature dimension.

Unlike most studies of multisensory attention in vision and touch which usually involved spatial elements (Macaluso et al., 2002b; Eimer et al., 2002b; Chambers et al., 2004b), we used a task that involved sustaining attention to a single location only (left hand side). This enables the elucidation of multisensory feature-based attention without possible contamination of spatial-related activations. This approach accords with recent neuroimaging studies investigating the neural bases of vibrotactile feature attention (Burton et al., 2008; Wacker, 2011). Furthermore, we employed a variant of feature-based attention that required participants to selectively attend to a specific feature of a stimulus while simultaneously ignoring other irrelevant competing features present in that stimulus (McMains et al., 2007; Mirabella et al., 2007; Chen et al., 2012); this stands in contrast to most feature-based attention studies that investigated preferential processing of whole objects that matched a target feature among other competing objects (Maunsell and Treue, 2006; Schenkluhn et al., 2008; Liu and Hou, 2011). Using a single object that contains multiple features instead of multiple objects with numerous features enables us to study the neural bases of feature-based attention without the influence of object-selective or spatially-selective processes. Experiments using similar tasks have been conducted by Mirabella et al. (2007) in macaques monkeys, where they recorded responses of V4 neurons during attention to either colour or orientation of a single bar stimulus, and in macaque area MT by Chen et al. (2012), where they trained the monkeys to either attend to the direction of motion or the colour of the moving gratings.

A central point of contention in the study of the neural bases of attention is to what extent the mechanisms of endogenous orienting are generalized with regards to the sensory modality. In the present study, we asked the question concerning the generality and specificity of feature-selective attention in the visual and somatosensory modalities. Specifically, using classical univariate analysis we first investigated whether orienting of attention within vision and touch recruited similar fronto-parietal regions commonly associated with the attentional control network. Secondly, we applied MVPA searchlight analyses to examine whether these potentially supramodal regions contained distributed population coding that could reliably distinguish the attended modality. In the third stage of the analysis, we investigated the top-down modulatory effect of feature-selective attention on the respective sensory regions using both univariate and multivariate methods.

5.4.1 Potential Supramodal Frontoparietal Regions

In the first stage of analysis, we aimed to investigate to what extent the brain regions recruited for orienting of attention to visual features overlap with the regions activated while attention was oriented to tactile features. To visualize these regions, univariate conjunction analyses were computed between attend-visual and attend-tactile contrasts, separately for each feature dimension. Generally, a similar pattern of activity was observed regardless of whether attention was selectively directed towards the shape or frequency of the stimulus. Consistent activations throughout both modalities and feature dimensions were revealed bilaterally in the posterior parietal cortex (PPC), comprising regions near the IPS, SMG, and TPJ, an area commonly believed to be part of the dorsal and ventral frontoparietal network (Corbetta and Shulman, 2002; Corbetta et al., 2008). In the frontal cortex, attention to stimulus frequency evoked greater responses than attention to shape. When stimulus frequency was attended, prominent clusters of activations were observed in the bilateral IFG, right middle frontal gyrus (MFG), and pre-SMA, whereas during the attend-shape condition, the frontal activity was only visible in the right IFG. This result might indicate that orienting to stimulus frequency were cognitively more demanding than orienting to shape, thereby requiring increased neural resources in the frontal lobe (Sunaert et al., 2000).

Overall, the fronto-parietal networks observed in this study were consistent with the commonly reported dorsal and ventral attention networks (Corbetta and Shulman, 2002) in previous neuroimaging studies involving strategic attention to particular features (Giesbrecht et al., 2003; Slagter et al., 2007) and sensory modalities (Macaluso, 2010). Together, these findings suggest that this network is ubiquitous for orienting of attention across sensory modalities and stimulus dimensions including location, features, and objects. Previous neuroimaging studies have revealed that the dorsal frontoparietal network was pre-activated during preparatory attention while the subject was expecting the stimulus to appear (Corbetta et al., 2008). Based on this evidence, the dorsal system was thought to play a central role in initiating and maintaining endogenous attentional signals, and for selectively biasing relevant sensory regions in a top-down manner. Complementary to the dorsal network is the ventral frontoparietal network, which is activated when task-relevant targets are detected (Corbetta et al., 2008). It has been proposed that the function of this network is akin to a ‘circuit breaker’, interrupting ongoing attentional biases in the dorsal network when unexpected new input is detected and triggering reorienting of attention towards the new stimulus. Recruitment of both dorsal and ventral networks seen in the current study is consistent with this hypothesis because the task that we used contained both elements of endogenous selective attention (i.e. sustained attention to certain modality and feature) and bottom-up stimulus driven input.

In comparison to Experiment 4 (discussed in Chapter 4), the amount of overlapping activations observed in this experiment was comparatively less, indicating the possibility that orienting of attention to stimulus features might depend more on modality-specific fronto-parietal regions than attention to spatial location. Nevertheless, the degree of modality specificity between feature and spatial attention could not be compared directly because here we used two different tasks. Future experiments that investigate this particular issue should adopt a task that combines both elements of spatial and feature orienting in a single paradigm, similar to the approaches which has been taken previously when comparing neural basis of spatial and feature-based attention in vision (Giesbrecht et al., 2003; Slagter et al., 2007; Greenberg et al., 2010). In these studies, it was shown that orienting to a location recruited more medial dorsal parietal and frontal regions than orienting to stimulus feature, suggesting the existence of both general and dimension-specific mechanisms in these regions (Slagter et al., 2007).

Another notable findings of this study compared to the results of Experiment 4 is the absence of significant common activations in the FEF, an area which is attributed to be important for both attention and eye movements (Rizzolatti et al., 1987; Corbetta et al., 1998b; Craighero and Rizzolatti, 2010). This observation might indicate that this prefrontal region is only necessary for orienting of feature-based selective attention to one modality but not the other (i.e. modality-specific). However, further univariate and multivariate analysis contrasting visual and tactile conditions (described in Section 5.3.2.2 and 5.3.2.3) did not reveal any evidence of modality-specific activity within this region. An alternate explanation for the lack of FEF activation might be related to the fact that in the current paradigm there was no requirement for covertly shifting attention between locations (i.e. stimuli were always presented in one location on the left hand side) and the size of the stimulus was very small. Most other visual and crossmodal attention experiments that reported FEF activation either involved spatial orienting towards stimuli in various locations (Macaluso et al., 2002b; Slagter et al., 2007; Greenberg et al., 2010) or using a stimulus that covered a large sector of the visual field, requiring their subjects to spread their attention spatially (Liu, 2003). Interestingly, in a recent vibrotactile feature-attention study using a small tactile stimulus applied to the right index finger (Wacker, 2011), similar lack of FEF activation was also observed.

5.4.2 Common Activation in the Sensory Regions

In addition to activations in the fronto-parietal regions, univariate conjunction analysis also revealed significant overlapping responses in the relevant sensory regions, including secondary somatosensory cortex (SII), superior temporal sulcus (STS), lingual gyrus, and right V5/hMT+. In line with previous neuroimaging studies which reported that vibrotactile stimulation of a fingertip strongly modulated neural responses in bilateral SII (Burton et al., 2008; Wacker et al., 2011), similar SII activations in the current study indicate that the tactile input was processed in this region regardless of which sensory modality was task relevant. However, no overlapping activation was observed in contralateral SI and this area was significantly increased only during tactile conditions. Presentation of concurrent visuo-tactile stimuli also activated the STS, an area which has been shown to be important for multisensory integration of visual, auditory, and tactile signals (Macaluso and Driver, 2005; Beauchamp et al., 2008). The involvement of the STS might indicate that although there was no task-relevant demand for multisensory integration, nonetheless there might still have been some form of automatic or pre-attentive integration across modalities.

5.4.3 Modality Specific Activity (MVPA Analysis)

We have shown in the previous analysis (Section 5.3.2.1) that regions in the fronto-parietal attention network were both activated during orienting of attention to visual and tactile features. These findings suggests that some of these regions might contain populations of supramodal neurons necessary for controlling attention to both modalities, as has been previously proposed in other multisensory attention studies (Macaluso et al., 2002b; Eimer et al., 2002b; Green et al., 2011). However, due to the nature of an fMRI voxel which generally contain millions of neurons (Logothetis, 2008), it is possible that the specific underlying neural populations that were recruited might be unique for each condition. Activations of overlapping but functionally distinct neuronal populations could give rise to a small bias in each voxel, and by pooling these biases across adjacent voxels it may be possible to discriminate the task conditions that were previously inseparable (Kamitani and Tong, 2005; Tong and Pratte, 2012). This principle underlies the MVPA technique that we performed in this analysis for finding potential cortical regions that might contain population coding of modality- or dimension-specific information. A recently published study comparing the sources of spatial and feature-based attention also applied similar logic to investigate whether overlapping regions in the frontal-parietal ROIs contain dimension specific information (Greenberg et al., 2010). Using a linear-SVM classifier, they found that common activations in the PPC can significantly classify whether the subject was attending to a location or to a stimulus feature, but this was not the case with common activations in the frontal ROIs.

We applied MVPA searchlight analysis (Kriegeskorte et al., 2006; Kriegeskorte and Bandettini, 2007) to map brain regions that contained modality-specific information, separately for each feature dimension (i.e. shape or frequency). During the attend-shape condition (Figure 5.5a), above chance classification of attended modality was found in bilateral parietal cortex, with discriminative peaks observed in bilateral SMG, spreading posteriorly to the right IPS, and anteriorly to the primary and secondary somatosensory cortices (SI and SII). In frontal regions, a small cluster of informative voxels was also observed in the left IFG. By contrast, fewer distributed activations were found during the attend-frequency condition (Figure 5.5b). Disconnected clusters of discriminative voxels were observed in the right IPS, right SII, right premotor cortex, and around left STS, but almost no activations at all around the SMG in either hemisphere.

This searchlight result raises the interesting possibility that the degree of modality specificity of SMG might also depend on which type of feature requires attention. When attention was directed towards shape, searchlight MVPA revealed that SMG operated in a modality-specific manner. In contrast, even though attention to stimulus frequency also strongly activated bilateral SMG for both modalities (as shown in the result of conjunction analysis), no modality-specific information was found by searchlight analysis in these regions, suggesting possible existence of common supramodal neural mechanism for orienting towards stimulus frequency. The findings of modality-specific regions in SMG during attention to stimulus shape further corroborates previous TMS studies which provide evidence that SMG has a critical role in orienting of attention to visual, but not to somatosensory events (Chambers et al., 2004b). Likewise, in a related study investigating specificity and generality of spatial and feature-based attention in vision, it has been shown that disruption of the SMG only affected strategic orienting to a spatial location, with no impairment observed when attention was oriented to a stimulus colour (Schenkluhn et al., 2008). The present study further extends these TMS studies by suggesting that specific function of the SMG might also be modulated by competing intrinsic features that need to be attended. Although SMG was activated during both attention to shape and frequency, as discussed in the result of univariate analysis in Section 5.3.2.1, MVPA searchlight analyses revealed that this region contained modality-specific information only when shape was attended. This result suggests that SMG might be an important hub for top-down regulation of intermodal attention to shape-specific features but not to temporal-features like stimulus frequency.

In contrast, regions in the right IPS were able to classify the attended modality in shape and frequency conditions, showing modality specificity of this region across features dimensions. However, a closer observation revealed that the location of informative clusters in IPS during attention to shape were slightly more posterior than during attention to frequency (Section 5.3.2.3), indicating recruitment of anatomically distinct IPS sub-regions. Furthermore, cross-generalization searchlight analysis classifying the attended modality across both feature dimensions (modality-specific but feature non-specific information; Section 5.3.2.4) uncovered no significant voxels after correction for multiple comparisons. There was a trend towards significance in the right anterior IPS which overlaps with the location of informative clusters in IPS during the attend-shape condition. Together, these results indicate that although there was modality-specific information in the IPS during attention to shape and frequency, their specific anatomical locations were rather distinct, and thus cross-generalization searchlight analysis was unable to detect significant voxels that were both modality-specific and dimension-nonspecific.

Observation of modality-specific yet anatomically distinct region in IPS echoes a recent finding of resting state fMRI reported by Anderson et al. (2010). They investigated the internal architecture of IPS by tracing its connectivity to other brain regions using maximal connectivity clustering, and found that connectivity between IPS and other regions were topographically organized, with each connection specialized to different sensory modalities. The present results are also in line with similarly motivated MVPA study that investigated domain-specific information within overlapping activations in frontoparietal regions elicited by strategic spatial and feature-based attention (Greenberg et al., 2010). They found that region in the posterior parietal cortex (PPC; which includes IPS), but not in the frontal cortex, could reliably distinguished spatial and feature-based attention shifts, suggesting domain-specificity of the PPC regions.

5.4.4 Top-Down Modulatory Effect of Feature-Based Attention on Visual Cortex

Evidence from electrophysiological recordings in monkeys (Martinez-Trujillo, 2011) and human neuroimaging studies (Maunsell and Treue, 2006) have demonstrated that orienting strategic attention to a particular feature of the visual stimuli can modulate visual regions that are specific for processing those feature dimensions. In an early PET study, Corbetta et al. (1990) discovered feature-specific modulatory effects in the extrastriate cortex induced by various stimulus attributes including colour, shape, and velocity. Later studies using fMRI have further confirmed and extended these findings by showing that attention to visual motion selectively increased activity in visual area V5/hMT+ (Beauchamp et al., 1997; Shulman et al., 1999; Saenz et al., 2002), whereas attention to colours elicited modulatory effects within the colour-selective regions of the visual cortex (V4/V8; Liu, 2003; Schoenfeld et al., 2007). Interestingly, a growing body of evidence has also suggested that modulatory effects of feature-based attention could also spread beyond the current spotlight of attention (McAdams and Maunsell, 2000; Martinez-Trujillo and Treue, 2004; Bichot et al., 2005; Liu and Mance, 2011), extending even to distant unstimulated locations (Serences and Boynton, 2007).

In the present study, we applied classical ROI-based analysis and ROI-based MVPA classification to identify modality- and feature-specific modulatory effects in the visual and somatosensory cortex. We initially compared mean BOLD signals in retinotopic regions elicited during attention to visual-shape vs. attention to visual-frequency to identify feature-specific modulation within vision (discussed in Section 5.3.3.2). Specifically, we asked whether attention to visual-frequency evoked stronger responses in the motion sensitive regions (V5/hMT+) than attention to visual-shape. Contrary to our expectations, we detected no significant differences in the mean evoked response between these two attentional states in any retinotopic ROIs.

Although counterintuitive, the absence of feature-selective modulatory effects in V5 echoes recent findings of an fMRI study (McMains et al., 2007) that employed similar feature-based attention task used here. In their study, they compared the effect of attention to an object with a single feature (i.e. just colour or motion) with attention to an object with multiple features (i.e. containing both colour and motion). They discovered that when their participants were presented with a coloured object, baseline activity in V4 was significantly increased compared to when a moving object was displayed, with the opposite pattern observed in V5. By contrast, barely noticeable differences were observed in the baseline activity of V4 and V5 when a competing colour or motion within an object was attended. These findings indicate that attending to a competing feature within an object might automatically engage object-based attentional processes that highlight the object holistically and facilitate processing of unattended features within that object. We further investigated whether modulatory effects on visual cortex during attention to visual stimuli were truly feature-independent by applying ROI-based MVPA classification to decode attended feature dimension from patterns of activity in retinotopic ROIs (discussed in Section 5.3.3.2). Above -chance discrimination of the attended feature was observed in the late visual regions (V4 – V8), but not in the early visual regions (V1 – V3). This finding suggests the existence of feature-specific modulations in the higher visual regions that selectively bias preference towards currently attended feature dimensions, consistent with previous studies that found increasing attentional modulation effects as we ascend the hierarchy of visual regions (Tootell et al., 1998; Liu et al., 2005).

In the other part of the analysis, we investigated whether attention to vision elicited greater activity in the visual cortex compared to attention to touch (i.e. intermodal modulatory effects). Contrary to expectations, both visual and somatosensory attention elicited equally strong activations in the visual cortex, and no significant differences of mean BOLD signals were found between these two modalities. We further applied ROI-based MVPA classification to probe whether patterns of activity within these retinotopic ROIs were different between attention to vision vs. touch. The results revealed that most of the regions in the early and late visual cortex could significantly discriminate the currently attended modality, indicating the presence of multimodal and modality-specific modulatory activity in visual cortex.

In the paradigm used in the present study, we employed presentation of bimodal visuo-tactile stimuli. Hence, there was a possibility that activity in the visual cortex during tactile attention might simply be induced by spread of attention to irrelevant visual distracters, and not induced by any top-down multisensory effects from other regions. To test this hypothesis, we trained an ROI-based MVPA classifier to discriminate attended feature dimension (i.e. shape or frequency) in one modality (i.e. vision) and then used the trained classifier to distinguish attended feature dimension in the other modality (i.e. touch), and vice versa (cross-generalization procedure). We reasoned that if activity in the visual cortex during tactile attention was caused by spread of feature-based attention to the unattended visual distracter, then the patterns of activity that distinguished shape vs. frequency in the visual condition should be similar to the patterns of activity that distinguished shape vs. frequency in the tactile condition (i.e. activities in both conditions were driven by attentional modulation of visual input signals). The outcome of the classification analysis revealed that none of these retinotopic ROIs contained modality-nonspecific encoding of the attended feature dimension, suggesting the existence of modality-specific top-down modulatory effects on the visual regions.

Many plausible accounts might be able to explain this crossmodal influence of tactile attention on visual cortex, including the existence of multisensory representations in higher visual regions that facilitate top-down mental imagery. Several studies comparing neural activity of visual and tactile processing have demonstrated that some visual regions traditionally regarded as *unisensory* are involved not only during processing of visual information but also during processing of tactile information, including the lateral occipital complex (LOC; Amedi et al., 2002; Beauchamp, 2005; Lucan et al., 2010; Kim and Zatorre, 2011) and V5/hMT+ (Hagen et al., 2002; Blake et al., 2004; Summers et al., 2009; Wacker et al., 2011). Based on these observations, Sathian and colleagues have proposed a model for multisensory object recognition that relies on common mental imagery mechanisms, shared across multiple sensory modalities (Stilla and Sathian, 2008; Lacey and Sathian, 2011). According to this account, the LOC and IPS host shared multisensory representations that are flexibly accessible in a bottom-up or top-down manner along the continuum of mental imagery (Peltier et al., 2007). Related evidence for imagery-related representations in late visual cortex was recently reported in an MVPA study that demonstrated the existence of common population coding underlying visual perception and mental imagery in the LOC (Stokes et al., 2009a).

Previous multisensory spatial attention studies have demonstrated that attending to tactile stimuli could also evoke crossmodal activity in visual cortex at the commonly attended location (Macaluso et al., 2000; Driver and Noesselt, 2008). These crossmodal influences might be induced by multisensory integration processes, such as those demonstrated in the touch-induced visual illusion (Violentyev et al., 2005; Shams and Kim, 2010) or by the spread of object-based attention to task-irrelevant stimuli (Busse et al., 2005). Busse et al. (2005) applied fMRI and ERP to investigate the crossmodal spread of object-based attention between the visual and auditory modalities. The participants in their study were cued to covertly attend to either the left or right visual field, and to discriminate visual targets displayed on the attended side, while ignoring irrelevant visual targets in the unattended sides. On each trial, a task-irrelevant, centrally presented auditory stimulus was also simultaneously delivered with the visual targets. They found that evoked responses in the auditory cortex were significantly enhanced when accompanying visual stimulus was attended vs. unattended. The complementary ERP recordings revealed that this effect emerged relatively late in the processing stream, suggesting the manifestation of object-based attentional effects that group visual and auditory stimuli into a single multisensory object.

Another notable finding in the present study is the evidence for the spread of modality-specific information to the unstimulated and unattended part of the visual cortex (left hemisphere, Section 5.3.3.2), corroborating and extending analogous findings reported in previous studies. Several electrophysiological studies in non-human primates have provided evidence for the spread of feature-specific enhancements beyond the current locus of spatial attention, extending to distant unattended locations (McAdams and Maunsell, 2000; Martinez-Trujillo and Treue, 2004; Bichot et al., 2005). A more recent study using combination of fMRI and MVPA has further confirmed these findings by showing that feature-specific attentional effects could even spread to visual regions that contained no stimulus (Serences and Boynton, 2007). Our complementary finding further suggested that not only feature-specific information but also modality-specific information could spread to unstimulated part of the visual cortex.

5.4.5 Summary

In this study, we focused our investigation on the neural basis of intermodal feature-based attention in vision and touch. Specifically, using univariate conjunction analysis, we first inquired whether attention to visual and tactile features exhibit similar patterns of activity in the frontoparietal regions. We then applied MVPA searchlight analyses to locate modality-specific information within these regions. In the final stage of the analysis, we also investigated the top-down modulatory effects of feature-based attention on visual and somatosensory cortex.

Overall, the findings suggest that while feature-selective attention in vision and touch activated a similar fronto-parietal network, most of the regions in the posterior parietal cortex (PPC) could reliably classify patterns of activity associated with the attended modality, lending support to the existence of overlapping but modality-specific subpopulations of neurons throughout this region (Chambers et al., 2004b). Furthermore, MVPA searchlight analysis also revealed that the frontoparietal attention network recruited during attention to shape was distinct from the network activated when attending to stimulus frequency, providing evidence for the existence of dimension-specific attention networks in the brain. We also found that the pattern of activity in visual cortical regions was selectively modulated not only during attention to the visual stimulus but also when attention was directed toward the tactile stimulus; however these patterns were clearly distinguishable, signifying the existence of modality-specific attentional modulation within sensory brain regions.

Chapter 6 - Concurrent TMS/fMRI Study of Feature-based Attention in Vision

In this study, we examined feature-based attentional modulatory effects in retinotopic visual cortex using combination of simultaneous TMS/fMRI and MVPA analysis. Two pilot experiments will be discussed in this chapter, the first using fMRI and the second using simultaneous TMS/fMRI. The chapter begins with a brief review of previous TMS/fMRI studies and description of the task paradigm used. Experimental and analysis methods will then be presented, followed by discussion of the findings.

6.1 Introduction

Previous neuroimaging studies have provided evidence for the involvement of dorsal frontoparietal regions during strategic orienting of attention to various dimensions and modalities (Kastner and Ungerleider, 2000; Corbetta and Shulman, 2002; Corbetta et al., 2008). These dorsal regions, which includes the frontal eye fields (FEF) and the intraparietal sulcus (IPS), are implicated as the potential sources for attentional control signals that bias lower-level sensory regions. Novel statistical analysis methods of neuroimaging data have been developed to identify patterns of *functional connectivity* between cortical regions (Friston et al., 2003; Goebel et al., 2003; Friston, 2007) and these methods have been applied to indirectly infer top-down attentional effects on sensory regions. However, direct proof of causality cannot be obtained solely from neuroimaging due to its correlational nature. As an alternative, causal relationships between a cortical region and task-specific cortical networks can be investigated using interventional approaches including microstimulation or concurrent TMS/fMRI.

