Modulation of sensory processing during simultaneous bimodal stimulation: Effects of sensorimotor integration

By

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AUTHOR’S DECLARATION FOR ELECTRONIC SUBMISSION OF A THESIS

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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ABSTRACT

Illusions such as the McGurk (McGurk and MacDonald, 1976) and ventriloquist (Radeau and Bertelson, 1974) effects or visual capture sensorimotor deficits (Holmes et al., 2004) demonstrate that our perception of and interaction with our environment is shaped by our ability to extract and integrate relevant sensory inputs across multiple modalities. Physiologically extraction occurs through a mechanism that facilitates relevant sensory representations and/or suppresses irrelevant ones within secondary sensory cortices, areas traditionally viewed as “modality-specific” cortex. This mechanism is commonly called “attention”. The purpose of the current thesis is to investigate the influence of motor requirements upon attentional modulation of sensory processing. It was hypothesized that different task demands associated with sensory processing for continuous movement rather than perception would result in earlier loci and/or different mechanisms of attentional modulation. Two studies used functional magnetic resonance imaging (fMRI) to investigate intermodal influences between a vibrotactile and visuospatial stimulus during a continuous sensorimotor task. These studies revealed that attention to vibrotactile stimulation guiding a continuous movement resulted in decreased activation in primary somatosensory cortex (S1) relative to when the same stimulus was an irrelevant distracter. This was regardless of the spatial or temporal properties of the two modalities. In a third study, somatosensory evoked potentials (SEPs) demonstrated that somatosensory processing is influenced as early as arrival to S1 from thalamic-cortical projections, however, SEPs did not demonstrate decreased activation during vibrotactile tracking. A fourth study using transcranial magnetic stimulation (TMS) confirmed differential excitability of S1 dependent upon whether the same sensory stimulus was used for perception or to guide a continuous sensorimotor transformation. Finally, a fifth study using behavioral measures demonstrated that the intramodal signal to noise ratio is an important factor in determining intermodal influence. This thesis provides insight into the influence of motor requirements upon sensory processing and demonstrates its importance in understanding how information is extracted from our environment. Understanding this has important implications for the interpretation/development of future work investigating intermodal influences upon sensory-processing.

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ABBREVIATIONS

ANOVA = Analysis of Variance
BA = Brodmann Area
BOLD = Blood Oxygen Level Dependent
CS = TMS Conditioning Stimulus
DLPFC – Dorsolateral Pre-frontal Cortex
ERP = Event-Related Potential
fMRI = Functional Magnetic Resonance Imaging
LED = Light-Emitting Diode
M1 = Primary Motor Cortex
MEG = Magnetoencephalography
MT = Middle Temporal Area
MST – Medial Superior Temporal Cortex
PET = Positron Emission Technology
PPC = Posterior Parietal Cortex
rCBF = Regional Cerebral Blood Flow
RMSE = Root Mean Square Error
RMT = Resting Motor Threshold
S1 = Primary Somatosensory Cortex
SEP = Somatosensory Evoked Potential
TS = TMS Test Stimulus
TMS = Transcranial Magnetic Stimulation
TPJ = Temporal Parietal Junction (or Temporo-parietal Junction)
V1 = Primary Visual Cortex
VEP = Visual Evoked Potential

ADDITIONAL MANUSCRIPTS

The following is a list of published and submitted manuscripts done during the course of my PhD degree at the University of Waterloo that are not part of my thesis.

Legon, W., Meehan, S. K., & Staines, W. R. (2008). The relationship between frontal somatosensory-evoked potentials and motor planning. *Neuroreport*, *19*(1), 87-91.

Fowler, B., Meehan, S., & Singhal, A. (submitted). Perceptual-Motor Performance and Associated Kinematics in Space. *Experimental Brain Research*

CHAPTER 1 – INTRODUCTION

1.1 Overview of thesis

This thesis begins with the statement of the overall objective. Following the statement of the overall objective literature relevant to the thesis will be reviewed in the following areas (1) sensory processing in vision and somatosensation, (2) attentional modulation within one modality, (3) attentional modulation across modalities and 4) the influence of motor interactions upon sensory processing. Finally, the last section of Chapter 1 will introduce the specific research questions that guided the path of this thesis. Subsequent chapters detail the research studies performed to address the research questions.

1.2 General objective of thesis

The overall objective of this thesis is to investigate how sensorimotor requirements interact with attention during sensory-guided movement, specifically during cases of multimodal stimulation. Although vast research has investigated intermodal links in multisensory integration, the mechanisms of intermodal selective attention have largely been investigated only using perceptual paradigms. However, perceiving an object or stimulus and performing a sensory-guided action place very different demands on processing pathways. Therefore, understanding the mechanisms involved with intermodal selective attention during sensory-guided movements is extremely important and may provide valuable insight into sensorimotor deficits in a number of patient populations.

1.3 Background Research

The use of sensory information in our environment has broadly been divided into two purposes: perception and action. Nowhere is this more evident than visual processing (Goodale & Milner, 1992; Haxby et al., 1991), although there is increasing evidence that this dissociation is also present in a number of other modalities including the somatosensory system (Caselli, 1993; De Santis, Spierer, Clarke, & Murray, 2007; Reed, Klatzky, & Halgren, 2005) and audition (Arnott, Binns, Grady, & Alain, 2004; Rauschecker & Tian, 2000). However, despite the dissociation of deficits observed with damage to the areas within each pathway optimal motor performance is a function of both perception and action. Further, our ability to interact with our environment is a function of our ability to detect and categorize individual sources of sensory information into relevant signal or noise and extract the signal at the expense of the noise for the proper transformation into a motor plan. The following reviews sensory processing in vision and touch, selection of relevant information within one modality and selection of relevant information between modalities. Finally, the influence of motor cortex and inter-hemispheric interactions upon sensory processing will be highlighted.

1.3.1 Sensory Processing and Perception

Each of our senses has evolved receptors to detect specific types of stimulus energy. Although each receptor can provide only limited information with respect to a complex stimulus the combination of information from multiple receptors, each detecting a stimulus attribute, can be used to generate an overall picture of a complex stimulus or environment. This process can be quite efficient despite the fact that information related to the same event or unrelated simultaneous events is initially detected in distinct forms and processed within modality-specific areas before being integrated at later processing sites in the cortex. In the following section sensory processing of visual and somatic information will be reviewed with an emphasis on the macro- and micro-anatomical and functional organization prior to discussing multisensory interactions between these two modalities.

1.3.1.1 Vision

Visual input first arrives at the primary visual cortex (V1) and is organized within V1 in a retinotopic manner. From V1 visual input is processed along two streams, a dorsal and a ventral stream (Goodale & Milner, 1992; Haxby et al., 1991). The ventral stream terminates in the inferior temporal cortex. In contrast the dorsal stream terminates in posterior parietal cortex. Within this gross division of visual processing there is an apparent hierarchical organization where as visual information is passed from V1 to intermediate and later hierarchical areas each stage appears to integrate smaller receptive fields from the previous stage into newer larger more abstract receptive fields, eventually representing the visual information in systems related more to perception/motor output than sensory input (Kandel, Schwartz, & Jessell, 2000).

It was first proposed that the ventral stream was the “what” pathway concerned with object identification (Ungerleider & Mishkin, 1982). This is in line with inputs from V4, an area of the cortex involved with the processing of color and form (Kandel et al., 2000). In contrast, the dorsal stream was proposed to be the “where” pathway involved with localizing objects in space (Ungerleider & Mishkin, 1982). This is in line with inputs from MT and MST that are involved with detecting stimulus motion and optic flow (Kandel et al., 2000). These “what” and “where” distinctions were supported by early neuroimaging studies using static matching and spatial localization tasks (Haxby et al., 1991), during color or motion viewing (Zeki et al., 1991) and even during attention to various stimulus attributes (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991). Evidence suggests that these two pathways can be better characterized by their respective outputs with the ventral stream mediating visual perception (“what”) and the dorsal stream mediating visually guided action (“how” to interact with the stimulus) (Goodale & Milner, 1992). These new designations have been supported by comparison of patients exhibiting visual agnosia and optic ataxia. Patient DF, who has visual agnosia, a deficit associated with improper processing in the ventral stream, demonstrated an intact ability to adjust grip aperture despite an inability to indicate the size of visually inspected objects with the same fingers (Goodale, Milner, Jakobson, & Carey, 1991). In contrast, Patient RV who initially presented with optic ataxia associated with damage to the parietal cortex could accurately compare shapes of objects but was not able to use this information during precision gripping (Goodale et al., 1994).

One of the most interesting aspects of the visual system is that the dual visual pathways may actually be present prior to those observed in the cortex (Livingstone & Hubel, 1988). The segregation is largely based upon anatomical evidence but is also supported by functional observations as well. In the visual system the photoreceptors in the retina project to retinal ganglion cells via various interneurons that determine the type of information reflected by each ganglion cell. The most prominent ganglion cells in primates are parasol and midget cells (Kandel et al., 2000). These ganglion cells remain anatomically distinct and project to different layers in the LGN in a retinotopic organization (Kastner, Schneider, & Wunderlich, 2006). Parasol retinal ganglion cells project to the magnocellular layers of the LGN while midget cells project to the parvocellular layer. These layers of the thalamus then project to separate layers of the primary visual cortex (V1) in a retinotopic organization. Functionally, the anatomical dichotomy is replicated as parasol cells have larger receptive fields, they respond optimally to large objects and can detect rapid changes in a visual stimulus (Maunsell, 1992). In contrast, midget cells are more numerous but have smaller receptive fields that favor specific wavelengths that contribute to form and color detection (Maunsell, 1992).

In addition to pre-cortical functional and anatomical evidence it has also been suggested that the magnocellular pathway is the primary driving input for the superior parietal lobule (SPL) of the dorsal pathway (Maunsell, 1992). However, evidence that the ventral pathway is exclusively linked to the parvocellular pathway is less concrete. The sensitivity of parvocellular cells to color and similar properties but not to motion suggests projections to the ventral pathway. This has been shown as the LGN parvocellular pathway projections terminate in the layers of V1 and V2 that ultimately project to area V4. However, there is also evidence of magnocellular inputs to ventral processing. Lesions to the parvocellular layers of the LGN fail to produce object related deficits for properties such as shape discrimination and stereopsis (Maunsell, 1992). The magnocellular inputs may reflect the need for the spatial arrangement of object attributes.

1.3.1.2 Somatosensation

Somatosensory input first arrives at the primary somatosensory cortex. Unlike V1 there are four distinct cytoarchitectural areas (Brodmann Areas 3a, 3b, 1 and 2) of the primary somatosensory cortex (S1). This difference is likely associated with the multitude of modalities within somatosensation with information detected by not one, but many different types of sensory receptors. In the context of this thesis, in which vibrotactile stimulation will be used, the receptors of interest are the mechanoreceptors.

The majority of afferent thalamic connections terminate in areas 3a and 3b that in turn somatotopically project to areas 1 and 2. It is the projections from posterior ventrolateral (VPL) thalamic relay nucleus to area 3b and the cortico-cortical connections between areas 3b and 1 that transmit and process vibrotactile (as well as other mechanoreceptive) information in the cortex. Within areas 3b and 1 there are modality maps with spatially distinct domains for the various types of stimulation detected by the different mechanoreceptors (Friedman, Chen, & Roe, 2004). However, the distinction between processing reflected in areas 3a/2 and 3b/1 is not exclusive as there is evidence for large interconnections between all of these areas that may be involved with integrating somatic information at a very early level. In addition, both areas 1 and 2 do also receive direct thalamic inputs that may supplement early integration (Rowe, Turman, Murray, & Zhang, 1996).

From SI there are a number of additional areas involved in somatosensory processing. A review of attention to touch (Johansen-Berg & Lloyd, 2000) listed five additional cortical areas that primarily reflect somatosensory processing including, the secondary somatosensory cortex (SII), the granular insula, retroinsular cortex and areas 5 and 7b of the posterior parietal cortex. As in the visual system, the progression of somatosensory input is associated with a hierarchical structure in which somatosensory inputs arriving at the cortex representing small receptive fields are integrated at each step and transformed into more and more abstract representations (Kandel et al., 2000)

Recent research has also suggested that, like visual processing, somatosensory processing within each of these cortical areas can be grouped into two broad categories "what" and "where" (Reed et al., 2005). Evidence from lesion studies (Caselli, 1993; Reed, Caselli, & Farah, 1996) as well as direct comparisons between tactile object recognition and tactile object localization studies (Reed, Shoham, & Halgren, 2004; Reed et al., 2005) suggest a ventrolateral pathway, involving SII, inferior parietal, parietal insula and pre-motor areas, for object recognition and a dorsomedial pathway involving the superior parietal areas 5 and 7, precuneus (BA 19) and premotor areas, for object localization.   In addition, research has also demonstrated a dissociation of a "how" from "where" pathway (Rossetti, Rode, & Boisson, 1995) in patients with lesions to the dorsomedial network. These designations are homologous to the "what" and "where" (Haxby et al., 1991) and "what" and "how" (Goodale & Milner, 1992) pathways described earlier in the visual system. In addition there appears to be a similar amount of anatomical overlap in the later areas of these pathways despite the absence of primary visual cortical activation during somatosensory activation and vice versa during visual conditions suggesting potential loci for integration (Reed et al., 2005). This notion is further supported by studies suggesting the presence of multisensory neurons in the posterior parietal cortex (Andersen, Snyder, Bradley, & Xing, 1997).

In addition there is also evidence for pre-cortical somatotopy in the somatosensory pathways not only based upon body-coordinates but receptor-based as well. Not only are mechanoreceptors a subset of the somatic receptors but there are also four different mechanoreceptors; 1) Meissner's corpuscles, 2) Merkel's discs, 3) Pacinian corpuscles and 4) Ruffini corpuscles. Each mechanoreceptor conveys different information about the touch stimulus that depends upon its location, firing properties and receptive field (Kandel et al., 2000).

1.3.2 Signal Detection and Attention Within One Modality

Within any environment one key aspect to sensory processing is our capability to distinguish between different sources of sensory information as well as any changes within these sources of sensory information. In order to achieve this the difference in the amplitude between that which is relevant (signal) and that which is irrelevant (noise) must be sufficient in order to detect the relevant stimulus. Whether this difference is between two sources within one modality or two sources from different modalities it appears that we have the ability to alter the signal to noise ratio of various sensory events that we are processing, a mechanism commonly referred to as "attention". The use of attention is important upon two fronts 1) our representation of our environment is dominated by the most salient (highest signal to noise ratio) representation (Ernst & Banks, 2002) and 2) the influence of the irrelevant sensory representation is strongest when the relevant stimulus is at its weakest (Hecht, Reiner, & Karni, 2008). In the following section a brief review of attention will be followed by its application to cases of intramodal competition.

1.3.2.1 Attention

Attention was first comprehensively defined in the late 1800's (James, 1890) and today is most commonly regarded as a cognitive construct for dealing with the limited processing capacity of the brain (Pashler, 1998). Early behavioral investigations of attention focused upon perceptual overload tasks (Kahneman, 1973). These tasks were largely driven by the increasing complexity of work environments and demonstrated the fundamental problem: as processing demands increased task performance decreased. It was accepted that attention must be the mechanism by which the most relevant aspects of a task were selected at the expense of less relevant aspects due to limitations imposed by processing ability. Over the years the mechanism of attention has taken many forms. The earliest debates of attention centered upon the loci at which a filter served to select relevant information (Broadbent, 1958; Deutsch & Deutsch, 1963; Moray, 1959; Treisman, 1960; Welford, 1952). It was not until the 1960's that the principles of facilitation and suppression were included in the debate (Treisman, 1960). This resulted in a shift of thought from attention being a filter that blocked irrelevant information to a mechanism by which the irrelevant information was suppressed (Treisman, 1960). In the subsequent years the fundamental issue: that we cannot process all incoming sensory information shifted the conceptualization of attention to a sensory processing mechanism (Kahneman, 1973; Wickens, 1992).

Through the early nineties advances in various imaging techniques led to the evolution of attention research from primarily behavioral to physiologically based responses associated with information processing. Although neuropsychological and neurophysiological research still aims to determine the locus of attention the focus has been on changing signaling properties of populations of neurons (Hillyard, Vogel, & Luck, 1998) associated with task performance.

It has been demonstrated since the early nineties that attention to a stimulus feature results in an increase in neural activity compared to when that stimulus is irrelevant and not being attended (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1990). These changes in neural activity were suggested to reflect an enhancement of relevant sensory information whereby the relevant information receives a competitive advantage through a higher signal to noise ratio (Hillyard et al., 1998). In addition, it has been proposed that selective attention induced changes in blood flow can also manifest as a tonic shift in baseline neural activity (Hillyard et al., 1998). Tonic shifts in baseline activity have been linked to cases where incoming sensory cues are compared to a "template" of the attended stimulus, such as in the attentional trace theory of auditory attention (Naatanen, 1990).

In addition to amplification of the relevant sensory information, evidence from studies of visual selective attention suggest that attention works by a mechanism that weights stimulus representations not only through facilitation of the relevant sensory inputs but also through a concomitant suppression of the irrelevant sensory inputs (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005b), thereby not only increasing the signal to noise ratio of the relevant stimulus but decreasing that of the irrelevant stimulus at the same time. This stimulus weighting system has been suggested to involve cortical structures, such as sensory cortex and dorsolateral prefrontal cortex (DLPFC), as well as sub-cortical structures, such as the thalamic relay nuclei and the thalamic reticular nucleus (Guillery, 2005; Sherman & Guillery, 2002).

The focus of attention as changes in neural activity within the sensory processing pathways appears to circumvent the early debate about the locus (or loci) of attention in the early behavioral cognitive theories of attention by providing physiological evidence that attention can work at multiple levels. Further the neuroanatomical structure of information processing pathways both cortically and sub-cortically support the notion that attention can work at multiple levels with its locus perhaps dependent upon both stimulus properties and task demands.

1.3.2.3 Attention Within One Modality

As mentioned earlier, the introduction of imaging techniques has shifted the focus from investigating attention through behavioral deficits to searching for loci of altered activation. This search has largely been driven by the notion that stimulus inputs are first represented most precisely in small receptive fields that feed into larger receptive fields with more abstract representations that then feedback to the smaller precise inputs to modify their contribution. The conceptualization of feedforward/feedback convergence has largely shaped the view that attention serves to extract relevant information for further processing while limiting the relay of irrelevant sensory information.

There are generally two aspects to attentional research: 1) determining what areas are responsible for the control and selection of relevant information and 2) the site at which the feedback control is exerted. The former is concerned with determining the attentional networks at work during a task while the latter is more concerned with the extraction of relevant information associated with the given task.

Recently, Corbetta and Shulman (2002) surveyed evidence from functional imaging studies of stimulus detection and proposed an extension of earlier attentional network models (Mesulam, 1990; Posner & Petersen, 1990). Corbetta and Shulman

(2002) proposed the presence of two complementary attentional networks. The first a dorsal frontal-parietal network for goal-directed (or voluntary) stimulus-response selection (i.e. orientation) involving the posterior parietal cortex (PPC) and the frontal eye fields of the superior frontal cortex. The purpose of this network was to prepare and apply top-down selection of task-relevant stimuli and the appropriate responses. The second, a ventral frontal-parietal network for the detection of behaviorally relevant stimuli involving the temporal-parietal and inferior frontal cortex. The purpose of which was to re-orient the dorsal system to a salient potentially relevant stimulus. These attentional networks have been shown to reflect not only spatial attention but attention to objects or even object features. In the case of the former it has been shown that top-down orienting signals from the PPC can effect sustained changes in extrastriate cortex facilitating contralateral while inhibiting ipsilateral extrastriate cortex after an attention shift (Yantis et al., 2002). These results suggest that the mechanism by which attention works is to release competitive inhibition between the relevant stimulus and surrounding competitors by increasing the signal to noise ratio for one representation giving it increased salience (a competitive advantage) facilitating selection of the relevant stimulus. However, it is not only extrastriate cortex that demonstrates attentional modulation and it has recently been suggested that visual attention should be viewed as a multilevel selection process working at the level of the thalamus, early cortical and later cortical processing sites (Guillery et al., 1998; Kastner and Pinsk 2004; Kastner et al., 2006).

Within the somatosensory modality it appears as though feedback attentional modulation in early sensory areas is mediated by a prefrontal-cortical sensory system (Schaefer, Heinze, & Rotte, 2005; Staines, Graham, Black, & McIlroy, 2002). Concurrent facilitation of S1 and DLPFC suggest that it plays an important modulation role in the extraction of task-relevant information (Staines et al., 2002). This is consistent with other results demonstrating the notion that the DLPFC is involved with the extraction of task-relevant information via top-down modulation of S1 and the inhibition of task-irrelevant tactile information (Knight, Staines, Swick, & Chao, 1999; Schaefer et al., 2005; Woods & Knight, 1986; Yamaguchi & Knight, 1990). Evidence from fMRI, EEG and single cell recordings suggest, at least within one modality, these effects are associated with changes at the level of S1 (Burton & Sinclair, 2000; Legon & Staines, 2006; Schaefer et al., 2005; Staines et al., 2002). Further, research investigating the firing properties of thalamic relay neurons and their anatomical connections to the thalamic reticular nucleus suggests a role in modulating the transmission of peripheral sensory information to S1 (Guillery, Feig, & Lozsadi, 1998; Guillery, 2005; Sherman & Guillery, 2002). The thalamic reticular nucleus is ideally positioned to influence the relay of sensory information from the thalamus to cortex, located between the thalamus and internal capsule (Guillery et al., 1998; Guillery & Harting, 2003). It receives excitatory connections from thalamic-cortical and the reverse cortico-thalamic projections and influences relay nuclei activity through GABAergic feedback projections, as well as to other relay nuclei via collateral projections to adjacent reticular neurons (Guillery et al., 1998; Guillery, 2005; Pinault, 2004). These collateral connections between thalamic reticular nuclei also have the potential to limit spatial transmission.

The role of the thalamus in restricting the relay of irrelevant information to the cortex was demonstrated in thalamic lesion stroke patients (Staines, Black, Graham, & McIlroy, 2002). Patients with lesions in the thalamus demonstrated decreased perceptual thresholds to contralateral stimuli when presented with a concurrent ipsilateral distracter. Changes in perceptual thresholds were only associated with bilateral stimulation and approached unilateral thresholds with thalamic recovery.

Whether the attentional mechanisms and their loci of influence discussed above are similar for competing stimuli from different sensory modalities has been a recent area of interest.

1.3.3 Sensory Processing and Attention Between Modalities

Research suggests that information relating to the same sensory event is integrated in the parietal cortex. Although, there is debate over whether the posterior parietal cortex reflects motor intention (Snyder, Batista, & Andersen, 1997) or attention (Gottlieb, Kusunoki, & Goldberg, 1998) the presence of neurons that reflect both motor effector and stimulus properties suggests that it may bridge the sensorimotor gap. In addition, the presence of multisensory neurons representing stimuli in common reference frames further supports the role of the PPC in sensorimotor integration (Andersen et al., 1997). The integration of various sensory inputs at the level of the PPC has been shown to rely on spatial and temporal relationships between the representations of the stimulus within each modality. However, in any given environment task-relevant information from one or multiple modalities needs to be extracted from task-irrelevant information. Failure to efficiently extract relevant information can result in detriments to behavior. Therefore important questions are at what level is this information extracted and what areas modulate this extraction?

Evidence from multisensory integration studies demonstrates convergent routes and reciprocal connections between modality-specific cortices and heteromodal areas such as the ventral intraparietal sulcus (VIP), superior temporal gyrus (STG) and ventral premotor areas (PMv) (Macaluso, 2006). Based upon the assumption that intermodal extraction is a form of multisensory integration it is likely that similar areas are involved with the extraction of relevant sensory cues.

A number of studies have demonstrated intermodal influences at various loci in the brain using EEG (Eimer & Driver, 2001; Eimer & Van Velzen, 2002; Hotting, Rosler, & Roder, 2003; Macaluso & Driver, 2001; Ohara, Lenz, & Zhou, 2006; Taylor-Clarke, Kennett, & Haggard, 2002), fMRI (Balslev, Nielsen, Paulson, & Law, 2005; Macaluso, Eimer, Frith, & Driver, 2003; 2005; Petkov et al., 2004; Tanabe, Kato, Miyauchi, Hayashi, & Yanagida, 2005), MEG (Kida, Inui, Wasaka, Akatsuka, Tanaka, & Kakigi, 2007a) and PET (Macaluso, Frith, & Driver, 2002a). These studies have demonstrated that the amount of processing in early sensory areas is linked to the relevance of the stimulus to the task (Johnson & Zatorre, 2005; 2006; Macaluso, Frith, & Driver, 2002b; Petkov et al., 2004; Shomstein & Yantis, 2004), the spatial relationship between the target modality and the distracter modality (Eimer & van Velzen, 2005; Macaluso, Frith, & Driver, 2002b; Macaluso et al., 2003; 2005) and the temporal relationship between the two (Lange & Roder, 2006; Shore, Barnes, & Spence, 2006).

In addition to perceptual studies, recent investigations of neural correlates of intermodal selective attention have demonstrated increased activation in the task-relevant modality-specific cortices and a concomitant decrease in task-irrelevant sensory cortices during both sustained (Johnson & Zatorre, 2005; 2006) and transient (Shomstein & Yantis, 2004) intermodal selective attention tasks. ERP and MEG studies have further shown that these modulations are generally associated with amplitude changes in components generated in modality-specific areas beyond primary sensory cortex (Eimer & Driver, 2000; Kida et al., 2004; Kida, Inui, Wasaka, Akatsuka, Tanaka, & Kakigi, 2007a; Ohara et al., 2006; Taylor-Clarke et al., 2002). In addition, effects in modality-specific cortices are not always associated with task-relevance despite the recruitment of a network of areas associated with attentional modulation (Downar, Crawley, Mikulis, & Davis, 2001).

There are a number of possible explanations for the lack of modulation of primary sensory cortex and the discrepancy in modality-specific modulation. Two major sources are 1) the neurophysiological techniques and 2) the experimental paradigms employed. In the case of the former, fMRI does provide excellent spatial resolution however, it has been demonstrated that a voxel-based approach to investigating attentional modulation of S1 is insensitive (Johansen-Berg, Christensen, Woolrich, & Matthews, 2000). Instead ROI analyses are preferred but rarely employed in studies of intermodal modulation. In addition to fMRI, the use of ERPs also may miss early modulation of sensory processing as the earliest potentials that are generally elicited are at 50 ms, approximately 30 ms after the first arrival of somatosensory information to primary somatosensory cortex.

In the case of the latter, the experimental paradigms often require simple detection of a discrete stimulus with an associated button press or verbal/counting response. These studies, while easier to control for various aspects often have two faults 1) the tasks are not overly demanding and 2) the stimuli are often not presented simultaneously, instead they are presented in rapid oddball sequences in which one modality is defined as a target. In these cases intermodal effects upon sensory processing are inferred by investigating neurophysiological responses to a modality when it is presented at a spatial location at which the target in the other modality is expected.

As attention has been suggested to be a multilevel selection process it is possible that attentional effects observed in these studies may only be part of the attentional modulations that have occurred. Also using techniques that can probe the earliest cortical processing and tasks that impose greater demands upon the sensory processing system may reveal earlier modulatory effects.

One potential locus of early cortical modulation of sensory processing is sensory gating associated with interactions between the thalamus and thalamic reticular nuclei. It has been shown that collateral projections in the thalamic reticular nucleus, mediated by both thalamic-cortical and cortical-thalamic projections, can alter the firing rates of both first-order (peripheral-central) and second order (cortico-cortical) relay nuclei of other modalities (Crabtree & Isaac, 2002). These collaterals may serve as low-level sensory connections and/or part of a prefrontal cortical system that weights information transmitted to primary sensory cortex.

The absence of early cortical observations may result from the task demands imposed by previous studies, with perceptual detection and sensorimotor transformations resulting in different firing properties in the relay nuclei.

1.3.4 Influence of Motor Cortex on Sensory Processing and Inter-hemispheric Interactions

Two additional considerations of importance to somatosensory processing during movement are the role of 1) primary motor cortex and 2) inter-hemispheric interactions between motor-somatosensory as well as somatosensory-somatosensory areas.