TMS enables non-invasive, reversible *virtual* lesion of a target region that causally influences the behaviour (Pascual-Leone et al., 2000; Siebner and Rothwell, 2003; Chambers and Mattingley, 2005; Stewart and Walsh, 2006). Recent behavioural TMS studies have demonstrated the crucial role of the right angular gyrus (AG; Rushworth et al., 2001; Chambers et al., 2004a; Chambers and Mattingley, 2005) and the right supramarginal gyrus (SMG; Chambers et al., 2004b, 2007; Schenkluhn et al., 2008) for strategic orienting of attention in various domains and modalities. Behavioural TMS studies, however, were unable to distinguish between local effects on the target site with remote TMS effects on the interconnected task-related cortical regions. Moreover, the exact nature of TMS intervention on neural processing is still heavily debated (Harris et al., 2008; Siebner et al., 2009a).

Recent technical advances have enabled successful combination of concurrent TMS with fMRI (Bohning et al., 2003; Bestmann et al., 2008; Siebner et al., 2009b; Weiskopf et al., 2009; Bungert et al., 2012b, 2012a), which allows direct measurements of local and remote effects of TMS on whole-brain BOLD responses, providing a novel interventional approach to study functional connectivity of the brain. In early pioneering studies, TMS has been successfully combined with PET (Fox et al., 1997; Siebner et al., 1999) and EEG (Ilmoniemi et al., 1997). Subsequently, the feasibility of combining TMS and MRI was first demonstrated by Bohning and colleagues (1998) using MR-safe ferromagnetic-free materials for the TMS coil to preserve the homogeneity of the main magnetic field (B_0) of the scanner. There were many technical challenges associated with concurrent TMS/fMRI, especially concerning the positioning of the TMS coil inside the MR scanner (Bohning et al., 2003; Moisa et al., 2010; Bungert et al., 2012b), and reducing the MR artefact caused by the leakage currents (Weiskopf et al., 2009) and radiofrequency (RF) interference leaked through the lead of the TMS into the scanner room (Bungert et al., 2012a). Additional complications in delivering TMS pulses inside the scanner are related to the issue of loud auditory artefacts produced by the TMS coil and tactile sensations on the scalp that might cause unwanted artefacts in the measured BOLD signals.

Early TMS/fMRI studies primarily focused on the study of the motor system and revealed that stimulation of the M1 not only affected the BOLD signal at the stimulation site, but also remote regions connected with M1, including dorsal premotor cortex, SMA, and other subcortical structures (Bestmann et al., 2004; Denslow et al., 2005). In the later developments, several TMS/fMRI studies have also extended the investigation to probe functional interactions between the frontoparietal network and the sensory regions. In a key study reported by Ruff et al. (2006), they showed that TMS over the right FEF could modulate activity in the retinotopic visual regions in a topographically specific manner, during rest or visual stimulation. Specifically, they found that higher intensity TMS pulse over the right FEF increased BOLD activity for representations of the peripheral visual field (in V1-V4), but reduced the activity for the representations of the central visual field. This finding has corroborated and extended previous observations in microstimulation of macaque FEF neurons which demonstrated that FEF stimulation could modulate remote activities in V4 neurons (Moore and Armstrong, 2003; Armstrong and Moore, 2007). In a subsequent study, Ruff et al. (2008) have also demonstrated that TMS over the right intraparietal cortex could lead to distinct effects on visual cortex, and these remote influences were predominantly stronger in the right-hemisphere, implicating hemispheric lateralization of the parietal cortex (Ruff et al., 2009).

Although these concurrent TMS/fMRI studies by Ruff and colleagues were able to show remote influences of the dorsal frontoparietal region on the visual cortex activity, in their experimental design they did not manipulate the top-down attentional state of the participants, instead their participants were asked to hold a central fixation throughout the experiment. More recently, Blankenburg et al. (2010) applied TMS over the posterior parietal cortex (PPC) during visuospatial attention task to investigate task-dependent effect of the TMS on early visual processing. The visual stimuli in their study were held constant across conditions and only their participants' attentional state were manipulated, so that varying BOLD signals on the visual cortex could be attributed to coupling between remote influences of TMS and top-down attentional factors. They found that the impact of parietal TMS on visual cortex activity depended critically on the current attentional state. TMS on the right PPC increased BOLD activity in the right extrastriate cortex when attending to the left visual field, but decreased the activity of the same region when attending to the right visual field. The opposite, but less pronounced effect was found in the left extrastriate cortex. These findings have provided evidence for remote influence of TMS on the patterns of *effective connectivity* between PPC and visual cortex that dynamically vary as a function of the attentional state. In a related TMS/fMRI study reported by Heinen et al. (2011), TMS was applied over the right parietal cortex during exogenously cued visuospatial attention task. Consistent with the results of Blankenburg et al. (2010), they also found that TMS over the right AG could dynamically modulates neural responses in the visual cortex depending on the trajectory of spatial attention.

In the present pilot study, we aimed to investigate attention-dependent modulatory effects associated with TMS over FEF during sustained feature-based attention. Classical ROI-analysis was applied to find top-down modulatory effects in the extrastriate cortex, in combination with ROI-based MVPA analysis to probe the effect of remote TMS on the patterns of distributed information in the visual cortex. Two separate experiments were conducted. In the first experiment, we used fMRI to examine the feasibility of the attention paradigm, and in the second pilot experiment, we applied concurrent TMS/fMRI over the FEF during the feature-based attention task.

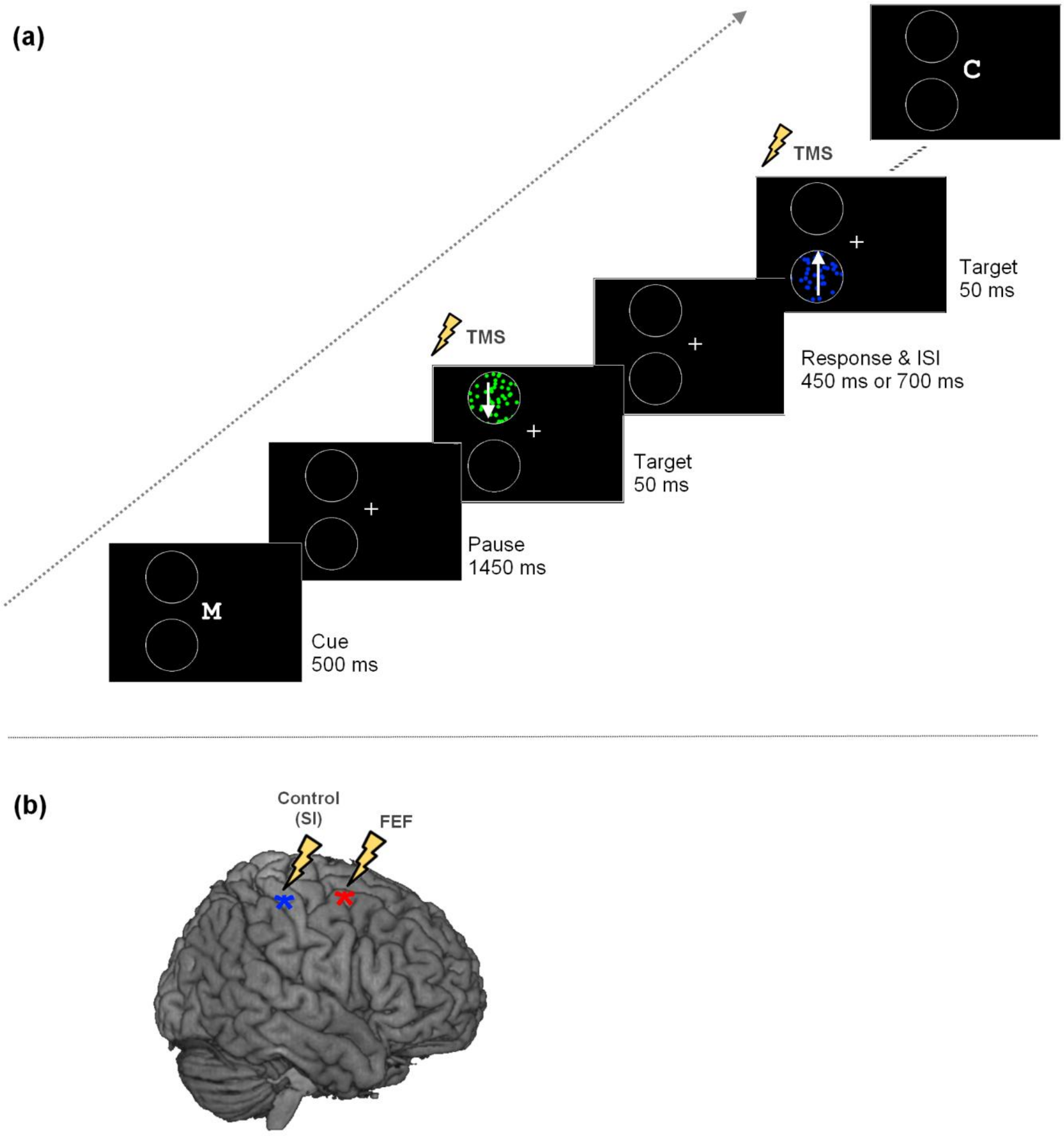


Figure 6.1. (a) Schematic illustration of the sequence of events. A central cue was presented in the beginning of each block, informing the participants to sustain their attention to either colour (C) or direction of motion (M) of the target stimuli. Following a 1450 ms pause, coloured moving dots were presented inside one of the circular placeholders located in the upper and lower part of the left visual field. Participants discriminated the attended target feature while simultaneously ignoring the task-irrelevant feature dimension. There were two possible targets for each feature dimension: green or blue

colours, and upward or downward motion. In the concurrent TMS/fMRI experiment, single pulse TMS was delivered within two different time windows after the onset of the visual stimulus, early (40, 50, or 60 ms after stimulus onset) or late (140, 150, or 160 ms after stimulus onset). TMS was applied with either low intensity (30% of motor threshold/MT) or high intensity (120% of MT). **(b)** Illustration of the TMS target site (right FEF) and TMS control site (region in the somatosensory cortex parallel to the location of the right FEF). The TMS target site was localized on an individual subject basis using separate functional localizer scans.

The participants were instructed to sustain their attention to the colour or direction of motion of the visual stimulus (Figure 6.1a). On each trial, the stimulus was presented in the upper or lower part of the left visual field. The stimulus consisted of moving coloured dots (green or blue) that moved either in an upward or downward direction for 50 ms. Overall sensory inputs were held constant across conditions, with only the participant's attentional state manipulated throughout the experiment.

For the fMRI experiment, we examined attention-specific top-down modulation in the relevant retinotopic visual regions. Specifically, we asked whether attending to one feature dimension (i.e. colour) would selectively modulate activity in the functionally relevant visual region (i.e. V4 for colour; V5 for motion). We first applied ROI-analysis to compare mean BOLD activations in visual region V4 and V5 during the different attentional conditions, and then used ROI-based MVPA to decode attention- and target-specific information in these retinotopic regions. For the concurrent TMS/fMRI experiment, we applied similar ROI-analysis and MVPA classification comparing TMS-induced remote modulatory effects in V4 and V5 during the different attentional conditions. Two different TMS intensities were used (low: 30% of motor threshold/MT, and high: 120% of MT). To control for site non-specific artefacts of TMS, stimulation was also applied to the control site on the somatosensory cortex, in a separate experiment (Figure 6.1b).

6.2 Materials and Methods

6.2.1 Participants

Eight healthy right-handed participants (ages 19 - 41, mean 27, 5 females) with normal or corrected-to-normal vision took part in the fMRI experiment. Three of this group (3 males) also volunteered to take part in the concurrent TMS/fMRI experiment. The study was approved by the Ethics Committee of the School of Psychology, Cardiff University, and informed written consent was obtained from each participant.

6.2.2 Stimuli and Procedure

All visual stimuli were rendered on a black background and back-projected onto a screen using the MR projector system installed at CUBRIC. A central fixation cross and two circular placeholders (subtending ~2^o radius) located in the upper and lower part of the left visual field were always present throughout the experiment (Figure 6.1). The horizontal distance from the central fixation to the circular placeholder was ~ 6^o. On each trial, moving dots were presented inside one of the circular placeholder, randomly, and these dots were either colored in green or blue, and moving either upwards or downwards.

The participants were instructed to maintain central fixation throughout the experiment. At the beginning of each block, a central cue was presented to indicate the task-relevant target feature that needed to be attended during the upcoming block (M for attend motion and C for attend colour). The cue was presented for 500 ms and then followed by a 1450 ms pause. Each sustained attention block consisted of 6 individual trials, with randomly assigned inter-trial intervals (ITI) of 450ms or 700 ms. On each trial, coloured moving dots were presented for 50 ms. Depending on the block instruction, the participants were responding to the target's colour (green or blue) or the target's motion (up or down) by pressing one of the button boxes. The responses were collected in a non-speeded way within 2s window after the stimulus onset. The stimulus was calibrated individually for each participant to achieve ~80% correct performance on all attentional conditions. In the second half of the experiment, the response mapping was reversed to avoid correlating target features with motor effectors in the MVPA decoding.

6.2.3 Data Acquisition: fMRI Experiment and Concurrent TMS/fMRI Experiment

Data for the fMRI experiment were acquired on a General Electric 3T MRI scanner at CUBRIC. Multi-slice T2-weighted echo-planar imaging (EPI) volumes were acquired with a repetition time (TR) of 2500ms, echo time (TE) of 35ms, flip angle of 90^o, matrix size of 64 ×

64, 38 contiguous slices, and a voxel resolution of 3.2 × 3.2 × 3.2 mm. Ten experimental runs were collected for each participant. Each runs consisted of 132 volumes, lasting for ~5.5 min.

Functional volumes for the concurrent TMS/fMRI experiment were acquired using T2-weighted EPI imaging with a repetition time (TR) of 2000ms, echo time (TE) of 35ms, flip angle of 90^o, matrix size of 64 × 64, 30 contiguous slices, and a voxel resolution of 3.4 × 3.4 × 3.4 mm. A 500ms gap was included between acquisitions of subsequent EPI volumes to allow sufficient time for applying TMS pulse without corrupting the functional images. A single TMS pulse was applied on each trial within this temporal gap. There were two different timings for the TMS pulse: early (40ms, 50ms, or 60ms after the onset of the target stimulus) or late (140ms, 150ms, 160ms after the onset of the target stimulus), delivered in a balanced random order. Two levels of TMS intensities were used, low (30%) or high (120%) of participants' motor threshold (MT). TMS/fMRI data were collected in two sessions, the first session with TMS over the FEF and the second session with TMS over the control site (somatosensory cortex), and the order was counterbalanced for one of the subject. Twelve experimental runs were obtained for each session, and in each run, 125 volumes were acquired, lasting for ~5.3 min. Real-time eye tracking and physiological monitoring of the cardiac and respiratory cycle were also performed throughout all TMS/fMRI sessions, however, the data will not be presented in this thesis.

Cortical stimulation was delivered via Magstim Rapid stimulator (The Magstim Company Ltd, Wales, UK) with specialized radiofrequency (RF) filter for concurrent TMS/fMRI (Bungert et al., 2012a). An MR-compatible figure-of-eight TMS coil (10 turns on each side, 70 mm average diameter) with built-in passive shim for reducing image artefacts was used (Bungert et al., 2012b). Before the TMS/fMRI session, the target TMS site on the participants' scalp was initially localized and marked outside of the scanner using a miniBIRD^{TM} 500 tracking device (Ascension Technologies) and MRIcro/MRIreg image coregistration software (Rorden and Brett, 2000). Inside the scanner, the TMS coil was positioned approximately over the marked location using a custom-build MR-compatible coil-holder (designed and constructed by Andreas Bungert; Figure 6.2).

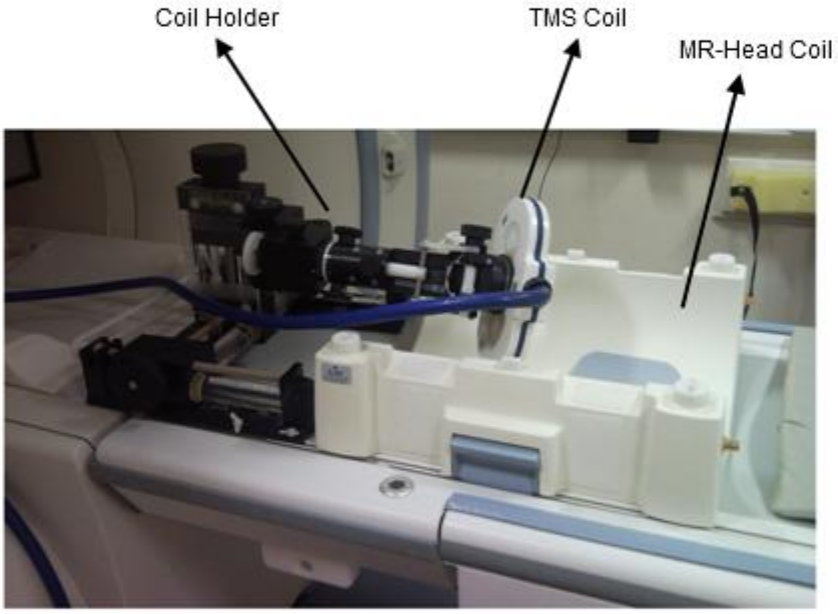
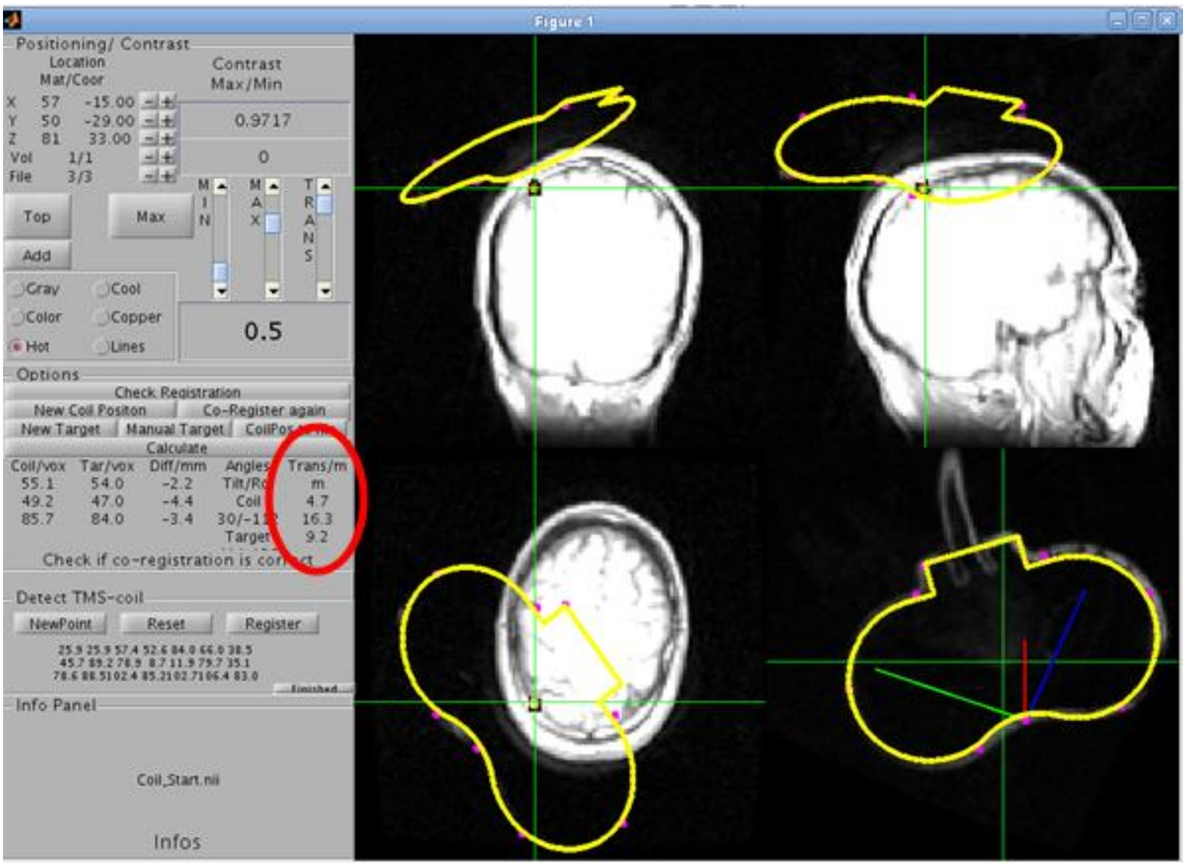


Figure 6.2. A custom built MR-compatible TMS coil holder with six degree of freedom (designed and constructed by Andreas Bungert), shown with a TMS coil attached and mounted at the end of the MR-head coil.

After initial positioning of the coil, a whole-head 3D FSPGR volume (TR = 5.4ms, TE = 1.7ms, flip angle of 20^o, matrix size of 128 × 128 × 128) was acquired to visualize the coil location relative to the head. Based on this 3D volume, the relative distance between the centre of the TMS coil and the target site on the surface of the scalp was automatically estimated using a custom in-house MATLAB script (developed by Andreas Bungert; for screenshot see Figure 6.3). When necessary, the coil position was manually re-adjusted to bring it closer to the target location, and these steps (acquiring 3D volumes of the head and calculating the distance) were repeated until the gap was small enough (~10 mm).

In addition to the functional images, we also acquired data for the retinotopic mapping analysis and 3D anatomical image of the head. Whole head T1-weighted structural images were acquired with 1 × 1 × 1 mm voxel resolution, repetition time (TR) of 8ms, echo time (TE) of 3ms, flip angle of 20^o, matrix size of 256 × 256, and 172 slices. Data for the retinotopic mapping analysis were obtained using a T2-weighted EPI pulse sequence, with a TR of 3000ms, TE of 35ms, flip angle of 90^o, matrix size of 128 × 128, 37 slices, and a voxel resolution of 2 × 2 × 2 mm. Two scanning runs were acquired. Each run consisted of 100 volumes, lasting for 5 min.



X 57 -15.00
Y 50 -29.00
Z 81 33.00
Vol 1/1
File 3/3

0.9717

0

0.5

Coil/vox	Tar/vox	Diff/mm	Angles	Trans/mm
55.1	54.0	-2.2	Tilt/Ro	
49.2	47.0	-4.4	Coil	4.7
85.7	84.0	-3.4	30/-11	16.3
			Target	9.2

Check if co-registration is cor ct

25.9 25.9 57.4 52.6 84.0 66.0 38.5
45.7 89.2 78.9 8.7 11.9 79.7 35.1
78.6 88.5102.4 85.2102.7106.4 83.0

Coil_Start.nii

Figure 6.3. Screenshot of the coil positioning script for estimating the distance between the TMS target site and the centre of the TMS coil (developed by Andreas Bungert). The outline of the TMS coil was shown in yellow and the target location was highlighted with the green crosshair. The red ellipse on the panel denotes the estimated distance (mm) in three different axis (X, Y, and Z).

6.2.4 Data Analysis

In the first analysis, we applied ROI-analysis to compute mean BOLD activity within the retinotopic visual regions. Before analysis, the EPI volumes were initially pre-processed using SPM8 software. The volumes were realigned to correct for possible head movements artefacts, and then smoothed using 8mm isotropic Gaussian kernel and a high-pass filtered at 128s to remove slow drifts in the time series. For the fMRI experiment, four beta contrasts were estimated for 2 attentional conditions (attend colour or motion) × 2 target locations (upper or lower visual field), in an event related design time-locked to the stimulus onset. For the concurrent TMS/fMRI experiment, eight beta contrasts were estimated for 2 attentional conditions × 2 target locations × 2 TMS intensities (high or low). The contrast regressors were modelled using a stick function (i.e. target onset) convolved with a canonical haemodynamic response function. Mean BOLD activity for each ROI was computed using a custom MATLAB script, individually for each subject and task condition, and then averaged across subjects yielding a single activation value for each ROI and condition. The retinotopic mapping data were obtained using the same task and analysis procedures described in section 4.2.6.

In the second analysis, we analysed the imaging data using ROI-based MVPA classification in retinotopic visual regions V4 and V5. The MVPA classification was undertaken using the Princeton MVPA Toolbox for MATLAB (Detre et al., 2006) and the linear support vector machine (SVM) as the learning algorithm (Cortes and Vapnik, 1995). The pattern analysis was performed in individual native space using raw, unsmoothed EPI volumes. Initially, the EPI time series were loaded together with the ROI mask, and then normalized using a z-score transformation. Sample volumes corresponding to the onset of each trial were labelled according to categories corresponding to the task conditions of interest (i.e. green vs. blue or upward motion vs. downward motion), specifying the regressor matrix. To compensate for haemodynamic lag in the BOLD signals, the regressor was shifted by 6 seconds (2 TRs). A leave-one-run-out cross-validation was then undertaken and overall classification accuracy was computed by averaging the classification accuracies of N times of training and testing runs (N is a number of fMRI runs). Group level statistical significance of the classification was estimated using a two-tailed single-sample t-test statistics against chance (50%).

6.3 Results

6.3.1 Behavioural Results

Mean behavioural performance of the fMRI experiment and concurrent TMS/fMRI experiments are depicted in Figure 6.4. No significant differences in mean performance were observed between different attentional conditions (paired sample t-test, fMRI: $p = 0.604$, TMS FEF: $p = 0.398$, TMS control site: $p = 0.871$).

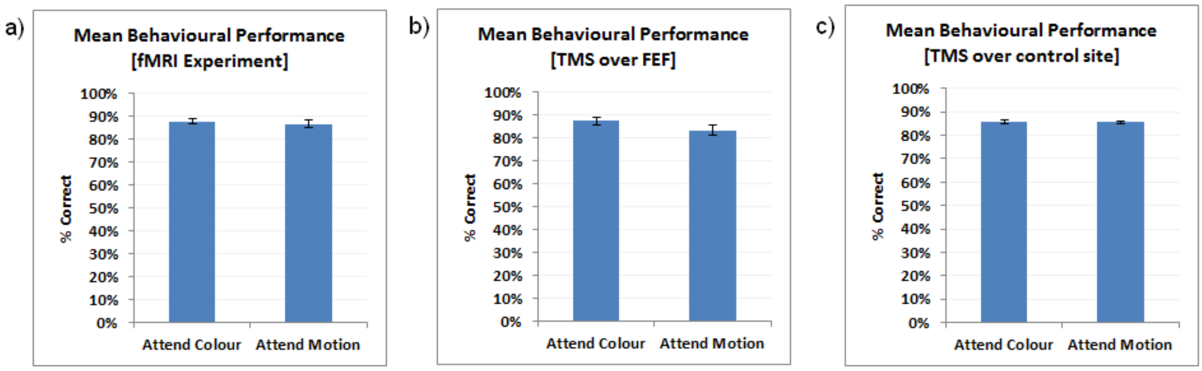


Figure 6.4. Mean behavioural performance during the fMRI experiment (**a**, attend-colour: 88%; attend-motion: 87%) and concurrent TMS/fMRI experiment targeting the FEF (**b**, attend-colour: 88%; attend-motion: 83%) and control site (**c**, attend-colour: 86%; attend-motion: 86%).

6.3.2 Result of the fMRI Experiment

In this analysis, we examined the top-down modulatory effect of feature-based attention in the retinotopic visual regions using ROI-analysis. We hypothesized that attention to colour (vs. motion) would increase the mean BOLD response in the right V4, whereas attention to motion (vs. colour) would increase the mean response in the right V5, irrespective of the location of the stimuli. Contrary to expectations, we found no significant mean differences between the two attentional conditions in any regions and target locations (Figure 6.5). When averaged across target locations, there was a trend towards higher responses in V5 during attention to motion than attention to colours, but no such differences were observed in V4. Subsequently, we applied ROI-based MVPA classification to discriminate attended feature dimensions from the patterns of activity in the V4 and V5 regions (Figure 6.6). There was a trend towards significant information in the right V4 when the targets were presented in the upper visual field, but classification accuracies for all other conditions approximated chance. Altogether, the ROI-analysis and the MVPA classifications were unable to find any significant top-down modulatory effect of feature-based attention on visual area V4 and V5.

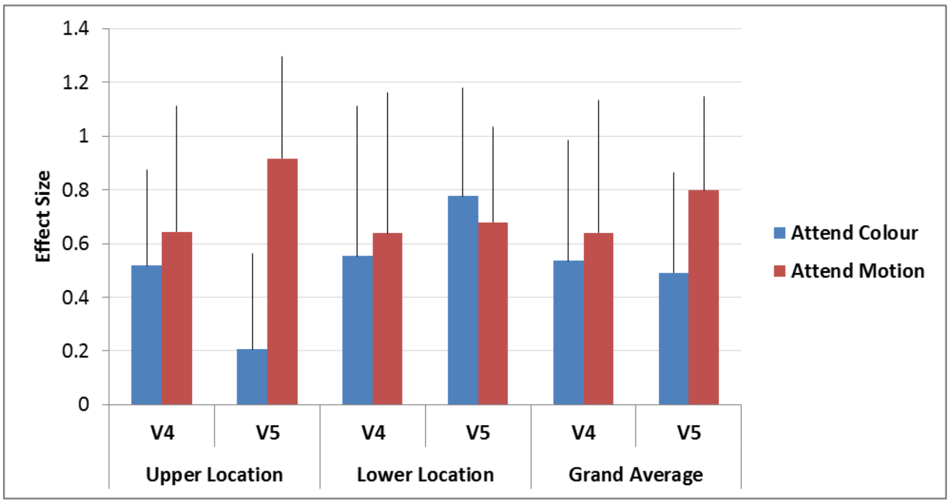


Figure 6.5. Mean BOLD activity in the right V4 and V5 of eight participants while attending to colour or direction of motion. The plots were grouped by the location of the target stimuli (upper visual field, lower visual field, and their average). No significant differences in the mean activity were observed between attention to colour and motion, in any regions and targets locations. However, there was a trend towards significantly larger mean response during attention to motions than attention to colours in area V5, when the targets were presented in the upper visual field ($p=0.07$).

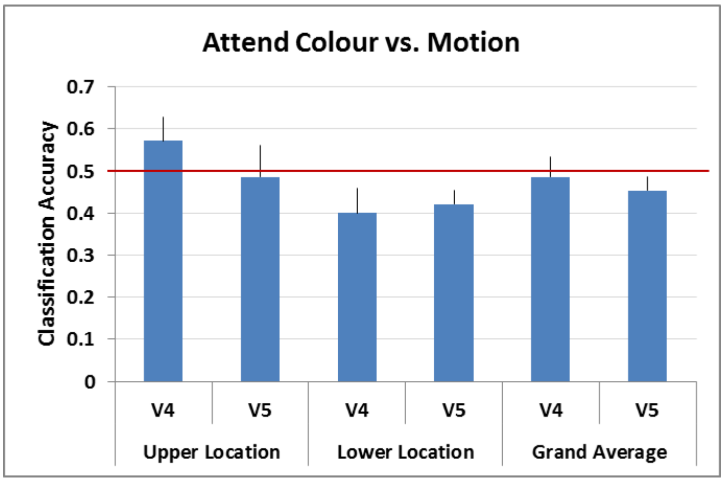


Figure 6.6. Results of ROI-based MVPA classifying attended feature dimension (attend colour vs. motion) in the right visual region V4 and V5, grouped by the location of the targets. None of the regions contained significant information about the attended feature dimension (chance is 0.5).

We further applied MVPA classification to decode the actual visual target within the attended feature dimension (i.e. decoding green vs. blue when colour was attended and decoding upward vs. downward when motion was attended; Figure 6.7). We hypothesize that decoding performance of the attended target in the functionally relevant retinotopic regions (i.e. colours in V4, and motion in V5) would be better than decoding performance of the attended target in the functionally irrelevant regions (i.e. colours in V5, and motion in V4). For the second time, no significantly above chance classification was found in any visual regions and target locations.

Lastly, to verify the validity of the MVPA classification procedure applied to this imaging data, we also performed a diagnostic analysis to classify the location of the displayed visual stimuli (upper vs. lower visual field). As expected, information about the location of the stimuli was present in almost all retinotopic visual regions (V1 – V4; Figure 6.8). Thus the failure of the classifier to decode attended modalities and visual targets in the previous analyses could not be attributed to the error in the classification procedure, but indicates the lack of significant information about the task conditions in these visual regions.

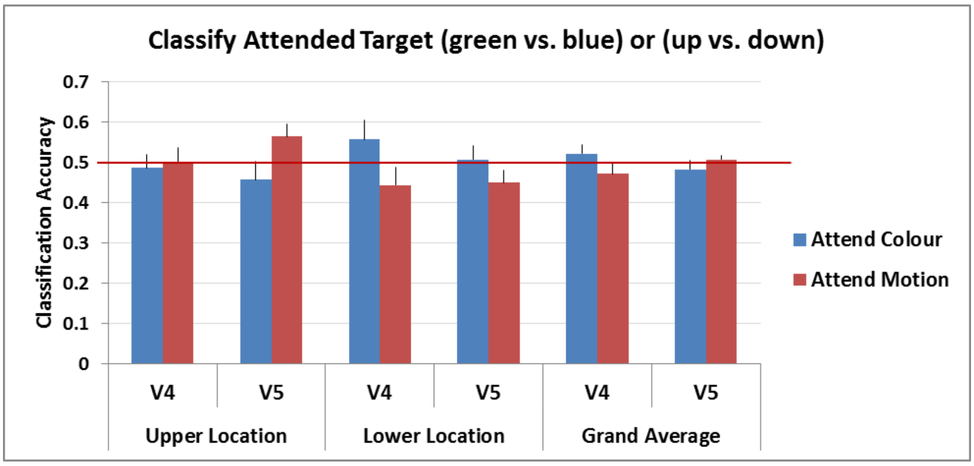


Figure 6.7. Results of ROI-based MVPA decoding of attended target colour (green vs. blue) or motion (up vs. down) in the retinotopic regions V4 and V5, grouped by the location of the stimulus (upper visual field, lower visual field, and averaged of both). No significantly above chance discrimination was found in any visual regions and locations (chance is 0.5).

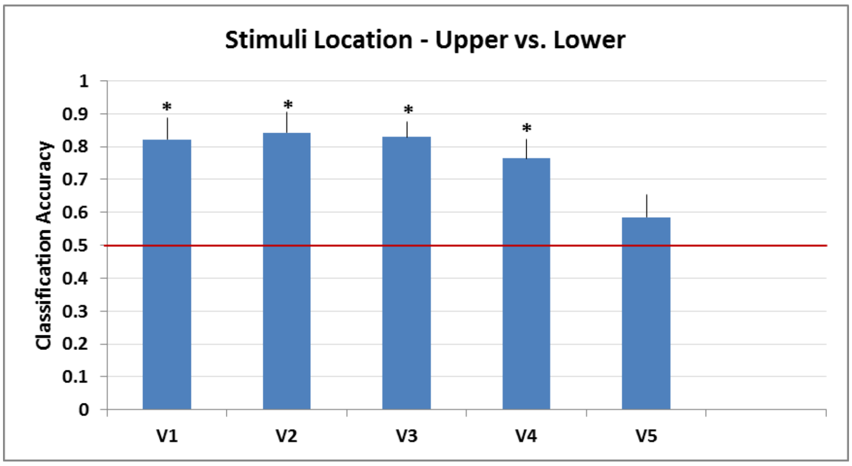


Figure 6.8. Results of MVPA decoding of the locations of the stimuli (upper vs. lower visual field) in the retinotopic visual regions. As expected, significantly above chance (> 0.5) classification were observed in almost all regions (V1 – V4; * $p < 0.01$).

6.3.3 Result of the Concurrent TMS/fMRI Experiment

In the previous section, we have reported the outcome of fMRI experiment investigating top-down modulatory effects of feature-based attention in the visual region V4 and V5 using both ROI-analysis and MVPA classification. The lack of significant attentional modulatory effects in the relevant visual regions might indicate the infeasibility of the attentional task paradigm for the purpose of the present study. Nevertheless, in the same time period during the fMRI data collection, we have also collected concurrent TMS/fMRI pilot data on three subjects using the same task paradigm. Therefore, for completeness, we have also analysed the data and presented the results in this section.

Figure 6.9a shows the mean BOLD response in visual regions V4 and V5 induced by the TMS (high intensity minus low intensity) over the right frontal eye fields (FEF). In V4, FEF TMS decreased the mean activity when colour was attended, and the opposite effect was observed when motion was attended (increased mean activity). However, no statistically significant mean signal differences between two attentional conditions were found in either V4 or V5. Similar null-results were observed during application of TMS on the control site (Figure 6.9b).

In the last analysis, we applied ROI-based MVPA classification to compare the influence of low vs. high intensity TMS on decoding accuracy of visual targets in V4 and V5, within currently attended feature dimension (i.e. classify green vs. blue in attend colour condition and classify upward vs. downward in attend motion condition). There was no significantly above chance classification during both FEF TMS and control TMS in both visual regions and attentional conditions (Figure 6.10), replicating the null-results found in the fMRI experiment reported in Section 6.3.2.

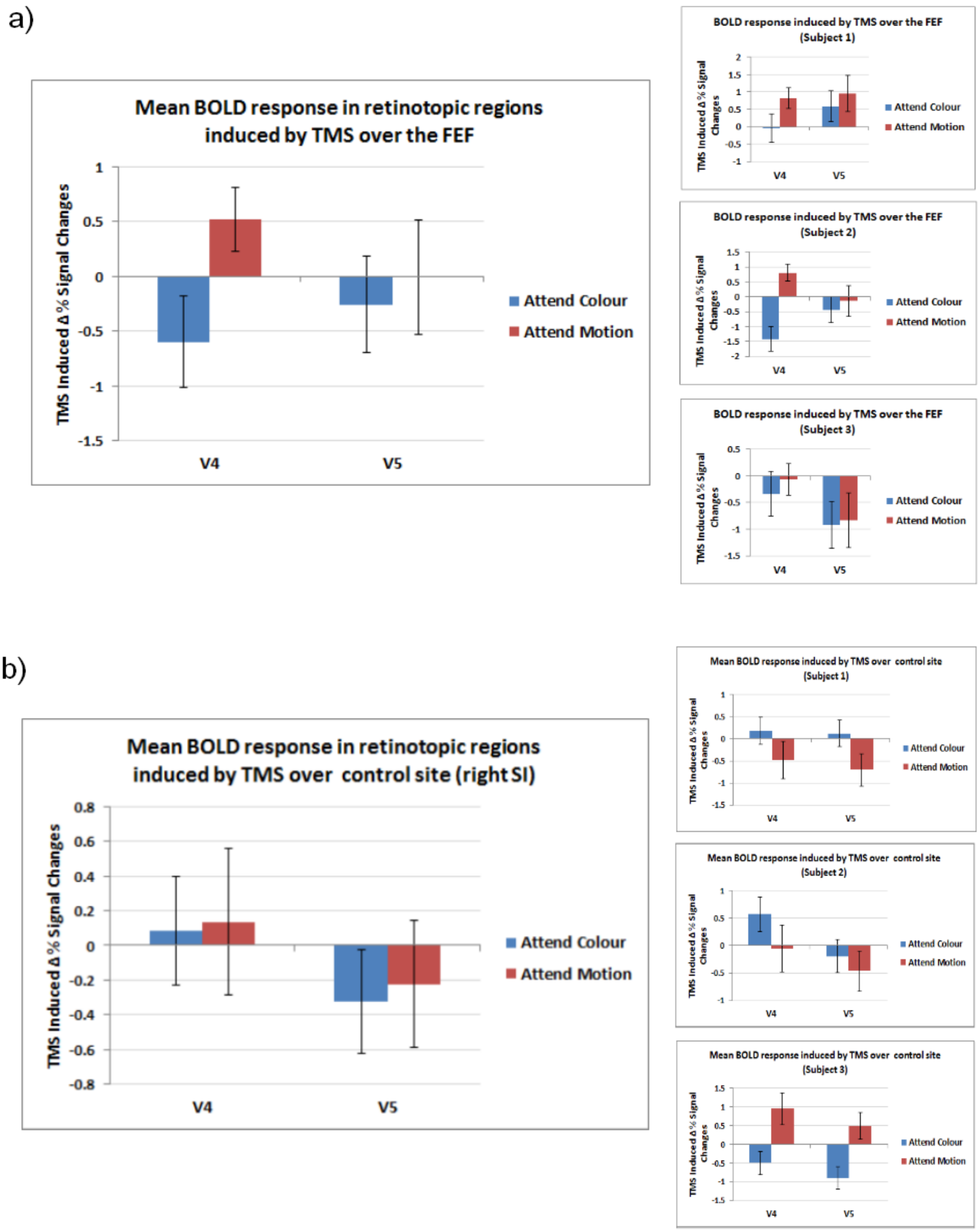
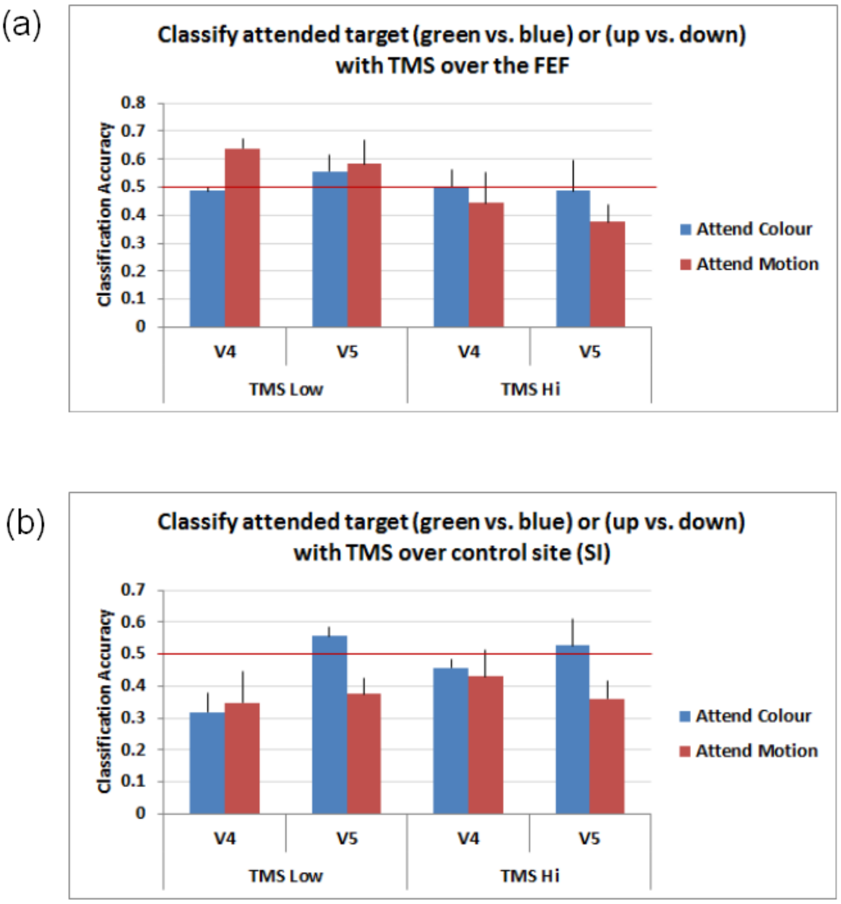


Figure 6.9. (a) Effects of high vs. low-intensity TMS over the FEF in the retinotopic visual regions V4 and V5. Mean BOLD signals changes induced by the TMS (high intensity minus low intensity) were shown for each attentional condition (attend colour and attend motion) alongside with mean signal changes in each subject. FEF TMS reduced mean activity in area V4 during attention to colours, but increased mean activity in the same region during attention to motions. However, the mean signal difference was not statistically significant (paired t-test, *p = 0.19*). Similarly, no significant difference in TMS induced effects during attend colour vs. attend motion was observed in area V5. **(b)** Effects of TMS over control site (right somatosensory cortex) in visual regions V4 and V5. There were no significant differences in TMS induced mean BOLD signals changes between two attentional conditions in both visual regions.


(a)

Classify attended target (green vs. blue) or (up vs. down) with TMS over the FEF

(b)

Classify attended target (green vs. blue) or (up vs. down) with TMS over control site (SI)

Figure 6.10 (a) Results of MVPA decoding of attended target colour (green vs. blue) or motion (up vs. down) in visual regions V4 and V5 during application of concurrent TMS over the FEF. No statistically significant information (chance is 0.5) about attended targets was found in any regions for both TMS intensities. Classification accuracy in V4 when attending to motion and during application of low intensity TMS was close to significance when uncorrected for multiple comparisons across the eight conditions (*p=0.063*). **(b)** Results of MVPA decoding of attended targets in visual regions V4 and V5 during application of concurrent TMS over control site (SI). Similarly, no significant information about the visual targets was found by the MVPA classifier.