Primary motor cortex can exhibit strong modulatory influences upon afferent information projected to primary somatosensory cortex (Canedo, 1997). In the upper limbs it has been demonstrated that cortical potentials as early as the P27 SEP component are suppressed from approximately 100 ms prior to the start of movement and lasting until the movement ends. These effects were localized to the cortical representations supplied by the median nerve (the nerve of stimulation) (Cohen & Starr, 1987; Tapia, Cohen, & Starr, 1987). This attenuation is commonly referred to as “movement-related gating” and is generally associated with active inhibition of afferent information relayed to somatosensory cortex during movement. However, there is evidence that these effects are instead localized to any cortical representations involved in the task (Hoshiyama & Kakigi, 1999) as gating has been observed in ipsilateral somatosensory cortex, in addition to the traditionally observed contralateral somatosensory cortex during skilled motor performance with the non-dominant hand. It was hypothesized that skilled performance required contributions from the dominant hemisphere and thus gating was present in both hemispheres. This effect was regardless of which hemisphere represented the dominant hand.

More recently interactions between ipsilateral motor and somatosensory cortices have been demonstrated by actively influencing one or the other. Depending upon stimulation parameters both facilitatory (Kujirai, Sato, Rothwell, & Cohen, 1993; Seyal, Browne, Masuoka, & Gabor, 1993)and inhibitory (Enomoto et al., 2001) effects of stimulation of primary motor cortex have been shown in S1. These effects are largely associated with an inverse relationship between M1 and S1 cortical excitability.

Although movement-related gating is a commonly observed phenomenon, it appears that this attenuation can be modulated itself depending upon the relevance of the sensory information to the guidance of the movement (Staines, Brooke, & McIlroy, 2000). This suggests that cortical mechanisms have the ability to overcome gating by disinhibiting afferent inputs at the level of the spinal chord or facilitating the gated afferent inputs at higher levels.

In addition to ipsilateral effects on somatosensory processing, it has also been demonstrated that motor cortical activation can influence somatosensory processing in the contralateral somatosensory cortices. Low frequency rTMS over M1 has been shown to increase (Mochizuki et al., 2004) or reduce (Seyal, Shatzel, & Richardson, 2005) the amplitude of the early cortical potentials depending upon stimulation parameters. Using 1 Hz rTMS at 110% of resting motor threshold appears to result in a facilitation of S1 cortical activity while rTMS at 0.3 Hz appears to have the opposite effect. It has been suggested that these inter-hemispheric effects are the result of ipsilateral (relative to rTMS)-contralateral M1 effects that then result in altered contralateral M1-S1 effects (Mochizuki et al., 2004). Further, perceptual detection thresholds co-varied with SEP amplitude demonstrating that these effects have important implications for behavior (Seyal et al., 2005).

Finally, in order to disentangle the effects of a continuous sensory-guided motor task on sensory processing the last consideration is inter-hemispheric interactions between the sensory cortices themselves. Cooling of ipsilateral S1 results in a facilitation and increase in receptive fields of contralateral S1 single neurons (Clarey, Tweedale, & Calford, 1996). Further, evidence relating to selective attention within one modality demonstrates a concurrent suppression of ipsilateral S1 during unilateral tactile stimulation (Hlushchuk & Hari, 2006; Staines et al., 2002). It has been suggested that this suppression is the result of S1-S1 inter-hemispheric connections (Hlushchuk & Hari, 2006).

Both motor-sensory and sensory-sensory inter-hemispheric interactions are an important factor in interpreting any attentional modulations observed when the sensory receptor and motor effector are located on different hands, as in the studies that will be presented in this thesis.

1.4 Specific Research Questions

The following are the specific research questions and hypotheses that guided the studies that address the general purpose of the thesis. In all cases the research was carried out using healthy participants in order to establish motor influences upon attentional modulation of sensory processing. The primary questions all serve to investigate these influences at the level of the earliest arrival of somatosensory information to the cortex, as well as any potential networks mediating this early modulation. In all cases the term “intermodal” refers to the simultaneous presentation of tactile and visual information.

1.4.1 Research Question 1

Does intermodal selective attention alter sensory processing at the level of primary somatosensory cortex? Does the spatial relationship between the target and distracter modalities influence sensory processing? What areas serve as potential top-down modulators of sensory processing?

Although there has been a focus upon intermodal selective attention these studies are largely restricted to perceptual detection tasks during which participants do not need to continuously extract relevant information. Instead they involve the presentation of discrete sensory events that require a transient response and do not account for the continuous nature generally associated with action.

In addition, intermodal effects are often measured by comparing activation when a stimulus of one modality is unattended and presented at an unattended location and subtracting this neural activity from that when the same modality is unattended but presented at an attended location to which a target in another sensory modality is expected. Although this comparison does offer insight into processing of unattended stimuli it does not reflect true environmental conditions where both the relevant modality and irrelevant modality are present at the same time.

Hypotheses: 1) Continuous tracking would be associated with increased activation in S1 when a tactile stimulus was to be tracked relative to when the same stimulus was a task-irrelevant distracter during visual tracking. 2) Increasing the spatial relationship between the target and distracter modalities would result in decreased tracking performance. 3) A spatially related vibrotactile distracter would result in increased activation in S1 compared to when the same distracter arose from a spatially distinct location. 4) Intermodal selective attention would be associated with differential recruitment of a frontal-parietal network.

1.4.2 Research Question 2

Does the temporal synchrony between the target and distracter modalities influence intermodal modulation of sensory processing? What is the potential network involved with the control of these modulations?

The synchrony between two modalities appears to be an important factor in determining the salience of the distracter modality. Two examples of this are the McGurk (McGurk & MacDonald, 1976) and ventriloquist effects (Radeau & Bertelson, 1974). Two interesting questions that arise from these illusions are 1) to what degree is an irrelevant modality processed? and 2) do the temporal similarities between intermodal stimuli influence sensory processing?

Hypotheses: 1) Increasing the temporal synchrony between the target and distracter modalities would result in improved tracking performance relative to when the same stimuli were asynchronous. 2) Increased temporal synchrony would increase S1 activation when the vibrotactile stimulus was a distracter. 3) Increasing temporal synchrony would be associated with a network of heteromodal cortical areas, including the superior temporal sulcus, inferior parietal lobe and insula that have previously been implicated in detecting stimulus synchrony.

1.4.3 Research Question 3

Do the attentional modulations observed using fMRI represent modulation of somatosensory information at the level of first arrival to the somatosensory cortex? Are spatial relationship and/or temporal synchrony represented by modulation of early processing within S1?

Although there is limited evidence for intermodal effects early in sensory processing the studies addressing the previous two research questions suggests that task demands may play an important role. ERP studies offer limited insight into early cortical processing as the earliest potentials observable are about 50 ms post-stimulus and may reflect 30 ms of cortical processing. In any event these studies rarely observed early effects with effects being localized to potentials (both magneto- and electroencephalographic) thought to be generated in secondary somatosensory areas. One problem with fMRI is that, despite excellent spatial resolution, the time associated with the haemodynamic response and data acquisition (2 s) means that a number of processes may be reflected in one data point. Therefore, an interesting question arises, were the early effects on S1, observed in the first two studies of this thesis, the result of influences from other areas/additional processes occurring later in time or were the changes observed in fMRI associated with modulation of thalamic-cortical projections? SEPs offer a distinct advantage in this area as the temporal resolution allows for investigation of the temporal nature of this processing.

Hypotheses: 1) Early cortical potentials, as early as the first arrival of somatosensory information to the cortex, would have reduced amplitude during continuous tactile tracking compared to visual tracking. 2) These early cortical potentials would be insensitive to changes in the spatial relationship and/or temporal synchrony of the target and distracter modalities.

1.4.4 Research Question 4

Is the decreased excitability of S1 observed in fMRI studies of continuous sensory-guided tracking associated with the continuous motor aspect of the task? Does this decreased excitability have behavioral implications?

From the studies addressing Research Questions 1 and 2 of this thesis an interesting hypothesis emerged. It was hypothesized that decreased excitability of contralateral S1 during vibrotactile tracking was the result of an interaction between tracking demands associated with the continuous nature of the task and traditional facilitory mechanisms associated with intermodal selective attention. If this hypothesis were true then it is possible that local cortical networks in contralateral S1 may demonstrate different states of excitability during a continuous tracking task versus a discrete detection task in the presence of bimodal stimulation. Paired-pulse TMS has been shown to elicit tactile extinction that is associated with increased excitability of local cortical networks. Therefore, TMS offers a unique advantage to probe differences in local cortical excitability during various sensory-guided motor responses.

<u>Hypotheses:</u> 1) Decreased local cortical excitability in S1 associated with the continuous tracking task would result in decreased susceptibility to the effects of excitatory paired-pulse stimulation over S1 compared to discrete detection using the same tactile stimulus. 2) These differential effects would be observed as differences in stimulus perception during continuous and discrete sensorimotor tasks.

1.4.5 Research Question 5

Is the benefit associated with the presence of a temporally synchronous distracter restricted to the modality that has a lower signal to noise ratio? Can we predict whether an overtly indicated task-irrelevant distracter that contains task-relevant information will be used to supplement target modality tracking?

A second interesting set of results from the studies addressing Research Questions 2 and 3 was the limited effects of the temporally synchronous distracter. In the fMRI study logistical constraints had participants lying on their back with the visuospatial stimulus located on a screen at their feet. This required the use of a small reflecting mirror placed in the birdcage coil above the participants' head so that they could see the stimulus. In contrast, during the SEP study an intensity-based stimulus was used with participants sitting at a table. In the former study participants benefited from a synchronous vibrotactile distracter but not from a synchronous visuospatial distracter while in the latter participants benefited from a synchronous visual distracter but not a synchronous vibrotactile distracter. It was suggested that these effects might be mediated by the suitability, as reflected in the ability to detect and transform signal changes into a motor output, of each modality. Therefore, an interesting question arises, were the differential effects between these studies the result of differences in the relative reliability of the target and distracter modalities with respect to the sensorimotor transformation required? If so, increasing the noise in the target modality should result in a greater benefit of a synchronous distracter modality regardless of which is initially better suited to guide motor output.

<u>Hypotheses:</u> 1) Increasing the signal to noise ratio within a modality during bimodal stimulation would result in decreased tracking performance when that modality is the task-relevant target. 2) The benefit of a temporally synchronous distracter modality would be greatest when the signal to noise ratio of the target modality is degraded to a greater extent. 3) This effect will be largest during vibrotactile tracking due to visual dominance.

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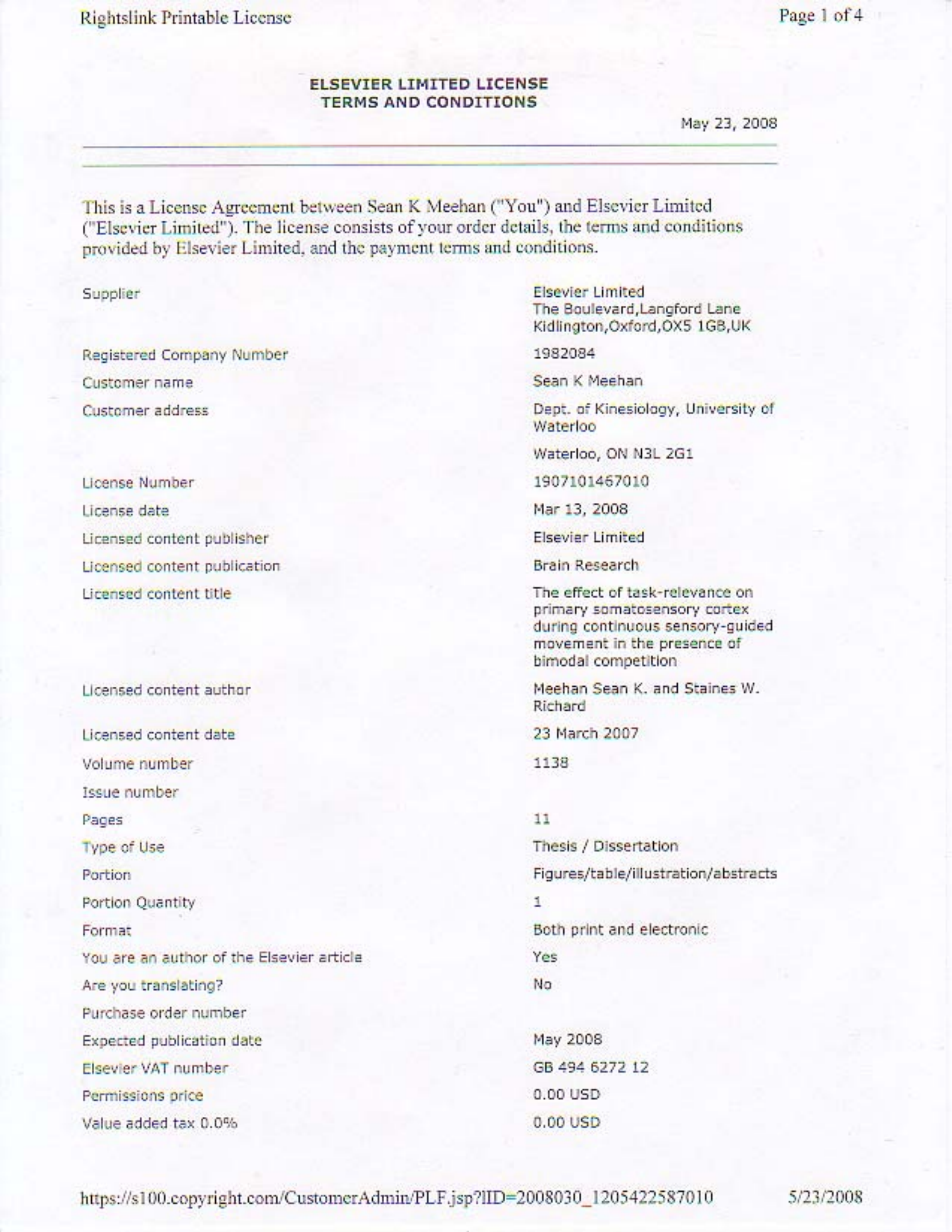

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CHAPTER 2 – Task-relevance, spatial relationship and bimodal competition

Meehan, S. K., & Staines, W. R. (2007). The effect of task-relevance on primary somatosensory cortex during continuous sensory-guided movement in the presence of bimodal competition. *Brain Research, 1138*, 148-158.

2.1 Abstract

Recent perceptual neuroimaging studies have shown that intermodal selective attention extracts relevant information from one modality at the expense of another at the level of unimodal sensory cortex. The present paper sought 1) to determine the effects of intermodal selective attention on primary somatosensory cortex (S1) during continuous sensorimotor transformations, 2) to investigate the interactions of spatial relationship between the target and distracter modalities on S1 and 3) to identify any potential modulators during continuous sensorimotor transformations. Functional MRI was acquired while participants (n=10) received simultaneous vibrotactile and visuospatial stimulation. In each condition, participants tracked either vibrotactile stimulation (25 Hz), applied to the right index finger with variable intensity, or a visuospatial stimulus, a centrally presented dial where the spatial position of a needle randomly moved, by applying graded force to a force sensing resistor. The distracter modality either originated from a location that was spatially related or distinct to the target that guided movement. Vibrotactile tracking resulted in decreased S1 activation relative to when it was task-irrelevant. Neither S1 activity nor tracking performance was influenced by spatial relationship. In addition the superior parietal lobe/precuneus (BA 7), inferior parietal lobe (BA 40), precentral gyrus (BA 6) and secondary visual areas (BA 18 and 19) may modulate the extraction of task-relevant information while the insula (BA 13) may do so during cases of spatial conflict. We conclude that modulation of S1 is important to the proper execution of sensory-guided movements and that sensorimotor requirements determine the mechanisms of intermodal selective attention.

2.2 Introduction

The performance of sensorimotor tasks requires the analysis and integration of sensory inputs that arise from multiple modalities. These inputs initially arrive and are processed at very distinct, modality-specific areas of the cortex before being integrated at later processing sites (Stein, Wallace, Stanford, & Jiang, 2002). Recent research has suggested that the integration of task-relevant information from multiple modalities may occur in multimodal neurons that have been described in the parietal cortex (Andersen et al., 1997). However, in any given environment task-related information also needs to be extracted from information that is irrelevant to the ongoing behavior. It has been suggested that this extraction occurs through a system that weights stimulus representations through facilitation of the relevant and suppression of the irrelevant sensory inputs (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005a) and involves heteromodal areas in the frontal and parietal cortices (Downar et al., 2001). Extraction of task-relevant somatosensory input has been associated with enhanced activity in cortical processing areas as early as the primary somatosensory cortex (S1). Concurrent facilitation of the heteromodal dorsolateral prefrontal cortex (DLPFC) suggests that it may play an important modulatory role (Staines et al., 2002). These results are consistent with the notion that the DLPFC is involved with the extraction of task-relevant information via top-down modulation of S1 (Knight et al., 1999; Schaefer et al., 2005; Yamaguchi & Knight, 1990).

Recently, one question that has generated interest is how task-relevant information from one modality is extracted from irrelevant information from other modalities. Evidence from recent multisensory integration studies (for a review see Macaluso, 2006) suggests that an area of potential interest is primary sensory cortex. Despite demonstrating convergent routes to heteromodal temporo-parietal and frontal areas such as the ventral intraparietal sulcus, superior temporal gyrus and ventral premotor areas, multisensory studies have also shown reciprocal influences between areas traditionally assigned as modality-specific. Therefore, one possibility is that similar mechanisms as those demonstrated in the heteromodal and modality-specific areas in integration studies are involved with intermodal selective attention when individuals are presented with non-corresponding sensory inputs.

A number of studies have demonstrated intermodal influences of modality-specific sensory cortex during perceptual tasks using electroencephalography (Eimer & Driver, 2001; Eimer & Van Velzen, 2002; Hotting et al., 2003; Macaluso & Driver, 2001), positron emission tomography (PET) (Macaluso, Frith, & Driver, 2002a) and fMRI (Balslev et al., 2005; Macaluso et al., 2003; 2005; Petkov et al., 2004; Tanabe et al., 2005). These studies have demonstrated that the amount of stimulus processing in the early sensory areas depends upon the relevance of the stimulus to the task (Johnson & Zatorre, 2005; 2006; Macaluso, Frith, & Driver, 2002b; Petkov et al., 2004; Shomstein & Yantis, 2004) and the spatial relationship between the target and distracter modalities (Eimer & van Velzen, 2005; Macaluso & Driver, 2001; Macaluso, Frith, & Driver, 2002a; 2002b; Macaluso et al., 2003; 2005).

In addition to these perceptual studies recent investigations of the neural correlates of intermodal selective attention have demonstrated increased activation in the sensory cortex of the relevant modality and a concomitant decrease in that of the irrelevant modality during both sustained (Johnson & Zatorre, 2005; 2006) and transient (Shomstein & Yantis, 2004) intermodal selective attention tasks. Further event-related potential (ERP) investigations of bimodal divided attention have shown a reduction in amplitude of not only components reflecting modality unspecific components but also those thought to reflect perceptual processes in modality-specific sensory cortex(Kida et al., 2004). However, not all studies investigating intermodal selective attention demonstrate modulation at the level of the primary sensory cortex. Recently, Downar et al. (2001) presented subjects with simultaneous visual and auditory stimuli but failed to observe any influence of task-relevance/intermodal selective attention on the primary sensory cortices. However, Downar et al. (2001) did observe a more extensive network of areas that demonstrated increased activations to task-relevant events including the temporo-parietal junctions (TPJ), precuneus, anterior insula, anterior cingulate cortex and thalamus suggesting that these areas may be involved in the top-down control of intermodal selective attention.

Despite the evidence cited above, very few studies have investigated cross-modal modulation of primary somatosensory cortex and its top-down control, especially during continuous and simultaneous bimodal stimulation. This is of particular interest because task-demands may play a crucial role in the mechanisms recruited under more demanding conditions like continuous sensory-guided movements, where motor commands need to be constantly updated, compared to transient attention shifts (Shomstein & Yantis, 2004), to memory encoding (Johnson & Zatorre, 2005; 2006) and to perceptual discrimination (Downar et al., 2001). From the literature there appears to be a gradient of bimodal effects within primary sensory cortex with discrete non-simultaneous tasks demonstrating effects in heteromodal association areas and more demanding continuous and simultaneous bimodal tasks demonstrating the strongest bimodal interactions in primary sensory cortices. The latter conditions are predominant in many natural behaviors that require continuous sensory-guided movement.

In addition to these modality task-relevancy changes within the sensory cortices, studies often demonstrate spatially specific but modality independent changes in frontal and parietal areas, commonly referred to as supramodal areas. FMRI and PET studies suggest that these changes may be associated with changes in activation in the anterior intraparietal sulcus (Macaluso, Frith, & Driver, 2002a; 2002b; Tanabe et al., 2005) and superior frontal cortex in sustained vigilance (Macaluso, Frith, & Driver, 2002b) and the temporo-parietal junction and inferior frontal cortex during orientation (Downar, Crawley, Mikulis, & Davis, 2000; Macaluso, Frith, & Driver, 2002b; Macaluso et al., 2003). The fact that these changes are independent of modality has led to the hypothesis that these areas may mediate the cross-modal influences observed within traditionally modality-specific areas (Eimer & Van Velzen, 2002; Macaluso & Driver, 2001). However, despite these observations the question still remains, does the spatial relationship between relevant and irrelevant tactile and visual stimuli lead to interactions at the level of S1? Further, the specific role of these areas in parsing out the distracter modality from the target modality during sensory-guided movements is not clear.

The purpose of the current paper was threefold: 1) to assess the effects of task-relevancy/intermodal selective attention on S1 during continuous sensorimotor transformations in the presence of a cross-modal distracter, 2) to assess the additional effects of the spatial relationship on the tactile/visual interactions at the level of S1 and 3) to identify potential top-down modulators of such interactions. To assess the intermodal interactions of task-relevancy on S1, fMRI was performed while subjects tracked either continuous intensity changes of a vibrotactile stimulus or continuous changes in spatial position of a visual stimulus by applying graded force to a force-sensing resistor. In any given condition subjects were instructed to track one modality and ignore the other. It was hypothesized that the demanding continuous tracking task would result in a facilitation of S1 when the vibrotactile stimulus was task-relevant as opposed to when the participants tracked the visuospatial stimulus (vibrotactile stimulus was task-irrelevant) despite the physical stimulus being virtually identical. No specific hypotheses were made about primary visual cortex, as time did not permit the proper individual retinotopic mapping required to investigate such effects.

In addition to the relevant modality we manipulated the spatial relationship between the task-relevant and distracter modalities by increasing or reducing the distance between the stimuli. Macaluso et al. (2003) have suggested that directing attention to a particular locus of space results in increased processing of unattended stimuli and a subsequent involuntary perceptual integration of the attended and unattended stimuli. Therefore, it was hypothesized that tracking performance would decrease when the target and distracter modalities were spatially aligned relative to when they were presented from distinct locations. Further, it was hypothesized that a vibrotactile distracter presented in spatial alignment with the visuospatial stimulus would increase its S1 representation relative to when the same tactile distracter was presented at a distinct spatial location. Finally, it was hypothesized that the intermodal selection of the relevant stimulus may be accompanied by a differential recruitment of areas within the previously described fronto-parietal network of heteromodal areas responsible for the top-down control of both visual and somatosensory intermodal selective attention.

2.3 Results

2.3.1 Behavioral Data

The means of the main effects of Modality and Spatial Relationship are shown in Figure 2-1. The two-way ANOVA on the data in Figure 2-1 revealed a significant main effect of Modality [$F(1, 9) = 23.91$, $p < 0.001$]. This effect can be attributed to an increase in RMSE during visuospatial tracking. None of the other effects were significant.

2.3.2 fMRI Data - S1 ROI Analyses

The mean volume of activation expressed as a percentage of the total volume of the anatomical ROI is shown in Figure 2-2A, while the percent signal change for the areas activated is shown in Figure 2-2B. A two-way ANVOA on the volume data in Figure 2-2A revealed a main effect of Modality ($F(1,9) = 6.61$, $p < 0.03$). This effect can be attributed to a greater increase in the volume of activation relative to rest in the visuospatial tracking conditions compared to the vibrotactile tracking. No other analyses were significant. The corresponding analyses on the percent signal change data shown in Figure 2-2B were not significant.

2.3.3 fMRI Data – Random Effects Analysis

2.3.3.1 – Modality Effects

Figure 2-3 shows the statistical contrast maps for the Track Tactile versus Track Visual comparisons. Those areas that demonstrate a greater BOLD signal when the visuospatial stimulation was task-relevant and the vibrotactile stimulation was task-irrelevant are shown in Figure 2-3 and the center of gravity and t-statistics are shown in Table 2-1 (top). There were no areas that demonstrated a greater BOLD response when the vibrotactile stimulus was task-relevant, although an area of the right inferior frontal gyrus failed to meet the 135 μl volume criteria (cluster size 118 μl).

2.3.3.2 – Spatial Relationship Effects

There were no areas that demonstrated a differential BOLD response for the Spatially Related relative to Spatially Distinct conditions. Therefore two subsequent analyses were performed to compare the Spatially Related and Spatially Distinct conditions during the vibrotactile and visuospatial tracking. Figure 2-4 shows the statistical contrast maps for the Spatially Distinct vs. Spatially Related comparisons for the visuospatial tracking conditions. Only the left insula demonstrated an increase in the BOLD signal when the tactile distracter was presented within the visual field (Spatially Related) relative to when the distracter was presented outside of the visual field (Spatially Distinct) are shown. There were no significant areas that demonstrated a greater BOLD signal when the distracter was spatially distinct. Further, the corresponding contrast map for the Track Tactile condition Spatially Distinct vs. Spatially Related comparison is not shown because there were no significant changes in BOLD signal. Center of gravity and t-statistics for the statistically significant activations are shown in Table 2-1 (bottom).

2.3 Discussion

The present study sought to assess the effects of task-relevancy and intermodal selective attention on S1 during sensorimotor transformations in the presence of a cross-modal distracter and the additional effects of the spatial relationship between the two competing modalities at this level. Subjects tracked changes in one modality during simultaneously presented vibrotactile and visuospatial stimulation that arose from related or distinct locations. It was observed, regardless of the spatial relationship between the task-relevant and distracter modalities that intermodal selective attention to the vibrotactile stimulation resulted in a decrease in the volume of S1 activation relative to when it was ignored. Further, these changes were not influenced by the spatial relationship between the vibrotactile distracter and visuospatial tracking target nor when the vibrotactile stimulus was task-relevant and visuospatial stimulus the distracter. Finally, despite an overall increase in tracking performance on the vibrotactile tracking task, manipulating the spatial relationship did not have any additional effects on tracking performance.

A key finding of this study was that intermodal selective attention to the vibrotactile stimulus resulted in a decreased BOLD response relative to when it was a task-irrelevant distracter. To our knowledge this is the first study to demonstrate intermodal attentional modulation in S1, in particular during a continuous sensorimotor task. However, this result was surprising as it was hypothesized that the volume of activation would increase when it was task-relevant, demonstrating a facilitation of the relevant information or a release of inhibition, relative to when it was task-irrelevant. This change was due to a greater increase in volume relative to rest when the vibrotactile stimulus was task-irrelevant compared to the increase in volume when the vibrotactile stimulus was task-relevant.