6.4 Discussion

The aim of the present study was to probe attention-dependent modulatory effects of TMS on functionally relevant visual regions during sustained feature-based attention to vision. Two pilot experiments were conducted, the first was fMRI experiment to validate the feasibility of the attention task paradigm, and the second was concurrent TMS/fMRI experiment to probe remote modulatory effects of TMS over FEF on visual cortex.

In this study, we adopted a variant of feature-based attention paradigm that required participants to selectively discriminate a specific feature dimension (i.e. colour) of a stimulus while simultaneously ignoring task-irrelevant competing feature dimension (i.e. motion) presents in that stimulus (Nobre et al., 2006; Mirabella et al., 2007; Chen et al., 2012). We hypothesize that visual areas specialized for processing of a particular feature dimension (i.e. V5 for motion; V4 for colour) would be differentially modulated depending on which competing feature was currently attended (i.e. greater activation or better MVPA decoding performance in V5 during attention to motion vs. attention to colour, and vice versa for V4). We then asked whether application of TMS over the right FEF would selectively influence these attention-dependent modulatory effects in V4 and V5.

The outcome of the ROI-analysis revealed no significant influence of top-down attention on the mean BOLD activity in V4 and V5. This finding is consistent with a recent fMRI study that employed similar feature-based attention paradigm, which also reported absence of attention-dependent modulatory effects in the mean BOLD response in V4 and V5 (McMains et al., 2007). The authors interpreted their findings as an indication for an object-based spread of attention that facilitate processing of both attended and unattended features within that object (Beauchamp et al., 1997; O'Craven et al., 1999; Melcher and Vidnyánszky, 2006).

MVPA classifications decoding attended visual targets also failed to identify target-specific information in V4 and V5, indicating that the distributed patterns of activity which encode the relevant target might be too weak to be detected. One possible reason for the absence of target related information in visual cortex was due to the very short duration of the presented visual stimulus (50 ms). In a previous MVPA study that demonstrates successful decoding of attended direction of motion in retinotopic visual cortex (Serences and Boynton, 2007), much longer stimulus duration was used (14 s).

There were several other limitations in the concurrent TMS/fMRI paradigm used in the present study. Only single TMS pulse was delivered on each trial due technical and regulatory limitations of the presently installed TMS/fMRI system in our lab. In comparison, previous TMS/fMRI studies which shown remote TMS effects on retinotopic visual cortex have applied three to five pulses of TMS bursts on each trial (Ruff et al., 2006; Blankenburg et al., 2010; Heinen et al., 2011), and longer target durations were employed in these studies (270 ms and 570 ms). Moreover, only three participants were tested in the current TMS/fMRI study, so there might not be enough statistical power to demonstrate remote TMS effects.

7 - General Discussion

7.1 Summary of the Experimental Results

Chapter 3 discussed the development of an MRI compatible fibre-optic stimulus presentation system for multisensory experiments and described three fMRI experiments that established the feasibility and capability of this device for delivering reliable visual stimuli during scanning. We have designed and constructed a custom fibre-optic system to solve the technical challenges of presenting visual stimuli above the participants' hands, in close proximity with the tactile stimulation device, which could not be achieved using ordinary projection screens or binocular goggles. The fibre-optic system was implemented using programmable microcontrollers circuits that are able to control several hundred coloured LEDs in an analogous way as manipulating pixels on an LCD screen, providing the user great flexibility in displaying stimulus with various shapes, colours, contrasts, or frequency.

In the first experiment described in Chapter 3, we applied the fibre-optic device to deliver flashing checkerboard-like stimuli in the left and right visual field alternately, and found that the visual stimuli could induce strong and reliable haemodynamic response in the contralateral occipital cortex. In the second experiment, we tested the reliability of the device for displaying coloured stimuli using a simple colour discrimination task, and confirmed that chromatic stimuli delivered via the fibre-optic system could reliably activate expected ventral occipital regions (V4). The third and last experiment reported in this chapter was conducted to test the feasibility of combining the fibre-optic device together with the Quaerosys^{TM} tactile stimulator in a multisensory interaction experiment. Contrasting the activations of bimodal visuo-tactile processing vs. unimodal processing, we observed widespread activations in the bilateral superior temporal sulcus (STS), an area thought to be important for multisensory integration (Beauchamp, 2005). The results from these experiments confirmed the reliability of the fibre-optic device for presenting complex, spatio-temporally coordinated visual stimuli for multisensory experiments inside the scanner.

In chapter 4, we discussed our study that investigated the generality and specificity of the frontoparietal networks in controlling endogenous spatial attention in vision and touch. We conducted this fourth fMRI experiment using a behavioural paradigm that involved sustained spatial attention to one modality and side, similar to the paradigm used by Macaluso et al. (2002a). Fibre-optic system described in Chapter 3 and Quaerosys^{TM} tactile stimulator were used in this experiment to deliver bimodal and bilateral visuo-tactile stimuli. Consistent with previous neuroimaging studies of attention in various modalities, using classical univariate analysis we found common widespread activity in the frontoparietal network (Corbetta and Shulman, 2002; Corbetta et al., 2008) during both attention to vision and touch. We then examined whether activations in these overlapping regions were truly supramodal by applying ROI-based MVPA analysis to decode attended modality from distributed patterns of activity within the frontoparietal ROIs found by univariate analysis. Our results revealed that overlapping activations in the right parietal cortex could reliably discriminate currently attended modality in both sides, indicating the presence of modality-specific information in this region. Moreover, most of the ROIs in the frontal cortex also contained information about attended modality during attention to targets on the left hand side, but almost no frontal ROIs could significantly discriminate attended modality during attention to targets on the right hand side.

To confirm these results and to visualize cortical regions that contains information about attended modality and/or attended sides, we also conducted three separate exploratory MVPA searchlight analyses on the imaging data. The results of our whole-brain searchlight analyses provided additional evidence for the existence of modality-specific and location non-specific coding in the frontoparietal regions that includes the dorsalFP network (IPS and FEF) and the ventralFP network (SMG/TPJ and IFG). In contrast, searchlight analysis did not find any evidence for location-specific that generalise across modality, refuting the hypothesis that supramodal coding of attended location was present in the frontoparietal network. Finally, we performed another searchlight analysis to find modality-specific and location-specific information, and found informative regions in the right parietal cortex, in the vicinity of IPS and SMG. Overall, our results have provided evidence that although there might be some isolated cortical regions that were activated in supramodal manner, the majority of frontoparietal regions contained modality-specific distributed patterns of activity.

In chapter 5, we presented the third study that investigated the neural basis of intermodal feature-based attention in vision and touch. The experiment conducted in this study also utilized the fibre-optic system and Quaerosys^{TM} tactile stimulator for stimuli presentation. Our study was among the first to probe the cortical networks involved in visuo-tactile feature-based attention using fMRI. Simultaneous presentation of bimodal and bidimensional stimuli were used in this experiment, and the participants were asked to focus their attention either to the shape or frequency of the stimulus in one modality, discriminating the property of the target stimulus. Using univariate conjunction analysis, we inquired whether maintaining sustained attention to visual features recruited anatomically similar cortical regions with sustained attention to tactile features. Our results revealed that during attention to stimulus shape, common activations shared by attention to vision and touch were found mostly in the posterior parietal cortex (PPC), STG, right hMT+/V5, and right IFG. Although the overall patterns of common activations were similar, attention to stimulus frequency elicited a slightly more widespread activity in the frontal regions that includes right MFG, IFG, and pre-SMA areas. We further investigated the nature of distributed patterns of activity contained within these overlapping regions by applying searchlight analysis, and discovered that some regions in the PPC contained modality-specific information.

In the second part of this study, we investigated the effect of top-down feature-based attentional modulation on the visual and somatosensory cortex using conventional ROIs analysis and ROI-based MVPA analysis. Mean signal changes in the retinotopically defined ROIs revealed that attention to tactile targets activated early and late visual cortex as strongly as when attention was directed towards visual targets, suggesting the presence of crossmodal influence of tactile processing on visual cortex (Macaluso et al., 2000; Driver and Noesselt, 2008) or multisensory integration effects (Shams and Kim, 2010; Mozolic et al., 2008a). To probe this question further, we applied MVPA classification on these retinotopic ROIs to test whether visual cortical activity during tactile attention was caused by spread of attention to visual distracters or caused by crossmodal influence of tactile processing. We found that patterns of modulatory activity in the right visual cortex were significantly different between attention to vision and touch, indicating that the effect was not simply processing of visual distracters but might also be caused by crossmodal modulation. Additionally, using cross-generalization MVPA analyses we also found that early visual regions (V1-V3) contained modality-specific but feature non-specific information (i.e. could not discriminate currently attended feature), whereas the late visual regions were modality-specific and feature-specific. This result provides an evidence that feature-specific attentional modulations occurs primarily in the higher visual regions where the receptive fields were more attuned to those attended feature dimensions (i.e. processing of frequency/motion in hMT+/V5). Interestingly, in these analyses we also found modality-specific information in the unstimulated left visual cortex, in line with previous MVPA findings that reported spread of feature-selective attention to empty visual fields (Serences and Boynton, 2007).

7.2 Frontoparietal Attention Network: Supramodal and Modality-Specific ?

The involvement of frontoparietal attention network (Corbetta and Shulman, 2002; Corbetta et al., 2008) in mediating attention to various modalities and dimensions has been the subject of debate during the last decade. Many influential neuroimaging studies have suggested the existence of supramodal control region involved in allocating attention independent of modalities (Macaluso et al., 2002b; Macaluso, 2010; Smith et al., 2010; Green et al., 2011). However, other studies have also provided evidence against this supramodal hypothesis (Bushara et al., 1999; Chambers et al., 2004b, 2007; Anderson et al., 2010).

The proposal of supramodal hypothesis was partly motivated by the discovery of crossmodal links in various behavioural studies of spatial attention (Farah et al., 1989; Driver and Spence, 1998; McDonald et al., 2000; Spence et al., 2000; Macaluso and Driver, 2001) as well as by the evidence of common frontoparietal brain regions recruited during attention to various modalities (Macaluso et al., 2002a; Smith et al., 2010; Green et al., 2011). Many behavioural studies using endogenous and exogenous paradigms have demonstrated that orienting attention to one location in one sensory modality can enhance processing of targets presented at the same location but in different modality (Spence, 2010). The findings of crossmodal facilitatory effect have prompted the possibility of common attentional control system that biases stimuli processing across sensory modalities (Farah et al., 1989; Driver and Spence, 1998).

The quest for supramodal control system has been supported by evidence gathered from many neuroimaging studies using PET, fMRI, and EEG in various combination of sensory modalities (Macaluso et al., 2002b; Eimer et al., 2002b; Green et al., 2011). A pioneering fMRI study conducted by Macaluso and Driver (2001) have shown that orienting of endogenous spatial attention to visual and tactile stimuli produced common activations in the frontoparietal regions that includes the anterior part of the IPS, FEF, and TPJ/STG. Subsequent studies using a crossmodal spatial cuing task (Macaluso et al., 2002b) and sustained spatial attention paradigm (Macaluso et al., 2002a) also reported similar overlapping activations in these regions. Other supporting evidence for the existence of supramodal attention network was also reported in an fMRI study investigating voluntary shift of strategic spatial attention to visual and auditory modality (Shomstein and Yantis, 2004) and in a more recent study using orthogonal cuing in visuo-auditory spatial attention task (Smith et al., 2010).

Although influential, the interpretation of overlapping fMRI activations or similar ERP activity as evidence for the existence of supramodal control system has been challenged partly because the spatiotemporal limitations of these neuroimaging methods. Since a typical fMRI voxel summarize an activity of several millions of neurons (Logothetis, 2008), there is a possibility that a commonly activated voxel might actually contain spatially overlapping but anatomically distinct sub-voxel neuronal populations that are modality specific, arranged in a topographic manner (Klemen and Chambers, 2012). Moreover, observation of common activations in several regions does not automatically imply that all of these regions are necessary for directing attention to all modalities. Because we cannot directly infer causality from the fMRI data, it is possible that only a subset of these activated regions is crucial for controlling attention to a specific modality (Chambers et al., 2004b).

In a TMS experiment using a similar spatial cueing paradigm reported by Macaluso et al. (2002b), Chambers and colleagues (2004) have provided direct experimental evidence that refutes the existence of supramodal attention network in the parietal cortex. Specifically, they have demonstrated that transient disruption of the right SMG impaired only strategic orienting to the visual modality but had no significant effect on orienting to the somatosensory modality. A subsequent TMS study using an exogenous spatial cueing task has also found similar modality-specific roles of the parietal cortex (right AG and right SMG) during reflexive orienting of attention to visual and tactile events (Chambers et al., 2007).

Motivated by this unresolved debate, we have applied multivoxel pattern analysis (MVPA) method to investigate whether overlapping fMRI activation patterns found during focusing of spatial and feature-based attention to vision and touch were modality-specific or supramodal. Many studies have shown that MVPA technique were very sensitive in detecting fine-grained bias in the distributed patterns of voxels activity that could discriminate different task conditions or cognitive states (Haynes and Rees, 2006; Norman et al., 2006; Wagner and Rissman, 2010; Tong and Pratte, 2012). As demonstrated in an early application of MVPA by Haxby et al. (2001), the fact that they could reliably decode object categories from the patterns of activity in the ventral temporal (VT) regions has provided new perspective and methodologies to tackle long standing debate as to whether similar brain regions were involved in object and face recognitions (Spiridon and Kanwisher, 2002; Peelen and Downing, 2007; Stokes et al., 2009a). Successful discrimination of low level features like orientations (Kamitani and Tong, 2005; Haynes and Rees, 2005) or motions (Kamitani and Tong, 2006) in the occipital lobe also provided another proof that MVPA method could be useful in decoding information that is organized topographically at the scale below the spatial resolution of the fMRI voxels (Swisher et al., 2010).

In the study described in Chapter 4, we have applied similar logic to decode modality-specific information in the overlapping frontoparietal regions elicited during sustained spatial attention task. We found evidence for modality-specific information in the right parietal cortex during attention to either sides, and in the left inferior parietal cortex when attending to the right side. Interestingly, we only discovered one frontal region (right medial frontal) that could significantly classify attended modality in the right visual field, but almost all frontal regions contained modality-specific information when attending to the left visual field. Less prominent frontal activations were observed during attend-right condition than attend-left condition. We speculated that this might be caused by slightly more demanding cognitive load (Sunaert et al., 2000) when attending to the left side compared to the right side, despite the absence of noticeable differences in behavioural performance. Therefore, when attention was sustained on the left visual field, the frontal regions might contain more task relevant information that needs to be maintained in the working memory (Woolgar et al., 2011a).

Additional evidence for the existence of modality-specific regions was obtained using MVPA searchlight analysis looking for common encoding of attended modality, irrespective of attended location. Large clusters of modality-specific but location non-specific regions were observed in the bilateral PPC that includes IPS and SMG/TPJ. Smaller clusters of informative regions were also found in the frontal regions including the IFG, FEF, and SMA. In contrast, searchlight analysis did not find any regions that could distinguish attended location irrespective of attended modality (i.e. supramodal regions that selects attended location across modalities). This result is inconsistent with the hypothesis of the supramodal dFP regions that biases relevant spatial location in a modality non-specific manner (Macaluso, 2010).

Furthermore, searchlight analysis looking for location-specific coding in the respective modality found distinct informative regions between visual and tactile attention. Information about attended location was found prominently in the occipital lobe during visual attention, whereas during tactile attention location-specific regions were found in the anterior parietal cortex (near SI and SII). Lack of location-specific information in the frontoparietal cortex might also be caused by the limitation of sustained attention paradigm used in our study. Since the participants only need to shift their spatial attention in the beginning of each block, the brain might not need to send top-down signals that encodes attended location continuously throughout the block, thus we did not observe location-specific information in the higher regions. Overall, our results have provided evidence that although most of the frontoparietal regions (especially the posterior parietal cortex) were modality-specific, the existence of potentially supramodal regions could not be ruled out completely because we still observed some commonly activated regions that contained no modality-specific information (such as the anterior part of the frontal cortex and pre-SMA). Therefore both modality-specific and supramodal regions might actually work in a complementary way to mediate deployment of spatial attention in various sensory modalities.

In Chapter 5, we have reported an experiment to identify the neural basis of sustained feature-based attention in vision and touch. In accordance with activations observed during multimodal spatial attention, classical univariate analysis have identified similar, but less pervasive overlapping frontoparietal regions involved in feature-based attention to both modalities. Reliable activations throughout both modalities and feature dimensions were found predominantly in the PPC, comprised of the IPS, SMG, and TPJ, accompanied with fewer shared activations in the IFG. These findings are consistent with previous studies that reported similar frontoparietal networks recruited during orienting of feature-based attention in vision (Shulman et al., 2002; Liu, 2003; Giesbrecht et al., 2003; Luks and Simpson, 2004; Slagter et al., 2007), as well as with results reported in a recent vibrotactile feature-based attention studies (Wacker, 2011).

We subsequently applied MVPA searchlight procedure to identify modality-specific information within these overlapping frontoparietal regions and discovered modality-specific regions in the PPC. A large patch of modality-specific regions were found in the IPS and SMG, bilaterally, when attention was focused to stimulus shape, whereas during attention to stimulus frequency, only a small cluster in the right IPS contained information about attended modality. This outcome suggests that the amount of modality-specific information within the PPC regions were inextricably linked with the attended feature dimension, indicating distinct functional role of this region for processing different feature dimensions such as shape and frequency. Additionally, cross-generalization searchlight analysis looking for modality-specific but dimension non-specific coding found no significant voxels that survived correction for multiple comparisons (although there was a trend towards significant classification in the anterior IPS and ventral part of the SMG), providing additional evidence for the existence of distinct modality-specific coding for different attended feature dimensions. The discovery of modality-specific information in the SMG during attention to stimulus shape also corroborates previous TMS study that demonstrated distinct role of the SMG in strategic orienting of attention to visual and somatosensory targets (Chambers et al., 2004b). Furthermore, the present searchlight analysis results have also indicated that the SMG might function differently depending the type of stimulus features that needs to be attended, an observation that can be verified in the future TMS experiments. Overall, together these findings have provided evidence for the involvement of both modality-specific (IPS and SMG) and potentially supramodal regions (IFG) that mediates sustained feature-based attention to vision and touch.

The findings of modality-specific information in the PPC associated with both attention to locations and stimulus features echoes many recent studies that demonstrated functional specificity of the PPC regions using novel fMRI analysis methods. An MVPA study reported by Greenberg and colleagues (2010) has pointed to the existence of domain-specific information within the PPC region that selectively control shifts of spatial and feature-based attention in vision. Using similar logic employed in the present study, they have shown that despite the observation of common, domain-independent transient signals in the PPC revealed by univariate analysis, surface based MVPA classification were able to dissociate distinct spatiotemporal profiles associated with attention shifts to different domains. In a related study conducted by the same research group, Chiu and Yantis (2009) have provided evidence for the involvement of the PPC not only during shifts of spatial attention but also during shifts between categorization rules. Using univariate conjunction analysis, they discovered common transient signals manifested during preparatory cues in both domains of control, suggesting the existence of domain-independent mechanism in the PPC. However, upon closer inspection using MVPA classification, distinct spatiotemporal patterns of activity between attention shifts and rule shifts were discovered within the overlapping PPC region (Esterman et al., 2009). Additional evidence for the existence of modality-specific processes in the PPC was reported in a recent functional connectivity study using resting state fMRI method to investigate connectivity between IPS and other attentional regions (Anderson et al., 2010). The results of their study have indicated that functional connectivity between IPS and other cortical regions were topographically organized into several modality-specific clusters, providing evidence for the existence of spatially overlapping but anatomically distinct neuronal populations that mediates attention in various sensory modalities. Altogether, evidence obtained from earlier studies and our present studies point to likely conclusion that the PPC region contained both domain- and modality-specific neural substrates.

Attentional control signals might be deployed on multiple hierarchical levels. The frontal cortex might contain information about attended modality and location when the subjects initiated their intention to attend to something (Haynes et al., 2007; Woolgar et al., 2011b). This frontal region will then transmit signals to the parietal cortex which in turn will modulate relevant sensory cortex. However, this idea of hierarchical information transmission does not solve the conundrum of where does this attentional signal first initiated and how. Is there any specific anatomical region from where these attentional signals were first generated (Miller and D'Esposito, 2005) ? or is it possible that complex phenomenon like attention was initiated and maintained by some kind of emergent 'virtual processes' that requires coordination of multiple brain regions (Metzinger, 2008) ? To answer these questions we may need to escape from the dichotomy of functional segregation and functional integration, and seek a way to look for interactions of both processes in the brain (Friston, 1994, 2011).

Dividing the brain into various modules is beneficial to identify various regions involved in a cognitive task. However, simply assigning fixed roles and labels to each identified region might also limit our understanding of how these modules actually operate and interrelate with each other. Moreover, each of these macroscopic regions identified using neuroimaging techniques might actually contain finer-level mesoscopic (intermediate) and microscopic (local) circuits with various functions. This kind of problems concerning the level of abstractions might be inherent in reverse-engineering of complex systems like the brain (Varela et al., 2001). In order to truly understand the spatiotemporal brain dynamics, data recording and computational modelling from multiple spatial and temporal scales should be obtained and integrated (Freeman and Kozma, 2000; Varela et al., 2001).

On one level, modular thinking is very useful, because we can first identify large elements of the system and observe its functions on a macroscopic level during various cognitive states. Once we observed how the system works on the macroscopic level, we should however try to look down at the lower level of abstraction in order to understand more detailed processes that are invisible on the higher level of abstractions and vice versa. In relation to the present study, recent advances in fMRI analysis methods such as MVPA, spatiotemporal MVPA (Fogelson et al., 2011; Su et al., 2012), and complex brain network analysis (Bullmore and Sporns, 2009; Rubinov and Sporns, 2010; Telesford et al., 2011) has provide us with various tools to investigate finer level of details so that we can understand the mechanics of brain functions in terms of information and functional connectivity on various spatiotemporal scales, complementing orthodox location based analysis. Moreover, future research on multisensory attention would also benefit from combined multimodal neuroimaging with different spatiotemporal scales such as fMRI, MEG, EEG, and simultaneous TMS/fMRI, in combination with computational and mathematical modelling to integrate the findings (Dale and Halgren, 2001; Friston, 2009; Blinowska et al., 2009; McDonald et al., 2010; Sui et al., 2011).

7.3 Future Directions

There are several limitations in the multisensory attention studies discussed in this thesis. We employed sustained attention paradigms instead of cued attention paradigm. One reason for this decision was to simplify the analysis and to increase statistical power for the MVPA decoding. However, with sustained attention tasks, there is no way to dissociate anticipatory processes with target processing. Therefore, it remains possible that modality-specific information discovered in the frontoparietal regions might be contaminated by feedback signals from the sensory cortices to the higher regions, as opposed to purely top-down attentional control signals. Future studies may consider combining multisensory cueing paradigms with event-related MVPA to investigate transient shifts of endogenous multisensory attentional control. Furthermore, it would be interesting to investigate the similarity between modality-specific neural coding during preparatory attention with modality-specific coding during target processing using the cross-generalization searchlight analysis.

In the present studies, we were unable to decode target-specific information in any cortical regions during the multisensory attention task. One possible reason for this might be related to the very short duration of the presented target stimuli. Successful decoding of target-specific information might require longer stimulus durations or better MVPA decoding techniques. Alternatively, we could also employ a variant of multisensory attention paradigms in which streams of visuo-tactile stimuli are presented continuously and the task is to detect transient shifts of the target within the cued modality, in similar vein with paradigms employed in Serences and Boynton (2007) and Greenberg et al. (2010) studies.

Appendix A – Additional Figures for Chapter 4

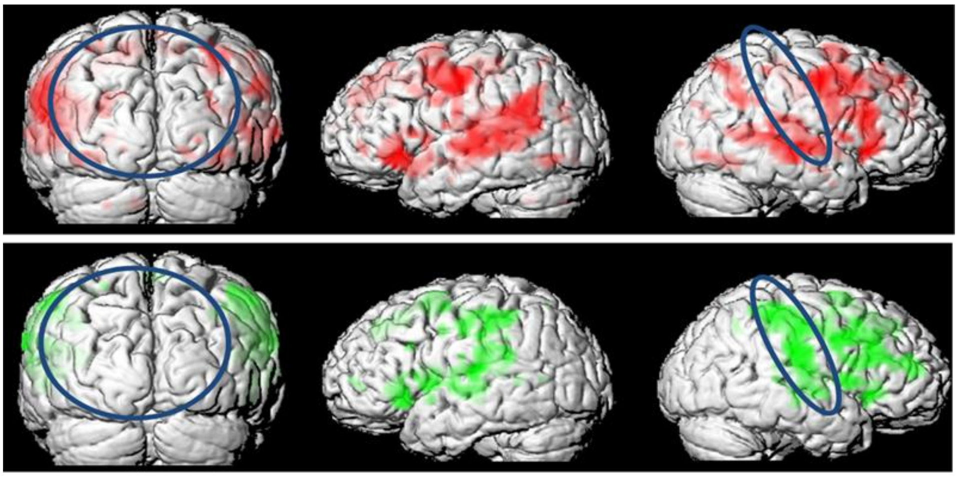


Figure A.1. Group level whole brain BOLD activations correlated with visual (red) and tactile (green) attentional condition (14 subjects, $p < 0.01$, FDR-corrected), collapsed across attended sides. Activations in visual cortex is more prominent in visual conditions, whereas activations along the post-central gyrus (SI and SII) was more prominent during tactile conditions.

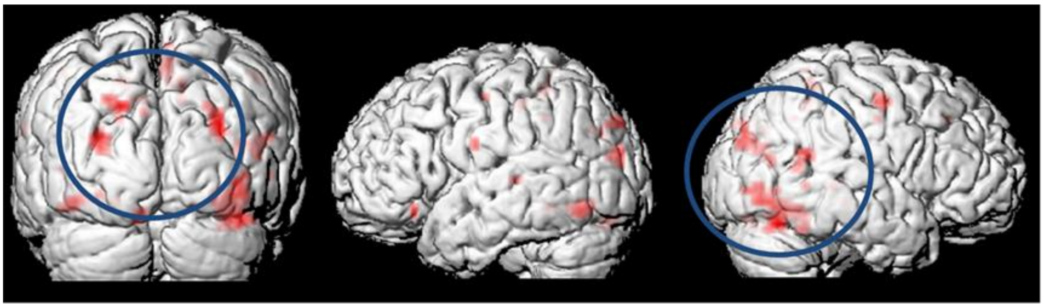


Figure A.2. Regions with greater activation in visual condition compared to tactile condition (visual minus tactile contrast), collapsed across attended sides (14 subjects; $p < 0.001$, uncorrected).

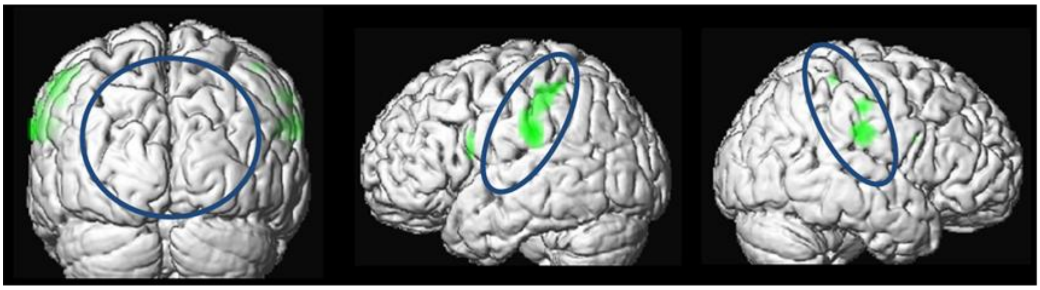


Figure A.3. Regions with greater activation in tactile condition compared to visual condition (tactile minus visual contrast), collapsed across attended sides (14 subjects; $p < 0.001$, uncorrected).

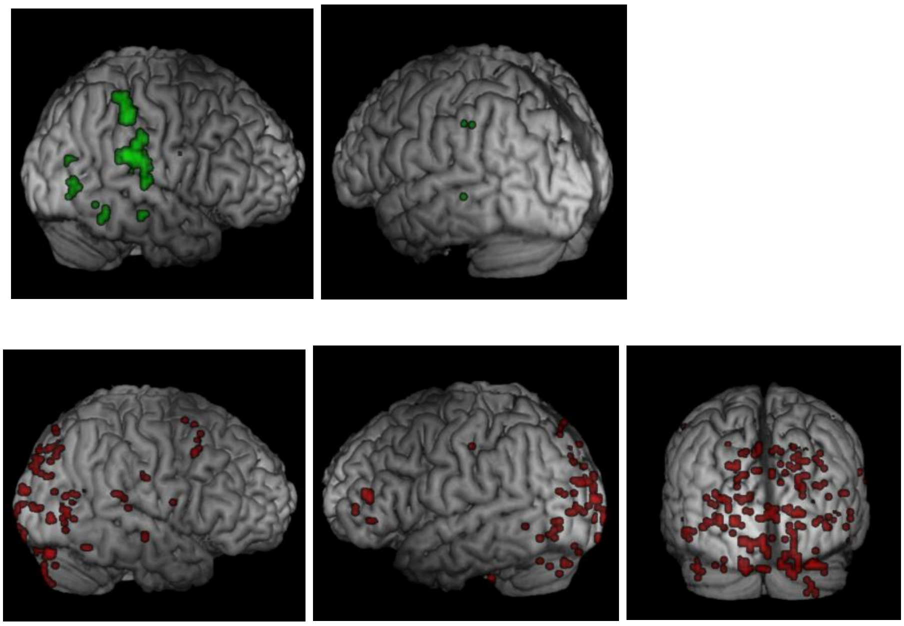
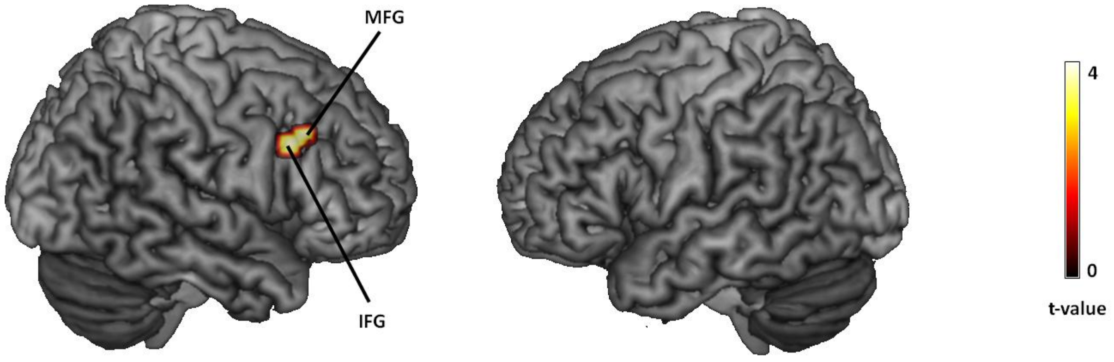


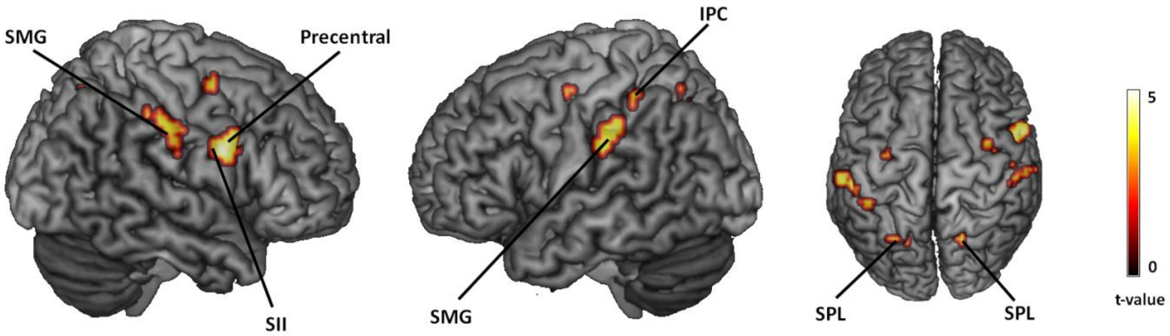
Figure A.4. Result of whole-brain MVPA searchlight classification trained to distinguish attended location (left vs. right) for tactile attention condition (above, $p < 0.001$, uncorrected) and visual attention condition (below, $p < 0.00001$, uncorrected).

Appendix B - Additional Figures for Chapter 5



* (p < 0.001, uncorrected)

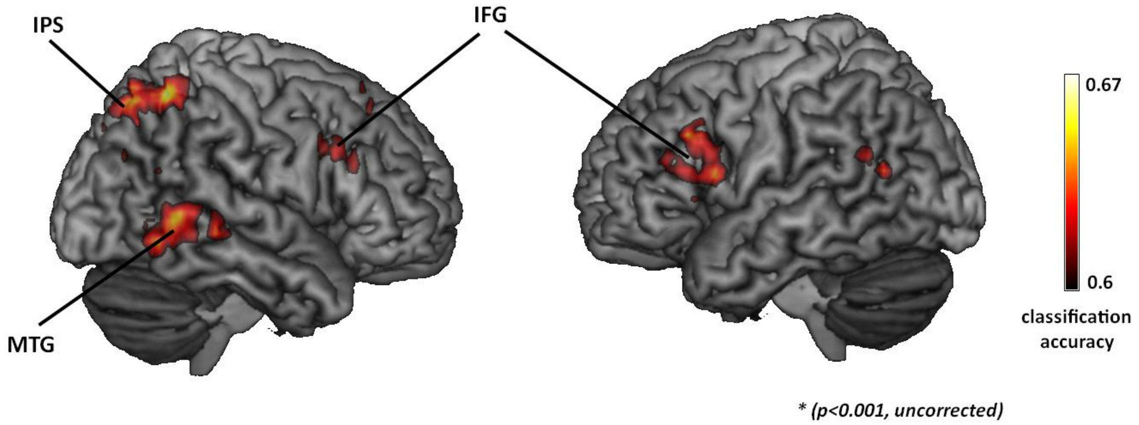
a) Univariate contrast for visual-shape vs. visual-frequency condition



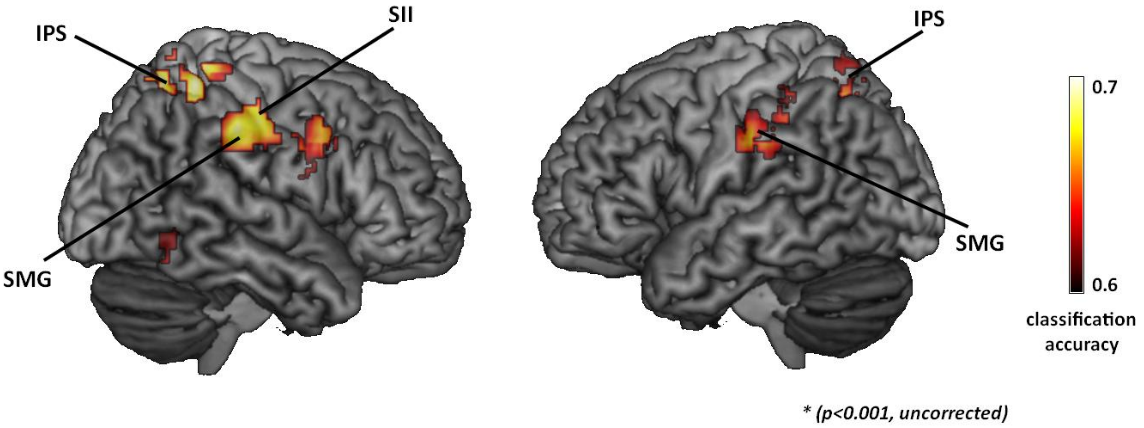
* (p < 0.001, uncorrected)

b) Univariate contrast for tactile-shape vs. tactile-frequency condition

Figure B.1. (a) Feature-specific activations during attention to visual modality, obtained using univariate conjunction analysis with attend visual-shape vs. attend visual-frequency as the contrast. Although no voxel survived correction for multiple comparisons, a small but close to significant cluster of activity was observed in inferior frontal gyrus (IFG), extending to middle frontal gyrus (MFG), indicating possible function of this frontal region in biasing selection towards distinct feature dimensions in vision. **(b)** Feature-specific activations while attending to tactile modality with attend tactile-shape vs. attend tactile-frequency as the contrast. There was no voxel that survived multiple comparisons in this contrast. Nevertheless, trends towards significance were observed in a few regions, including bilateral supramarginal gyrus (SMG), bilateral superior parietal lobe (SPL), and left inferior parietal cortex (IPC).



a) MVPA searchlight discriminating visual-shape vs. visual-frequency

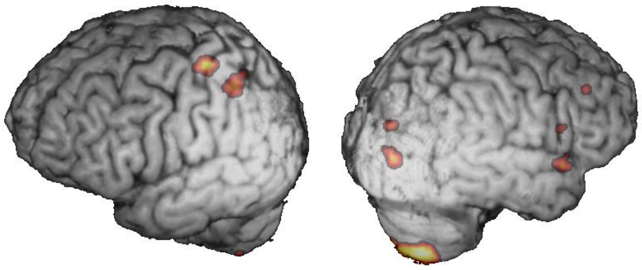


b) MVPA searchlight discriminating tactile-shape vs. tactile-frequency

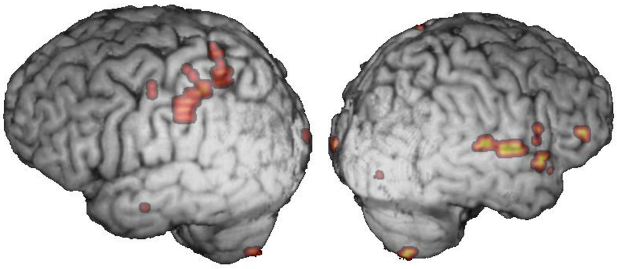
Figure B.2. (a) Searchlight map contrasting attend visual-shape vs. attend visual frequency condition revealed a trend toward significant classification in several fronto-parietal regions, including right intraparietal sulcus (IPS), bilateral inferior frontal gyrus (IFG), and right middle temporal gyrus (MTG). However, none of these clusters survived correction for multiple comparisons. **(b)** Result of searchlight analysis contrasting attend tactile-shape vs. attend tactile-frequency. Similarly, although there was a trend towards informative clusters in several regions, none of these were significant enough to pass multiple comparisons test.

Figure B.3. Results of individual subject conjunction analysis contrasting visual vs. tactile condition were shown below. The maps were produced using the first half of the fMRI data (odd runs only).

Subject 1

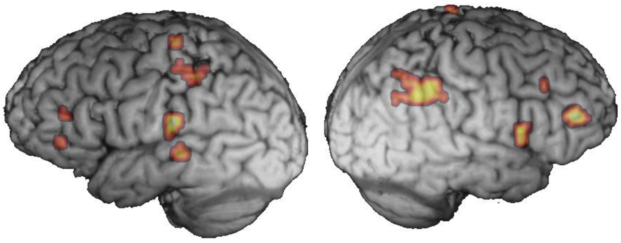


[Visual Shape AND Tactile Shape]

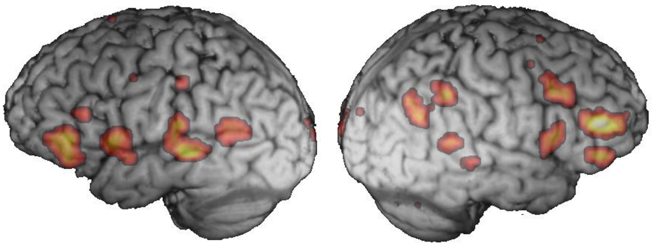


[Visual Freq AND Tactile Freq]

Subject 2

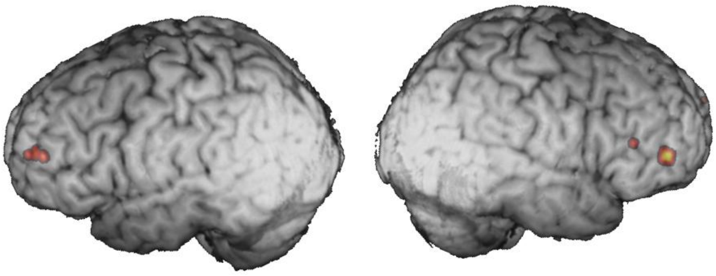


[Visual Shape AND Tactile Shape]

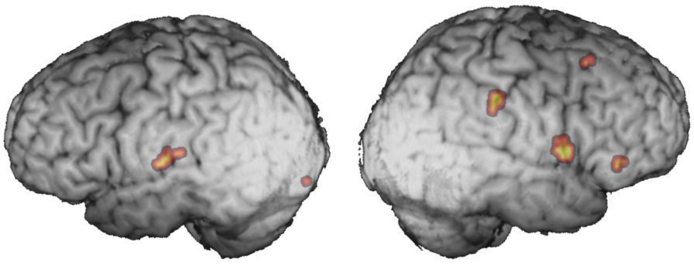


[Visual Freq AND Tactile Freq]

Subject 3

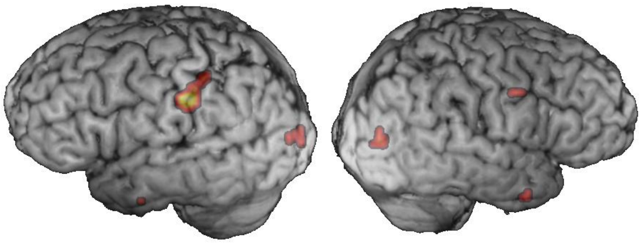


[Visual Shape AND Tactile Shape]

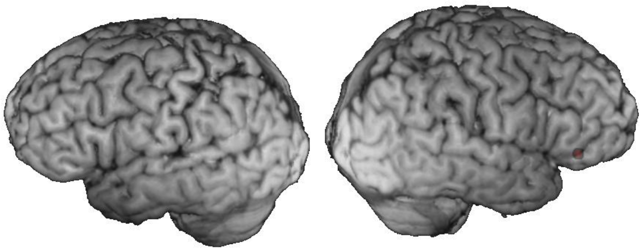


[Visual Freq AND Tactile Freq]

Subject 4



[Visual Shape AND Tactile Shape]



[Visual Freq AND Tactile Freq]

Appendix C - List of Abbreviations

AG	Angular Gyrus
BOLD	Blood Oxygenation Level-Dependent
CPU	Central Processing Unit
CUBRIC	Cardiff University Brain Research Imaging Centre
EEG	Electroencephalogram
EPI	Echo-Planar Imaging
ERP	Event-Related Potential
FDR	False-Discovery Rate
FEF	Frontal Eye Fields
FWE	Family-wise Error
GLM	General Linear Model
IC	Integrated Circuits
IFG	Inferior Frontal Gyrus
IPS	Intraparietal Sulcus
LCD	Liquid Crystal Display
LED	Light Emitting Diode
MEG	Magnetoencephalography
MFG	Middle Frontal Gyrus
MRI	Magnetic Resonance Imaging
MVPA	Multi Voxel Pattern Analysis
PC	Personal Computer
PET	Positron Emission Tomography
PLL	Phase-Locked Loop
PPC	Posterior Parietal Cortex
PWM	Pulse Width Modulation

ROI	Region of Interest
SI	Primary Somatosensory Cortex
SII	Secondary Somatosensory Cortex
SPI	Serial Peripheral Interface
SPL	Superior Parietal Lobe
SPM	Statistical Parametric Mapping
STS	Superior Temporal Sulcus
TMS	Transcranial Magnetic Stimulation
TPJ	Temporoparietal Junction
TTL	Transistor-Transistor Logic
USB	Universal Serial Bus
fMRI	Functional Magnetic Resonance Imaging

References

Adams, R. C., and Chambers, C. D. (2012). Mapping the timecourse of goal-directed attention to location and colour in human vision. Acta psychologica *139*, 515–523.

Al-Rawi, M. S., and Silva Cunha, J. P. (2012). On using permutation tests to estimate the classification significance of functional magnetic resonance imaging data. Neurocomputing *82*, 224–233.

Amedi, A., Jacobson, G., Hendler, T., Malach, R., and Zohary, E. (2002). Convergence of visual and tactile shape processing in the human lateral occipital complex. Cerebral Cortex *12*, 1202–1212.

Amiez, C., and Petrides, M. (2009). Anatomical organization of the eye fields in the human and non-human primate frontal cortex. Progress in neurobiology *89*, 220–230.

Anderson, J. S., Ferguson, M. A., Lopez-Larson, M., and Yurgelun-Todd, D. (2010). Topographic maps of multisensory attention. Proceedings of the National Academy of Sciences of the United States of America *107*, 20110–20114.