One possible explanation for the increased activation volume in S1 when the vibrotactile stimulus was task-irrelevant could be due to the task demands imposed by the continuous sensorimotor task. One commonality among previous studies that have demonstrated attention-related increases in either S1 under unimodal stimulation conditions (Staines et al., 2002) or in unimodal sensory cortices under bimodal stimulation conditions (Johnson & Zatorre, 2005; 2006) is the emphasis on the perceptual discrimination of the stimuli and the absence of a requirement to transform continuous stimulus changes into motor responses. Johnson and Zatorre (2005; 2006) suggested that top-down modulation was responsible for the modulatory affects observed in sensory cortex, in particular the influence of the superior temporal sulcus. However, in contrast to Johnson and Zatorre (2005; 2006) the increase in the S1 volume in the current study appears to mimic a mechanism of task-relevant inhibition, rather than global mechanisms that facilitate task-relevant and/or inhibit task-irrelevant modalities. One possible explanation is that the continuous tracking task resulted in increased surround inhibition during vibrotactile tracking. In such a case the need to extract the continuous vibrotactile information from only the ventral surface of the right index finger in order to accurately perform the sensorimotor task may have led to surround inhibition within S1 resulting in a decrease in the volume of activation. Surround inhibition to neighboring S1 representations has been demonstrated when stimuli to very specific parts of the skin are anticipated (Drevets et al., 1995). In contrast, during the visuospatial tracking condition the need to extract the irrelevant tactile information is much less and surround inhibition may have been released resulting in a global increase in the volume of activation within S1 because of the continued presence of the vibrotactile stimulation during visuospatial tracking.

A second, but not mutually exclusive possibility is corticocortical inhibition that contributed to the decrease in S1 activation during vibrotactile tracking. These corticocortical influences have been demonstrated during complex highly skilled movements performed by the non-dominant hand and have been suggested to reflect sensorimotor contributions from the dominant hemisphere (Hoshiyama & Kakigi, 1999; Rossini et al., 1999). It is possible that the sensorimotor transformations during tracking may have modulated the incoming sensory information of the ipsilateral hemisphere.

An alternative explanation to the surround/corticocortical inhibition explanations is the role of low-level links between sensory areas in multisensory integration. Recent multisensory integration studies (for a review seeMacaluso, 2006) have suggested that interactions between modality-specific sensory cortices may also occur not only through top-down feedback projections but via more direct parallel low level connections between sensory areas. Such direct connections have been supported by electrophysiological (Foxe et al., 2000) and anatomical studies (Cappe & Barone, 2005). It is possible that the increased volume in S1 may represent a second complementary mechanism of intermodal selective attention for the purposes of generating quick and accurate adjustments in motor output. The continuous tracking requirement of the current study may have placed a greater emphasis on rapid multisensory effects, potentially mediated by low-level connections linking the visual and somatosensory cortices, rather than lengthier feedback pathways that may mediate the cognitive processes required by the tasks of Johnson and Zatorre (2005; 2006) and other studies of intermodal selective attention. Therefore, another possibility that cannot be excluded is that the increased S1 activation observed during the visuospatial tracking may be due to an increase in S1 interneuron activity mediated by these low-level connections from visual cortex. While these two pathways provide alternative routes for multisensory effects in sensory cortex they are likely not mutually exclusive and may both be invoked differentially depending on task demands.

In addition to the changes in S1 associated with the task-relevance of the vibrotactile stimulus a number of other cortical areas demonstrated an increased BOLD response in the visuospatial tracking conditions including; the right lingual gyrus (BA 19), precentral gyrus (BA 6), superior parietal lobe (BA 7) and precuneus (BA 7), as well as the left inferior occipital gyrus (BA 19) and inferior parietal lobule (BA 40). It is possible that these areas may reflect top-down influences on primary sensory cortex as the pre-central gyrus (BA 6), superior parietal lobe (BA 5) and inferior parietal lobe (BA 40) have been implicated in the control of both unimodal and intermodal visual selective attention (Corbetta & Shulman, 2002; Shomstein & Yantis, 2004). However, in the current study subjects generally demonstrated decreased tracking performance during visuospatial tracking compared to vibrotactile tracking that may be attributable to potential extra transformations required to convert a representation of a visuospatial stimulus into a representation of isometric force. The superior parietal lobe, in particular, is thought to be involved in this process (Buneo & Andersen, 2006). Therefore one possibility that cannot be ruled out is the sensitivity of these areas to any potential additional visuomotor transformations required to perform the visuospatial sensorimotor task.

A second key finding from this study was the lack of additional effects on S1 activation associated with the spatial origin of the two competing modalities. It was originally hypothesized that a distracter stimulus, presented from a similar spatial location as the target modality, would receive enhanced processing at the level of the S1 (Macaluso et al., 2003). However, a recent study by Murray et al. (2005) suggests that these effects as well as those seen in the ventriloquism (Radeau & Bertelson, 1974) and McGurk (McGurk & MacDonald, 1976) effects may be perceptual and mediated at higher levels and do not occur at early levels of sensory processing. To our knowledge the current study is the first study to demonstrate this effect between tactile and visual stimuli during continuous sensorimotor transformations.

Based upon the work of Murray et al. (2005) one possible explanation for the insensitivity to the spatial relationship between the visuospatial target and vibrotactile distracter may be the lack of an implicit link between the two modalities at a higher cognitive representation. It has been demonstrated that presenting an unattended or irrelevant stimulus from one modality at the spatial position at which a target stimulus from another modality will appear results in an increase in the representation of the unattended stimulus in unimodal sensory cortex (Eimer & van Velzen, 2005; Macaluso & Driver, 2001; Macaluso, Frith, & Driver, 2002a; 2002b; Macaluso et al., 2003; 2005). However, these studies often use an “oddball” paradigm in which a target is defined by the spatial location at which it is presented. One possible explanation for the lack of spatial interaction between the visuospatial target and vibrotactile distracter was that there was no cognitive or perceptual relevance attached to the spatial attributes and therefore sustained attention was not directed to location but to some other stimulus attribute despite the similar locus of origin. Within this same argument, studies investigating modality-specific influences in multisensory integration often use stimuli that are implicitly or explicitly linked by some spatial attribute whether it be the locus in space or by spatial origin with respect to an object. This was not the case in the current study. Therefore, without any top-down spatial influences the mechanisms working at the level of S1 were identical between the two spatial manipulations and only reflected the extraction of the relevant modality.

A second alternative follows the framework of direct sensory-sensory links. Under this framework it is possible that the demands imposed by the continuous sensorimotor transformations required to perform the task may have put a premium on direct sensory-sensory connections rather than top-down feedback. Based upon the results of Murray et al. (2005) there should be no changes in processing with changes in the spatial relationship because the interactive mechanism is insensitive.

One interesting note is that the random effects analysis comparing the spatially related versus spatially distinct conditions did not reveal any significant activations. Post-hoc analyses comparing these two conditions separately for visuospatial and vibrotactile tracking revealed only one area, the left insula (BA 13), that demonstrated differential activation only when the visuospatial target and vibrotactile distracter were spatially related relative to when they were spatially distinct. It has been suggested that the left insula is part of a network involved with detecting relevant sensory events not only based upon relevant modality but also on behavioral context (Downar et al., 2001). Due to the different transformations required by the vibrotactile and visuospatial stimuli it is possible that having a spatially related vibrotactile distracter enhanced the relevance of the visuospatial target to be tracked but did not alter the relevance of the distracter. This would account for the both the activation of the insula and the insensitivity of S1 activation to the spatial relationship of the target and distracter modalities.

Another interesting result is that there was no differential modulation of S1 when the vibrotactile stimulus was task relevant and the visual distracter originated from a distinct or similar spatial location. It was hypothesized that there may be a facilitation of S1 when the visuospatial distracter was spatially related relative to when it was spatially distinct via feedback connections in order to compensate for the increased the increased representation of the visual distracter. However, this was not the case and further supports the two explanations outlined above.

In conclusion, this study was the first to show task-relevant modulation of primary somatosensory cortex associated with intermodal selective attention during continuous sensory-guided movement. However, unlike previous studies task-relevant modulation of the somatosensory cortex did not appear to reflect a global facilitation but a loss of specificity when the vibrotactile stimulation was task-irrelevant. This does not rule out that this mechanism was present, but that a second potential mechanism of intermodal selective attention may have interacted with traditional top-down influences. This differential mechanism may be a result of two distinct features of the current study relative to those reviewed: 1) the same vibrotactile and visuospatial stimuli were presented continuously and simultaneously in all conditions, and 2) subjects were required to perform a continuous sensory-guided movement based on the changes in one of the modalities. Further, contrary to previous work this study demonstrated an insensitivity of the representation in S1 of a task-irrelevant distracter to spatial influences. These results suggest that task-demands may play an important role in the type of mechanism used to extract task-relevant information and needs to be considered in future work.

2.4 Materials and Methods

2.4.1 Subjects

Ten healthy volunteers (5 male, 5 female, age range 22-34, mean 26.1 years) were recruited. All subjects gave their informed consent to participate in the study and the experimental procedures were approved by the Sunnybrook and Women's College Health Sciences Centre Ethics Committee and by the Office of Research Ethics at the University of Waterloo.

2.4.2 Experimental Tasks

For each of the ten participants, functional MRI was performed in the presence of independent but simultaneous binocular visuospatial and unilateral right vibrotactile stimulation. Independent bimodal stimulation was delivered in a blocked design (10 s stimulation/20 s no stimulation, 10 repetitions). Prior to the start of each scan subjects were instructed to either track the intensity/position of one modality (target) while ignoring position/intensity of the other modality (distracter). Tracking was carried out by applying graded force to a force-sensing resistor mounted on a rigid plastic tube under the thumb of their left hand.

During the vibrotactile tracking conditions subjects were instructed to apply graded force that followed the intensity of the vibrotactile stimulation, so that as the intensity of the vibrotactile stimulation increased, force applied to the resistor increased and as vibrotactile intensity decreased the force applied decreased (Track Tactile) (Figure 2-5). During the visuospatial tracking conditions subjects were instructed to apply graded force in such a fashion that a needle position equivalent to seven o'clock represented minimal force, five o'clock represented maximal force and twelve o'clock represented intermediate force (Track Visual) (Figure 2-5).

In addition to tracking the target modality, the spatial proximity of the target and distracter modalities were also manipulated. In one set of conditions, the participants were instructed to place the hand receiving the tactile stimulation on their stomach resulting in that hand being visible to the subject at the bottom of the visual dial serving as the visual stimulus (Spatially Related). In another set of conditions the subjects were instructed to place their right hand at their side so that the hand receiving tactile stimulation was not visible (Spatially Distinct). The purpose of this manipulation was to induce a stronger spatial relationship between the target and distracter modalities, with the assumption that subjects' performance would decrease when the target and distracter appeared to originate from similar rather than distinct spatial locations.

The experiment consisted of a 2 x 2 repeated measures design with four conditions in all: 1) Track Tactile, Spatially Related 2) Track Tactile, Spatially Distinct 3) Track Visual, Spatially Related and 4) Track Visual, Spatially Distinct. In addition, each condition was performed during a separate scan for a total of four functional scans per subject each five minutes in duration.

2.4.3 Somatosensory Stimulation

Somatosensory stimuli were presented via a custom-made MRI-compatible vibrotactile device (Graham, Staines, Nelson, Plewes, & McIlroy, 2001). The vibrotactile device consisted of a plastic tube with a wooden dowel (1 cm diameter) extending from the body such that the index finger, when extended, rested over the dowel's surface. The wooden dowel was controlled to vibrate at varying forces by passing fluctuating current through coils within the body of the vibrotactile device according to a 25 Hz sine wave with random intensity fluctuations. Vibrotactile stimulation was controlled by digitally generating waveforms that were converted to an analog signal (DAQCard 6024E, National Instruments, Austin, Texas) and then amplified (Bryston 2B-LP, Peterborough, Ontario, Canada). Variation in amplitude of the driving voltage at a given frequency (25 Hz) led to proportionate increases in force applied by the dowel onto the finger. The vibrotactile waveform varied in average frequency from 0.10Hz – 0.50Hz superimposed upon the underlying 25 Hz vibration and was generated as a random combination of 4 sinusoid waveforms of varying amplitude and frequency using Labview software (version 7.1, National Instruments, Austin, Texas). Output from the computer was routed through a penetration panel to the magnet room using a filtered 9-pin D sub-connector and shielded cable to ensure that no perceptible torque was produced by currents induced by radio-frequency transmit pulses or time-varying magnetic field gradients during imaging.

2.4.4 Visual Stimulation

The visuospatial stimulus was back projected (BoxLight 6000) onto a white screen placed at the bore of the magnet and viewable to the subject via an angled mirror placed within the head coil. The visuospatial stimulus consisted of a white dial presented against a black background. Within the dial was a yellow needle that moved back and forth (with a maximum range of five to seven o'clock, via twelve o'clock) according to a randomly generated composite sine wave. The position of the needle was controlled by computer using the same Labview software as the vibrotactile device with an average frequency between 0.10 and 0.5 Hz.

2.4.5 Data Acquisition

Functional and anatomical imaging was performed at Sunnybrook and Women's College Health Science Centre on a 3 T clinical whole body MRI scanner (GE HealthCare, Milwaukee, WI, USA) using a standard birdcage head coil with the head immobilized. Blood oxygenation level dependent (BOLD) images were acquired axially using gradient echo imaging with single-shot spiral in-out readout (TR = 2000 ms, TE = 30 ms, flip angle $\theta = 70°$, FOV = 20, 26 slices, 5 mm slice thickness). Prior to acquisition of the functional data subjects underwent a high-resolution anatomical scan (TR = 12.4 ms, TE = 5.4 ms, flip angle $\theta = 35°$, FOV = 20 x 16.5, 124 slices, 1.4 mm slice thickness) for later co-registration with the functional maps. Total scan time was approximately 40 minutes.

2.4.6 fMRI Data Analyses

For each scan a time series consisting of 154 images per slice location was generated by offline gridding and reconstruction of the raw data. The reconstructed time courses were analyzed using BrainVoyager QX 1.7 software (Brain Innovation, Masstricht, The Netherlands). Prior to further analysis, the first 4 volumes at each slice location were excluded to prevent artifact from transient signal changes as the brain reached a steady magnetized state. The following pre-processing steps were performed prior to co-registration: linear trend removal, temporal high pass filtering to remove non-linear low-frequency drift of 3 cycles or less per second and three-dimensional motion correction (using trilinear interpolation) to detect and correct for small head movements during the scan by spatially realigning all subsequent volumes to that first acquired (the fifth volume). Estimated translation and rotation measures were visually inspected and never exceeded 0.78 mm and 1.2 degrees, respectively. The functional data sets were transformed into Talairach space (Talairach & Tournoux, 1988) through coregistration with spatially transformed 3D anatomical data sets for each individual subject. The resulting volume time courses were filtered using an 8 mm Gaussian kernel at full width half maximum.

In order to statistically evaluate the relative differences across the four experimental conditions a multiple regression approach was employed using four predictors: 1) Tactile Spatially Related 2) Tactile Spatially Distinct 3) Visual Spatially Related and 4) Visual Spatially Distinct, with the 20 s of no stimulation serving as a baseline. Four stimulation protocols using dummy-predictors (for those predictors not included in a given scan) were adopted and convolved with a boxcar haemodynamic response function (Boynton, Engel, Glover, & Heeger, 1996) to account for the expected shape and temporal delays of the physiological response. The resulting reference functions served as the model for the response time course functions used in the general linear model. We employed two different general linear models.

First, in order to assess the relative effects of the experimental manipulations on S1 a fixed effects general liner model was employed for each individual subject.

Anatomical markers were used to create a mask of the left (contralateral to the vibrotactile stimulation) S1 as defined in each individual according to the following landmarks: the central sulcus anteriorly, the medial wall of the "hand knob" medially and the most lateral edge of the of the post-central gyrus (Nelson, Staines, Graham, & McIlroy, 2004). Any significant voxels that exceeded the Bonferroni corrected value of $p < 0.05$ and were part of a cluster greater than three contiguous voxels (i.e. > 135 μl) were included in region of interest (ROI) analyses. Task-related changes were then quantified as changes in the intensity and volume of the ROI analyses. For the intensity measurements the individual time course data for all significantly activated voxels within a cluster were extracted and averaged across each individual subject and condition. This resulted in one time series per subject per condition representing signal changes for the tracking relative to the rest blocks for a given scan. BOLD signal changes were expressed as a percentage relative to the baseline rest. For the volume measurements the total number of voxels that met the outlined criteria were represented as a percentage of the total number of voxels in the anatomical region defined using the landmarks stated. Both the intensity and volume measures were first analyzed using a 2 (Tracking Modality: Tactile, Visual) x 2 (Spatial relationship: Related, Distinct) repeated measures analysis of variance (ANOVA) to assess any potential interactions between the tracking modality or spatial relationship. *A priori* contrasts were used to test the specific hypotheses and statistical significance was defined as $p < 0.05$.

Second, in order to identify other areas that were sensitive to the experimental manipulations a random effects approach was employed using the same predictors outlined above. Contrast maps were calculated to show the relative changes, using a voxel based approach, for the following comparisons: 1) Modality: Track Tactile vs. Track Visual and 2) Spatial Relationship: Spatially Distinct vs. Spatially Related. In addition two more *a priori* contrasts were performed to look for significant changes for the following comparisons: 1) Spatial Relationship – Tactile: Track Tactile, Spatially Related vs. Track Tactile, Spatially Distinct and 2) Spatial Relationship - Visual: Track Visual, Spatially Related vs. Track Visual, Spatially Distinct. Voxels were deemed significant if the threshold exceeded $p < 0.001$ uncorrected and formed a cluster of three contiguous voxels (i.e. > 135 μl). The center of gravity and t-statistics for each significant cluster were then extracted.

2.4.7 Behavioral Data Analysis

Tracking performance during each scan was quantified by calculating the average root mean square error (RMSE) of the difference waveform derived from the graded motor response and that driving the task-relevant target. Average RMSE was calculated according to the following. First, the amplitude of the task-relevant waveform was normalized to that of the motor response. The motor output waveform was then subtracted from the task-relevant sensory input at each data point, yielding a difference waveform. The average RMSE was then derived by taking the average value of this waveform across all the time points for each condition and each subject. Therefore, a decrease in the average RMSE implies that a decrease in the difference between the motor output generated and the sensory task-relevant target supplied, or an increase in tracking performance. In contrast an increased average RMSE implies that the difference between the motor output and sensory target increased, or tracking performance decreased.

Behavioral performance was assessed with a 2 (Tracking Modality: Tactile, Visual) x 2 (Spatial Relationship: Related, Distinct) repeated measures ANOVA using the average RMSE as the dependent variable in order to assess any potential interactions between Tracking Modality and Spatial Relationship.

Table 2-1: Center of gravity and t-statistics for those clusters demonstrating a significant increase in BOLD response from the Random Effects Analysis. Contrasts are specified in table (see text for details).

Condition	Anatomical (Brodmann) Area	X	Y	Z	t-statistic
Visuospatial > Vibrotactile Tracking					
	Rt. Precentral Gyrus (BA 6)	27	-10	49	5.72
	Rt. Superior Parietal Lobe (BA 7)	13	-63	58	6.39
	Rt. Precuneus (BA 7)	15	-52	47	5.53
	Rt. Precuneus (BA 7)	7	-78	43	6.36
	Rt. Lingual Gyrus (BA 19)	31	-73	-1	12.89
	Lt. Inferior Occipital Gyrus (BA 19)	-36	-74	-2	10.94
	Lt. Inferior Parietal Lobule (BA 40)	-31	-49	44	7.78
Visual Tracking – Spatially Related > Spatially Distinct					
	Lt. Insula (BA 13)	13	-35	-8	9.50

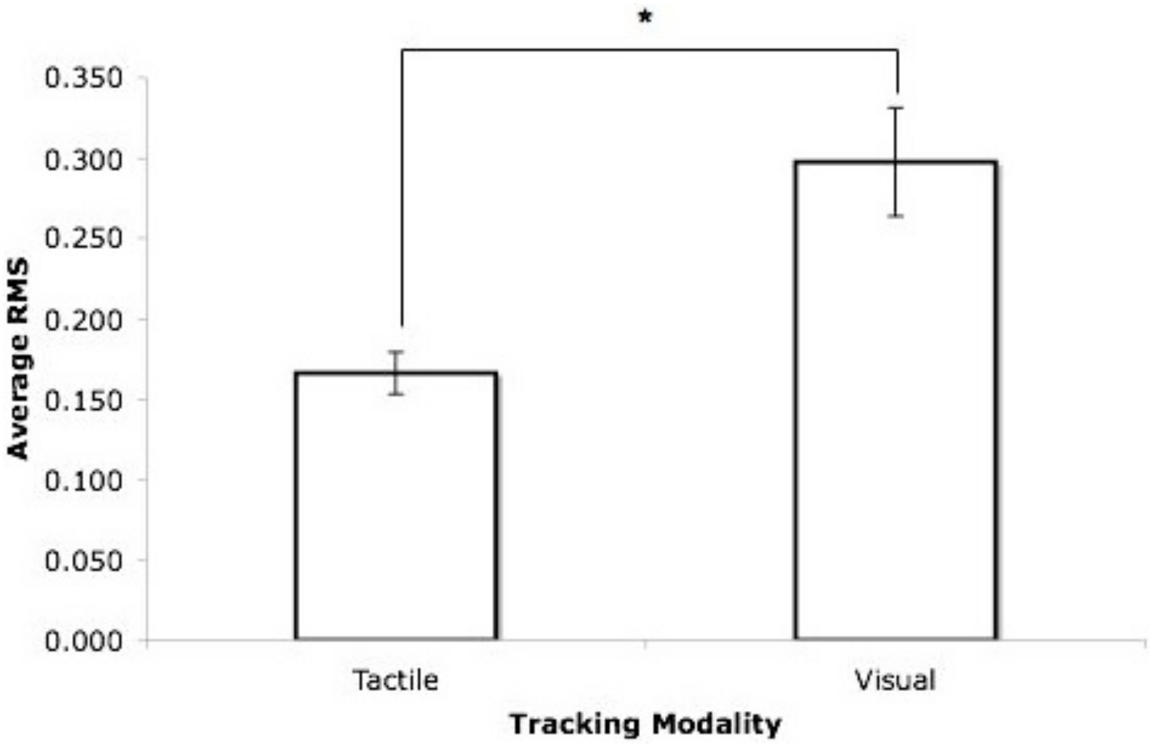

Figure 2-1: A plot of the average normalized RMS values for the main effects of tracking modality. Error bars represent standard errors. Asterix denotes $p < 0.05$.

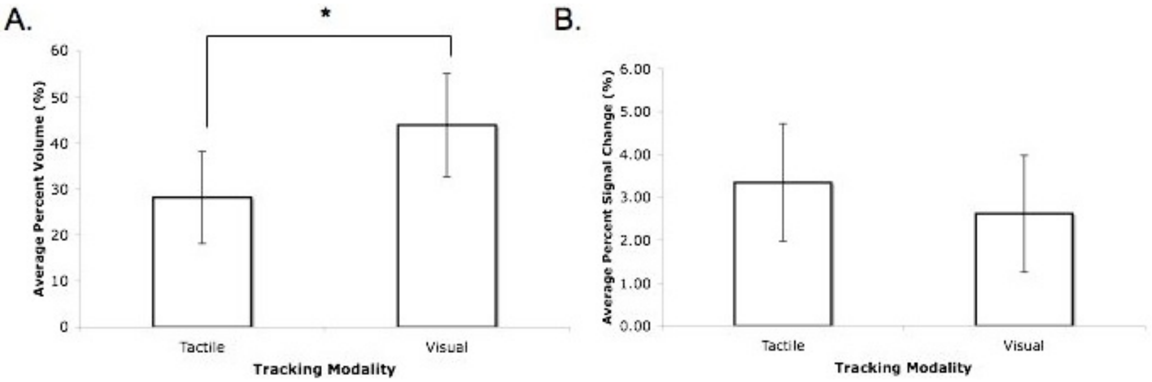

Figure 2-2: (A) A plot of the average percent of volume of activated voxels for each tracking condition. Volume is defined as the percentage of significantly active voxels relative to the total volume of the anatomically defined primary somatosensory cortex (see text). (B) A plot of the average signal percent change for the activated voxels with the anatomically defined primary somatosensory cortex. Error bars represent standard errors. Asterix denotes $p < 0.05$.

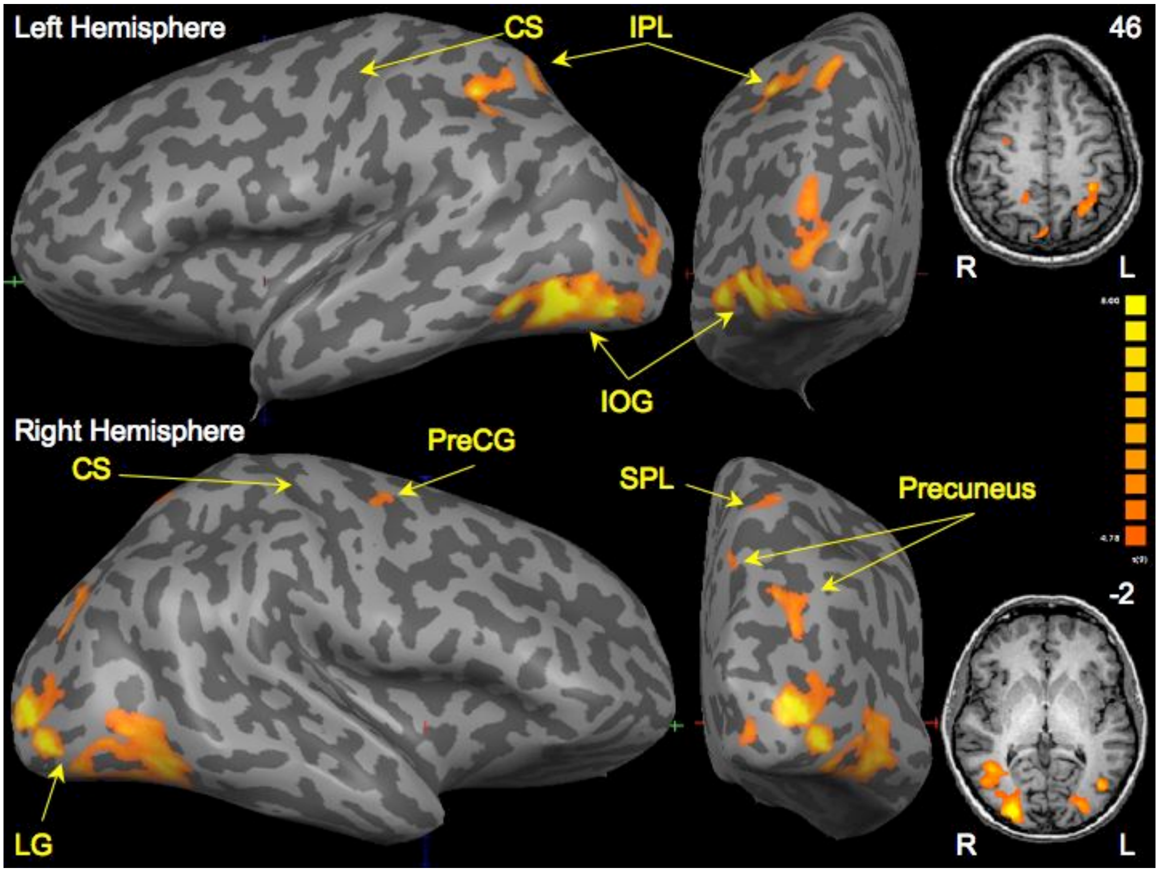

Figure 2-3: (A) RFX statistical contrast map for the main effect of task-relevance. The contrast map is overlaid on an individual's cortex. Those areas in red/yellow demonstrated a greater magnitude BOLD signal when the vibrotactile stimulation was task-irrelevant relative to when it was task-relevant. (B) An axial slice depicting those areas demonstrated on the inflated cortex. Slice levels are indicated on the bottom right. CS – central sulcus, IPL – inferior parietal lobe, IOG – inferior occipital gyrus, pre-CG – precentral gyrus, SPL – superior parietal lobule, LG – lingual gyrus