Anllo-Vento, L., and Hillyard, S. A. (1996). Selective attention to the color and direction of moving stimuli: electrophysiological correlates of hierarchical feature selection. Perception And Psychophysics *58*, 191–206.

Armstrong, K. M., and Moore, T. (2007). Rapid enhancement of visual cortical response discriminability by microstimulation of the frontal eye field. Proceedings of the National Academy of Sciences of the United States of America *104*, 9499–9504.

Aron, A. R., Robbins, T. W., and Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. Trends in cognitive sciences *8*, 170–177.

Ashkenazi, A., and Marks, L. E. (2004). Effect of endogenous attention on detection of weak gustatory and olfactory flavors. Perception And Psychophysics *66*, 596–608.

Backes, W. H., Mess, W. H., Van Kranen-Mastenbroek, V., and Reulen, J. P. (2000). Somatosensory cortex responses to median nerve stimulation: fMRI effects of current amplitude and selective attention. Clinical Neurophysiology *111*, 1738–1744.

Barrett, N. A., Large, M. M., Smith, G. L., Michie, P. T., Karayanidis, F., Kavanagh, D. J., Fawdry, R., Henderson, D., and O'Sullivan, B. T. (2001). Human cortical processing of colour and pattern. Human Brain Mapping *13*, 213–225.

Bartfeld, E., and Grinvald, A. (1992). Relationships between orientation-preference pinwheels, cytochrome oxidase blobs, and ocular-dominance columns in primate striate cortex. Proceedings of the National Academy of Sciences of the United States of America *89*, 11905–11909.

Beauchamp, M. S. (2005). See me, hear me, touch me: multisensory integration in lateral occipital-temporal cortex. Current opinion in neurobiology *15*, 145–153.

Beauchamp, M. S., Cox, R. W., and DeYoe, E. A. (1997). Graded effects of spatial and featural attention on human area MT and associated motion processing areas. (Am Physiological Soc).

Beauchamp, M. S., Haxby, J. V., Jennings, J. E., and DeYoe, E. A. (1999). An fMRI version of the Farnsworth-Munsell 100-Hue test reveals multiple color-selective areas in human ventral occipitotemporal cortex. (Oxford Univ Press).

Beauchamp, M. S., Pasalar, S., and Ro, T. (2010). Neural Substrates of Reliability-Weighted Visual-Tactile Multisensory Integration. Frontiers in systems neuroscience *4*, 11.

Beauchamp, M. S., Yasar, N. E., Frye, R. E., and Ro, T. (2008). Touch, sound and vision in human superior temporal sulcus. NeuroImage *41*, 1011–1020.

Beck, D. M., and Kastner, S. (2009). Top-down and bottom-up mechanisms in biasing competition in the human brain. Vision Research *49*, 1154–1165.

Beer, A. L., and Röder, B. (2004). Attention to motion enhances processing of both visual and auditory stimuli: an event-related potential study. Brain Research *18*, 205–225.

Berman, R. A., Colby, C. L., Genovese, C. R., Voyvodic, J. T., Luna, B., Thulborn, K. R., and Sweeney, J. A. (1999). Cortical networks subserving pursuit and saccadic eye movements in humans: an FMRI study. Human brain mapping *8*, 209–225.

Bestmann, S., Baudewig, J., Siebner, H., Rothwell, J., and Frahm, J. (2004). Functional MRI of the immediate impact of transcranial magnetic stimulation on cortical and subcortical motor circuits. European Journal of Neuroscience *19*, 1950–1962.

Bestmann, S., Ruff, C. C., Blankenburg, F., Weiskopf, N., Driver, J., and Rothwell, J. C. (2008). Mapping causal interregional influences with concurrent TMS-fMRI. Experimental Brain Research *191*, 383–402.

Bichot, N. P., Rossi, A. F., and Desimone, R. (2005). Parallel and serial neural mechanisms for visual search in macaque area V4. Science *308*, 529–534.

Bishop, C. M. (2006). Pattern Recognition and Machine Learning M. Jordan, J. Kleinberg, and B. Schölkopf, eds. (Springer).

Blake, R., Sobel, K. V., and James, T. W. (2004). Neural synergy between kinetic vision and touch. Psychological Science *15*, 397–402.

Blankenburg, F., Ruff, C. C., Bestmann, S., Bjoertomt, O., Josephs, O., Deichmann, R., and Driver, J. (2010). Studying the Role of Human Parietal Cortex in Visuospatial Attention with Concurrent TMS–fMRI. Cerebral Cortex *20*, 2702–2711.

Blinowska, K., Müller-Putz, G., Kaiser, V., Astolfi, L., Vanderperren, K., Van Huffel, S., and Lemieux, L. (2009). Multimodal Imaging of Human Brain Activity: Rational, Biophysical Aspects and Modes of Integration. Computational intelligence and neuroscience *2009*, 813607.

Bohning, D. E., Denslow, S., Bohning, P. A., Walker, J. A., and George, M. S. (2003). A TMS coil positioning/holding system for MR image-guided TMS interleaved with fMRI. Clinical Neurophysiology *114*, 2210–2219.

Bohning, D. E., Shastri, A., Nahas, Z., Lorberbaum, J. P., Andersen, S. W., Dannels, W. R., Haxthausen, E. U., Vincent, D. J., and George, M. S. (1998). Echoplanar BOLD fMRI of brain activation induced by concurrent transcranial magnetic stimulation. NeuroReport *33*, 943–948.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., and Cohen, J. D. (2001). Conflict monitoring and cognitive control. Psychological review *108*, 624–652.

Botvinick, M. M., Cohen, J. D., and Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. Trends in cognitive sciences *8*, 539–546.

Boynton, G. M. (2005). Imaging orientation selectivity: decoding conscious perception in V1. Nature neuroscience *8*, 541–542.

Boynton, G. M., Ciaramitaro, V. M., and Arman, A. C. (2006). Effects of feature-based attention on the motion aftereffect at remote locations. Vision Research *46*, 2968–2976.

Brouwer, G. J., and Heeger, D. J. (2009). Decoding and reconstructing color from responses in human visual cortex. Journal of Neuroscience *29*, 13992–14003.

Bruce, C., Desimone, R., and Gross, C. G. (1981). Visual properties of neurons in a polysensory area in superior temporal sulcus of the macaque. Journal of neurophysiology *46*, 369–384.

Bullmore, E., and Sporns, O. (2009). Complex brain networks: graph theoretical analysis of structural and functional systems. Nature Reviews Neuroscience *10*, 186–198.

Bungert, A., Chambers, C. D., Long, E., and Evans, C. J. (2012a). On the importance of specialized radiofrequency filtering for concurrent TMS/MRI. Journal of neuroscience methods *210*, 202–205.

Bungert, A., Chambers, C. D., Phillips, M., and Evans, C. J. (2012b). Reducing image artefacts in concurrent TMS/fMRI by passive shimming. NeuroImage *19*, 2011–2011.

Burton, H., Sinclair, R. J., and McLaren, D. G. (2008). Cortical network for vibrotactile attention: a fMRI study. Human Brain Mapping *29*, 207–221.

Bushara, K. O., Weeks, R. A., Ishii, K., Catalan, M. J., Tian, B., Rauschecker, J. P., and Hallett, M. (1999). Modality-specific frontal and parietal areas for auditory and visual spatial localization in humans.

Busse, L., Roberts, K. C., Crist, R. E., Weissman, D. H., and Woldorff, M. G. (2005). The spread of attention across modalities and space in a multisensory object. Proceedings of the National Academy of Sciences of the United States of America *102*, 18751–18756.

Carlson, T. A., Schrater, P., and He, S. (2003). Patterns of activity in the categorical representations of objects. Journal of Cognitive Neuroscience *15*, 704–717.

Castiello, U. (1990). Size of the attentional focus and efficiency of processing. Acta Psychologica *73*, 195–209.

Chambers, C. D., and Mattingley, J. B. (2005). Neurodisruption of selective attention: insights and implications. Trends in Cognitive Sciences *9*, 542–550.

Chambers, C. D., Payne, J. M., and Mattingley, J. B. (2007). Parietal disruption impairs reflexive spatial attention within and between sensory modalities. Neuropsychologia *45*, 1715–1724.

Chambers, C. D., Payne, J. M., Stokes, M. G., and Mattingley, J. B. (2004a). Fast and slow parietal pathways mediate spatial attention. Nature Neuroscience *7*, 217–218.

Chambers, C. D., Stokes, M. G., and Mattingley, J. B. (2004b). Modality-Specific Control of Strategic Spatial Attention in Parietal Cortex. Neuron *44*, 925–930.

Chelazzi, L., Duncan, J., Miller, E. K., and Desimone, R. (1998). Responses of neurons in inferior temporal cortex during memory-guided visual search. Journal of Neurophysiology *80*, 2918–2940.

Chelazzi, L., Miller, E. K., Duncan, J., and Desimone, R. (1993). A neural basis for visual search in inferior temporal cortex. Nature *363*, 345–347.

Chen, X., Hoffmann, K.-P., Albright, T. D., and Thiele, A. (2012). Effect of feature-selective attention on neuronal responses in macaque area MT. Journal of neurophysiology *107*, 1530–1543.

Chiu, Y.-C., and Yantis, S. (2009). A domain-independent source of cognitive control for task sets: shifting spatial attention and switching categorization rules. Journal of Neuroscience *29*, 3930–3938.

Chun, M. M., Golomb, J. D., and Turk-Browne, N. B. (2011). A taxonomy of external and internal attention. Annual Review of Psychology *62*, 73–101.

Ciaramitaro, V. M., Buracas, G. T., and Boynton, G. M. (2007). Spatial and cross-modal attention alter responses to unattended sensory information in early visual and auditory human cortex. Journal of neurophysiology *98*, 2399–2413.

Cohen, J. D., Botvinick, M., and Carter, C. S. (2000). Anterior cingulate and prefrontal cortex: who's in control? Nature neuroscience *3*, 421–423.

Constable, R. T., Pugh, K. R., Berroya, E., Mencl, W. E., Westerveld, M., Ni, W., and Shankweiler, D. (2004). Sentence complexity and input modality effects in sentence comprehension: an fMRI study.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., Linenweber, M. R., Petersen, S. E., Raichle, M. E., Van Essen, D. C., et al. (1998a). A common network of functional areas for attention and eye movements. Neuron *21*, 761–773.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., Linenweber, M. R., Petersen, S. E., Raichle, M. E., Van Essen, D. C., et al. (1998b). A common network of functional areas for attention and eye movements. Neuron *21*, 761–773.

Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L., and Petersen, S. E. (1990). Attentional modulation of neural processing of shape, color, and velocity in humans. Science *248*, 1556–1559.

Corbetta, M., Miezin, F. M., Shulman, G. L., and Petersen, S. E. (1993). A PET study of visuospatial attention. Journal of Neuroscience *13*, 1202–1226.

Corbetta, M., Patel, G., and Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. Neuron *58*, 306–324.

Corbetta, M., and Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience *3*, 201–215.

Cornelissen, F. W., Pelli, D. G., Farell, B., Huckins, S. C., and Szeverenyi, N. M. (1997). A binocular fiberscope for presenting visual stimuli during fMRI. Spatial Vision *11*, 75–81.

Cortes, C., and Vapnik, V. (1995). Support-vector networks. Machine Learning *20*, 273–297.

Coull, J. T., Frith, C. D., Büchel, C., and Nobre, A. C. (2000). Orienting attention in time: behavioural and neuroanatomical distinction between exogenous and endogenous shifts. Neuropsychologia *38*, 808–819.

Coull, J. T., and Nobre, A. C. (1998). Where and when to pay attention. Journal of Neuroscience *18*, 7426–7435.

Cox, D. D., and Savoy, R. L. (2003). Functional magnetic resonance imaging (fMRI) "brain reading": detecting and classifying distributed patterns of fMRI activity in human visual cortex. NeuroImage *19*, 261–270.

Craighero, L., and Rizzolatti, G. (2010). Premotor theory of attention. Acta Psychologica *136*, 181–186.

Culham JC, Gallivan J, Cavina-Pratesi C, and Quinlan DJ (2008). fMRI investigations of reaching and ego space in human superior parieto-occipital cortex. In Klatzky RL, Behrmann M, MacWhinney B, editors. Embodiment, Ego-Space and Action. Psychology Press: New York, 247–274.

Dale, A. M., and Halgren, E. (2001). Spatiotemporal mapping of brain activity by integration of multiple imaging modalities. Current Opinion in Neurobiology *11*, 202–208.

Van De Winckel, A., Sunaert, S., Wenderoth, N., Peeters, R., Van Hecke, P., Feys, H., Horemans, E., Marchal, G., Swinnen, S. P., Perfetti, C., et al. (2005). Passive somatosensory discrimination tasks in healthy volunteers: differential networks involved in familiar versus unfamiliar shape and length discrimination. (ACADEMIC PRESS INC ELSEVIER SCIENCE).

DeYoe, E. A., Carman, G. J., Bandettini, P., Glickman, S., Wieser, J., Cox, R., Miller, D., and Neitz, J. (1996). Mapping striate and extrastriate visual areas in human cerebral cortex. Proceedings of the National Academy of Sciences of the United States of America *93*, 2382–2386.

Denslow, S., Lomarev, M., George, M. S., and Bohning, D. E. (2005). Cortical and subcortical brain effects of transcranial magnetic stimulation (TMS)-induced movement: an interleaved TMS/functional magnetic resonance imaging study. (Society of Biological Psychiatry).

Derrfuss, J., Brass, M., Neumann, J., and Von Cramon, D. Y. (2005). Involvement of the inferior frontal junction in cognitive control: meta-analyses of switching and Stroop studies. Human brain mapping *25*, 22–34.

Desimone, R. (1998). Visual attention mediated by biased competition in extrastriate visual cortex. Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences *353*, 1245–1255.

Desimone, R., and Duncan, J. (1995a). Neural mechanisms of selective visual attention. Annual Review of Neuroscience *18*, 193–222.

Desimone, R., and Duncan, J. (1995b). Neural mechanisms of selective visual attention. Annual Review of Neuroscience *18*, 193–222.

Detre, G. J., Polyn, S. M., Moore, C. D., Natu, V. S., Singer, B. D., Cohen, J. D., Haxby, J. V., and Norman, K. A. (2006). The Multi-Voxel Pattern Analysis (MVPA) toolbox. Organization of Human Brain Mapping Florence 2006 *Jun 2006*.

Doesburg, S. M., Roggeveen, A. B., Kitajo, K., and Ward, L. M. (2008). Large-scale gamma-band phase synchronization and selective attention. Cerebral Cortex *18*, 386–396.

Dosenbach, N. U. F., Fair, D. A., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. A. T., Fox, M. D., Snyder, A. Z., Vincent, J. L., Raichle, M. E., et al. (2007). Distinct brain networks for adaptive and stable task control in humans. Proceedings of the National Academy of Sciences of the United States of America *104*, 11073–11078.

Dosenbach, N. U. F., Visscher, K. M., Palmer, E. D., Miezin, F. M., Wenger, K. K., Kang, H. C., Burgund, E. D., Grimes, A. L., Schlaggar, B. L., and Petersen, S. E. (2006). A core system for the implementation of task sets. Neuron *50*, 799–812.

Driver, J., and Noesselt, T. (2008). Multisensory Interplay Reveals Crossmodal Influences on “Sensory-Specific” Brain Regions, Neural Responses, and Judgments. Neuron *57*, 11–23.

Driver, J., and Spence, C. (1998). Cross-modal links in spatial attention. Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences *353*, 1319–1331.

Duhamel, J.-R., Colby, C. L., and Goldberg, M. E. (1998). Ventral intraparietal area of the macaque: Convergence visual and somatic response properties. Journal of Neurophysiology *79*, 126–136.

Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. Nature Reviews Neuroscience *2*, 820–829.

Duncan, J. (1998). Converging levels of analysis in the cognitive neuroscience of visual attention. Society *353*, 1307–1317.

Duncan, J., and Owen, A. M. (2000). A similar frontal lobe network recruited by diverse cognitive demands. Trends in Neurosciences *23*, 475–483.

Egly, R., Driver, J., and Rafal, R. D. (1994). Shifting visual attention between objects and locations: evidence from normal and parietal lesion subjects. Journal of experimental psychology General *123*, 161–177.

Eimer, M., and Schröger, E. (1998). ERP effects of intermodal attention and cross-modal links in spatial attention.

Eimer, M., Van Velzen, J., and Driver, J. (2002a). Cross-Modal Interactions between Audition, Touch, and Vision in Endogenous Spatial Attention: ERP Evidence on Preparatory States and Sensory Modulations. Journal of Cognitive Neuroscience *14*, 254–271.

Eimer, M., Velzen, V., and Jose, L. (2002b). Crossmodal links in spatial attention are mediated by supramodal control processes: evidence from event-related potentials. Psychophysiology *39*, 437–449.

Engel, S. A., Glover, G. H., and Wandell, B. A. (1997). Retinotopic organization in human visual cortex and the spatial precision of functional MRI. Cerebral Cortex *7*, 181–192.

Eriksen, C. W., and St James, J. D. (1986). Visual attention within and around the field of focal attention: a zoom lens model. Perception And Psychophysics *40*, 225–240.

Eriksen, C. W., and Yeh, Y. Y. (1985). Allocation of attention in the visual field. Journal of Experimental Psychology: Human Perception and Performance *11*, 583–597.

Esterman, M., Chiu, Y.-C., Tamber-Rosenau, B. J., and Yantis, S. (2009). Decoding cognitive control in human parietal cortex. Proceedings of the National Academy of Sciences of the United States of America *106*, 17974–17979.

Etzel, J. A., Gazzola, V., and Keysers, C. (2009). An introduction to anatomical ROI-based fMRI classification analysis. Brain Research *1282*, 114–125.

Etzel, J. A., Valchev, N., and Keysers, C. (2011). The impact of certain methodological choices on multivariate analysis of fMRI data with support vector machines. NeuroImage *54*, 1159–1167.

Fairhall, S. L., and Macaluso, E. (2009). Spatial attention can modulate audiovisual integration at multiple cortical and subcortical sites. European Journal of Neuroscience *29*, 1247–1257.

Fan, J., McCandliss, B. D., Fossella, J., Flombaum, J. I., and Posner, M. I. (2005). The activation of attentional networks. (Elsevier).

Farah, M. J., Wong, A. B., Monheit, M. A., and Morrow, L. A. (1989). Parietal lobe mechanisms of spatial attention: modality specific or supramodal? Neuropsychologia *44*, 1–26.

Filimon, F., Nelson, J. D., Hagler, D. J., and Sereno, M. I. (2007). Human cortical representations for reaching: mirror neurons for execution, observation, and imagery. NeuroImage *37*, 1315–1328.

Fogelson, S. V., Kohler, P. J., Hanke, M., Halchenko, Y. O., Haxby, J. V., Granger, R. H., and Tse, P. U. (2011). STMVPA: Spatiotemporal multivariate pattern analysis permits fine-grained visual categorization. Journal of Vision *11*, 814–814.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., and Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proceedings of the National Academy of Sciences of the United States of America *102*, 9673–9678.

Fox, P., Ingham, R., George, M. S., Mayberg, H., Ingham, J., Roby, J., Martin, C., and Jerabek, P. (1997). Imaging human intra-cerebral connectivity by PET during TMS. NeuroReport *8*, 2787–2791.

Freeman, W. J., and Kozma, R. (2000). Local-global interactions and the role of mesoscopic (intermediate-range) elements in brain dynamics. Behavioral and Brain Sciences *23*, 401–+.

Fries, P., Reynolds, J. H., Rorie, A. E., and Desimone, R. (2001). Modulation of oscillatory neuronal synchronization by selective visual attention. Science *291*, 1560–1563.

Friston, K. (2007). Dynamic causal models for fMRI. In Statistical Parametric Mapping, K. Friston, J. Ashburner, S. Kiebel, T. Nichols, and W. Penny, eds. (Elsevier), pp. 541–560.

Friston, K. (2011). Functional and effective connectivity: a review. Brain Connectivity *1*, 13–36.

Friston, K., Ashburner, J., Frith, C., Poline, J., Heather, J., and Frackowiak, R. (1995a). Spatial registration and normalization of images. Human Brain Mapping *3*, 165–189.

Friston, K. J. (1994). Functional and effective connectivity in neuroimaging: A synthesis. Human Brain Mapping *2*, 56–78.

Friston, K. J. (2009). Modalities, modes, and models in functional neuroimaging. Science *326*, 399–403.

Friston, K. J., Harrison, L., and Penny, W. (2003). Dynamic causal modelling. NeuroImage *19*, 1273–1302.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. P., Frith, C. D., and Frackowiak, R. S. J. (1995b). Statistical parametric maps in functional imaging: A general linear approach. Human Brain Mapping *2*, 189–210.

Friston, K. J., Penny, W. D., Ashburner, J., Kiebel, S. J., and Nichols, T. E. (2006). Statistical parametric mapping : the analysis of functional brain images K. J. Friston, J. T. Ashburner, S. J. Kiebel, T. E. Nichols, and W. D. Penny, eds. (Academic Press).

Friston, K., Penny, W., and Glaser, D. (2005). Conjunction revisited. NeuroImage *25*, 661–667.

Gallivan, J. P., Cavina-Pratesi, C., and Culham, J. C. (2009). Is that within reach? fMRI reveals that the human superior parieto-occipital cortex encodes objects reachable by the hand. Journal of Neuroscience *29*, 4381–4391.

Giesbrecht, B., Woldorff, M. G., Song, A. W., and Mangun, G. R. (2003). Neural mechanisms of top-down control during spatial and feature attention. NeuroImage *19*, 496–512.

Goebel, R., Roebroeck, A., Kim, D.-S., and Formisano, E. (2003). Investigating directed cortical interactions in time-resolved fMRI data using vector autoregressive modeling and Granger causality mapping. Magnetic Resonance Imaging *21*, 1251–1261.

Golland, P., and Fischl, B. (2003). Permutation tests for classification: towards statistical significance in image-based studies. C. Taylor and J. Noble, eds. (Springer-Verlag).

Green, J. J., Doesburg, S. M., Ward, L. M., and McDonald, J. J. (2011). Electrical Neuroimaging of Voluntary Audiospatial Attention: Evidence for a Supramodal Attention Control Network. Journal of Neuroscience *31*, 3560–3564.

Greenberg, A. S., Esterman, M., Wilson, D., Serences, J. T., and Yantis, S. (2010). Control of spatial and feature-based attention in frontoparietal cortex. Journal of Neuroscience *30*, 14330–14339.

Haenny, P., and Schiller, P. (1988). State dependent activity in monkey visual cortex. Experimental Brain Research *69*, 225–244.

Hagen, M. C., Franzen, O., McGlone, F., Essick, G., Dancer, C., and Pardo, J. V. (2002). Tactile motion activates the human middle temporal/V5 (MT/V5) complex. European Journal of Neuroscience *16*, 957–964.

Hamada, Y., Okita, H., and Suzuki, R. (2003). Effect of interstimulus interval on attentional modulation of cortical activities in human somatosensory areas. Clinical Neurophysiology *114*, 548–555.

Hanke, M., Halchenko, Y. O., Sederberg, P. B., Olivetti, E., Fründ, I., Rieger, J. W., Herrmann, C. S., Haxby, J. V., Hanson, S. J., and Pollmann, S. (2009). PyMVPA: A

Unifying Approach to the Analysis of Neuroscientific Data. Frontiers in neuroinformatics *3*, 13.

Harris, J. A., Clifford, C. W. G., and Miniussi, C. (2008). The functional effect of transcranial magnetic stimulation: signal suppression or neural noise generation? Journal of Cognitive Neuroscience *20*, 734–740.

Hastie, T., Tibshirani, R., and Friedman, J. (2009). The Elements of Statistical Learning: Data Mining, Inference, and Prediction Springer, ed. (Springer).

Haxby, J. V. (2012). Multivariate pattern analysis of fMRI: The early beginnings. NeuroImage.

Haxby, J. V., Gobbini, M. I., Furey, M. L., Ishai, A., Schouten, J. L., and Pietrini, P. (2001). Distributed and overlapping representations of faces and objects in ventral temporal cortex. Science *293*, 2425–2430.

Haynes, J., and Rees, G. (2006). Decoding mental states from brain activity in humans. Nature Reviews Neuroscience *7*, 523–534.

Haynes, J., and Rees, G. (2005). Predicting the orientation of invisible stimuli from activity in human primary visual cortex. Nature Neuroscience *8*, 686–691.

Haynes, J.-D., Sakai, K., Rees, G., Gilbert, S., Frith, C., and Passingham, R. E. (2007). Reading hidden intentions in the human brain. Current Biology *17*, 323–328.

Heinen, K., Ruff, C. C., Bjoertomt, O., Schenkluhn, B., Bestmann, S., Blankenburg, F., Driver, J., and Chambers, C. D. (2011). Concurrent TMS-fMRI reveals dynamic interhemispheric influences of the right parietal cortex during exogenously cued visuospatial attention. European Journal of Neuroscience *33*, 991–1000.

Hoffman, H. G., Richards, T. L., Magula, J., Seibel, E. J., Hayes, C., Mathis, M., Sharar, S. R., and Maravilla, K. (2003). A magnet-friendly virtual reality fiberoptic image delivery system. Cyberpsychology and Behavior *6*, 645–648.

Hopfinger, J. B., Büchel, C., Holmes, A. P., and Friston, K. J. (2000). A study of analysis parameters that influence the sensitivity of event-related fMRI analyses. NeuroImage *11*, 326–333.

Howard, J. D., Plailly, J., Grueschow, M., Haynes, J.-D., and Gottfried, J. A. (2009). Odor quality coding and categorization in human posterior piriform cortex. Nature Neuroscience *12*, 932–938.

Huang, R.-S., and Sereno, M. I. (2008). Visual stimulus presentation using fiber optics in the MRI scanner. Journal of Neuroscience Methods *169*, 76–83.

Huettel, S., Song, A., and Mccarthy, G. (2004). Functional Magnetic Resonance Imaging ({Sinauer Associates}).

Hämäläinen, H., Hiltunen, J., and Titievskaja, I. (2002). Activation of somatosensory cortical areas varies with attentional state: an fMRI study.

Ilmoniemi, R. J., Virtanen, J., Ruohonen, J., Karhu, J., Aronen, H. J., Näätänen, R., and Katila, T. (1997). Neuronal responses to magnetic stimulation reveal cortical reactivity and connectivity. NeuroReport *8*, 3537–3540.

Ito, M., and Gilbert, C. D. (1999). Attention modulates contextual influences in the primary visual cortex of alert monkeys. Neuron *22*, 593–604.

Jehee, J. F. M., Brady, D. K., and Tong, F. (2011). Attention improves encoding of task-relevant features in the human visual cortex. Journal of Neuroscience *31*, 8210–8219.

Johansen-Berg, H., Christensen, V., Woolrich, M., and Matthews, P. M. (2000). Attention to touch modulates activity in both primary and secondary somatosensory areas.

Johnson, J. A., and Zatorre, R. J. (2005). Attention to simultaneous unrelated auditory and visual events: behavioral and neural correlates. Cerebral Cortex *15*, 1609–1620.

Jung-Beeman, M. (2005). Bilateral brain processes for comprehending natural language. Trends in Cognitive Sciences *9*, 512–518.

Kalberlah, C., Chen, Y., Heinzle, J., and Haynes, J.-D. (2011). Beyond topographic representation: Decoding visuospatial attention from local activity patterns in the human frontal cortex. International Journal of Imaging Systems and Technology *21*, 201–210.

Kamitani, Y., and Tong, F. (2006). Decoding seen and attended motion directions from activity in the human visual cortex. Current Biology *16*, 1096–1102.

Kamitani, Y., and Tong, F. (2005). Decoding the visual and subjective contents of the human brain. Nature Neuroscience *8*, 679–685.

Kanwisher, N., Woods, R. P., Iacoboni, M., and Mazziotta, J. C. (1997). A locus in human extrastriate cortex for visual shape analysis. Journal of Cognitive Neuroscience *9*, 133–142.

Karns, C. M., and Knight, R. T. (2009). Intermodal auditory, visual, and tactile attention modulates early stages of neural processing. Journal of cognitive neuroscience *21*, 669–683.

Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R., and Ungerleider, L. G. (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron *22*, 751–761.

Kastner, S., and Ungerleider, L. G. (2000). Mechanisms of visual attention in the human cortex. Annual Review of Neuroscience *23*, 315–341.

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

Kay, K. N., Naselaris, T., Prenger, R. J., and Gallant, J. L. (2008). Identifying natural images from human brain activity. Nature *452*, 352–355.

Keeler, E. K., Casey, F. X., Engels, H., Lauder, E., Pirto, C. A., Reisker, T., Rogers, J., Schaefer, D. J., and Tynes, T. (1998). Accessory equipment considerations with respect to MRI compatibility. Journal of Magnetic Resonance Imaging *8*, 12–18.

Kim, J.-K., and Zatorre, R. J. (2011). Tactile-auditory shape learning engages the lateral occipital complex. Journal of Neuroscience *31*, 7848–7856.

Kimmig, H., Ohlendorf, S., Speck, O., Sprenger, A., Rutschmann, R. M., Haller, S., and Greenlee, M. W. (2008). fMRI evidence for sensorimotor transformations in human cortex during smooth pursuit eye movements. Neuropsychologia *46*, 2203–2213.

Kippenhan, J. S., Barker, W. W., Pascal, S., Nagel, J., and Duara, R. (1992). Evaluation of a neural-network classifier for PET scans of normal and Alzheimer’s disease subjects. Journal of nuclear medicine official publication Society of Nuclear Medicine *33*, 1459–1467.

Klein, A., Mensh, B., Ghosh, S., Tourville, J., and Hirsch, J. (2005). Mindboggle: Automated brain labeling with multiple atlases. BMC Medical Imaging *5*, 7.

Klemen, J., and Chambers, C. D. (2012). Current perspectives and methods in studying neural mechanisms of multisensory interactions. Neuroscience and biobehavioral reviews *36*, 111–133.

Koelewijn, T., Bronkhorst, A., and Theeuwes, J. (2010). Attention and the multiple stages of multisensory integration: A review of audiovisual studies. Acta Psychologica *134*, 372–384.

Kriegeskorte, N., and Bandettini, P. (2007). Analyzing for information, not activation, to exploit high-resolution fMRI. NeuroImage *38*, 649–662.

Kriegeskorte, N., Goebel, R., and Bandettini, P. (2006). Information-based functional brain mapping. Proceedings of the National Academy of Sciences of the United States of America *103*, 3863–3868.

Kriegeskorte, N., Simmons, W. K., Bellgowan, P. S. F., and Baker, C. I. (2009). Circular analysis in systems neuroscience: the dangers of double dipping. Nature Neuroscience *12*, 535–540.

Krishnan, A., Williams, L., Mcintosh, A. R., and Abdi, H. (2011). Partial Least Squares (PLS) methods for neuroimaging: A tutorial and review. NeuroImage *56*, 455–475.

Krumbholz, K., Nobis, E. A., Weatheritt, R. J., and Fink, G. R. (2009). Executive control of spatial attention shifts in the auditory compared to the visual modality. Human Brain Mapping *30*, 1457–1469.

Lacey, S., and Sathian, K. (2011). Multisensory object representation: insights from studies of vision and touch. Progress in Brain Research *191*, 165–176.

Langner, R., Kellermann, T., Boers, F., Sturm, W., Willmes, K., and Eickhoff, S. B. (2011). Modality-Specific Perceptual Expectations Selectively Modulate Baseline Activity in Auditory, Somatosensory, and Visual Cortices. Cerebral cortex (New York, N.Y. : 1991), bhr083–.

Lautrup, B., Hansen, L. K., Law, I., Mørch, N. J. S., Svarer, C., and Strother, S. C. (1994). Massive weight-sharing: A cure for extremely ill-posed problems. In Proceedings of the Workshop on Supercomputing in Brain Research From Tomography to Neural Networks, H. J. Hermann, D. E. Wolf, and E. Poeppel, eds. (World Scientific), pp. 137–148.

Lewis-Peacock, J. A., and Postle, B. R. (2012). Decoding the internal focus of attention. Neuropsychologia *50*, 470–478.

Liu, T. (2003). Cortical Mechanisms of Feature-based Attentional Control. Cerebral Cortex *13*, 1334–1343.

Liu, T., Hospadaruk, L., Zhu, D. C., and Gardner, J. L. (2011). Feature-specific attentional priority signals in human cortex. Journal of Neuroscience *31*, 4484–4495.

Liu, T., and Hou, Y. (2011). Global feature-based attention to orientation. Journal of Vision *11*, 1–8.

Liu, T., and Mance, I. (2011). Constant spread of feature-based attention across the visual field. Vision Research *51*, 26–33.

Liu, T., Pestilli, F., and Carrasco, M. (2005). Transient attention enhances perceptual performance and FMRI response in human visual cortex. Neuron *45*, 469–477.

Lloyd, D. M., Merat, N., McGlone, F., and Spence, C. (2003). Crossmodal links between audition and touch in covert endogenous spatial attention. Perception psychophysics *65*, 901–924.

Logan, G. D., and Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. Psychological Review *91*, 295–327.

Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. Nature *453*, 869–878.

Lucan, J. N., Foxe, J. J., Gomez-Ramirez, M., Sathian, K., and Molholm, S. (2010). Tactile shape discrimination recruits human lateral occipital complex during early perceptual processing. Human Brain Mapping *31*, 1813–1821.

Luks, T. L., and Simpson, G. V. (2004). Preparatory deployment of attention to motion activates higher-order motion-processing brain regions. NeuroImage *22*, 1515–1522.

Macaluso, E. (2006). Multisensory processing in sensory-specific cortical areas. The Neuroscientist a review journal bringing neurobiology neurology and psychiatry *12*, 327–338.

Macaluso, E. (2010). Orienting of spatial attention and the interplay between the senses. Cortex *46*, 282–297.

Macaluso, E., and Driver, J. (2005). Multisensory spatial interactions: a window onto functional integration in the human brain. Trends in Neurosciences *28*, 264–271.

Macaluso, E., and Driver, J. (2001). Spatial attention and crossmodal interactions between vision and touch. Neuropsychologia *39*, 1304–1316.

Macaluso, E., Driver, J., and Frith, C. (2003a). Multimodal spatial representations engaged in human parietal cortex during both saccadic and manual spatial orienting. Current Biology *13*, 990–999.

Macaluso, E., Eimer, M., Frith, C. D., and Driver, J. (2003b). Preparatory states in crossmodal spatial attention: spatial specificity and possible control mechanisms. Experimental Brain Research *149*, 62–74.

Macaluso, E., Frith, C. D., and Driver, J. (2002a). Directing attention to locations and to sensory modalities: multiple levels of selective processing revealed with PET. Cerebral Cortex *12*, 357–368.

Macaluso, E., Frith, C. D., and Driver, J. (2000). Modulation of human visual cortex by crossmodal spatial attention.

Macaluso, E., Frith, C. D., and Driver, J. (2005). Multisensory stimulation with or without saccades: fMRI evidence for crossmodal effects on sensory-specific cortices that reflect multisensory location-congruence rather than task-relevance. NeuroImage *26*, 414–425.

Macaluso, E., Frith, C. D., and Driver, J. (2002b). Supramodal effects of covert spatial orienting triggered by visual or tactile events. Journal of Cognitive Neuroscience *14*, 389–401.

Makin, T. R., Holmes, N. P., and Zohary, E. (2007). Is that near my hand? Multisensory representation of peripersonal space in human intraparietal sulcus. Journal of Neuroscience *27*, 731–740.

Martinez-Trujillo, J. (2011). Searching for the neural mechanisms of feature-based attention in the primate brain. Neuron *70*, 1025–1028.

Martinez-Trujillo, J. C., and Treue, S. (2004). Feature-based attention increases the selectivity of population responses in primate visual cortex. Current Biology *14*, 744–751.

De Martino, F., Valente, G., Staeren, N., Ashburner, J., Goebel, R., and Formisano, E. (2008). Combining multivariate voxel selection and support vector machines for mapping and classification of fMRI spatial patterns. NeuroImage *43*, 44–58.

Martínez, A., Anllo-Vento, L., Sereno, M. I., Frank, L. R., Buxton, R. B., Dubowitz, D. J., Wong, E. C., Hinrichs, H., Heinze, H. J., and Hillyard, S. A. (1999). Involvement of striate and extrastriate visual cortical areas in spatial attention. Nature Neuroscience *2*, 364–369.

Marx, E., Deutschländer, A., Stephan, T., Dieterich, M., Wiesmann, M., and Brandt, T. (2004). Eyes open and eyes closed as rest conditions: impact on brain activation patterns. NeuroImage *21*, 1818–1824.

Maunsell, J. H. R., and Cook, E. P. (2002). The role of attention in visual processing. Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences *357*, 1063–1072.

Maunsell, J. H. R., and Treue, S. (2006). Feature-based attention in visual cortex. Trends in Neurosciences *29*, 317–322.

Maunsell, J. H., Sclar, G., Nealey, T. A., and DePriest, D. D. (1991). Extraretinal representations in area V4 in the macaque monkey. Visual Neuroscience *7*, 561–573.

McAdams, C. J., and Maunsell, J. H. (2000). Attention to both space and feature modulates neuronal responses in macaque area V4. Journal of Neurophysiology *83*, 1751–1755.

McDonald, C. R., Thesen, T., Carlson, C., Blumberg, M., Girard, H. M., Trongnetrpunya, A., Sherfey, J. S., Devinsky, O., Kuzniecky, R., Dolye, W. K., et al. (2010). Multimodal imaging of repetition priming: Using fMRI, MEG, and intracranial EEG to reveal spatiotemporal profiles of word processing. NeuroImage *53*, 707–717.

McDonald, J. J., Teder-Sälejärvi, W. A., and Hillyard, S. A. (2000). Involuntary orienting to sound improves visual perception. Nature *407*, 906–908.

McIntosh, A. R., Bookstein, F. L., Haxby, J. V., and Grady, C. L. (1996). Spatial pattern analysis of functional brain images using partial least squares. NeuroImage *3*, 143–157.

McMains, S. A., Fehd, H. M., Emmanouil, T.-A., and Kastner, S. (2007). Mechanisms of feature- and space-based attention: response modulation and baseline increases. Journal of Neurophysiology *98*, 2110–2121.

Meador, K. J., Allison, J. D., Loring, D. W., Lavin, T. B., and Pillai, J. J. (2002). Topography of somatosensory processing: cerebral lateralization and focused attention. Journal of the International Neuropsychological Society JINS *8*, 349–359.

Mehta, A. D., Ulbert, I., and Schroeder, C. E. (2000a). Intermodal selective attention in monkeys. I: distribution and timing of effects across visual areas. Cerebral cortex New York NY 1991 *10*, 343–358.

Mehta, A. D., Ulbert, I., and Schroeder, C. E. (2000b). Intermodal selective attention in monkeys. II: physiological mechanisms of modulation. Cerebral cortex New York NY 1991 *10*, 359–370.

Melcher, D., and Vidnyánszky, Z. (2006). Subthreshold features of visual objects: unseen but not unbound. Vision Research *46*, 1863–1867.

Menz, M. M., McNamara, A., Klemen, J., and Binkofski, F. (2009). Dissociating networks of imitation. Human Brain Mapping *30*, 3339–3350.

Meredith, M. A., and Stein, B. E. (1983). Interactions among converging sensory inputs in the superior colliculus. Science New York NY *221*, 389–391.

Metzinger, T. (2008). Empirical perspectives from the self-model theory of subjectivity: a brief summary with examples. Progress in Brain Research *168*, 215–245.

Meyer, E., Ferguson, S. S., Zatorre, R. J., Alivisatos, B., Marrett, S., Evans, A. C., and Hakim, A. M. (1991). Attention modulates somatosensory cerebral blood flow response to vibrotactile stimulation as measured by positron emission tomography. Annals of Neurology *29*, 440–443.

Mikl, M., Marecek, R., Hlustík, P., Pavlicová, M., Drastich, A., Chlebus, P., Brázdil, M., and Krupa, P. (2008). Effects of spatial smoothing on fMRI group inferences. Magnetic Resonance Imaging *26*, 490–503.

Miller, B. T., and D'Esposito, M. (2005). Searching for "the top" in top-down control. Neuron *48*, 535–538.

Mima, T., Nagamine, T., Nakamura, K., and Shibasaki, H. (1998). Attention modulates both primary and second somatosensory cortical activities in humans: a magnetoencephalographic study. Journal of Neurophysiology *80*, 2215–2221.

Mirabella, G., Bertini, G., Samengo, I., Kilavik, B. E., Frilli, D., Della Libera, C., and Chelazzi, L. (2007). Neurons in area V4 of the macaque translate attended visual features into behaviorally relevant categories. Neuron *54*, 303–318.

Mitchell, T. M. (2006). The Discipline of Machine Learning. Machine Learning *17*, 1–7.

Mitchell, T. M., Hutchinson, R., Niculescu, R. S., Pereira, F., Wang, X., Just, M., and Newman, S. (2004). Learning to Decode Cognitive States from Brain Images. Machine Learning *57*, 145–175.

Miyawaki, Y., Uchida, H., Yamashita, O., Sato, M.-aki, Morito, Y., Tanabe, H. C., Sadato, N., and Kamitani, Y. (2008). Visual image reconstruction from human brain activity using a combination of multiscale local image decoders. Neuron *60*, 915–929.

Moisa, M., Pohmann, R., Uludağ, K., and Thielscher, A. (2010). Interleaved TMS/CASL: Comparison of different rTMS protocols. NeuroImage *49*, 612–620.

Moore, T., and Armstrong, K. M. (2003). Selective gating of visual signals by microstimulation of frontal cortex. Nature *421*, 370–373.

Moran, J., and Desimone, R. (1985). Selective attention gates visual processing in the extrastriate cortex. Science *229*, 782–784.

Mozolic, J. L., Hugenschmidt, C. E., Peiffer, A. M., and Laurienti, P. J. (2008a). Modality-specific selective attention attenuates multisensory integration. Experimental Brain Research *184*, 39–52.

Mozolic, J. L., Joyner, D., Hugenschmidt, C. E., Peiffer, A. M., Kraft, R. A., Maldjian, J. A., and Laurienti, P. J. (2008b). Cross-modal deactivations during modality-specific selective attention. BMC Neurology *8,* 35.

Müller, H. J., and Humphreys, G. W. (1991). Luminance-increment detection: Capacity-limited or not? Journal of Experimental Psychology Human Perception and Performance *17,* 107–124.

Naselaris, T., Prenger, R. J., Kay, K. N., Oliver, M., and Gallant, J. L. (2009). Bayesian reconstruction of natural images from human brain activity. Neuron *63,* 902–915.

Nishimoto, S., Vu, A. T., Naselaris, T., Benjamini, Y., Yu, B., and Gallant, J. L. (2011). Reconstructing Visual Experiences from Brain Activity Evoked by Natural Movies. Current Biology *21,* 1–6.

Nobre, A. C., Rao, A., and Chelazzi, L. (2006). Selective attention to specific features within objects: behavioral and electrophysiological evidence. Journal of Cognitive Neuroscience *18,* 539–561.

Nobre, A., Correa, A., and Coull, J. (2007). The hazards of time. Current opinion in neurobiology *17,* 465–470.

Noesselt, T., Hillyard, S. A., Woldorff, M. G., Schoenfeld, A., Hagner, T., Jäncke, L., Tempelmann, C., Hinrichs, H., and Heinze, H.-J. (2002). Delayed striate cortical activation during spatial attention. Neuron *35,* 575–587.

Norman, K. A., Polyn, S. M., Detre, G. J., and Haxby, J. V. (2006). Beyond mind-reading: multi-voxel pattern analysis of fMRI data. Trends in Cognitive Sciences *10,* 424–430.

Obermayer, K., and Blasdel, G. G. (1993). Geometry of orientation and ocular dominance columns in monkey striate cortex. New York *13,* 4114–4129.

O'Connor, D. H., Fukui, M. M., Pinsk, M. A., and Kastner, S. (2002). Attention modulates responses in the human lateral geniculate nucleus. Nature Neuroscience *5,* 1203–1209.

O'Craven, K. M., Downing, P. E., and Kanwisher, N. (1999). fMRI evidence for objects as the units of attentional selection. Nature *401,* 584–587.

O'Craven, K. M., Rosen, B. R., Kwong, K. K., Treisman, A., and Savoy, R. L. (1997). Voluntary attention modulates fMRI activity in human MT-MST. Neuron *18,* 591–598.

O'Toole, A. J., Jiang, F., Abdi, H., and Haxby, J. V. (2005). Partially distributed representations of objects and faces in ventral temporal cortex. Journal of Cognitive Neuroscience *17,* 580–590.

O'Toole, A. J., Jiang, F., Abdi, H., Pénard, N., Dunlop, J. P., and Parent, M. A. (2007). Theoretical, statistical, and practical perspectives on pattern-based classification approaches to the analysis of functional neuroimaging data. Journal of Cognitive Neuroscience *19,* 1735–1752.