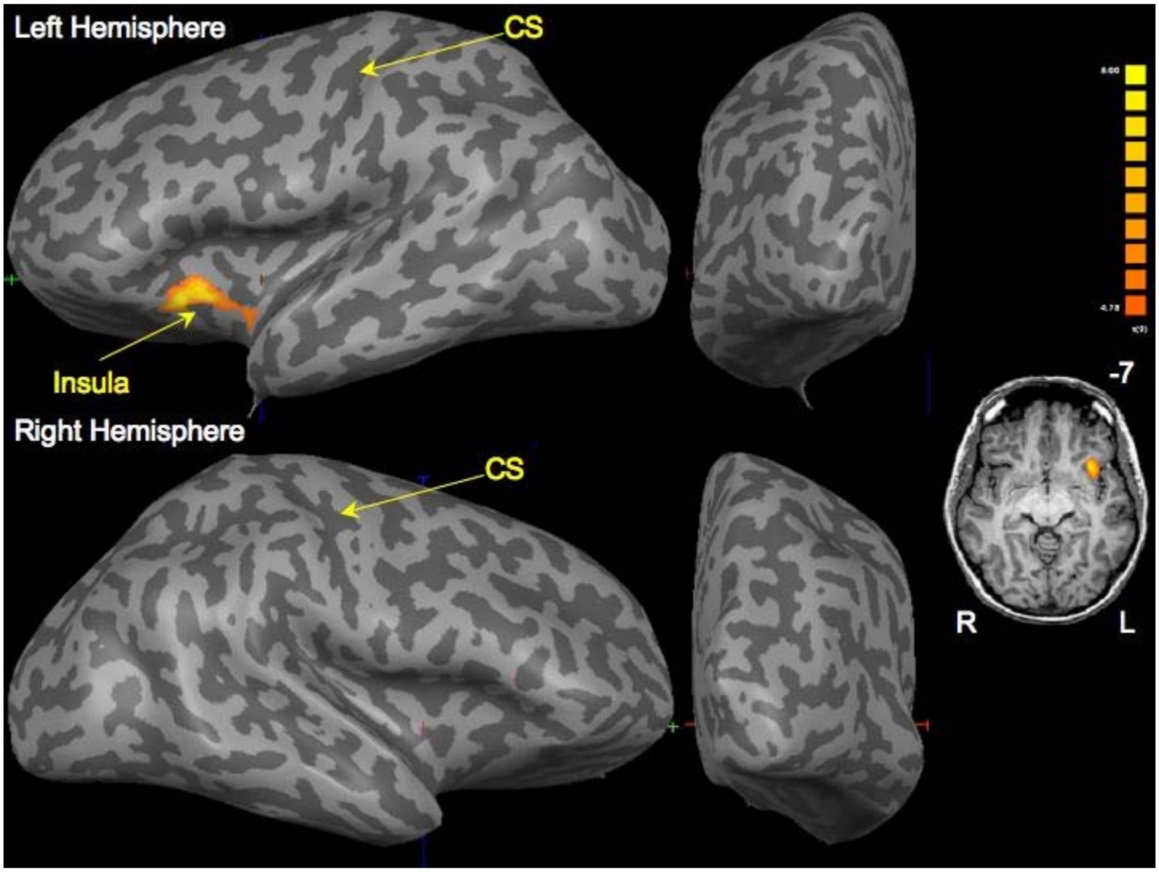

Figure 2-4: (A) RFX statistical contrast map for the effect of spatial relationship during visuospatial tracking. The contrast map is overlaid on an individual's cortex. Those areas in red/yellow demonstrated a greater magnitude BOLD signal when the vibrotactile stimulation was task-irrelevant relative to when it was task-relevant. (B) An axial slice depicting those areas demonstrated on the inflated cortex. Slice levels are indicated on the bottom right. CS – central sulcus

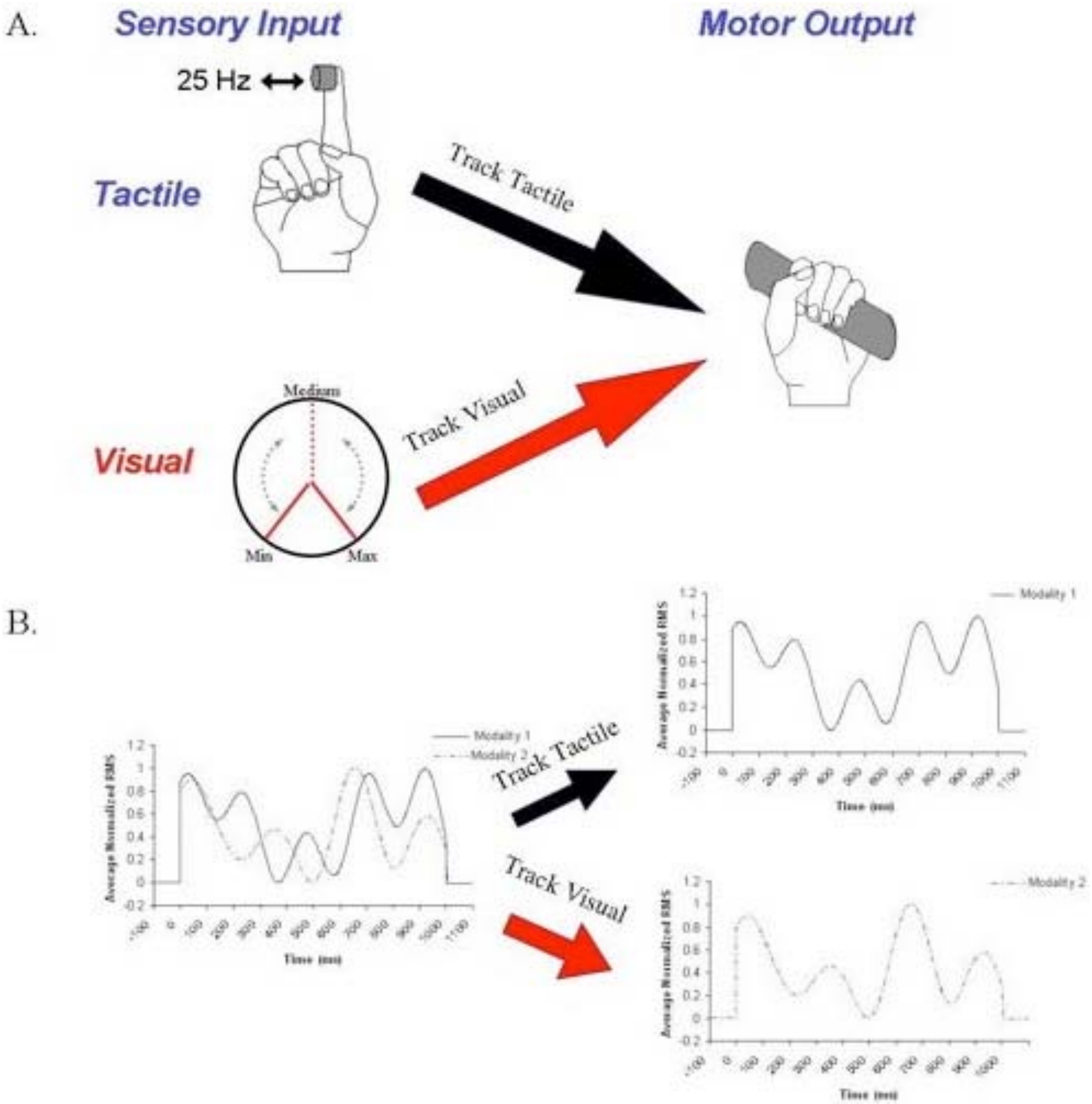

Figure 2-5: (A) Example of the experimental design. Subjects were presented with a vibrotactile stimulus on their right index finger and a bilateral visuospatial stimulus, simultaneously. On any given scan subjects tracked either the intensity of the vibrotactile stimulus or the spatial position of the needle of the dial by applying graded force to a force sensing resistor in their left hand. In the case of track visuospatial, movement of the needle to the right was a sign for subjects to apply greater force to the FSR while movement to the left required less force to be applied. (B) An example of the stimulus waveforms and the motor output required under the track tactile and track visual conditions. Prior to the start of the scan subjects were instructed to track one of the modalities and ignore the other.

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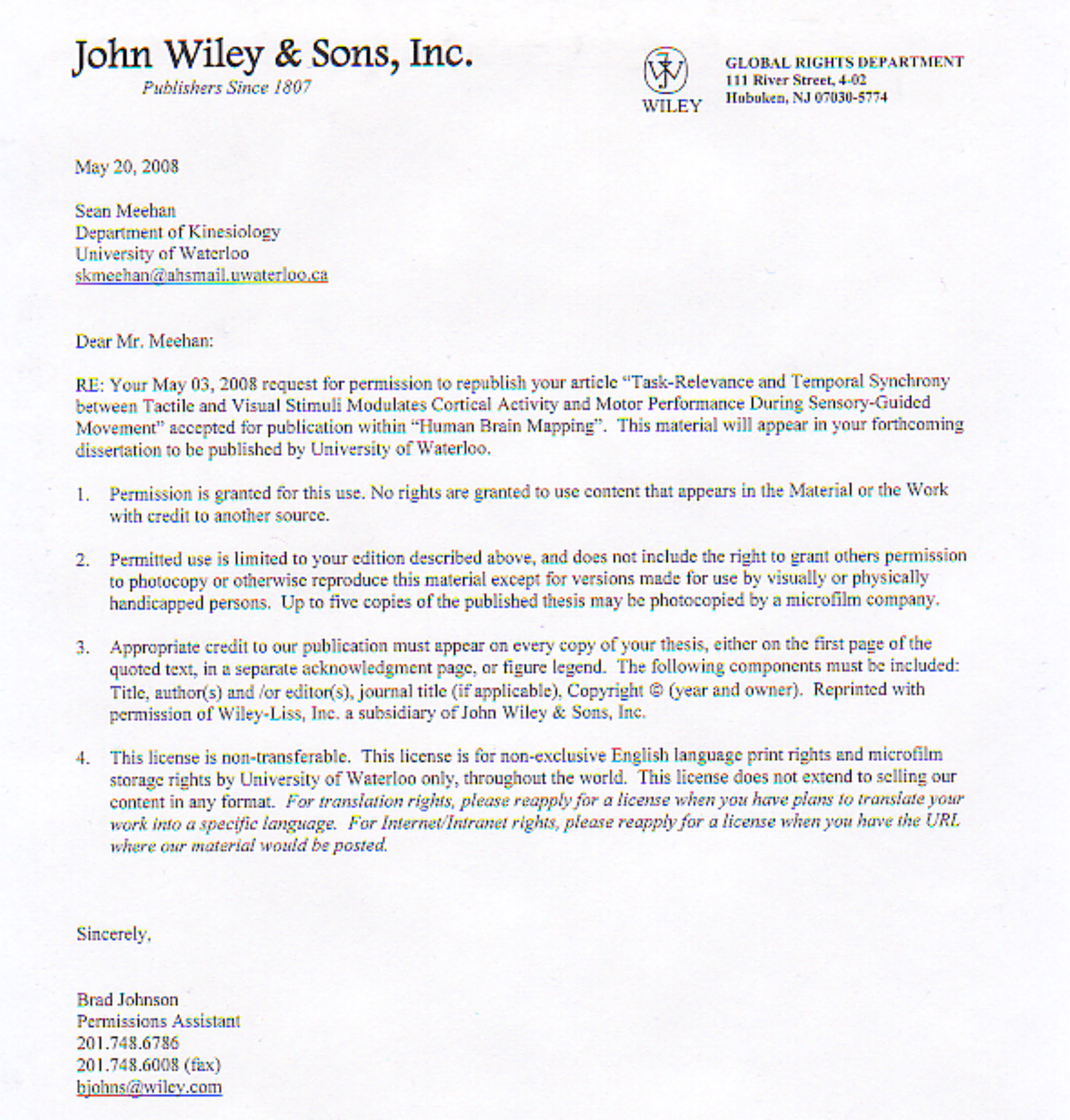

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May 20, 2008

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CHAPTER 3 – Task-relevance, temporal synchrony and bimodal competition

Meehan, S. K., & Staines, W. R. (epub - 2007). Task-relevance and temporal synchrony between tactile and visual stimuli modulates cortical activity and motor performance during sensory-guided movement. *Human Brain Mapping,* (DOI: 10.1002/hbm.20520)

3.1 Abstract

Sensory-guided movements require the analysis and integration of task-relevant sensory inputs from multiple modalities. The present paper sought to: 1) assess effects of intermodal temporal synchrony upon modulation of primary somatosensory cortex (S1) during continuous sensorimotor transformations, 2) identify cortical areas sensitive to temporal synchrony and 3) provide further insight into the reduction of S1 activity during continuous vibrotactile tracking previously observed by our group (S. K. Meehan & Staines, 2007a). Functional MRI was acquired while participants received simultaneous bimodal (visuospatial/vibrotactile) stimulation and continuously tracked random changes in one modality, by applying graded force to a force-sensing resistor. Effects of intermodal synchrony were investigated, unbeknownst to the participants, by varying temporal synchrony so that sensorimotor transformations dictated by the distracter modality either conflicted (low synchrony) or supplemented (high synchrony) those of the target modality. Temporal synchrony differentially influenced tracking performance dependent upon tracking modality. Physiologically, synchrony did not influence S1 activation, however the insula and superior temporal gyrus were influenced regardless of tracking modality. The left temporal-parietal junction demonstrated increased activation during high synchrony specific to vibrotactile tracking. The superior parietal lobe and superior temporal gyrus demonstrated increased activation during low synchrony specific to visuospatial tracking. As previously reported, vibrotactile tracking resulted in decreased S1 activation relative to when it was task-irrelevant. We conclude that while temporal synchrony is represented at higher levels than S1, interactions between inter- and intramodal mechanisms determines sensory processing at the level of S1.

3.2 Introduction

Sensory-guided movements require the analysis and integration of task-relevant sensory inputs from one or multiple modalities. Recent perceptual research has shown that multiple modalities representing the same sensory event are integrated along a hierarchical processing stream. These inputs initially arrive and are processed at very distant, distinct modality-specific cortical regions before being integrated at later heteromodal processing sites (Stein et al., 2002). However, growing evidence suggests that multisensory effects may even be present within traditionally viewed modality-specific cortices governed by feedback projections from the traditional heteromodal areas (Macaluso & Driver, 2005) as well as more direct, shorter latency projections between the modality-specific cortices (Foxe & Schroeder, 2005).

It has been suggested that modulation of modality-specific cortex is contingent upon the temporal synchrony and/or spatial relationship between the two sensory modalities (Macaluso & Driver, 2005). In contrast, evidence from auditory-tactile multisensory interactions suggests that they can occur along a diverse range of spatiotemporal alignments at very short processing latencies (Murray et al., 2005). However, despite the benefits, both behavioral and physiological, of integrating sensory inputs across modalities (Murray et al., 2005) failure to extract task-relevant from irrelevant information can have adverse effects on behavior. The most common examples of this failure are the ventriloquist (where concurrent auditory stimuli are mislocalized to visual stimuli) and the McGurk (alteration of speech perception by concurrent yet conflicting lip movements) effects. It has been suggested that the extraction of task-relevant sensory information occurs through a system that weights stimulus representations through facilitation of the relevant and a relative suppression of the irrelevant sensory inputs (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005a; Staines et al., 2002) and it is the failure to properly weight the simultaneous sensory cues, largely due to the spatial/temporal synchrony, that results in these perceptual deficits (McGurk & MacDonald, 1976; Radeau & Bertelson, 1974).

Investigations of intermodal selective attention, like those of multisensory integration, have demonstrated task-dependent modulation of modality-specific sensory cortex primarily during perceptual detection tasks. Recent imaging studies of both sustained and transient shifts of intermodal selective attention have shown not only increased activation of the modality-specific sensory cortex of the relevant modality but a concomitant decrease in activation within the sensory representation of the irrelevant modality (Johnson & Zatorre, 2005; 2006; Shomstein & Yantis, 2004). Converging evidence is also provided by event-related potential (ERP) studies of visual-tactile divided attention that demonstrate a reduction in the amplitude of sensory-specific perceptual somatosensory ERP components in addition to later heteromodal somatosensory ERP components compared to selective attention conditions (Kida et al., 2004). Further, studies investigating the spatial/temporal factors have shown that the suppression within the sensory cortex of the task-irrelevant modality can depend upon its spatial/temporal relationship with the facilitated target modality during perceptual detection tasks (Eimer & van Velzen, 2005; Kida, Inui, Wasaka, Akatsuka, Tanaka, & Kakigi, 2007a; Macaluso & Driver, 2001; 2002a; Macaluso, Frith, & Driver, 2002b; Macaluso et al., 2003; 2005). However, intermodal selective attention is not universally associated with modulation of modality-specific cortex with effects localized solely to higher order heteromodal areas (Downar et al., 2001).

Two interesting questions arise from the reviewed literature. Does changing task-demands, by introducing a continuous tracking requirement, result not only in changes in sensory-specific cortices but in primary sensory cortex? If so are task-demands attributed to intermodal properties such as the spatial relationship/temporal synchrony between task-relevant and irrelevant modalities reflected at this level? It is possible that the presence of intermodal effects or lack thereof in the reviewed literature may be attributable to differences in the demands associated with the various tasks, such as differences in sensory-sensory interactions or the required response, that determine where in the sensory processing stream intermodal effects manifest.

Recently, our group investigated intermodal selective attention during continuous sensorimotor transformations in the presence of simultaneous conflicting vibrotactile and visuospatial stimulation (S. K. Meehan & Staines, 2007a). In contrast to previous unimodal (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005a; Staines et al., 2002) and bimodal (Johnson & Zatorre, 2005; 2006; Shomstein & Yantis, 2004) perceptual studies, the introduction of the continuous motor response resulted in a decrease in S1 activation contralateral to the finger of stimulation, when the vibrotactile stimulus was task-relevant relative to visuospatial tracking where the vibrotactile stimulus was irrelevant. Further, these changes in S1 activation were insensitive to the spatial relationship between the simultaneously presented modalities. However, whether modulation of S1 is sensitive to task-demands associated with the temporal synchrony between two simultaneously presented stimuli, a factor that may have a stronger influence upon multisensory processing, during a continuous tracking task is unknown.

The purpose of the current paper was threefold: 1) to assess the influence of temporal synchrony upon task-relevant modulation of S1 during continuous sensory-guided movements in the presence of bimodal stimulation, 2) to identify potential modulators involved with the extraction of task-relevant information and 3) to replicate and provide further insight into the reduction of activity in S1 during continuous vibrotactile tracking observed previously by Meehan and Staines (2007a). Functional MRI (fMRI) and behavioral measures were acquired while participants applied graded force to a force-sensing resistor according to the intensity of a continuous vibrotactile stimulus or the spatial position of a simultaneously presented continuous visual stimulus. Unbeknownst to the participants we varied the temporal synchrony between the simultaneously presented target and distracter modalities by driving the continuous fluctuations in the vibrotactile and visuospatial stimuli with distinct or identical waveforms. Synchrony was manipulated without prior knowledge of the participant to avoid biasing the participants to a particular modality regardless of its task-relevance. In the case of low temporal synchrony the motor response dictated by the tracking target and distracter were distinct and tracking the task-irrelevant distracter modality resulted in poor tracking performance. However, in the high temporal synchrony case there was no such penalty to tracking the distracter, reducing sensorimotor conflict between the modalities. In all cases participants did not receive feedback as to their tracking accuracy. To address the purposes stated above we tested four hypotheses. 1) Tracking performance would benefit when the sensory-guided responses required by the target and distracter were not in conflict (high temporal synchrony) relative to when the simultaneous inputs conflicted in the required motor response (low temporal synchrony). 2) The increase in temporal synchrony would modulate S1 activation. 3) Reducing distraction by increasing temporal synchrony would be associated with increased activation in heteromodal areas such as the superior temporal sulcus, inferior parietal lobe and insula that have been previously implicated in detecting intermodal stimulus synchrony. 4) A comparison of the vibrotactile versus visuospatial tracking under low temporal synchrony would replicate our previous findings that S1 activity would be lower in the vibrotactile-tracking task (S. K. Meehan & Staines, 2007a).

3.3 Materials and Methods

3.3.1 Participants

Ten healthy volunteers (4 male, 6 female, age range 22-53) were recruited. All participants gave their written informed consent to participate in the study. The experimental procedures were approved by the Sunnybrook Health Sciences Centre Ethics Committee and the Office of Research Ethics at the University of Waterloo.

3.3.2 Experimental Tasks

For each of the ten participants, fMRI was performed in the presence of simultaneous binocular visuospatial and unilateral right vibrotactile stimulation (details below). Independent bimodal stimulation was delivered in a blocked design (10 s stimulation/20 s no stimulation, 10 repetitions). Prior to the start of each collection block participants were instructed to either track the intensity/position of one modality (target) while ignoring position/intensity of the other modality (distracter). Tracking was carried out by applying graded force to a force-sensing resistor mounted on a rigid plastic tube under the thumb of their left hand. In all cases participants did not receive any feedback as to their tracking performance.

During the vibrotactile tracking conditions participants were instructed to apply graded force that followed the intensity of the tactile stimulation so that as the intensity of the tactile stimulation increased, force applied to the resistor increased and as tactile intensity decreased the force applied decreased (Track Vibrotactile) (Figure 3-1A). During the visual tracking conditions participants were instructed to apply graded force in such a fashion that a needle position equivalent to seven o'clock represented minimal force, five o'clock represented maximal force and twelve o'clock represented intermediate force (Track Visuospatial) (Figure 3-1A).

In addition to tracking the target modality, the temporal synchrony between the tracking target and distracter modalities was also manipulated. In one set of conditions, the waveforms driving the target and distracter were distinct, such that changes in the spatial position of the needle in the dial and the vibrotactile stimulus required different motor responses (Low Synchrony) (Figure 3-1B). In a second set of conditions the waveforms driving the target and distracter were identical, such that changes in the spatial position of the needle and the intensity of the vibrotactile stimulation were linked and associated with the same motor output at any given point in time (High Synchrony) (Figure 3-1C). Manipulations of temporal synchrony were done without the prior knowledge of the subject, in order to prevent them from being biased to one specific modality over the other.

The experiment consisted of a 2 (Tracking Modality: Vibrotactile, Visuospatial) x 2 (Temporal Synchrony: Low, High) repeated measures design with four conditions in all: 1) Track Vibrotactile, Low Synchrony, 2) Track Vibrotactile, High Synchrony, 3) Track Visuospatial, Low Synchrony, and 4) Track Visuospatial, High Synchrony. Each condition was performed during a separate scan for a total of four functional scans per subject each five minutes in duration.

3.3.3 Somatosensory Stimulation

Somatosensory stimuli were presented via a custom-made MRI-compatible vibrotactile device (Graham et al., 2001). The vibrotactile device consisted of a plastic tube with a wooden dowel (1 cm diameter) extending from the body such that the index finger, when extended, rested over the dowel’s surface. The wooden dowel was controlled to vibrate at varying forces by passing fluctuating current through coils within the body of the vibrotactile device according to a 25 Hz sine wave with random intensity fluctuations. Vibrotactile stimulation was controlled by digitally generating waveforms that were converted to an analog signal at a rate of 100 Hz (DAQCard 6024E, National Instruments, Austin, Texas) and then amplified (Bryston 2B-LP, Peterborough, Ontario, Canada). Variation in amplitude of the driving voltage at a given frequency (25 Hz) led to proportionate increases in force applied by the dowel onto the finger. The vibrotactile waveform varied in average frequency from 0.10 Hz – 0.50 Hz superimposed upon the underlying 25 Hz vibrations and was generated as a random combination of 4 sinusoid waveforms of varying amplitude and frequency using Labview software (version 7.1, National Instruments, Austin, Texas). Output from the computer was routed through a penetration panel to the magnet room using a filtered 9-pin D sub-connector and shielded cable to ensure that no perceptible torque was produced by currents induced by radio-frequency transmit pulses or time-varying magnetic field gradients during imaging.

3.3.4 Visual Stimulation

The visuospatial stimulus was back projected (BoxLight 6000) onto a white screen placed at the bore of the magnet, in spatial alignment with the vibrotactile device and viewable to the subject via an angled mirror placed within the head coil. The visuospatial stimulus consisted of a white dial presented against a black background. Within the dial was a yellow needle that moved back and forth (with a maximum range of five to seven o'clock, via twelve o'clock) according to a randomly generated composite sine wave. The position of the needle was controlled by computer using the same Labview software as the vibrotactile device with an average frequency between 0.10 and 0.5 Hz.

3.3.5 Data Acquisition

Functional and anatomical imaging was performed at Sunnybrook Health Sciences Centre on a 3 T clinical whole body MRI scanner (GE HealthCare, Milwaukee, WI, USA) using a standard birdcage head coil with the head immobilized. Blood oxygenation level dependent (BOLD) images were acquired axially using gradient echo imaging with single-shot spiral in-out readout (TR = 2000 ms, TE = 30 ms, flip angle θ = 70°, FOV = 20, 26 slices, 5 mm slice thickness). Prior to acquisition of the functional data subjects underwent a high-resolution anatomical scan (TR = 12.4 ms, TE = 5.4 ms, flip angle θ = 35°, FOV = 20 x 16.5, 124 slices, 1.4 mm slice thickness) for later co-registration with the functional maps. Total scan time was approximately 40 minutes.

3.3.6 fMRI Data Analyses

For each scan a time series consisting of 154 images per slice location was generated by offline gridding and reconstruction of the raw data. The reconstructed time courses were analyzed using BrainVoyager QX 1.8 software (Brain Innovation, Maastricht, The Netherlands). Prior to further analysis, the first 4 volumes at each slice location were excluded to prevent artifact from transient signal changes as the brain reached a steady magnetized state. The following pre-processing steps were performed prior to co-registration: linear trend removal, temporal high pass filtering to remove non-linear low-frequency drift of 3 cycles or less per second and three-dimensional motion correction (using trilinear interpolation) to detect and correct for small head movements during the scan by spatially realigning all subsequent volumes to the fifth volume acquired. Estimated translation and rotation measures were visually inspected and never exceeded 1 mm and 1 degree, respectively. The functional data sets were transformed into Talairach space (Talairach & Tournoux, 1988) through co-registration with spatially transformed 3D anatomical data sets for each individual subject. The resulting volume time courses were filtered using an 8 mm Gaussian kernel at full width half maximum.

In order to statistically evaluate the relative differences across the four experimental conditions a multiple regression approach was employed using four predictors: 1) Track Vibrotactile, Low Synchrony, 2) Track Vibrotactile, High Synchrony, 3) Track Visuospatial, Low Synchrony, and 4) Track Visuospatial, High Synchrony, with the 20 s of no stimulation serving as a baseline. Four stimulation protocols using dummy-predictors (for those predictors not included in a given scan) were adopted and convolved with a boxcar haemodynamic response function (Boynton et al., 1996) to account for the expected shape and temporal delays of the physiological response. The resulting reference functions served as the model for the response time course functions used in the general linear model.

In order to assess task-related modulations a two-step approach was employed. First, a region of interest (ROI) analysis was employed to assess the relative effects of the experimental manipulations on S1. This is consistent with previous studies investigating attentional modulation of S1 that demonstrate an insensitivity of voxel-based approaches to early attentional modulations within this area (Johansen-Berg et al., 2000). Second, a voxel-based approach was then employed to determine additional areas that demonstrated task-related modulation.

For the ROI analysis a fixed effects general liner model was employed for each individual subject, scan and ROI. Anatomical markers were used to create separate masks for both the left (contralateral to the vibrotactile stimulation) and right (ipsilateral to the vibrotactile stimulation) S1 as defined in each individual according to the following landmarks: the central sulcus anteriorly, the medial wall of the "hand knob" medially and the most lateral edge of the post-central gyrus (Nelson et al., 2004). Any significant voxels that exceeded the Bonferroni corrected value of $p < 0.05$ were included in ROI analyses. Task-related changes were then quantified as changes in the intensity and volume of individual voxels relative to rest. For the intensity measurements the individual time course data for all significantly activated voxels within a cluster were extracted and averaged across each individual subject and condition. This resulted in one time series per subject per condition representing signal changes for the tracking relative to the rest blocks for a given scan. BOLD signal changes were expressed as a percentage relative to the baseline rest. For the volume measurements the total number of voxels that met the outlined criteria was represented as a percentage of the total number of voxels in the anatomical region defined using the landmarks stated.

Both the volume and intensity measures were analyzed using a 2 (Hemisphere: Ipsilateral, Contralateral) x 2 (Tracking Modality: Vibrotactile, Visuospatial) x 2 (Temporal Synchrony: Low, High) repeated measures analysis of variance (ANOVA) to assess any potential interactions between Hemisphere, Tracking Modality and Temporal Synchrony. Significant results were interpreted using *a priori* contrasts (where applicable) and statistical significance was defined as $p < 0.05$.

For the voxel-based analysis the same predictors outlined above in the ROI analyses were used. A separate subjects model was employed in which one predictor per condition per subject was generated and subjected to a 2 (Tracking Modality: Vibrotactile, Visuospatial) x 2 (Temporal Synchrony: Low, High) repeated measures ANOVA. Voxels were deemed significant if the threshold exceeded a corrected value of $p < 0.0001$ with a cluster threshold of 377 contiguous voxels (Forman et al., 1995). The center of gravity, volume and absolute t-statistics for each significant cluster for the main effect of Temporal Synchrony and the Tracking Modality x Temporal Synchrony interaction were then extracted. Areas demonstrating main effect of Tracking Modality, having previously been reported (S. K. Meehan & Staines, 2007a) were not of interest in the current paper and these analyses are not included. Contrasts were then computed for areas demonstrating significant changes in activation for the main effect of Temporal

Synchrony or for the Tracking Modality by Temporal Synchrony interaction to interpret changes observed.

3.3.7 Behavioral Data Analysis

Tracking performance for each condition was quantified by calculating the root mean square error (RMSE) of the difference waveform derived from the graded motor response and that driving the task-relevant target. Average RMSE was calculated according to the following. First, the amplitude of the task-relevant waveform was normalized to that of the motor response. Second, the first second of tracking and last second of tracking for each block during the scan was then excluded to avoid artificial increases in RMSE associated with initial lags in participant responses. Third, the remaining motor output waveform was then subtracted from the task-relevant sensory input at each data point, yielding a difference waveform. Finally, the RMSE of the difference waveform was computed and averaged for each condition across subjects. Therefore, a decrease in the RMSE implies a decrease in the difference between the motor output generated and the sensory task-relevant target supplied, or an increase in tracking performance. In contrast an increased RMSE implies that the difference between the motor output and sensory target increased, or tracking performance decreased.

Behavioral performance was assessed with a 2 (Tracking Modality: Vibrotactile, Visuospatial) x 2 (Temporal Synchrony: Low, High) repeated measures ANOVA using RMSE as the dependent variable. Due to technical difficulties with the force-sensing resistors during collection the behavioral data from three subjects was dropped from the tracking performance analyses. In order to address issues related to sample size and power due to the loss of behavioral data, three additional participants not included in the original functional imaging data set were placed into the scanner under identical conditions to those faced by the original participants. No functional MRI data was acquired and the additional participants ran through an abbreviated block design (20s stimulation/5s no stimulation, 4 repetitions).

3.4 Results

3.4.1 Behavioral Tracking Data

The means for each of the four experimental conditions are shown in Figure 3-2. A 2 (Tracking Modality: Track Tactile/Track Visual) x 2 (Temporal Synchrony: High/Low) ANOVA revealed a significant interaction between Tracking Modality and Temporal Synchrony [$F(1, 9) = 7.77$, $p < 0.02$). An inspection of Figure 3-2 reveals that the interaction is due to an increase in tracking performance during visual tracking in the high synchrony condition relative to the low synchrony condition (contrast; $p < 0.02$) and a slight, non-significant decrease in tracking performance in the high synchrony condition compared to the low synchrony condition during vibrotactile tracking. An ANOVA on the original seven participants whose behavioral data was collected during fMRI acquisition revealed a trend for an interaction [$F(1,6) = 3.70$, $p < 0.1$) that was identical to the pattern of results observed with the three additional participants suggesting that this interaction was present in the original group.

3.4.2 fMRI Data – S1 ROI Analyses

The contralateral S1 (relative to the vibrotactile sensory stimulus) anatomical ROI analyses revealed a region of increased blood flow, relative to rest, lateral to the "hand knob" of the central sulcus (average center of gravity Talairach x,y,z co-ordinates (SD across subjects): -51 (6), -28 (7), 44 (5)). The ipsilateral S1 (relative to the vibrotactile sensory stimulus) ROI analyses revealed a region of increased blood flow, relative to rest, encompassing both the medial and lateral aspects of the hand knob of the central sulcus (average center of gravity: 40 (2), -27 (3), 49 (3)).

A three-way ANOVA on the mean volume of activation, expressed as a percentage of the total volume of the original S1 anatomical ROI, revealed a significant Hemisphere x Tracking Modality interaction [$F(1,9) = 5.09$, $p < 0.05$] as well as main effects of Hemisphere [$F(1,9) = 58.60$, $p < 0.00003$] and Tracking Modality [$F(1,9) = 14.53$, $p < 0.004$]. Contrasts revealed that the mean percent volume of activation was reduced during vibrotactile tracking compared to visuospatial tracking for both the contralateral and ipsilateral S1 ROIs, (both contrasts, $p < 0.01$) however this reduction was greater for ipsilateral S1 (Figure 3-3A).

A three-way ANOVA on the mean percent signal change, relative to rest, revealed a moderate trend for an effect of Tracking Modality [F(1,9) = 4.32, $p < 0.07$]. The main effect of Tracking Modality can be attributed to a greater percent signal change during visuospatial tracking compared to vibrotactile tracking for both the contralateral and ipsilateral S1 (Figure 3-3B).

3.4.3 fMRI Data – Whole Brain Analyses

3.4.3.1 Main Effect of Temporal Synchrony - Task-Related Changes Regardless of Tracking Modality

Figure 3-4 shows the statistical contrast maps for the main effect of Temporal Synchrony (Low Synchrony vs. High Synchrony regardless of modality tracked). The network of areas that demonstrated increased activation in the Low Synchrony relative to High Synchrony conditions are shown in Figure 3-4A. The center of gravity and t-statistics are shown in Table 3-1. These areas included a number of frontal areas, as well as bilateral insula (BA 13), bilateral superior temporal gyrus (BA 22) and areas of the primary and secondary visual cortices.

In addition another network of cortical areas demonstrated greater activation in the High Synchrony relative to Low Synchrony conditions. This left-hemisphere dominated network (contralateral to the vibrotactile stimulation) is shown in Figure 3-4B while the center of gravity and t-statistics are shown in Table 3-1. These areas included the superior and medial frontal gyri (BA 8 and 10), as well as the middle temporal gyrus (BA 39) and the fusiform gyrus (BA 37).

3.4.3.2 Interaction Effects: Tracking Modality x Temporal Synchrony

The interaction between Tracking Modality and Temporal Synchrony refers to those areas that demonstrated differential modality-specific modulation between High Temporal Synchrony and Low Temporal Synchrony. Those areas that demonstrated a significant interaction between tracking modality and temporal synchrony are shown in Figure 3-5. The center of gravity and t-statistics are shown in Table 3-2.

Contrasts revealed that the interaction near the TPJ centered on the middle temporal gyrus (BA 19, extending into BA 39) could be attributed to an increase in activation during vibrotactile tracking under high temporal synchrony (relative to low temporal synchrony) but no change in during visuospatial tracking. In contrast the significant interactions observed in the left post-central gyrus (BA 40) and inferior parietal lobule (BA 40) could be attributed to increased activation during vibrotactile tracking under low temporal synchrony.

The interaction effect observed in the left superior temporal gyrus can be attributed to an increase in activation during visuospatial tracking under high temporal synchrony (relative to low synchrony) but no change during vibrotactile tracking. In contrast the significant interactions observed in the right post-central gyrus (BA 5), right superior parietal lobe (BA 7) and right superior temporal gyrus (BA 22) can be attributed to an increase in activation during visuospatial tracking under low temporal synchrony but no change during vibrotactile tracking.

3.5 Discussion

The present study assessed the effect of temporal synchrony between simultaneously presented vibrotactile/visual stimuli upon task-relevant modulation of tracking performance and cortical activation (including S1) during continuous sensory-guided movement. Functional MRI was acquired when participants tracked changes in the target modality while ignoring those in an irrelevant distracter modality. Temporal synchrony was manipulated by changing the stimulus-response relationships between the simultaneously presented target and distracter modalities. The specific hypotheses were partially supported. As hypothesized tracking performance increased during visuospatial tracking during high temporal synchrony compared to low synchrony, however, this was not the case during vibrotactile tracking. Changes in temporal synchrony were not reflected at the level of S1 as tracking performance and S1 activation were dissociated. Instead changes in temporal synchrony were observed in networks of higher order heteromodal areas including networks sensitive to temporal synchrony regardless of the modality to be tracked, networks sensitive to temporal synchrony specific to vibrotactile tracking and those sensitive to temporal synchrony specific to visuospatial tracking. Finally, as hypothesized S1 activation was reduced during continuous vibrotactile tracking relative to during continuous visuospatial tracking in the presence of an irrelevant vibrotactile stimulus.

Participants tracked both the vibrotactile and visuospatial stimuli equally well and as hypothesized visuospatial tracking benefited from a non-conflicting temporally synchronous distracter modality. It was thought altered task-demands associated with increased temporal synchrony would result in increased tracking performance due to decreased feed-forward competition between the representations of each modality. There are two possible explanations for this benefit. First, intermodal selective attention was more effective at extracting the target modality due to a change in distracter salience when it was in temporal synchrony (required the same motor response) as the visuospatial target. Alternatively, it is possible that the task-irrelevant representation of the non-conflicting vibrotactile distracter simply fed forward along the hierarchical model and was integrated involuntarily into the motor response due to the spatial and temporal relationship between the target and distracter modalities resulting in a benefit to tracking performance (Murray et al., 2005), similar to the ventriloquist and McGurk effects without the detriment to performance (Macaluso, George, Dolan, Spence, & Driver, 2004). In contrast to the visuospatial task, vibrotactile-tracking performance was not altered by the temporal synchrony between the vibrotactile target and visuospatial distracter. During stimulus onset asynchrony visual-tactile congruency effects are larger when the visual stimulus precedes a tactile stimulus (Shore et al., 2006). Therefore, it is possible that the differential effect of temporal synchrony may be explained by differences in task-demands associated with the nature of the information extracted from a vibrotactile versus visuospatial stimulus.

A key finding in this study was that S1 activation volume was not influenced by the temporal synchrony between the target and distracter modalities. This is consistent with our previous work (S. K. Meehan & Staines, 2007a) and others (Murray et al., 2005) demonstrating insensitivity of S1/early cortical activity to the *spatial* relationship between simultaneous presented intermodal stimuli despite behavioral task performance differences. Previously we offered two alternate hypotheses to explain the lack of spatial interaction at the level of S1, 1) that there was a lack of explicit value associated with spatial location to the tracking task and/or 2) there was a lack of higher level feedback to S1. Similar to the manipulation of spatial location temporal synchrony does not appear to mediate primary cortical activity beyond that already associated with tracking modality.

This would suggest that intermodal selective attention works at the level of S1 to extract task-relevant information (possibly through low-level pathways) but works at subsequent processing levels to extract other features (via top-down feedback from heteromodal areas). This notion is supported by previous work demonstrating excitatory changes in primary visual cortex during somatosensory processing but inhibitory changes in secondary and subsequent visual areas (Merabet et al., 2007). Alternatively it is possible that the temporal synchrony manipulation was not strong enough to elicit any differences although this seems unlikely due to the behavioral interaction observed.

The decrease in S1 activation volume, contralateral to the vibrotactile stimulus, during vibrotactile tracking compared to visuospatial tracking was similar to that which we previously observed (S. K. Meehan & Staines, 2007a). This result was novel as previous studies investigating intermodal selective attention (Johnson & Zatorre, 2005; 2006; Shomstein & Yantis, 2004) are generally associated with increased activation over modality-specific cortices of the relevant modality. In the current study we also observed a decrease in the intensity of activation (% signal change) within the same contralateral S1 that mirrored the volume changes, a change not observed in our previous work. In addition, we also report similar changes in S1 activation, ipsilateral to the vibrotactile stimulus (but contralateral to the motor response). These additional results offer further insight into potential explanations originally offered (S. K. Meehan & Staines, 2007a) for this novel result. Although the decrease in volume of activation of contralateral S1 supports surround inhibition (Drevets et al., 1995) associated with vibrotactile tracking the concomitant decrease in signal intensity within contralateral S1 make it unlikely as one would expect to see either no change or an increase in signal intensity associated with a facilitation of the neuronal activity of the core set of relevant neurons. Of the two remaining explanations, the role of low-level influences (Cappe & Barone, 2005; Foxe et al., 2000) and/or inter-hemispheric cortical-cortical interactions (Hlushchuk & Hari, 2006; Hoshiyama & Kakigi, 1999; Seyal et al., 2005), the most plausible is that the decreased S1 activation is due to an interaction between inter-hemispheric and intermodal selective attention mechanisms brought about by the presence of functionally relevant somatosensory information in S1 ipsilateral to the vibrotactile stimulus but contralateral to the sensory feedback from the continuous movement.

Inter-hemispheric interactions have been demonstrated using cooling of ipsilateral S1 (Clarey et al., 1996) and repetitive TMS over ipsilateral M1 (Seyal et al., 2005). Cooling of ipsilateral S1 results in an increase in the receptive field of contralateral S1, thought to be mediated by the removal of tonic inhibition from the cooled ipsilateral S1 while repetitive TMS over ipsilateral primary motor cortex can reduce the amplitude of early SEP potentials in S1 as well as perceptual threshold. However, inter-hemispheric interactions are generally associated with a negative correlation between the hemispheres. Yet in the current study both contralateral and ipsilateral S1 demonstrate identical patterns of excitability changes, both demonstrating reduced excitability during vibrotactile tracking. Alternatively, the influence of low-level connections between the two modalities cannot be ruled out as it has been demonstrated that during tactile sensory processing, primary visual cortex demonstrates increased activity despite decreased activity in secondary visual cortices (Merabet et al., 2007). Therefore, it is possible that the increase in S1 activation may be attributable to co-activation during visuospatial tracking. However, under this explanation one might expect no difference in S1 activation during visuospatial and vibrotactile tracking. Therefore it is possible that the reduction in S1 activation may be attributable to an interaction between these mechanisms associated with the different task demands imposed by the continuous tracking requirement use currently and perceptual tasks used previously. We suggest that participants may employ a task-switching strategy, in order to perform the tracking task correctly, due to the need to simultaneously extract the vibrotactile sensory stimulus and monitor proprioceptive feedback from the motor effector that recruits intramodal selective attention mechanisms due to the competition between the two relevant somatosensory inputs. This mechanism results in a competitive disadvantage within S1 of both hemispheres that is not present during visuospatial tracking because the contralateral vibrotactile sensory inputs are irrelevant returning ipsilateral activation to baseline. However, intermodal mechanisms result in contralateral S1 activation associated during visuospatial tracking. Under this hypothesis one would expect a relative decrease in both ipsilateral and contralateral S1 during vibrotactile tracking relative to visuospatial tracking with the interaction between the two mechanisms resulting in parallel changes in activation with S1 of both hemispheres.

In addition to investigating changes in S1 we observed additional areas that were sensitive to the temporal synchrony between the target and distracter regardless of tracking modality. Areas that demonstrated increased activation during tracking under high synchrony compared to low temporal synchrony included an area of the middle temporal gyrus (BA 39) near the temporal-parietal junction, the fusiform gyrus (BA 37), superior frontal gyrus (BA 8) and medial frontal gyrus (BA 10). In particular, the superior frontal gyrus (BA 8) has been suggested to be part of a network, including the superior colliculus, involved in cross-modal integration of synchronous sensory inputs (Calvert, Hansen, Iversen, & Brammer, 2001). This area as well as those around the middle temporal (BA 39) and inferior frontal/fusiform gyri (BA 37) have also been implicated in the detection and extraction of task relevant information, presumably the detection, extraction and integration of the irrelevant modality during cases of high temporal synchrony.

In addition, a large network of areas demonstrated increased activity during tracking under low temporal relative to high temporal synchrony (Table 3-1 bottom). The increased activation in these areas likely reflects the increased task demands associated with extracting the relevant information and the subsequent sensorimotor transformations under low temporal synchrony. In particular, left insular activation (BA 13) has been associated with extraction of task-relevant information in the presence of cross-modal irrelevant distracters (Downar et al., 2001). The superior temporal gyrus (BA 22) is often associated with multisensory integration, however, the associated activation is generally reported in the posterior portions of the gyrus compared to the more anterior activation reported here, perhaps reflecting consciousness-related binding (Bischoff et al., 2007). Other areas including the medial frontal gyrus (BA 6) in the area of the SMA and the inferior frontal gyrus (BA 9) also known as the dorsolateral prefrontal cortex have been implicated with selective attention and the extraction of task-relevant information (Staines et al., 2002), demands that are more prevalent during tracking under low temporal synchrony.

In addition to areas that were influenced by temporal synchrony regardless of tracking modality there were a number of areas that demonstrated differential effects dependent upon the tracking modality and the irrelevant distracter modality (Table 3-2).

Only an area of the TPJ (middle temporal gyrus, BA 19/39) demonstrated increased activation during high temporal synchrony but only during vibrotactile tracking. This heteromodal area has been implicated in the extraction of task-relevant as well as multisensory integration (Matsuhashi et al., 2004) and may reflect the detection/extraction of potentially task-relevant information from the distracter modality due to the high temporal synchrony and resulting convergence of the vibrotactile and visuospatial representations. This is supported by the change in tracking performance. In contrast, areas of the inferior parietal lobule and post-central gyrus (BA 40) sensitive to low temporal synchrony specific to vibrotactile tracking supports evidence of their role in somatosensory processing (Johansen-Berg & Lloyd, 2000) and likely reflects task-relevant facilitation during situations where extraction of task-relevant somatosensory information is critical to task performance (Staines et al., 2002).

For the interaction between temporal synchrony of competing sensory targets and the specific task-relevant modality, only the middle to anterior portion of the left superior temporal gyrus (BA 22) demonstrated increased activation under high temporal synchrony specific to visuospatial tracking. Again, this area may reflect consciousness-related binding (Bischoff et al., 2007) and may be associated with increased tracking performance in this condition. In contrast a number of areas demonstrated increased activation during low temporal synchrony relative to high temporal synchrony that was specific to visuospatial tracking. This specific sensitivity can likely be attributed to the change in task demands associated with the visuospatial stimulus. In particular, increased activation in the right superior parietal lobe (BA 5) during visuospatial tracking under low synchrony could be attributed to the increased demand on these areas during visuomotor transformations, including reference frame transformations (Buneo & Andersen, 2006).

In conclusion, this study demonstrated that temporal synchrony between a visuospatial and vibrotactile stimulus is not reflected at the level of S1 despite previous evidence to suggest that it is reflected at the level of modality-specific cortex. Instead it appears that areas of the TPJ, superior temporal gyrus and anterior insula may mediate detection of temporal synchrony and task-relevance. In contrast to temporal synchrony, the relevance of the vibrotactile stimulus does appear to be reflected at the level of S1 when it is presented with a concurrent visuospatial stimulus regardless of temporal synchrony. Further, this relevance representation in S1, manifested as a decrease in activation when the vibrotactile stimulus is task-relevant, appears to be the result of inter-hemispheric influences between sensorimotor cortex associated with the continuous tracking aspect of the current task, not present during visuospatial tracking, that may interact with the traditional facilitatory intermodal selective attention mechanisms. This suggests that sensorimotor requirements may have an important modulatory role in modulating feed-forward activation within primary somatosensory cortex compared to top-down effects from heteromodal areas. This could have implications for the efficacy of rehabilitative strategies in functional recovery after sensorimotor damage.

Table 3-1: Activated Clusters from areas demonstrating a main effect of Temporal Synchrony. Areas are separated according to direction of significant effect

Condition	Anatomical (Brodmann) Area	X	Y	Z	t-statistic
Main Effect: Temporal Synchrony					
Areas demonstrating greater activation during Low Synchrony relative to High Synchrony					
	Lt. Medial Frontal Gyrus (BA 6)	-7	-7	62	4.70
	Rt. Inferior Frontal Gyrus (BA 9)	48	12	23	4.57
	Bil. Insula (BA 13)	-31/30	25/26	6/5	5.22/5.83
	Bil. Superior Temporal Gyrus (BA 22)	-65/59	-37/-35	10/14	5.06/5.61
	Rt. Superior Frontal Gyrus (BA 10)	34	49	24	4.78
	Rt. Inferior Occipital Gyrus (BA 17)	17	-89	-7	4.89
	Lt. Lingual Gyrus (BA 18)	-23	-69	-13	4.95
	Rt. Inferior Temporal Gyrus (BA 20)	50	-25	-15	5.94
	Rt. Cerebellum - Posterior Lobe, Tuber	37	-66	-25	4.99
	Rt. Cerebellum - Posterior Lobe, Cerebellar Tonsil	27	-41	-36	4.54
	Lt. Cerebellum – Posterior Lobe, Semi-lunar Lobule	-35	-63	-36	4.93
	Rt. Cerebellum – Anterior Lobe, Culmen	18	-54	-18	4.55
Areas demonstrating greater activation during High Synchrony relative to Low Synchrony					
	Lt. Superior Frontal Gyrus (BA 8)	-16	33	45	5.04
	Lt. Medial Frontal Gyrus (BA 10)	-2	68	13	4.62
	Lt. Middle Temporal Gyrus (BA 39)	-46	-70	20	5.58
	Lt. Fusiform Gyrus (BA 37)	-43	-51	-13	5.05

Table 3-2: Activated Clusters from areas demonstrating a Tracking Modality x Temporal Synchrony interaction effect. Areas are separated according to effects driving interaction as revealed by contrasts

Condition	Anatomical (Brodmann) Area	X	Y	Z	t-statistic
Interaction: Modality x Synchrony					
Areas demonstrating increased activation during High Synchrony relative to Low Synchrony during vibrotactile tracking only					
	Lt. Middle Temporal Gyrus (BA 19)	-43	-59	15	4.94
Areas demonstrating increased activation during Low Synchrony relative to High Synchrony during vibrotactile tracking only					
	Lt. Post-Central Gyrus (BA 40)	-64	-18	16	5.83
	Lt. Inferior Parietal Lobule (BA 40)	-53	-31	34	4.99
Areas demonstrating increased activation during High Synchrony relative to Low Synchrony during visuospatial tracking only					
	Lt. Superior Temporal Gyrus (BA 22)	-62	3	-5	5.56
Areas demonstrating increased activation during Low Synchrony relative to High Synchrony during visuospatial tracking only					
	Rt. Post-Central Gyrus (BA 5)	25	-40	64	4.77
	Rt. Precuneus (BA 7)	13	-57	61	4.63
	Rt. Superior Temporal Gyrus (BA 22)	52	-45	16	5.11

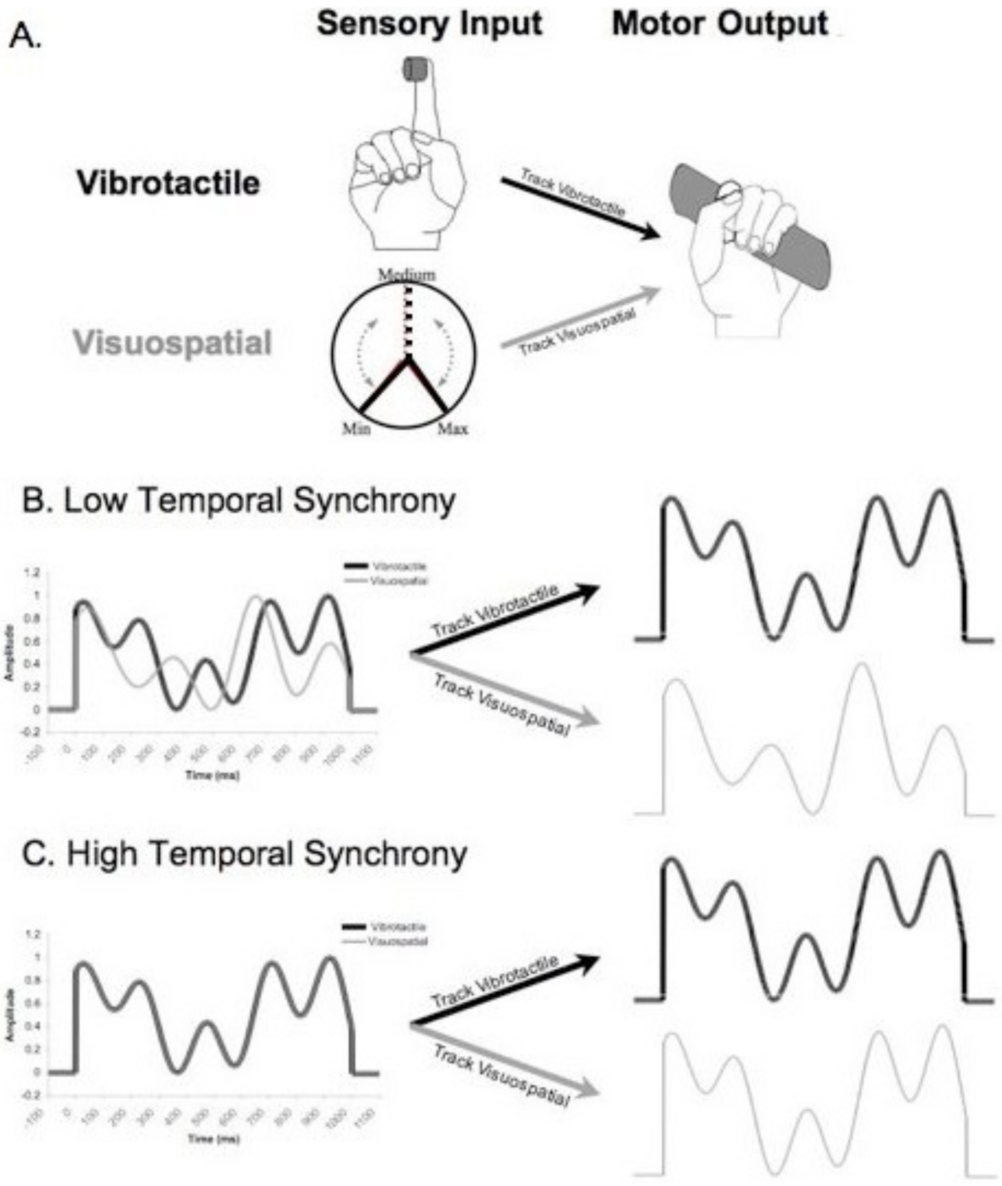


Figure 3-1: (A) Example of the experimental design. Subjects were presented with a vibrotactile stimulus on their right index finger and a bilateral visuospatial stimulus, simultaneously. On any given scan subjects tracked either the intensity of the vibrotactile stimulus or the spatial position of the needle of the dial by applying graded force to a force sensing resistor in their right hand. In the case of track visuospatial, movement of the needle to the right was a sign for subjects to apply greater force to the FSR while movement to the left required less force to be applied. Prior to the start of the scan subjects were instructed to track one of the modalities and ignore the other. (B) An example of the stimulus waveforms and the motor output required for the track tactile and track visual conditions in the presence of low temporal synchrony (see text for details). (C) An example of the stimulus waveforms and the motor output required for the vibrotactile and visuospatial tracking conditions in the presence of high temporal synchrony (see text for details).