Pascual-Leone, A., Walsh, V., and Rothwell, J. (2000). Transcranial magnetic stimulation in cognitive neuroscience--virtual lesion, chronometry, and functional connectivity. Current Opinion in Neurobiology *10*, 232–237.

Pashler, H. E. (1998). The psychology of attention C. E. Izard and J. L. Singer, eds. (MIT Press).

Peelen, M. V., and Downing, P. E. (2007). Using multi-voxel pattern analysis of fMRI data to interpret overlapping functional activations. Trends in Cognitive Sciences *11*, 4–5.

Peltier, S., Stilla, R., Mariola, E., LaConte, S., Hu, X., and Sathian, K. (2007). Activity and effective connectivity of parietal and occipital cortical regions during haptic shape perception. Neuropsychologia *45*, 476–483.

Pereira, F., and Botvinick, M. (2011). Information mapping with pattern classifiers: a comparative study. NeuroImage *56*, 476–496.

Pereira, F., Mitchell, T., and Botvinick, M. (2009). Machine learning classifiers and fMRI: A tutorial overview. NeuroImage *45*, S199–S209.

Petersen, S. E., and Posner, M. I. (2012). The Attention System of the Human Brain: 20 Years After. Annual Review of Neuroscience *35*, 73–89.

Poldrack, R. A. (2007). Region of interest analysis for fMRI. Social cognitive and affective neuroscience *2*, 67–70.

Polk, T. A., Drake, R. M., Jonides, J. J., Smith, M. R., and Smith, E. E. (2008). Attention enhances the neural processing of relevant features and suppresses the processing of irrelevant features in humans: a functional magnetic resonance imaging study of the Stroop task. Journal of Neuroscience *28*, 13786–13792.

Polyn, S. M., Natu, V. S., Cohen, J. D., and Norman, K. A. (2005). Category-specific cortical activity precedes retrieval during memory search. Science *310*, 1963–1966.

Posner, M. I. (1980). Orienting of attention. The Quarterly Journal Of Experimental Psychology *32*, 3–25.

Posner, M. I., Cohen, Y., and Rafal, R. D. (1982). Neural systems control of spatial orienting. Philosophical transactions of the Royal Society of London Series B Biological sciences *298*, 187–198.

Posner, M. I., and Petersen, S. E. (1990). The attention system of the human brain. Annual Review of Neuroscience *13*, 25–42.

Predko M (2002). Programming and Customizing PICmicro® Microcontrollers (USA: McGraw-Hill).

Preston, T. J., and Eckstein, M. P. (2010). Effect of fMRI study design on the classification accuracy of orientation discrimination. Journal of Vision *10*, 915–915.

Reddy, L., Tsuchiya, N., and Serre, T. (2010). Reading the mind's eye: decoding category information during mental imagery. NeuroImage *50*, 818–825.

Rizzolatti, G., Riggio, L., Dascola, I., and Umiltá, C. (1987). Reorienting attention across the horizontal and vertical meridians: evidence in favor of a premotor theory of attention. Neuropsychologia *25*, 31–40.

Roland, P. E. (1982). Cortical regulation of selective attention in man. A regional cerebral blood flow study. J Neurophysiol *48*, 1059–1078.

Rorden, C., and Brett, M. (2000). Stereotaxic display of brain lesions. Behavioural Neurology *12*, 191–200.

Rorden, C., Greene, K., Sasine, G., and Baylis, G. (2002). Enhanced tactile performance at the destination of an upcoming saccade. Current biology CB *12*, 1429–1434.

Rossi, A. F., and Paradiso, M. A. (1995). Feature-specific effects of selective visual attention. Vision Research *35*, 621–634.

Rubinov, M., and Sporns, O. (2010). Complex network measures of brain connectivity: uses and interpretations. NeuroImage *52*, 1059–1069.

Ruff, C., Blankenburg, F., Bjoertomt, O., Bestmann, S., Freeman, E., Haynes, J., Rees, G., Josephs, O., Deichmann, R., and Driver, J. (2006). Concurrent TMS-fMRI and psychophysics reveal frontal influences on human retinotopic visual cortex. Current Biology *16*, 1479–1488.

Ruff, C. C., Bestmann, S., Blankenburg, F., Bjoertomt, O., Josephs, O., Weiskopf, N., Deichmann, R., and Driver, J. (2008). Distinct causal influences of parietal versus frontal areas on human visual cortex: evidence from concurrent TMS–fMRI. Cerebral Cortex *18*, 817–827.

Ruff, C. C., Blankenburg, F., Bjoertomt, O., Bestmann, S., Weiskopf, N., and Driver, J. (2009). Hemispheric differences in frontal and parietal influences on human occipital cortex: direct confirmation with concurrent TMS-fMRI. Journal of Cognitive Neuroscience *21*, 1146–1161.

Rushworth, M. F. S., Ellison, A., and Walsh, V. (2001). Complementary localization and lateralization of orienting and motor attention. Nature Neuroscience *4*, 656–661.

Saalmann, Y. B., Pigarev, I. N., and Vidyasagar, T. R. (2007). Neural mechanisms of visual attention: how top-down feedback highlights relevant locations. Science New York NY *316*, 1612–1615.

Saenz, M., Buracas, G. T., and Boynton, G. M. (2002). Global effects of feature-based attention in human visual cortex. (Association for Research in Vision and Ophthalmology).

Saito, D. N., Okada, T., Morita, Y., Yonekura, Y., and Sadato, N. (2003). Tactile-visual cross-modal shape matching: a functional MRI study. Brain Research *17*, 14–25.

Salmi, J., Rinne, T., Degerman, A., Salonen, O., and Alho, K. (2007). Orienting and maintenance of spatial attention in audition and vision: multimodal and modality-specific brain activations. Brain structure function *212*, 181–194.

Saupe, K., Schröger, E., Andersen, S. K., and Müller, M. M. (2009). Neural Mechanisms of Intermodal Sustained Selective Attention with Concurrently Presented Auditory and Visual Stimuli. Frontiers in human neuroscience *3*, 13.

Schenkluhn, B., Ruff, C. C., Heinen, K., and Chambers, C. D. (2008). Parietal stimulation decouples spatial and feature-based attention. Journal of Neuroscience *28*, 11106–11110.

Schmahmann, J. D., and Pandya, D. N. (1991). Projections to the basis pontis from the superior temporal sulcus and superior temporal region in the rhesus monkey. The Journal of comparative neurology *308*, 224–248.

Schoenfeld, M. A., Hopf, J.-M., Martinez, A., Mai, H. M., Sattler, C., Gasde, A., Heinze, H.-J., and Hillyard, S. A. (2007). Spatio-temporal analysis of feature-based attention. Cerebral Cortex *17*, 2468–2477.

Scolari, M., and Serences, J. T. (2010). Basing perceptual decisions on the most informative sensory neurons. Journal of Neurophysiology *104*, 2266–2273.

Sengpiel, F., and Hübener, M. (1999). Visual attention: spotlight on the primary visual cortex. Current Biology *9*, R318–R321.

Serences, J. T., and Boynton, G. M. (2007). Feature-based attentional modulations in the absence of direct visual stimulation. Neuron *55*, 301–312.

Serences, J. T., Schwarzbach, J., Courtney, S. M., Golay, X., and Yantis, S. (2004a). Control of object-based attention in human cortex. Cerebral Cortex *14*, 1346–1357.

Serences, J. T., Yantis, S., Culberson, A., and Awh, E. (2004b). Preparatory Activity in Visual Cortex Indexes Distractor Suppression During Covert Spatial Orienting. Brain *92*, 3538 –3545.

Sereno, M. I., Dale, A. M., Reppas, J. B., Kwong, K. K., Belliveau, J. W., Brady, T. J., Rosen, B. R., and Tootell, R. B. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. Science New York NY *268*, 889–893.

Shams, L., and Kim, R. (2010). Crossmodal influences on visual perception. Physics of life reviews *7*, 269–284.

Shepherd, M., and Müller, H. J. (1989). Movement versus focusing of visual attention. Perception psychophysics *46*, 146–154.

Shibata, K., Yamagishi, N., Goda, N., Yoshioka, T., Yamashita, O., Sato, M.-aki, and Kawato, M. (2008). The effects of feature attention on prestimulus cortical activity in the human visual system. Cerebral Cortex *18*, 1664–1675.

Shomstein, S., and Behrmann, M. (2006). Cortical systems mediating visual attention to both objects and spatial locations. Proceedings of the National Academy of Sciences of the United States of America *103*, 11387–11392.

Shomstein, S., and Yantis, S. (2004). Control of attention shifts between vision and audition in human cortex. Journal of Neuroscience *24*, 10702–10706.

Shulman, G. L., d' Avossa, G., Tansy, A. P., and Corbetta, M. (2002). Two attentional processes in the parietal lobe. Cerebral Cortex *12*, 1124–1131.

Shulman, G. L., Ollinger, J. M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Petersen, S. E., and Corbetta, M. (1999). Areas involved in encoding and applying directional expectations to moving objects. Journal of Neuroscience *19*, 9480–9496.

Siebner, H., Hartwigsen, G., Kassuba, T., and Rothwell, J. (2009a). How does transcranial magnetic stimulation modify neuronal activity in the brain? Implications for studies of cognition. Cortex *45*, 1035–1042.

Siebner, H. R., Bergmann, T. O., Bestmann, S., Massimini, M., Johansen-Berg, H., Mochizuki, H., Bohning, D. E., Boorman, E. D., Groppa, S., Miniussi, C., et al. (2009b). Consensus paper: Combining transcranial stimulation with neuroimaging. Brain stimulation *2*, 58–80.

Siebner, H. R., Peller, M., Willoch, F., Auer, C., Bartenstein, P., Drzezga, A., Schwaiger, M., and Conrad, B. (1999). Imaging functional activation of the auditory cortex during focal repetitive transcranial magnetic stimulation of the primary motor cortex in normal subjects. Neuroscience letters *270*, 37–40.

Siebner, H. R., and Rothwell, J. (2003). Transcranial magnetic stimulation: new insights into representational cortical plasticity. Experimental Brain Research *148*, 1–16.

Silver, M. A., Ress, D., and Heeger, D. J. (2007). Neural correlates of sustained spatial attention in human early visual cortex. Journal of Neurophysiology *97*, 229–237.

Slagter, H. A., Giesbrecht, B., Kok, A., Weissman, D. H., Kenemans, J. L., Woldorff, M. G., and Mangun, G. R. (2007). fMRI evidence for both generalized and specialized components of attentional control. Brain Research *1177*, 90–102.

Slotnick, S. D., Schwarzbach, J., and Yantis, S. (2003). Attentional inhibition of visual processing in human striate and extrastriate cortex. NeuroImage *19*, 1602–1611.

Smith, A. T., Singh, K. D., and Greenlee, M. W. (2000). Attentional suppression of activity in the human visual cortex.

Smith, D. T., and Schenk, T. (2012). The Premotor theory of attention: Time to move on? Neuropsychologia *50*, 1104–1114.

Smith, D. V., Davis, B., Niu, K., Healy, E. W., Bonilha, L., Fridriksson, J., Morgan, P. S., and Rorden, C. (2010). Spatial attention evokes similar activation patterns for visual and auditory stimuli. Journal of Cognitive Neuroscience *22*, 347–361.

Somers, D. C., Dale, A. M., Seiffert, A. E., and Tootell, R. B. H. (1999). Functional MRI reveals spatially specific attentional modulation in human primary visual cortex. Proceedings of the National Academy of Sciences of the United States of America *96*, 1663–1668.

Soon, C. S., Brass, M., Heinze, H.-J., and Haynes, J.-D. (2008). Unconscious determinants of free decisions in the human brain. Nature Neuroscience *11*, 543–545.

Spence, C. (2010). Crossmodal spatial attention. Annals Of The New York Academy Of Sciences *1191*, 182–200.

Spence, C., and Driver, J. (1996). Audiovisual links in endogenous covert spatial attention. Journal of experimental psychology Human perception and performance *22*, 1005–1030.

Spence, C., and Driver, J. (1997a). Audiovisual links in exogenous covert spatial orienting. Perception psychophysics *59*, 1–22.

Spence, C., and Driver, J. (1998). Auditory and audiovisual inhibition of return. Perception And Psychophysics *60*, 125–139.

Spence, C., and Driver, J. (1997b). On measuring selective attention to an expected sensory modality. Perception psychophysics *59*, 389–403.

Spence, C. J., and Driver, J. (1994). Covert spatial orienting in audition: Exogenous and endogenous mechanisms. Journal of Experimental Psychology Human Perception and Performance *20*, 555–574.

Spence, C., and McDonald, J. (2004). The cross-modal consequences of the exogenous spatial orienting of attention. In Handbook of Multisensory Processes, G. Calvert, C. Spence, and B. Stein, eds. (USA: MIT Press), pp. 3–25.

Spence, C., Nicholls, M. E., and Driver, J. (2001). The cost of expecting events in the wrong sensory modality. Perception psychophysics *63*, 330–336.

Spence, C., Nicholls, M. E., Gillespie, N., and Driver, J. (1998). Cross-modal links in exogenous covert spatial orienting between touch, audition, and vision. Perception psychophysics *60*, 544–557.

Spence, C., Pavani, F., and Driver, J. (2000). Crossmodal links between vision and touch in covert endogenous spatial attention. Journal of Experimental Psychology: Human Perception and Performance *26*, 1298–1319.

Spence, C., Pavani, F., Maravita, A., and Holmes, N. (2004). Multisensory contributions to the 3-D representation of visuotactile peripersonal space in humans: evidence from the crossmodal congruency task. Journal Of Physiology Paris *98*, 171–189.

Spiridon, M., and Kanwisher, N. (2002). How distributed is visual category information in human occipito-temporal cortex? An fMRI study. Neuron *35*, 1157–1165.

Stein, B. E., and Stanford, T. R. (2008). Multisensory integration: current issues from the perspective of the single neuron. Nature reviews Neuroscience *9*, 255–266.

Stewart, L., and Walsh, V. (2006). Transcranial Magnetic Stimulation in Cognitive Neuroscience. In Nature Reviews Neuroscience (MIT press), pp. 73–79.

Stilla, R., and Sathian, K. (2008). Selective visuo-haptic processing of shape and texture. Human Brain Mapping *29*, 1123–1138.

Stokes, M., Thompson, R., Cusack, R., and Duncan, J. (2009a). Top-down activation of shape-specific population codes in visual cortex during mental imagery. Journal of Neuroscience *29*, 1565–1572.

Stokes, M., Thompson, R., Nobre, A. C., and Duncan, J. (2009b). Shape-specific preparatory activity mediates attention to targets in human visual cortex. Proceedings of the National Academy of Sciences of the United States of America *106*, 19569–19574.

Stoppel, C. M., Boehler, C. N., Sabelhaus, C., Heinze, H.-J., Hopf, J. M., and Schoenfeld, M. A. (2007). Neural mechanisms of spatial- and feature-based attention: a quantitative analysis. Brain Research *1181*, 51–60.

Sturm, W., and Willmes, K. (2001). On the functional neuroanatomy of intrinsic and phasic alertness. NeuroImage *14*, S76–S84.

Su, L., Fonteneau, E., Marslen-Wilson, W., and Kriegeskorte, N. (2012). Spatiotemporal Searchlight Representational Similarity Analysis in EMEG Source Space. In 2012 Second International Workshop on Pattern Recognition in NeuroImaging (IEEE), pp. 97–100.

Sui, J., Adali, T., Yu, Q., Chen, J., and Calhoun, V. D. (2011). A Review of Multivariate Methods for Multimodal Fusion of Brain Imaging Data. Journal of Neuroscience Methods *204*, 68–81.

Summers, I. R., Francis, S. T., Bowtell, R. W., McGlone, F. P., and Clemence, M. (2009). A functional-magnetic-resonance-imaging investigation of cortical activation from moving vibrotactile stimuli on the fingertip. Journal of the Acoustical Society of America *125*, 1033–1039.

Sunaert, S., Van Hecke, P., Marchal, G., and Orban, G. A. (2000). Attention to speed of motion, speed discrimination, and task difficulty: an fMRI study. NeuroImage *11*, 612–623.

Swisher, J. D., Gatenby, J. C., Gore, J. C., Wolfe, B. A., Moon, C.-H., Kim, S.-G., and Tong, F. (2010). Multiscale pattern analysis of orientation-selective activity in the primary visual cortex. Journal of Neuroscience *30*, 325–330.

Szczepanski, S. M., Konen, C. S., and Kastner, S. (2010). Mechanisms of spatial attention control in frontal and parietal cortex. Journal of Neuroscience *30*, 148–160.

Sàenz, M., Buraĉas, G. T., and Boynton, G. M. (2003). Global feature-based attention for motion and color. Vision Research *43*, 629–637.

Talsma, D., Senkowski, D., Soto-Faraco, S., and Woldorff, M. G. (2010). The multifaceted interplay between attention and multisensory integration. Trends in cognitive sciences *14*, 400–410.

Talsma, D., and Woldorff, M. G. (2005). Selective attention and multisensory integration: multiple phases of effects on the evoked brain activity. Journal of cognitive neuroscience *17*, 1098–1114.

Telesford, Q. K., Simpson, S. L., Burdette, J. H., Hayasaka, S., and Laurienti, P. J. (2011). The brain as a complex system: using network science as a tool for understanding the brain. Brain connectivity *1*, 295–308.

Thiel, C. M., Zilles, K., and Fink, G. R. (2004). Cerebral correlates of alerting, orienting and reorienting of visuospatial attention: an event-related fMRI study. (Elsevier).

Ting Siok, W., Kay, P., Wang, W. S. Y., Chan, A. H. D., Chen, L., Luke, K.-K., and Hai Tan, L. (2009). Language regions of brain are operative in color perception. Proceedings of the National Academy of Sciences of the United States of America *106*, 8140–8145.

Tong, F., and Pratte, M. S. (2012). Decoding patterns of human brain activity. Annual Review of Psychology *63*, 483–509.

Tootell, R. B., Hadjikhani, N., Hall, E. K., Marrett, S., Vanduffel, W., Vaughan, J. T., and Dale, A. M. (1998). The retinotopy of visual spatial attention. Neuron *21*, 1409–1422.

Trenner, M. U., Heekeren, H. R., Bauer, M., Rössner, K., Wenzel, R., Villringer, A., and Fahle, M. (2008). What Happens in Between? Human Oscillatory Brain Activity Related to Crossmodal Spatial Cueing. PloS one *3*, 10.

Treue, S., and Martínez Trujillo, J. C. (1999). Feature-based attention influences motion processing gain in macaque visual cortex. Nature *399*, 575–579.

Turatto, M., Benso, F., Galfano, G., and Umiltà, C. (2002). Nonspatial attentional shifts between audition and vision. Journal of Experimental Psychology Human Perception and Performance *28*, 628–639.

Turatto, M., Galfano, G., Bridgeman, B., and Umiltà, C. (2004). Space-independent modality-driven attentional capture in auditory, tactile and visual systems. Experimental Brain Research *155*, 301–310.

Varela, F., Lachaux, J. P., Rodriguez, E., and Martinerie, J. (2001). The brainweb: phase synchronization and large-scale integration. Nature Reviews Neuroscience *2*, 229–239.

Vidyasagar, T. R. (1998). Gating of neuronal responses in macaque primary visual cortex by an attentional spotlight. NeuroReport *9*, 1947–1952.

Violentyev, A., Shimojo, S., and Shams, L. (2005). Touch-induced visual illusion. NeuroReport *16*, 1107–1110.

Vul, E., Harris, C., Winkielman, P., and Pashler, H. (2009). Puzzlingly High Correlations in fMRI Studies of Emotion, Personality, and Social Cognition. Perspectives on Psychological Science *4*, 274–290.

Vul, E., and Kanwisher, N. (2010). Begging the Question: The Non-Independence Error in fMRI Data Analysis. In Foundations and Philosophy for Neuroimaging, S. Hanson and M. Bunzl, eds. (MIT Press), pp. 71–91.

Wacker, E. (2011). Tactile feature processing and attentional modulation in the human somatosensory system.

Wacker, E., Spitzer, B., Lützkendorf, R., Bernarding, J., and Blankenburg, F. (2011). Tactile motion and pattern processing assessed with high-field FMRI. PLoS ONE *6*, e24860.

Wade, A. R., Brewer, A. A., Rieger, J. W., and Wandell, B. A. (2002). Functional measurements of human ventral occipital cortex: retinotopy and colour. Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences *357*, 963–973.

Wagner, A. D., and Rissman, J. (2010). Distributed representations in memory: insights from functional brain imaging. Annual Review of Psychology *63*, 110301102248092.

Weiskopf, N., Josephs, O., Ruff, C. C., Blankenburg, F., Featherstone, E., Thomas, A., Bestmann, S., Driver, J., and Deichmann, R. (2009). Image Artifacts in Concurrent Transcranial Magnetic Stimulation (TMS) and fMRI Caused by Leakage Currents: Modeling and Compensation. Journal of Magnetic Resonance Imaging *29*, 1211–1217.

Williams, M. A., Dang, S., and Kanwisher, N. G. (2007). Only some spatial patterns of fMRI response are read out in task performance. Nature Neuroscience *10*, 685–686.

Wojciulik, E., and Kanwisher, N. G. (1999). The generality of parietal involvement in visual attention. Neuron *23*, 747–764.

Wolfe, J. M. (2010). Visual search. Current Biology *20*, R346–R349.

Wolfe, J. M., and Horowitz, T. S. (2004). What attributes guide the deployment of visual attention and how do they do it? Nature Reviews Neuroscience *5*, 495–501.

Woolgar, A., Hampshire, A., Thompson, R., and Duncan, J. (2011a). Adaptive Coding of Task-Relevant Information in Human Frontoparietal Cortex. Journal of Neuroscience *31*, 14592–14599.

Woolgar, A., Thompson, R., Bor, D., and Duncan, J. (2011b). Multi-voxel coding of stimuli, rules, and responses in human frontoparietal cortex. NeuroImage *56*, 744–752.

Wright, R. D., and Ward, L. M. (2008). Orienting of Attention (New York: Oxford University Press).

Wu, C.-T., Weissman, D. H., Roberts, K. C., and Woldorff, M. G. (2007). The neural circuitry underlying the executive control of auditory spatial attention. Brain Research *1134*, 187–198.

Yeshurun, Y., and Carrasco, M. (1998). Attention improves or impairs visual performance by enhancing spatial resolution. Nature *396*, 72–75.

Zhang, W., and Luck, S. J. (2009). Feature-based attention modulates feedforward visual processing. Nature Neuroscience *12*, 24–25.