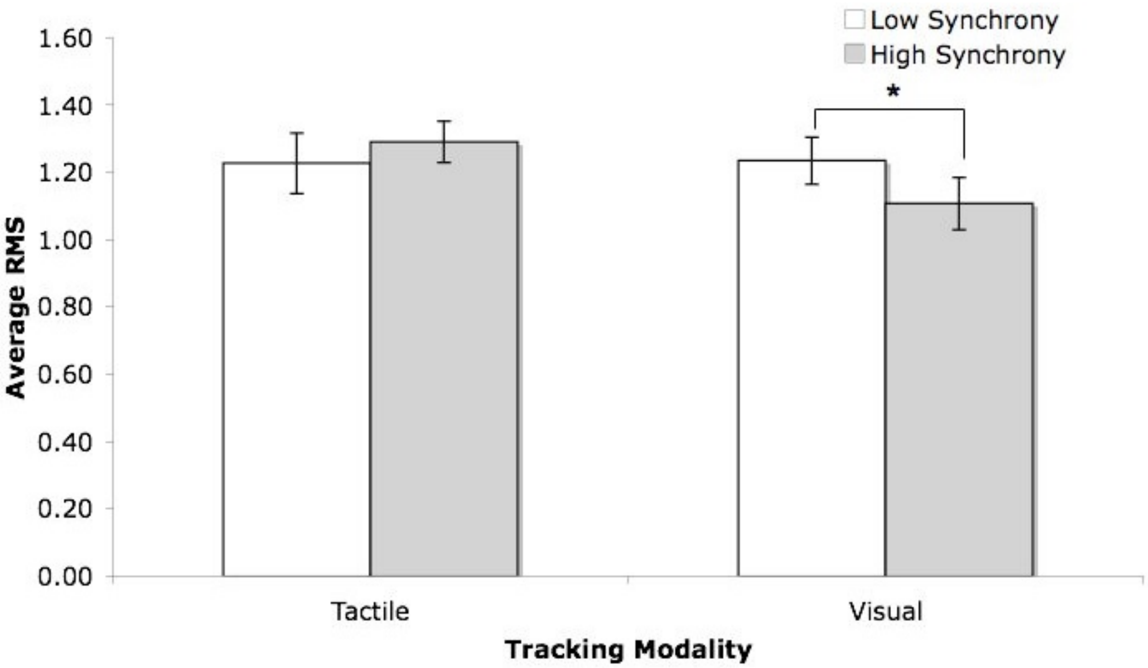


Figure 3-2: A plot of the average normalized RMS values for the tracking modality and temporal synchrony. * denotes $p < 0.05$. See text for details on calculation of average RMS.

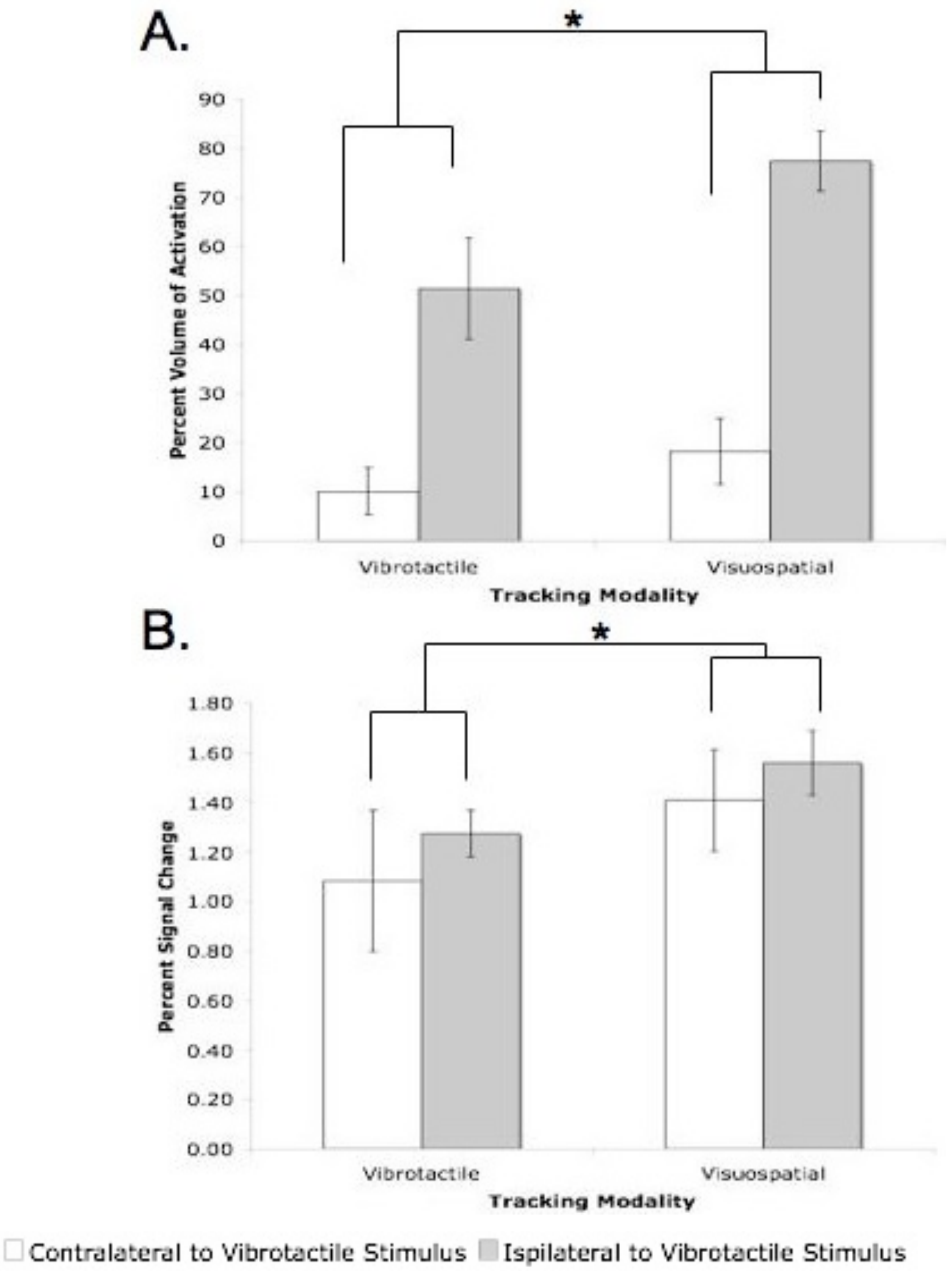


Figure 3-3: (A) Plot showing the means for the percent volume of activation for the significant Hemisphere (relative to the vibrotactile stimulus) x Tracking Modality interaction. Volume is defined as the percentage of significantly active voxels relative to the total volume of the anatomically defined primary somatosensory cortex (see text for details). (B) Plot showing the means for the percent signal change for the Hemisphere (relative to the vibrotactile stimulus) and Tracking Modality main effects. Signal change is defined as the percent signal change relative to the baseline signal for the significantly activated cluster within the anatomically defined primary somatosensory cortex (see text for details). * denotes $p < 0.05$.

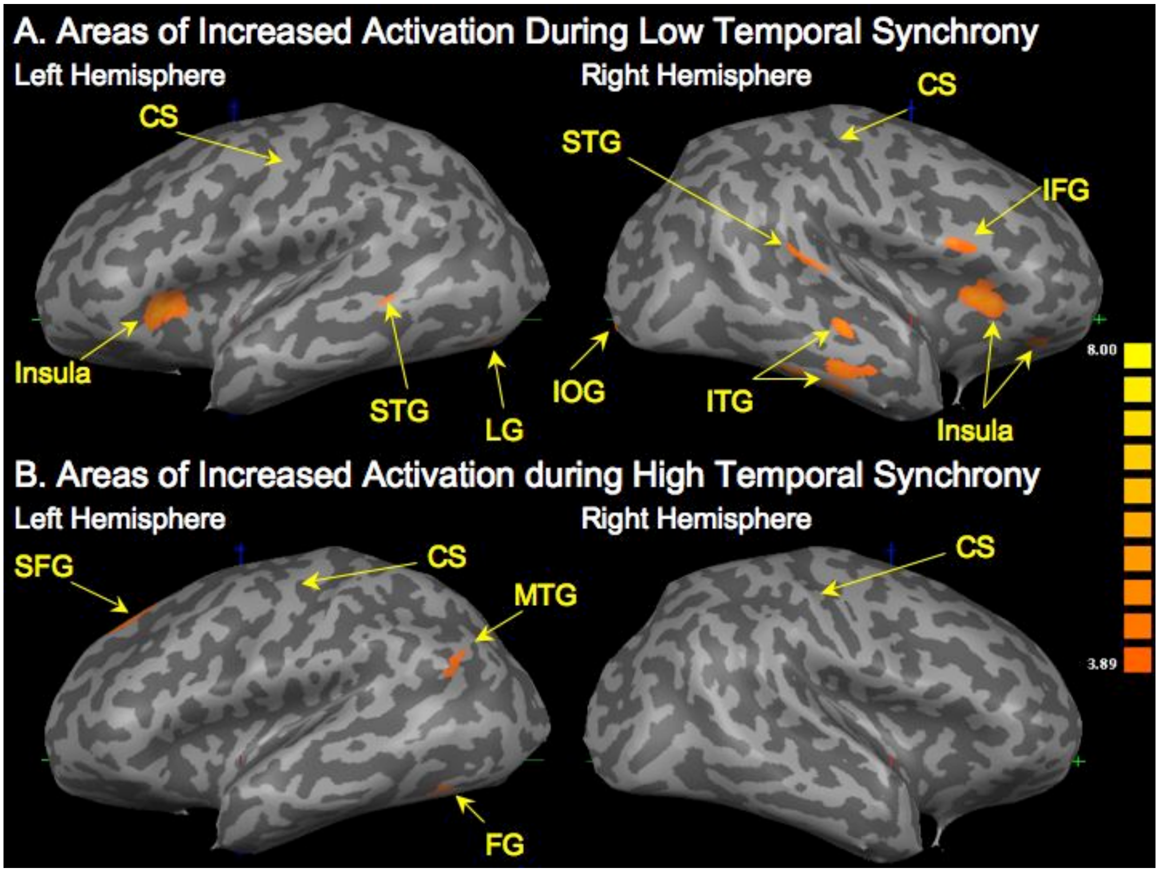


Figure 3-4: Map for areas demonstrating a main effect of Temporal Synchrony split according to direction of significant effect. (A) Map of areas demonstrating greater activation during low temporal synchrony relative to high temporal synchrony. Note, left medial frontal gyrus and right superior frontal gyrus not visible. (B) Map of areas demonstrating greater activation in during high temporal synchrony relative to low temporal synchrony. Note: medial frontal gyrus not visible. The maps are overlaid on an individual's inflated cortex and the colour scale reflects t-values. CS – central sulcus, IFG – inferior frontal gyrus, STG – superior temporal gyrus, ITG – inferior temporal gyrus, LG – lingual gyrus and IOG – inferior occipital gyrus.

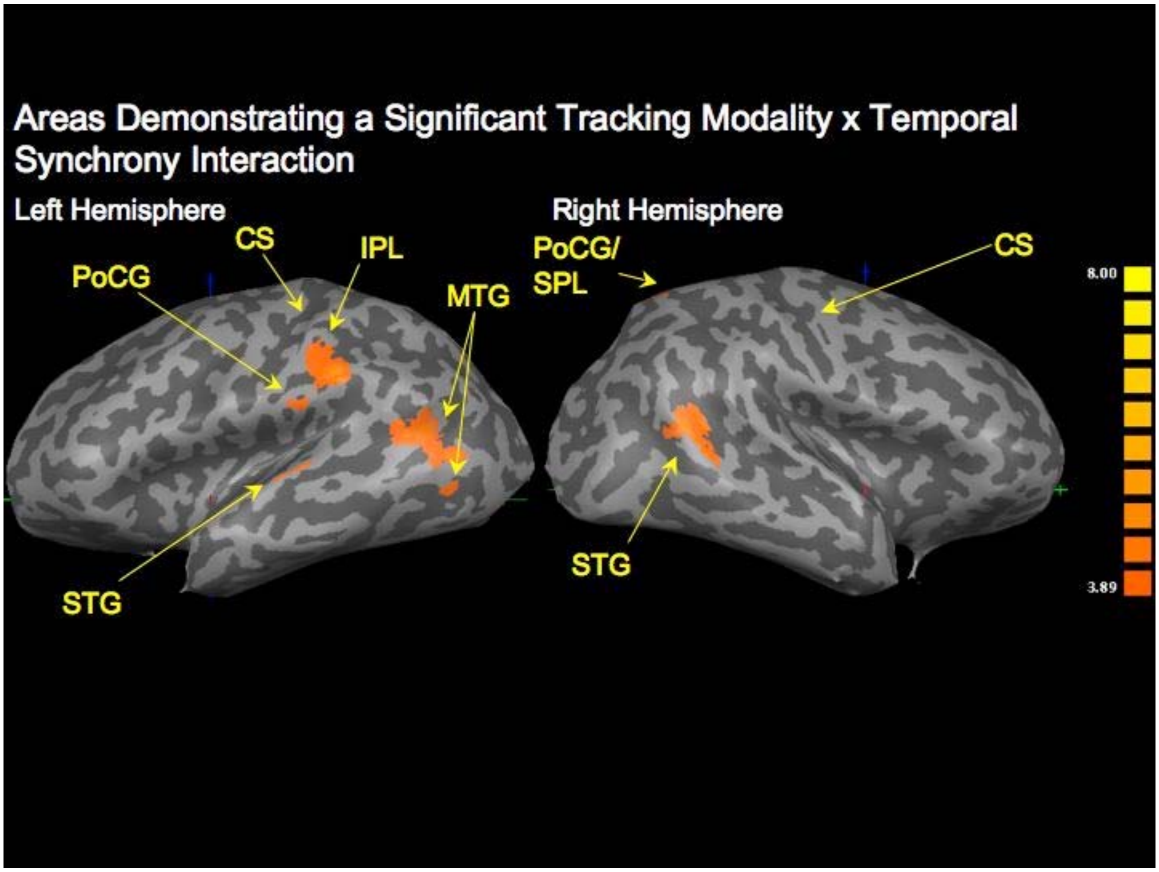


Figure 3-5: (A) Map for areas demonstrating a significant Tracking Modality x Temporal Synchrony interaction, see text and Table 2 for interpretation. The colour scale reflects t-values. CS – central sulcus, PoCG/SPL – post-central gyrus/superior parietal lobule, IPL – inferior parietal lobule, STG – superior temporal gyrus, MTG – middle temporal gyrus**.**

CHAPTER 4 – Intermodal modulation of early SEP components

4.1 Abstract

It has been demonstrated that attention can influence sensory processing as early as the first arrival of sensory information to primary somatosensory cortex (S1). However, intermodal effects upon sensory processing are generally observed much later. This may be attributable to differences in task demands and/or recording techniques. The present paper used somatosensory evoked potentials (SEPs) to 1) investigate intermodal attention effects upon early somatosensory processing in S1, 2) determine the role of spatial and temporal relationship between bimodal stimuli upon this processing and 3) the relationship this has to behavior. SEPs were evoked while participants received simultaneous bimodal (vibrotactile/visual) stimulation and continuously tracked random changes in one modality, by applying graded force to a force-sensing resistor. Spatial relationship was manipulated by placing the visual stimulus in the same or opposite hemi-field as the vibrotactile stimulus. Temporal synchrony was manipulated by altering the pattern of intensity changes such that they followed identical or different patterns. Increased spatial relationship reduced whereas increased temporal synchrony increased the amplitude of the P27 SEP component generated in Brodmann Area 1. Temporal synchrony also modulated P50 amplitude. In contrast, the N140 demonstrated greater amplitude during vibrotactile tracking as opposed to visual tracking. The results suggest that intermodal effects can occur much earlier than previously reported. In addition, behavioral performance appears to be associated with early SEP modulation and highlights the potential importance of early sensory processing to task performance. These results have implications for future studies investigating intermodal effects upon somatosensory processing.

4.2 Introduction

Neuroimaging studies of somatosensory processing have shown early attentional modulation of afferent somatosensory information as early as primary somatosensory cortex (S1) (Johansen-Berg et al., 2000; Staines et al., 2002). Electrophysiological studies have shown that these effects are present in the N140 component of the somatosensory event-related potential (ERP) (Eimer & Forster, 2003a; 2003b). Recently, it has been demonstrated that intermodal attention effects are also manifested within these same areas traditionally defined as modality specific (Kida, Inui, Wasaka, Akatsuka, Tanaka, & Kakigi, 2007b; Ohara et al., 2006; Taylor-Clarke et al., 2002). However, two issues with the use of ERPs to investigate changes in cortical activation within primary sensory cortex are 1) they typically do not elicit the earliest cortical potentials reflecting the first arrival of somatosensory information to S1 and 2) they are generally elicited using perceptual tasks that do not reflect the sensorimotor aspect associated with sensory processing.

Recently, it has been demonstrated using SEPs elicited by median nerve stimulation at the wrist, that somatosensory processing of a tactile stimulus shows attentional modulation as early as the P27 SEP component during a continuous sensory-guided tracking task (Legon & Staines, 2006). This modulation appears to reflect the attentional demands imposed by the task. In addition, it has been demonstrated that motor cortex can influence both ipsilateral and contralateral S1 (Mochizuki et al., 2004; Seyal et al., 2005) suggesting that the continuous motor requirement may have an influence upon sensory processing earlier than those processes reflected by later potentials like the N140. This notion was furthered by two recent neuroimaging studies investigating intermodal selective attention during a continuous sensorimotor task (S. K. Meehan & Staines, 2007a; 2007b). The continuous tracking requirement was associated with changes as early as S1 suggesting that intermodal attention effects may be mediated much earlier than previously observed in ERP studies.

The current study exploited the temporal resolution provided by SEPs to determine whether intermodal influences are present during the first steps of somatosensory processing, reflected in amplitude changes of the N20, P27 and P50 SEP components during a continuous sensorimotor task. These components have been localized to Brodmann areas 3b/1 and are generally believed to reflect thalamo-cortical projections to S1 (1991; Allison, McCarthy, & Wood, 1992). It was hypothesized that the amplitude of these potentials would be decreased during continuous tactile tracking compared to visual tracking, similar to the decreased activation in S1 reported previously. In addition to these early cortical potentials, N140 amplitude was also measured to investigate the intermodal effects previously observed during later stages of processing.

Further, we investigated the effects of spatial relationship and temporal synchrony between the two intermodal sources of information upon these early cortical potentials. Research using perceptual tasks has suggested that these factors can influence cortical processing during intermodal selective attention (Eimer & Van Velzen, 2002). However, recent neuroimaging studies (S. K. Meehan & Staines, 2007a; 2007b) suggest that these factors are not reflected at the level of S1. Based upon the latter it was hypothesized that early cortical potentials would be insensitive to these manipulations.

4.3 Materials and Methods

4.3.1 Participants

Thirteen healthy volunteers (6 male, 7 female, 21-31yrs) were recruited. All participants gave their informed consent to participate in the study and the experimental procedures were approved by the Office of Research Ethics at the University of Waterloo.

4.3.2 Tasks and Stimuli

For each of the participants, somatosensory and visual evoked potentials were elicited in the presence of simultaneous vibrotactile and visual stimulation. Vibrotactile stimulation was delivered via a modified speaker. Participants were instructed to rest their index finger upon a piece of Velcro® (1 cm x 1 cm) attached to the dust cap located at the center of the speaker’s diaphragm. The dust cap vibrated at varying forces by passing fluctuating current through the voice coil of the speaker via a 25 Hz sine wave with random intensity fluctuations. Vibrotactile stimulation was controlled by digitally generating waveforms that were converted to an analog signal (DAQCard 6024E, National Instruments, Austin, Texas) and then amplified (Bryston 2B-LP, Peterborough, Ontario, Canada). Variation in the amplitude of the driving voltage at the given frequency (25 Hz) led to proportionate increases in force on the volar surface of the finger. The vibrotactile waveform varied in average frequency from 0.10 Hz – 0.50 Hz superimposed upon the underlying 25 Hz vibrations and was generated as a random combination of 4 sinusoid waveforms of varying amplitude and frequency using custom software (Labview 7.1, National Instruments, Austin, Texas) (S. K. Meehan & Staines, 2007a; 2007b).

The visual stimulus consisted of a light-emitting diode (Bright Lite, 10 mm, 100 millicandle, red diffused LED) placed in front of a flat screen monitor (SyncMaster 171s) with a visual angle of 4°. Similar to the vibrotactile stimulus the intensity of the visual stimulus was controlled by passing randomly fluctuating voltage through a 5-volt resistor attached to the LED. Voltage was controlled by digitally generating waveforms that were converted to an analog signal using the same Labview software and digital to analog boards as those that controlled the vibrotactile stimulation.

Bimodal stimulation was delivered in a blocked design (45 s stimulation/15 s no stimulation, 4 repetitions). Prior to the start of each block, participants were instructed to track the amplitude of the intensity of one modality (target) while ignoring that of the other modality (distracter). Tracking was carried out by applying graded force to a pressure sensitive bulb held in their left hand. These signals were stored on computer for later analysis.

During the vibrotactile tracking (Vibrotactile) conditions participants were instructed to continuously track the amplitude of the vibrotactile stimulation on their right index finger by applying graded force to the bulb held in their left hand. During the visual tracking (Visual) conditions participants were instructed to apply graded force that followed the amplitude of luminance changes in the LED.

In addition to tracking the target modality there were two further experimental manipulations. In one set of conditions the spatial relationship was manipulated while in another set of conditions the temporal synchrony between the target and distracter modalities was manipulated. Spatial relationship had two levels, distinct and related, and was manipulated by placing the LED directly above the speaker on the same side (Related) or in the opposite hemi-space (Distinct) (Figure 1A). Temporal synchrony also had two levels, asynchronous and synchronous. In both cases spatial relationship was held constant in the Related configuration while the waveforms that drove the vibrotactile and visuospatial stimulation were either the same (Synchronous) or different (Asynchronous) (Figure 1B). Manipulations of temporal synchrony were done without the prior knowledge of the subject, in order to prevent an overt bias to one modality over the other. These manipulations resulted in eight experimental conditions (Target Modality, Distracter Characteristic): 1) Vibrotactile, Distinct, 2) Vibrotactile, Related, 3) Visual, Distinct, 4) Visual, Related, 5) Vibrotactile, Asynchronous, 6) Visual, Asynchronous, 7) Vibrotactile, Synchronous, 8) Visual, Synchronous. The Related and Asynchronous conditions were physically identical in terms of set-up and stimulation. These conditions were only performed once.

Three additional control conditions were performed: 1) Motor Control 2) Spatial Control and 3) Synchrony Control. For Motor Control, participants performed a self-paced gradual isometric squeezing of the bulb in their left hand, in the absence of vibrotactile and visual stimulation while in the latter two conditions participants received asynchronous or synchronous bimodal stimulation, respectively, but were not required to track either modality.

All conditions were performed in a sound-attenuating chamber (IAC, NY) with the lights off to maximize the luminance of the visual stimulus. Participants received 70 dB whitenoise (70 dB – Stim2, Neuroscan, Compumedics USA, Ltd. Corp., Charlotte, NC) throughout the experiment to prevent auditory perception of the vibrotactile stimulus. This was verbally confirmed with each participant.

4.3.3 Recording and Quantification of Evoked Potentials

Both somatosensory (SEPs) and visual evoked potentials (VEPs) were elicited during all conditions. SEPs were derived from electrical stimulation to the median nerve (MN) at the wrist of the right hand that received vibrotactile stimulation. Square wave pulses of 0.5 ms duration (GRASS S88X Stimulator with SIU-V isolation unit, West Warwick, RI) were delivered through surface electrodes fixed to the wrist. MN stimuli were pseudorandomly delivered with an average ISI of 1.2 s (range 0.7-1.7 s, Stim2, Neuroscan, Charlotte, NC) at a voltage sufficient to elicit a noticeable thumb twitch.

Surface electromyographic (EMG) electrodes were placed over the thenar eminence supplied by the stimulated MN to monitor M-wave amplitude in order to ensure consistency in the stimulus intensity delivered to the nerve. EMG recordings were amplified (2000 X), bandpass filtered (DC-200 Hz), digitized (1000 Hz, SynAmps2, model no. 8050, Neuroscan, Charlotte, NC) and stored for later analysis.

VEPs were derived from a flash stimulus presented on the flat screen placed behind the visual stimulus LED. The flash stimulus consisted of a bright red circle (13 cm in diameter, 27 ms in duration) delivered in a pseudorandom order with an average ISI of 1.2 s (range of 0.7-1.7 s, Stim2, Neuroscan, Charlotte, NC) fixed in a pattern such that no MN stimulation or visual evoking stimulus were presented within 300 ms of one another to avoid cross-contamination. VEP morphology was variable across participants and VEP data are not reported here.

Electroencephalographic (EEG) data was recorded from 60 electrode sites (64 channel Quick-Cap, Neuroscan) in accordance with the international 10-20 system for electrode placement, and referenced to linked mastoid electrodes. All channel recordings had impedances of 5 kΩ or less. Eye movements were recorded by electrooculogram (EOG). EEG and EOG data were amplified (20000x), filtered (DC-200 Hz, 6dB octave roll-off) and digitized (1000 Hz, SynAmps2, model no. 8050, Neuroscan) before being stored for off-line analysis.

EEG containing ocular and/or movement artifact was excluded from further analysis.

SEPs were extracted by averaging together epochs time locked to MN stimulation (-50 to 350 ms). SEPs were baseline corrected post-stimulus and filtered using a bandpass filter (1-200 Hz).

4.3.3 Data Analyses

Amplitudes and latencies of the parietal SEP components N20, P27, P50 and N140 were measured for each subject and each condition from electrode site CP3, where the amplitude was maximal. All fourteen participants showed clear SEP components. The only exception was the lack of a clearly defined P27 in one participant. This participant was excluded from the P27 analyses, however all other components were clear and thus they were included in all other analyses.

The statistical analyses were performed in two steps. First, a series of one-way ANOVAs were performed to investigate differences between the control conditions for the N20, P27, P50 and N140 components. None of the one-way ANOVAs demonstrated any differences and the traces from each control were subsequently averaged together to form a single SEP control to which the six experimental conditions were then compared. All reported means reflect the amplitude of specific components as a percentage of control values.

The effect of spatial relationship was analyzed using separate 2 (Vibrotactile/Visual) x 2 (Distinct/Related) ANOVAs for each SEP component. The effect of temporal synchrony was analyzed using separate 2 (Vibrotactile/Visual) x 2 (Asynchronous/Synchronous) ANOVAs for each SEP component. Post-hoc analyses were performed where appropriate.

M-wave amplitudes were quantified (peak-to-peak) from EMG electrodes placed over the thenar musculature of the hand receiving MN stimulation and analyzed using similar ANOVAs as detailed above to ensure MN stimulation did not vary and contribute to SEP differences.

Behavioral tracking performance for each condition was quantified by calculating the root mean square error (RMSE) of the difference between the graded motor response and the target stimulus. The first and last second of tracking for each block was dropped to avoid artificial increases in RMSE associated with initial lags in participant responses. A decrease in the RMSE represents a decrease in the difference between the motor output generated and the sensory task-relevant target supplied and thus an increase in tracking performance, whereas an increased RMSE represents decreased tracking performance.

Due to initial differences in the absolute voltages required to drive the vibrotactile and visual stimuli there were large differences in average RMSE between the two modalities. These differences were not related to tracking performance and this was confirmed by normalizing the amplitudes of the sensory waveforms to the participants' motor output. As we were not interested in tracking differences between the modalities, modality was dropped as a factor from the analyses and hypothesis guided t-tests were employed to investigate the differences in tracking performance for spatial and synchrony experimental manipulations within a single target modality.

4.4 Results

4.4.1 Tracking Performance

The spatial relationship effects upon tracking performance were investigated using two t-tests. A paired t-test investigating changes in tracking performance during vibrotactile tracking with a spatially distinct versus spatially related visual distracter revealed that tracking performance was poorer when the visual distracter was spatially related to the position of the vibrotactile stimulus [$t = -2.55$, $df = 12$, $p < 0.03$, Distinct = 0.54 (0.04), mean RMSE (±SEM), Related = 0.65 (0.06)]. The corresponding visual tracking analysis was not significant.

Tracking performance was improved when the visual distracter was synchronous compared to when the spatially related distracter was asynchronous [$t = 2.18$, $df = 12$, $p < 0.05$, Asynchronous = 0.65 (0.06), Synchronous = 0.61 (0.07)]. The corresponding vibrotactile tracking analysis was not significant.

4.4.2 M-wave

There were no differences for M-wave amplitudes for both the 2 (Vibrotactile/Visual) x 2 (Distinct/Related) and the 2 (Vibrotactile/Visual) x 2 (Asynchronous/Synchronous) ANOVAs.

4.4.3 SEP components

The grand average waveforms for both vibrotactile and visual tracking are shown in Figure 2. Both the spatial and temporal synchrony two-way ANOVAs on N20 amplitude failed to reach significance. In contrast, P27 amplitude demonstrated main effects of the Spatial Relationship [$F(1,4) = 5.10$, $p < 0.05$] (Figure 3A) and Temporal Synchrony [$F(1,4) = 6.81$, $p < 0.02$] (Figure 3B) of the visual distracter. The effect of spatial relationship can be attributed to a suppression (relative to the baseline control conditions) of the P27 SEP component during continuous sensorimotor tracking when the target and distracter modalities were spatially related. The effect of temporal synchrony can be attributed to a return to baseline control when the spatially related vibrotactile and visual stimuli are temporally synchronous.

The two-way ANOVA investigating the effects of spatial relationship upon the parietal P50 failed to reveal any significant effects, however the corresponding temporal synchrony analyses revealed a strong trend for a Tracking Modality x Temporal Synchrony interaction [F(1,12) = 4.68, $p < 0.06$] (Figure 3C). The trend for the interaction appears to be driven by a return in P50 amplitude back to baseline during vibrotactile tracking in the presence of a synchronous visual distracter compared to an asynchronous visual distracter (contrast, $p < 0.0008$) but no change during visual tracking with the temporal synchrony of the vibrotactile distracter (contrast, p = n.s.).

Finally, there was no effect of spatial relationship on the N140, however, temporal synchrony analysis revealed a significant main effect of Tracking Modality [F(1,12) = 6.74, $p < 0.02$] (Figure 4). The main effect can be attributed to a reduction in the amplitude of the negativity of the N140 component during visual tracking compared to during vibrotactile tracking.

4.5 Discussion

The current study produced two novel observations, 1) contrary to our hypothesis early SEP components, as early as the P27, demonstrated intermodal influences associated with the temporal and spatial properties of a concurrent distracter and 2) P27 changes were associated with changes in vibrotactile tracking performance.

It has been previously demonstrated that P27 amplitude is sensitive to intramodal attentional modulation of somatosensory processing (Legon & Staines, 2006). However, to our knowledge this is the first account of P27 modulation associated with intermodal influences. One hypothesis for this novel effect is that the task demands of the continuous sensorimotor transformation resulted in earlier modulation of sensory processing. However, the P27 component may be modulated in perceptual studies but methodological differences preclude observation of such early effects with ERPs. The earliest ERP potentials reported are often 50 ms post-stimulus while attentional effects are often reported no earlier than 80-140 ms post-stimulus (Eimer & Van Velzen, 2002; Ohara et al., 2006; Taylor-Clarke et al., 2002).

In the current study P27 amplitude decreased with spatially related bimodal stimulation. Decreased amplitude was associated with decreased tracking performance during vibrotactile tracking only. In contrast, spatially related bimodal stimulation that was synchronous, with respect to the random fluctuations in each modality, resulted in increased P27 amplitude that was associated with relative improvements in tracking performance specific to vibrotactile tracking.

The pattern of results suggests that the visual stimulus was the dominant modality with respect to the required sensorimotor transformation. Intermodal interactions are a function of the spatial and temporal properties of two simultaneously presented stimuli (Kayser & Logothetis, 2007) and occur in a statistically optimal manner with the stimulus with the highest signal to noise ratio dominating the multimodal representation (Ernst & Banks, 2002). If this statistically optimal model is extended to situations of intermodal competition then reduced ability to detect changes in the vibrotactile stimulus would result in decreased salience of that representation relative to the visual distracter representation. Therefore, the visual stimulus was likely a more salient distracter than a concurrent vibrotactile distracter. The greater salience of the visual distracter resulted in somatosensory gating, as reflected by the reduced P27 amplitude that in turn resulted in reduced ability to extract changes in the vibrotactile target. This is in line with previous intermodal attention research demonstrating increased sensory representations of an unattended modality presented at an attended location (Eimer & Driver, 2001; Eimer & Van Velzen, 2002). Further, during visual tracking the reduced salience of the vibrotactile stimulus resulted in traditional sensory gating associated with vibrotactile task-irrelevance that was stronger when the two modalities were spatially related (Shomstein & Yantis, 2004) but produced no additional change to behavior.

In contrast, when the distracter was spatially related but was temporally synchronous, so that the random changes in intensity were synchronous with the vibrotactile target, the increased salience of the visual distracter offered an advantage resulting in a benefit to vibrotactile tracking performance. This advantage was associated with an apparent return to baseline cortical excitability. This effect appears to reflect a reversal of the sensory gating of the vibrotactile stimulus when a spatially related stimulus is in conflict with the target modality. This may occur by simultaneous, synchronous convergence of the vibrotactile and visual sensory representations at the level of the temporal parietal junction (S. K. Meehan & Staines, 2007b). Although, P27 amplitude was also increased during visual tracking there was no behavioral effect of temporal synchrony during visual tracking because the salience of the visual stimulus was greater than the vibrotactile stimulus conferred no benefit. This is in line inverse effectiveness (Kayser & Logothetis, 2007) that posits stimuli with strong unisensory representations exhibit weak multisensory effects.

One possibility for reduced vibrotactile salience may be inter-hemispheric interactions associated with the continuous motor requirement. It has been shown that activation of primary motor cortex (M1) can have influences upon contralateral S1 and that these changes can influence perception thresholds (Mochizuki et al., 2004; Seyal et al., 2005). In the current task the continuous sensorimotor transformation may have initially reduced the signal detection capacity of the vibrotactile stimulus that was then further altered by the presence of the bimodal distracter.

The behavioral results in the current study are in contrast to previous studies using similar intermodal stimuli during continuous sensorimotor tracking that demonstrated a vibrotactile distracter influence upon visuospatial tracking (S. K. Meehan & Staines, 2007a; 2007b). This discrepancy is likely due to the use of a visuospatial stimulus and the imposed experimental setup from previous work. The use of a visuospatial stimulus outside peripersonal space and a reflecting mirror to view it may have weakened visuospatial salience as well as the spatial and temporal manipulations compared to the current study.

In addition to P27 amplitude changes the subsequent P50 SEP component was influenced by the synchrony between the vibrotactile target and visual distracter. The P50 most closely resembled the changes in behavioral tracking performance as it demonstrated an apparent return to baseline control amplitude only when participants were tracking the vibrotactile stimulus in the presence of a synchronous visual distracter. In contrast to the P27 where amplitude increased in the presence of a synchronous distracter regardless of tracking modality the P50 appears to reflect relief of visual influence on vibrotactile sensory processing associated with visual dominance. This differential pattern of results between these two potentials suggests that this effect is not a simple serial processing effect but might reflect a sensitivity of the P50 to feedback from heteromodal areas that is independent of those modulatory influences on the P27. This is supported by the notion that the P50 likely reflects a parallel afferent input of tactile information from the ventro-posterior lateral nucleus of the thalamus (Allison et al., 1992).

Few ERP studies report the P50 and those that do suggest that it is insensitive to intermodal modulation even when behavioral effects are present (Taylor-Clarke et al., 2002). The current modulation likely reflects a difference in task demands associated with the continuous tracking task. Previous research simply looked at the effect of passive vision upon perception of tactile stimulation. Although in the current study it can be argued that the visual stimulus was also passively viewed, the increase in task demands from perception to continuous sensorimotor tracking may result in the release of sensory gating at this thalamic-cortical synapse regardless of the passive or active role of vision.

An interesting result of the current study is the sensitivity of SEPs localized to S1 to the spatial and temporal manipulations, but no simple effects of tracking modality. This was contrary to the hypothesis based on previous fMRI studies using a similar continuous sensorimotor task that demonstrated increased activation, as reflected by the blood oxygenation dependent (BOLD) contrast, within S1 during visuospatial tracking compared to vibrotactile tracking. BOLD contrast was insensitive to spatial (S. K. Meehan & Staines, 2007a) or temporal (S. K. Meehan & Staines, 2007b) manipulations. One possible explanation for this difference may be due to the spatial and temporal properties inherent to each of these techniques (Arthurs, Johansen-Berg, Matthews, & Boniface, 2004). FMRI is a slower process that reflects a number of processing steps, each of which is incorporated into the BOLD response. In contrast the SEP is a short duration measurement in which each SEP component reflects a distinct process in time. Therefore, the spatial and temporal sensitivities reflected in the P27 and P50 may have been masked by additional processing in S1 due to the lower temporal resolution associated with measuring changes in BOLD.

In addition to changes in early SEP components believed to reflect generators within S1, the N140 demonstrated decreased amplitude to visual tracking relative to tactile tracking. This is supported by previous research demonstrating attentional effects upon the N140 (Eimer & Driver, 2001; Eimer & Van Velzen, 2002). It is interesting that this intermodal attention effect was only present as a main effect of modality in the temporal synchrony analyses. This likely can be attributed to two factors: 1) variability in the amplitude of the N140 was larger for vibrotactile tracking when pooled across spatial relationship and 2) N140 amplitude was reduced during visual tracking regardless of the vibrotactile distracter's temporal synchrony with the visual target. The former suggest that intermodal attention effects are affected by the spatial properties of the two modalities. This is supported by the interaction of spatial relationship and attention (Macaluso & Driver, 2005). The latter supports the behavioral data suggesting that the visual stimulus was deemed to be the more reliable stimulus for the sensorimotor interaction due to lower signal detection thresholds.

The current study is the first to demonstrate intermodal influences upon early somatosensory processing within S1. This was reflected in the P27, and to a lesser extent the P50 SEP components. Early SEP components were related to changes in behavior during the continuous tracking task. These results demonstrate the importance of early sensory modulation to behavior and highlight the potential importance of task demands and/or the limitations of ERPs in the interpretation of early attentional modulation in the somatosensory system.

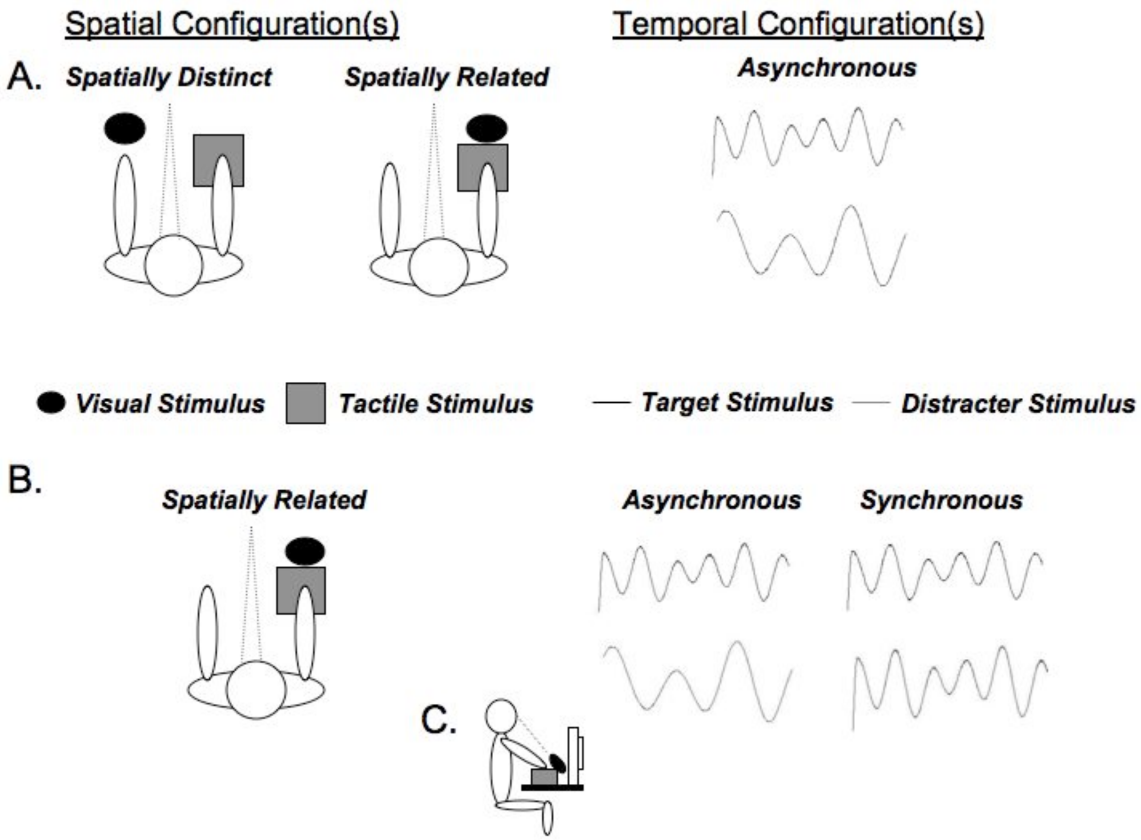


Figure 4-1: Schematic representation showing both the spatial and temporal configurations used for (A) the spatial and (B) the temporal experimental manipulations used in the task (see text for details). (C) Insert depicting the experimental setup from the side view.

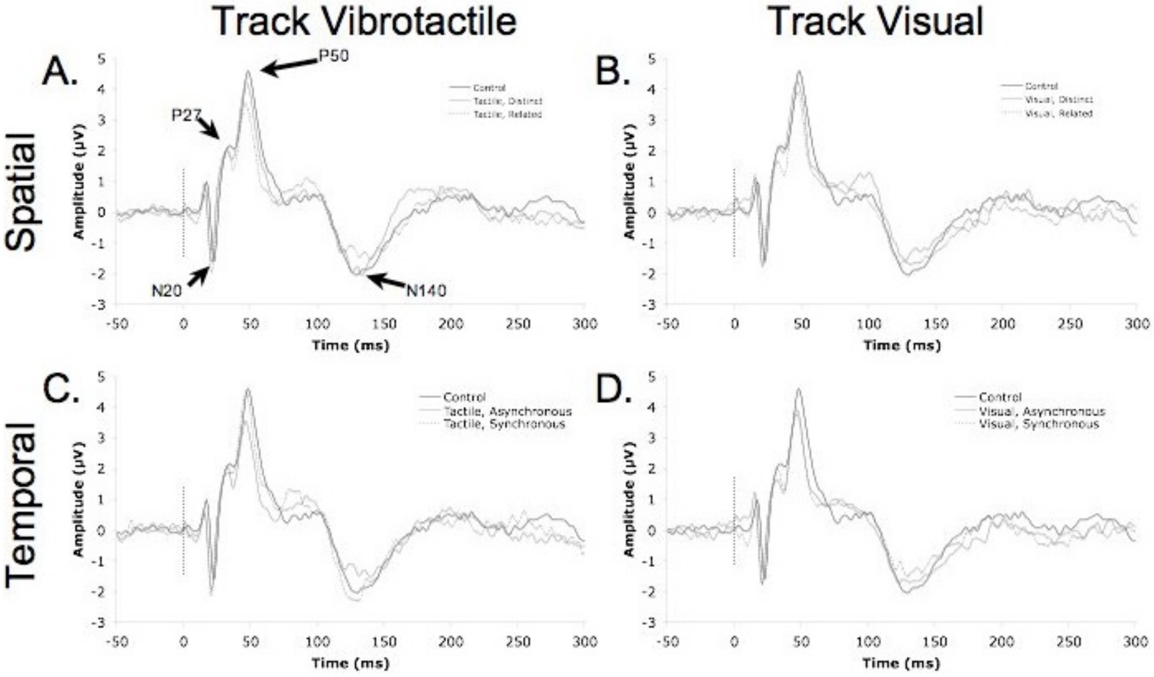


Figure 4-2: Grand average waveforms taken from the CP3 electrode site during the control, vibrotactile and visual tracking. (A) Vibrotactile tracking under the spatial manipulations, (B) Visual tracking under the spatial manipulations, (C) Vibrotactile tracking under the temporal manipulations and (D) Vibrotactile tracking under the temporal manipulations. SEP components of interest are indicated by arrows. SEP is time locked to MN stimulation (indicated by dashed line) elicited during continuous tracking.

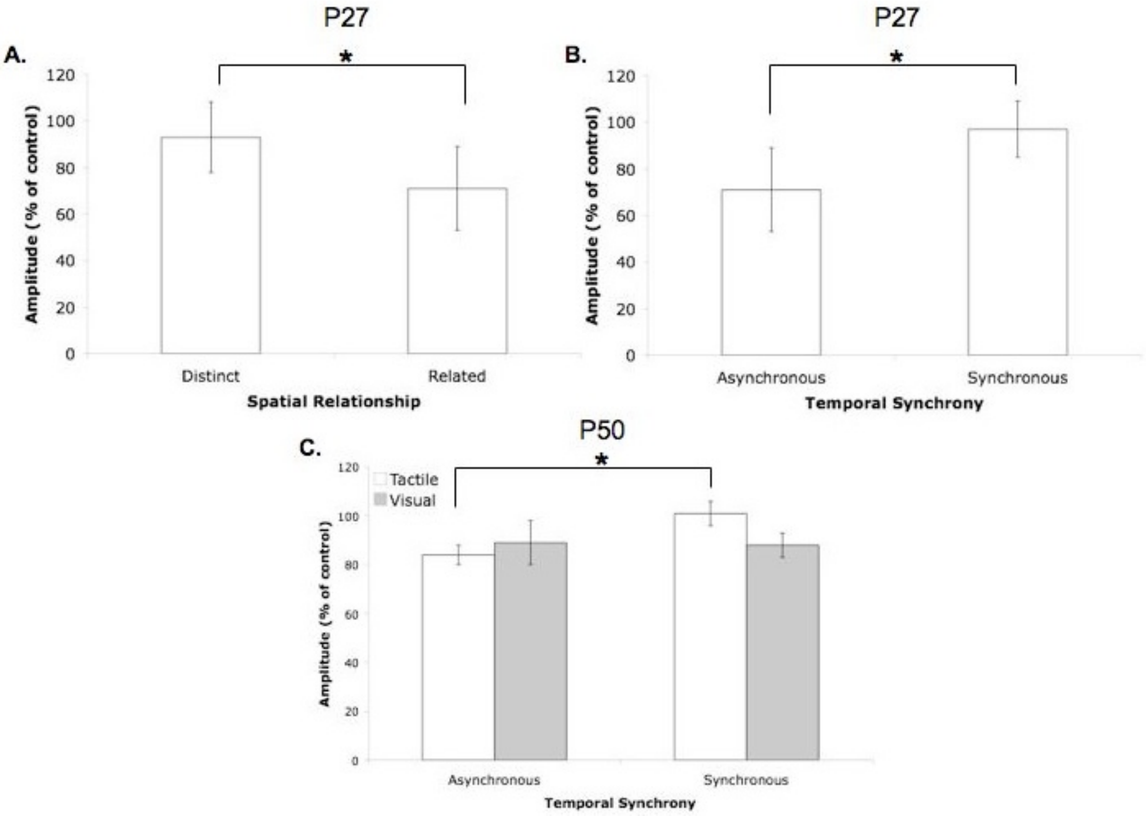


Figure 4-3: Normalized means for (A) the main effect of spatial relationship upon P27 amplitude, (B) the main effect of temporal synchrony upon P27 amplitude and (C) the Tracking Modality x Temporal Synchrony interaction upon P50 amplitude. All amplitudes are reported as a percentage of the baseline control values. Asterix denotes $p < 0.05$. Error bars indicate SEM values.

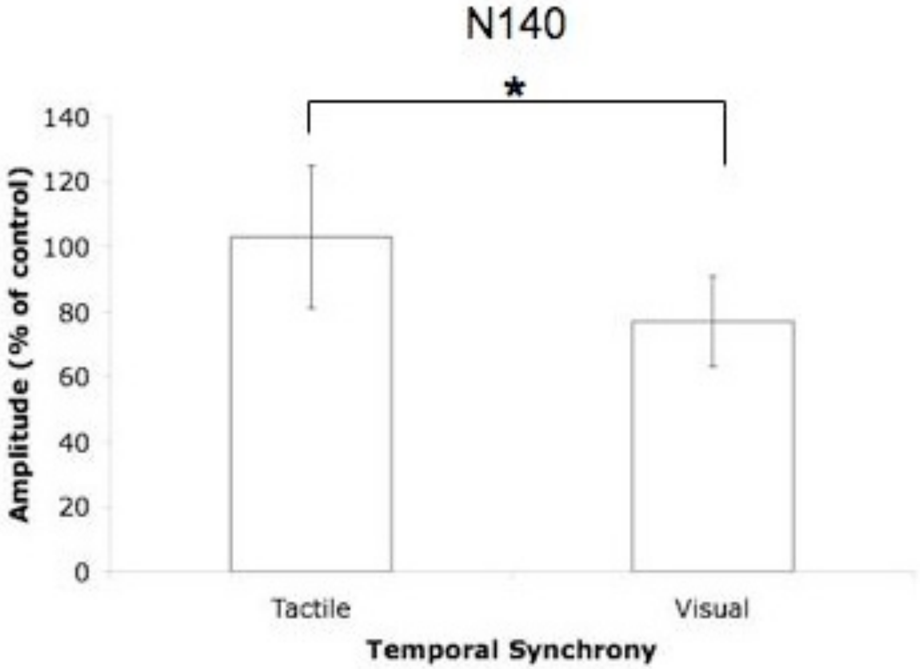


Figure 4-4: Normalized means for the main effect of Tracking Modality upon N140 amplitude. All amplitudes are reported as a percentage of the baseline control values. Asterix denotes $p < 0.05$. Error bars indicate SEM values.

CHAPTER 5 – Excitability Differences During Continuous and Discrete Motor Response

5.1 Abstract

Recent studies demonstrated reduced activation of primary somatosensory cortex (S1) with continuous vibrotactile tracking during bimodal stimulation. Reduced activation has been hypothesized to reflect an interaction between the motor and intermodal attention requirement of the task. The purpose of the current paper was to: 1) assess whether decreased S1 activation was associated with the continuous sensory-guided motor requirement and 2) determine the consequences to behavior. Single and paired-pulse transcranial magnetic stimulation (TMS) was used to investigate the excitability of S1 during a sensorimotor task that required either continuous or discrete sensorimotor responses. Reports suggest that a supra-threshold test stimulus (TS) preceded by a sub-threshold conditioning stimulus (CS) adversely affects perception. It was hypothesized paired-pulse TMS would have differential effects dependent upon the sensorimotor requirements associated with a vibrotactile stimulus. TMS was delivered while participants received simultaneous bimodal vibrotactile/visuospatial stimulation. Abrupt changes in amplitude were embedded within the continuous vibrotactile stimulus. Participants either responded discretely to the abrupt changes or continuously tracked amplitude changes, including the abrupt changes. Regardless of instruction single pulse TMS delivered over S1 decreased the number of abrupt changes in the sensorimotor response. Paired-pulse TMS decreased the number of abrupt changes detected only when participants responded discretely. This effect disappeared when the TS was replaced by a sub-threshold stimulus. These results suggest that the CS facilitates sensory output neurons during perceptual detection but that pre-existing differences in local cortical excitability in S1 suppress these effects during continuous sensory-guided movement.

5.2 Introduction

Studies of somatosensory processing demonstrate early task-related modulation of afferent sensory information as early as primary somatosensory cortex (S1) (Burton & Sinclair, 2000; Johansen-Berg et al., 2000; Staines et al., 2002). Somatosensory evoked potentials (SEPs) have shown that these effects can occur within the very first thalamic-cortical synapses (Legon & Staines, 2006) and that the integrity of these processes have an impact upon behavior (Staines et al., 2002).

However, in any given environment there are a multitude of multisensory sources of information that need to be integrated together or extracted from each other. Recent research has begun to investigate the loci at which intermodal modulation of afferent sensory input occurs. Perceptual studies have shown that afferent input is modulated during early sensory processing in secondary sensory cortices, areas traditionally designated as "modality specific" (Eimer & Driver, 2000; Johnson & Zatorre, 2005; Kida, Inui, Wasaka, Akatsuka, Tanaka, & Kakigi, 2007a; Ohara et al., 2006; Taylor-Clarke et al., 2002). It has recently been suggested that these early modulations have important feedforward consequences upon behavior related to the signal to noise ratio of each modality (Hecht et al., 2008; Kayser & Logothetis, 2007).

Recently early intermodal modulation of primary somatosensory cortex has been demonstrated using functional magnetic resonance imaging (fMRI) (S. K. Meehan & Staines, 2007a; 2007b). Using a continuous tracking paradigm, in place of a perceptual detection task, intermodal influences upon sensory processing were observed in Brodmann Area 1 of S1. However, in contrast to perceptual detection, continuous tracking of a vibrotactile stimulus resulted in decreased activation within S1, relative to when the same vibrotactile stimulus was a task-irrelevant distracter. It was hypothesized that this difference was associated with the continuous nature of the sensorimotor task and likely reflected an interaction between the intermodal sources of stimulation and inter-hemispheric interactions associated with the sensorimotor requirements of the task.

It has been demonstrated that there are inter-hemispheric interactions between ipsilateral (to an electrical stimulus) motor and contralateral (to an electrical stimulus) somatosensory cortices (Mochizuki et al., 2004; Seyal et al., 2005). It is hypothesized that these interactions are mediated by ipsilateral-contralateral M1-M1 effects that in turn result in M1-S1 effects on the side contralateral to the stimulus (Enomoto et al., 2001; Kujirai, Sato et al., 1993; Seyal et al., 1993). Further there is also evidence for ipsilateral and contralateral interactions between the somatosensory cortices (Clarey et al., 1996; Hlushchuk & Hari, 2006; Staines et al., 2002). It is possible that these inter-hemispheric interactions are associated with the continuous tracking task employed in our previous intermodal studies (S. K. Meehan & Staines, 2007a; 2007b) but not previous perceptual studies of intermodal selective attention and may explain the differential modulation of sensory cortices.

Transcranial magnetic stimulation (TMS) offers a unique method to study potential differences in cortical excitability within S1. A single supra-threshold, relative to resting motor threshold, TMS pulse delivered over sensorimotor cortex suppressed perception of a cutaneous electrical stimulation (Cohen, Bandinelli, Sato, Kufta, & Hallett, 1991; Seyal, Masuoka, & Browne, 1992). This suppression can in part be attributed to altered sensory cortical processing (McKay, Ridding, & Miles, 2003). Further, it has been shown that a sub-threshold conditioning stimulus (CS) prior to the single pulse supra-threshold test stimulus (TS) over S1 can further enhance this suppression (Koch, Franca, Albrecht, Caltagirone, & Rothwell, 2006). One hypothesis for the latter effect is that the CS results in a facilitation of sensory output neurons due to the 15 ms inter-pulse interval, an interval shown to have facilitatory effects upon output neurons in motor cortex (Kujirai et al., 1993).

The purpose of the current study was to use single TS and paired-pulse CS-TS TMS to investigate the excitability of S1 contralateral to a vibrotactile stimulus during continuous sensorimotor or a discrete sensorimotor response. In all cases participants received simultaneous continuous vibrotactile stimulation and visuospatial stimulation. Both the continuous vibrotactile and visuospatial stimulation randomly fluctuated in intensity. Embedded within the vibrotactile stimulation was abrupt changes in amplitude. Participants were instructed to either continuously track the vibrotactile stimulation by applying graded force according to the intensity at any given point in time or to respond discretely with a squeeze and release of the pressure sensing bulb when they detected an abrupt change in amplitude. The visuospatial stimulation was always a distracter and was used to maintain the intermodal component from previous work (S. K. Meehan &

Staines, 2007a; 2007b). TMS was delivered 20 ms after a discrete change regardless of sensorimotor response. It was hypothesized that the reduced excitability of S1 during vibrotactile tracking in the presence of a visuospatial distracter would result in decreased sensitivity of S1 to the effects of paired-pulse TMS during continuous tracking compared to discrete sensorimotor responses.

5.3 Materials and Methods

5.3.1 Subjects

Eleven healthy volunteers (6 male, 5 female, age range 21-39) were recruited. All participants gave their informed consent to participate in the study and the experimental procedures were approved by the Office of Research Ethics at the University of Waterloo.

5.3.2 Tasks and Stimuli

TMS was delivered while participants discretely detected changes in or continuously tracked a vibrotactile stimulus in the presence of a visuospatial distracter (Figure 5-1A). Vibrotactile stimulation was delivered via a modified speaker. Participants were instructed to rest their index finger upon a patch of Velcro® attached to the dust cap, located at the center of the speaker’s diaphragm. The dust cap was controlled to vibrate at varying forces by passing fluctuating current through the voice coil of the speaker according to a 25 Hz sine wave with random intensity fluctuations. Embedded within the random intensity fluctuations were abrupt changes in intensity. Vibrotactile stimulation was controlled by digitally generating waveforms that were converted to an analog signal (DAQCard 6024E, National Instruments, Austin, Texas) and then amplified (Bryston 2B-LP, Peterborough, Ontario, Canada). Variation in amplitude of the driving voltage at a given frequency (25 Hz) led to proportionate increases in force applied by the dust cap onto the finger. The vibrotactile waveform varied in average frequency from 0.10 Hz – 0.50 Hz superimposed upon the underlying 25 Hz vibration and was generated as a random combination of 4 sinusoid waveforms of varying amplitude and frequency. Following waveform generation the abrupt changes were inserted (0.2 mV, 50 ms duration). All waveforms were generated using a custom program written in Labview software (version 7.1, National Instruments, Austin, Texas).

The visuospatial stimulus was a dial similar to that that described previously (S. K. Meehan & Staines, 2007a; 2007b) and was presented upon the black background of a computer screen (SyncMaster 171s). The dial contained a needle that fluctuated between five o'clock and seven o'clock, passing through twelve o'clock. The position of the needle was controlled by waveforms generated and controlled using the same software as the vibrotactile stimulation. Unlike the vibrotactile stimulus there were no abrupt changes in the position of the needle.

The speaker was placed directly in front of the visuospatial stimuli presented upon the computer screen with the independent bimodal stimulation delivered in blocks (90 s stimulation, 2 repetitions). In all cases participants were instructed to fixate the center of the visual dial. In one set of conditions participants were instructed to respond to the abrupt changes in intensity embedded within the continuous vibrotactile stimulus while ignoring the visuospatial distracter (Discrete). Participants were instructed to discretely squeeze and release a pressure-sensing bulb (in their left hand) whenever they detected an abrupt change. In a second set of conditions participants were instructed to track the intensity of the vibrotactile stimulation exactly as they perceived it, including all the random fluctuations as well as the abrupt changes in intensity (Continuous). In the continuous condition participants were instructed to apply graded force that reflected the pattern of intensity of the stimulation. In total there were fourteen abrupt changes embedded within each 90s block of continuous vibrotactile stimulation.

During the experiment the visuospatial stimulus was never designated as the target stimulus, however prior to the start of the experiment participants were required to practice visuospatial tracking. For the visuospatial tracking practice participants were instructed that movement of the needle towards the five o'clock position was equivalent to an increase in vibrotactile intensity while movement back towards the seven o'clock position was the equivalent to a decrease in vibrotactile intensity. Visuospatial distraction was presented to maintain consistency with previous work in which an intermodal requirement was present (S. K. Meehan & Staines, 2007a; 2007b).

Throughout the experiment participants received 70 dB whitenoise (70 dB – Stim2, Neuroscan, Compumedics USA, Ltd. Corp., Charlotte, NC) to avoid vibrotactile tracking via audition.

5.3.3 Transcranial Magnetic Stimulation

TMS was delivered with a MagPro stimulator (Medtronic, Minneapolis, MN) using a figure-8 coil (Model No. MCF-B65). Prior to the experiment, high-resolution anatomical magnetic resonance images (MRI) were acquired for each participant (TR = 12.4 ms, TE = 5.4 ms, flip angle θ = 35°, FOV = 20 x 16.5, 124 slices, 1.4 mm slice thickness) on a 3 T clinical whole body MRI scanner (GE HealthCare, Milwaukee, WI, USA) using a standard birdcage head coil with the head immobilized. These images were then imported into the BrainSight TMS neuronavigation system (BrainSight v. 1.7, Montréal, QC) and used to position the TMS coil.

The location of stimulation for the S1 hand region was determined by identifying the site at which a single pulse reduced tactile perception (Harris, Miniussi, Harris, & Diamond, 2002; Knecht, Ellger, Breitenstein, Ringelstein, & Henningsen, 2003) during the discrete responses to the abrupt changes in the vibrotactile stimulus. This was further verified using paired-pulse subthreshold-suprathreshold stimulation during the same task to observe further decreases in tactile perception (Koch et al., 2006). In all stimulation conditions participants were monitored for muscle activation to ensure that stimulation effects could not be attributed to direct stimulation of motor output neurons. If stimulation resulted in motor activity the coil was repositioned until tactile perception was decreased in the absence of movement. The coil was placed tangentially over the skull directly posterior to the motor cortical “hot spot” of the right first dorsal interosseous representation; this site approximated the CP3 electrode site according to the 10-20 electrode placement standards. The handle of the coil was placed parallel to the midline to induce an anterior-posterior current in the underlying cortex. The position and orientation of the coil were marked using the BrainSight system to minimize variability in stimulation target variability within a block and across blocks of stimulation. In all cases the intensity of stimulation was determined relative to each individual participant’s resting motor threshold (RMT), defined according the international standards (Rossini et al., 1994).

5.3.4 Experiment 1

In the main experiment, participants performed either the discrete sensorimotor response or continuously tracked the vibrotactile stimulus, including abrupt changes while receiving TMS stimulation (Figure 5-1B). There were three types of TMS stimulation employed 1) sub-threshold TS (Sub TS), 2) supra-threshold TS (Supra TS) and 3) CS-TS paired-pulse stimulation (Paired CS-TS). For the Sub TS condition, a single TMS test stimulus (TS) was delivered at 70% of RMT. For the Supra TS condition the TS was set to 130% of RMT. In the Paired CS-TS condition a CS at 70% of RMT preceded the 130% of RMT TS.

For both the single and paired pulse stimulation protocols the TS was delivered 20 ms after a discrete abrupt change occurred in the vibrotactile stimulus. This delay was chosen as it corresponds to somatosensory transmission time (Cohen et al., 1991; Seyal et al., 1992) and has been shown to elicit the strongest suppressive effects on perception (Koch et al., 2006). During the paired pulse protocol the CS preceded the TS by 15 ms (Koch et al., 2006). Each stimulation protocol was delivered during a separate 90s block of vibrotactile stimulation.

To ensure that participants did not associate TMS with the occurrence of a discrete abrupt change in the vibrotactile stimulus four randomly chosen incidences of TMS occurred in the absence of an abrupt intensity change. In all, participants responded to less than 1% of these trials. Further, four abrupt changes in vibrotactile stimulation occurred in the absence of TMS to act as a control (Control) and ensure that participants performance was stable and that there were no longer lasting TMS effects during any given TMS protocol.

5.3.5 Experiment 2

Seven participants (3 males, 4 females) from Experiment 1 participated in this experiment to investigate the effects of the CS. Experiment 2 was similar to Experiment 1 except that participants performed the discrete and continuous sensorimotor tasks while receiving CS-TS paired-pulse TMS where both the CS and TS were 70% of RMT.

5.3.6 Data Analyses

In both experiments performance was assessed by the percent of abrupt changes detected during the Response Discrete and Response Continuous. In both sensorimotor conditions, a response was determined by a change in the participants force profile that was of 25% of their maximum force output during continuous tracking and occurred at a frequency of 100 Hz or greater. A correct response was determined by a deviation in the participants force profile between 50-300 ms post-stimulus. The absence of a deviation in force within this range was considered as a missed abrupt change and any deviations outside of the 50-300 ms range were considered false alarms.

The waveforms driving the sensory target and the participants' motor response were overlaid and the number of responses incorporated in the motor response were counted and expressed as a percentage of the total number of abrupt changes. This resulted in a percent detected for each participant and each condition.

In Experiment 1, a 2 (Response: Discrete/Continuous) x 4 (TMS: Control/SubTS/Single TS/Paired CS-TS) ANOVA was performed to assess the effect of TMS on task performance during both the discrete and continuous sensorimotor versions of the task. In Experiment 2, a t-test assessing task-performance during discrete and continuous tracking was performed.

5.4 Results

5.4.1 Experiment 1

A 2 (Response: Discrete/Continuous) x 4 (TMS: Control/SubTS/Single TS/Paired CS-TS) ANOVA revealed a significant Response x TMS interaction [$F(3,30) = 3.96$, $\varepsilon = 0.67$, $p < 0.04$] (Figure 5-2A). There was also a main effect of TMS [$F(3,30) = 28.42$, $\varepsilon = 0.87$, $p < 0.0000001$, mean % detected (±SEM), No TMS = 79% (4), Sub TS = 59 (8), Single TS = 47 (7), Paired CS-TS = 39 (6)]. The significant interaction can be attributed to a decrease in the percent of abrupt changes incorporated in the participants' motor response during the discrete sensorimotor condition compared to the continuous sensorimotor condition only during application of paired-pulse stimulation (contrast, $p < 0.01$).

5.4.2 Experiment 2

A t-test comparing task performance during paired-pulse stimulation where the TS pulse of 130% was replaced by a pulse of 70% of RMT failed to reveal any difference in percent incorporated into motor response during discrete sensorimotor compared to continuous sensorimotor (Figure 5-2B).

5.5 Discussion

The current study offers further evidence for paired-pulse interactions between a sub-threshold conditioning pulse and a supra-threshold eliciting pulse over S1. A sub-threshold conditioning stimulus prior to a supra-threshold condition pulse decreased detection of abrupt changes in the continuous vibrotactile stimulation when participants were required to respond discretely to these changes. However, the current study is unique in that detection of the abrupt changes was not altered by the presence of a sub-threshold conditioning pulse when participants were required to continuously track amplitude changes. This suggests that motor requirements have important influences upon the excitability of S1. Finally, the disappearance of the paired-pulse interaction when the supra-threshold pulse is replaced by a sub-threshold pulse suggests that the paired-pulse interaction is likely associated with recruitment of local facilitatory mechanisms that influence sensory output neurons decreasing the signal to noise ratio.

In the current study it was observed that application of a single supra-threshold TS, 20 ms after an abrupt change in the vibrotactile stimulus, resulted in a decrease in the participants' ability to detect and incorporate changes into their sensorimotor response regardless of whether participants were continuously tracking the vibrotactile stimulus or simply responded discretely to the abrupt changes. Inserting a sub-threshold CS 15 ms prior to the eliciting pulse resulted in a further decrease in perceptual detection compared to application of a single supra-threshold TS. In contrast, the CS had no additional effect when participants continuously tracked the vibrotactile stimulation.

These stimulation parameters were chosen based upon previous research demonstrating that perceptual detection of electrical stimulation applied to the thumb was optimally disrupted when application of the TS was delayed to account for somatosensory transmission time and preceded by a CS 15 ms prior (Koch et al., 2006). Although previous research has shown that the timing between a single supra-threshold pulse was not critical to the effects of the TS alone (McKay et al., 2003), the effects of the CS were strongest when the supra-threshold pulse was timed to the initial cortical processing of the electrical stimulation (Koch et al., 2006) demonstrating a specificity to the CS effects.

It was suggested that two potential mechanisms may be at work during TMS of somatosensory cortex and could explain the non-specific effects of the TS alone (McKay et al., 2003) and the specific effects of the CS (Koch et al., 2006): 1) TMS stimulation interferes with the afferent stimulation by disrupting or prematurely terminating processing and 2) TMS stimulation reduces perception by directly stimulating S1 output that then feeds forward and interferes with perception in higher processing areas. The former is akin to the silent period observed in M1 that is mediated by slower responding metabotropic receptors but persists over a longer period of time (Chen, 2000), while for the latter requires that the TS had to be timed to sensory output. Therefore, the specificity of the CS effects to the arrival of somatosensory information to S1 suggest that it recruits local cortical networks that either disrupt sensory processing by inhibiting sensory output neurons relevant to the stimulus or facilitating the excitability of additional irrelevant sensory output neurons.

Of these two possibilities, CS facilitation of sensory output neurons appears most likely based upon evidence from CS-TS stimulation of motor cortex where an inter-pulse interval of 15 ms, like that shown to elicit the strongest paired-pulse effects upon perception, facilitates motor output (Kujirai et al., 1993). This facilitation is short lasting and further supports the specificity of the CS-TS stimulation effects to the arrival of tactile information to somatosensory cortex.

The results of the current study support the current hypothesis that inter-hemispheric interactions associated with continuous tracking result in reduced excitability of S1. It has been shown using fMRI that tracking a continuous vibrotactile stimulus in the presence of a visual distracter was associated with a decrease in S1 activation (S. K. Meehan & Staines, 2007a; 2007b). In the current study CS-TS interaction was not observed when participants had to use the vibrotactile stimulus for the continuous sensory-guided tracking. The interaction was only present during perceptual detection, which is traditionally linked with increased activity in somatosensory cortex due to facilitation associated with attention (Burton & Sinclair, 2000; Ohara et al., 2006; Staines et al., 2002). It is hypothesized that previously observed decreases in excitability associated with the continuous sensorimotor tracking requirement (S. K. Meehan & Staines, 2007a; 2007b) mitigated the facilitatory effects of the CS. In contrast, the difference in the excitability of S1 during the discrete sensorimotor response requirement associated with the detection of the abrupt changes left S1 susceptible to the facilitatory effects of the CS. The end result was that during discrete detection increased sensory output fed forward to higher processing areas decreasing the signal to noise ratio of the discrete representation to the point where the discrete changes were difficult to detect from the background fluctuations of the vibrotactile stimulus. In contrast, sensory output activation was not substantially altered in the continuous tracking case and signal to noise ratio in higher processing areas was unchanged. This argument would hold true whether detection and incorporation of the abrupt changes was mediated by onset detection or offset detection of the abrupt change.

The disappearance of the paired-pulse interaction when the supra-threshold stimulus was replaced by a sub-threshold stimulus supports this hypothesis, as the paired-pulse interaction requires an eliciting stimulus that is above threshold to activate sensory output neurons in S1. Therefore the disappearance of the paired-pulse interaction can be attributed to the failure to recruit additional sensory output neurons and thereby adequately influence the signal to noise ratio in higher processing areas, provided there are substantial differences in activation thresholds between M1 and S1 neurons.

Another interesting observation from the current study is the absence of a differential effect of a TS stimulus depending upon how the continuous vibrotactile stimulus was to be used. In the current study, a single pulse at 70% of RMT resulted in a decrease in detection while a single pulse at 130% resulted in a further decrease in detection of the abrupt changes regardless of the required motor output. The similarities between the two sensorimotor conditions during single pulse but differential effects of paired-pulse stimulation suggest that local cortical networks in S1 mediate the CS-TS interaction. It is suggested that the application of the TS results in an increase in general interference, whose magnitude is dependent upon TS intensity, regardless of the excitability of S1 output neurons associated with sensorimotor requirements while the effects of a CS prior to this TS reflect a difference in the state of the local cortical networks controlling the excitability of these output neurons. The key factor being that this level of noise associated with the single pulse is not propagated during continuous tracking.

The current study is the first to demonstrate differential paired-pulse TMS interactions during a discrete sensorimotor task compared to a continuous sensorimotor task. These differences in the state of S1 with the differential use of an identical vibrotactile stimulus were reflected in the ability to detect abrupt changes in the sensory waveform. These results highlight the importance of motor requirements in determining the net effect of attentional modulation on somatosensory processing.

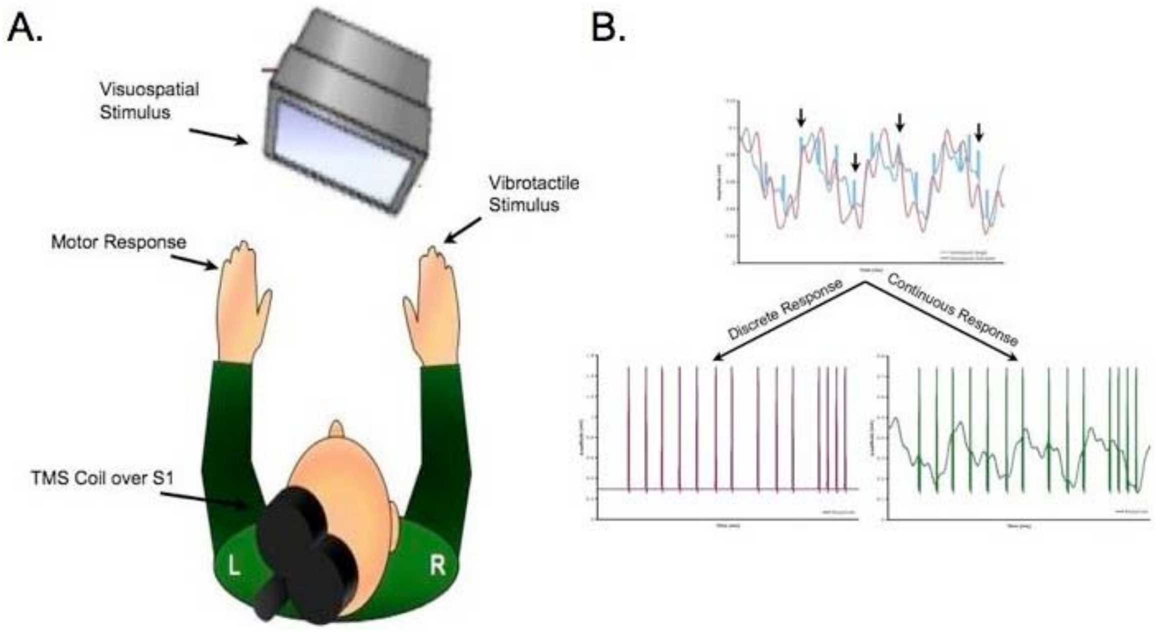


Figure 5-1: An example of the experimental design. (A) Participants were seated upright and facing a computer screen. Participants placed their right index finger on a speaker located directly in front of the computer screen. TMS was delivered over the S1 representation of the right index finger. (B) Top - An example of the waveforms driving the continuous random fluctuations in intensity of the vibrotactile (blue) and visuospatial (red) stimuli. The solid blue rectangles superimposed upon the vibrotactile waveform represent the abrupt changes in intensity while the black arrows designate the abrupt changes not associated with TMS. Bottom – Examples of the required motor response for the discrete detection of the abrupt changes (left) and the continuous tracking of the vibrotactile stimulus (right). In the latter participants were instructed to track the waveform exactly as they sensed it, including any abrupt deviations.

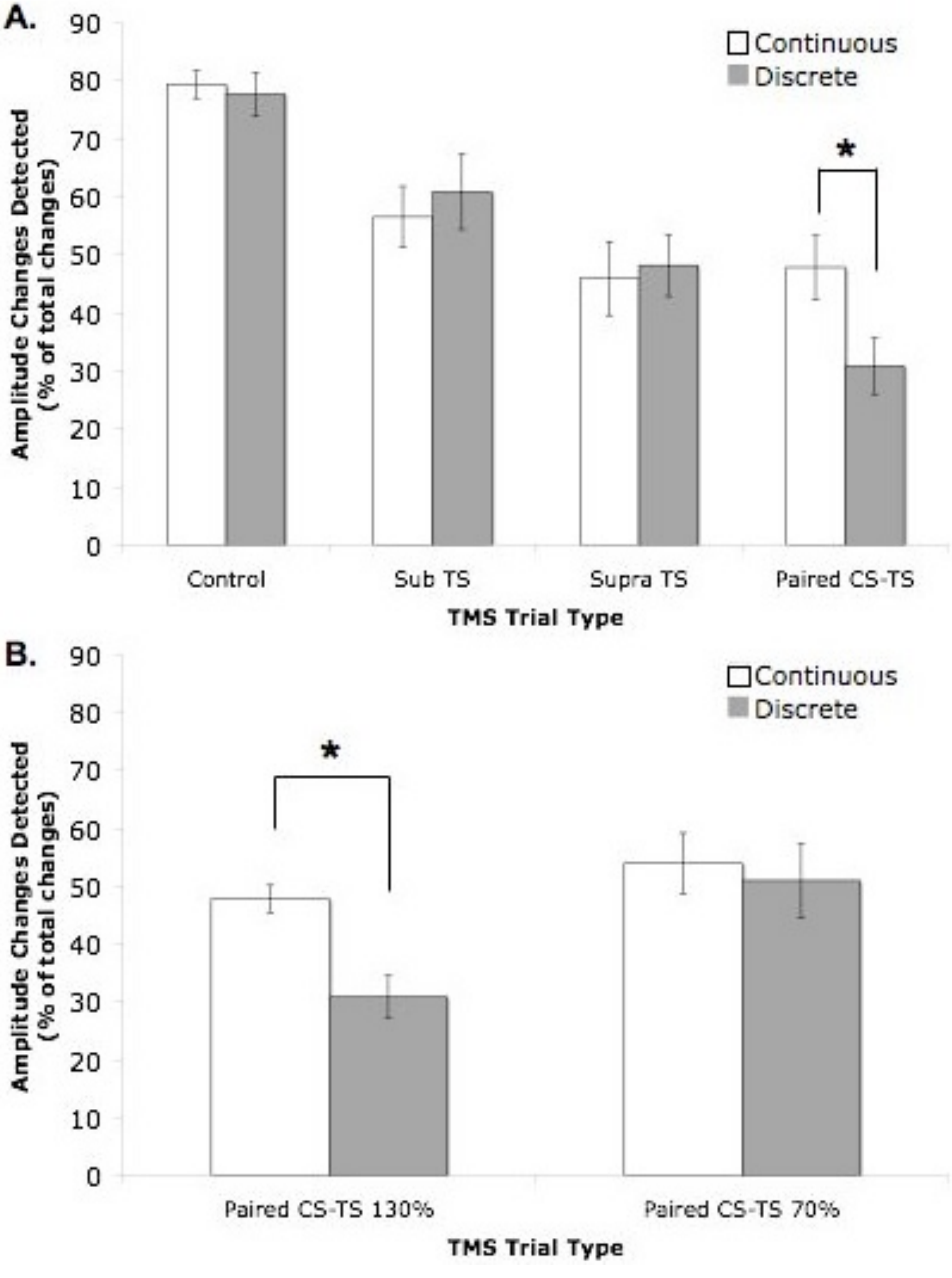


Figure 5-2: A) Plot of the mean percent of abrupt changes detected during the discrete and continuous sensorimotor conditions for the control changes and the sub-TS, supra-TS and CS-TS trials types. B) Plot of the mean percent of abrupt changes detected for both sensorimotor conditions for the CS-TS 130% and the CS-TS 70% trial types. Bars indicate SEM. * denotes $p < 0.05$

CHAPTER 6 – Influence of a temporally synchronous intermodal distracter under varying levels of intramodal noise

6.1 Abstract

Objects in our environment can be represented in a number of different modalities. To accurately form a percept of an object and interact with it there are two important factors 1) we need to efficiently and accurately extract the relevant information within each modality from noise within that modality, and 2) we need to integrate the representations from each modality into one unified percept. In contrast, there are circumstances where simultaneous modalities are in conflict with each other and integration can be detrimental to perception and action. The current study sought to investigate the role of intramodal noise in the extraction of an explicitly task-irrelevant modality, specifically whether this irrelevant modality could supplement the sensorimotor transformation required by the target modality. This question was investigated using bimodal vibrotactile/visual stimulation. For vibrotactile stimulation intramodal noise was manipulated by altering the relative intensity of a constant amplitude vibration applied to the palmar surface just below the metacarpo-phalangeal joint of the right index finger. Visual noise was manipulated by changing the range of fluctuation between the two states of intensity surrounding the visual target stimulus. For both vibrotactile and visual tracking, the presence of a non-conflicting synchronous distracter resulted in improved tracking performance only when there were high levels of noise within the relevant modality. This suggests that despite evidence for intermodal suppression of a task-irrelevant modality temporal similarities between the target and distracter stimuli do not completely suppress the distracter representation. Further, this representation can be used, voluntarily or involuntarily, to supplement sensorimotor transformations dictated by the relevant modality. This has implications for understanding intermodal links in attention and supports previous perceptual studies demonstrating illusions associated with strong similarities, either physical or cognitive, between two conflicting modalities.

6.2 Introduction

An object within our environment can be represented in a number of different modalities. The representation of that object in each modality is first processed in distinct areas, traditionally viewed as modality-specific. They are then integrated through convergent sensory processing routes that converge on heteromodal temporal-parietal and frontal areas such as the ventral intraparietal sulcus, superior temporal gyrus and ventral premotor areas (Macaluso, 2006). Neurons in these areas appear to have overlapping receptive fields for stimuli from multiple modalities whose representations converge upon the same neuron if they share a similar spatial origin and temporal occurrence (Meredith, 2002; Stein, 1998). Recently, there has been an increasingly popular view that feedforward convergence is supplemented by lateral connections between modality-specific areas (termed “low-level” connections) (Foxe & Schroeder, 2005; Kayser & Logothetis, 2007; Schroeder & Foxe, 2005).

These low-level connections and feedforward projections likely serve to manipulate the gain of the sensory representation such that events related to the same event are facilitated early in the processing pathway. As they proceed through the processing pathway from unimodal to heteromodal areas the representations from each attended modality are strongest and integrated while those unrelated to the event are lost as noise. Under this view intermodal selective attention is a parallel process to multisensory integration with multisensory illusions such as the McGurk (McGurk & MacDonald, 1976) and ventriloquist (Radeau & Bertelson, 1974) effects being a by-product of a breakdown between multisensory integration and intermodal selective attention. This breakdown can be attributed to distinct representations sharing spatial and temporal similarities.

Recently it has been demonstrated that a task-irrelevant stimulus that is spatially related with and synchronous to the task-relevant sensory stimulus can enhance behavioral tracking performance. It has been shown repeatedly (S. K. Meehan, Legon, & Staines, in prep; S. K. Meehan & Staines, 2007b) that during a continuous sensorimotor transformation altering the temporal properties of the distracter modality, unbeknownst to the participant, can result in improved tracking performance. However, this effect is not universal. One hypothesis put forward to explain the selectivity of this effect is that the most reliable of the stimuli, with respect to the required sensorimotor transformation, dominates the sensory representation that is converted to a motor response. This occurs despite overt instructions detailing the irrelevance of the distracter modality to the task. This hypothesis was based upon the observation that tracking a visuospatial stimulus, by applying graded force, in the presence of a synchronous vibrotactile stimulus resulted in an increase in tracking performance whereas the same visuospatial stimulus had no effect on tracking performance of the vibrotactile stimulus (S. K. Meehan & Staines, 2007b). This initial observation appears to go against the traditional view that vision tends to dominate our percepts (Holmes, Crozier, & Spence, 2004; McGurk & MacDonald, 1976; Radeau & Bertelson, 1974). In a subsequent study visual dominance was observed during sensorimotor transformations guided by the same vibrotactile stimulus or intensity based visual stimulus (see Chapter 3 of this thesis). Under these circumstances only vibrotactile tracking benefited from a synchronous visual distracter. One explanation for this difference is the difference in environment associated with functional magnetic resonance imaging (fMRI). In this environment the visuospatial stimulus was placed at the feet of the participant who was lying in the bore of the fMRI magnet and had to view the screen via a reflecting mirror located above their head.

If these effects are governed by the signal to noise ratio within the relevant modality then altering the signal to noise ratio by increasing the noise should result in differential benefits of a non-conflict irrelevant modality. It is hypothesized that increasing the noise, regardless of tracking modality, in the presence of a synchronous bimodal distracter will result in larger benefits when intramodal noise is high compared to when it is lower. Further, it is hypothesized that this benefit will be largest for the vibrotactile stimulus due to the tendency for vision to dominate perception.

To address this hypothesis, participants received bimodal stimulation and were required to track one modality while being instructed to ignore the other. Unbeknownst to participants the temporal synchrony was manipulated in some conditions such that both the vibrotactile and visual stimuli were temporally synchronous. Noise level within a modality was manipulated by either having a constant low intensity or high intensity stimulus presented at the same location of the randomly fluctuating vibrotactile/visual stimulation. In all cases the simultaneous distracter modality was presented with the low noise configuration.

6.3 Materials and Methods

6.3.1 Tasks and Stimuli

Thirteen healthy volunteers (5 male, 8 female, 19-24 yrs) were recruited. All participants gave their informed consent to participate in the study and the experimental procedures were approved by the Office of Research Ethics at the University of Waterloo.

For each of the participants, simultaneous somatosensory and visual stimulation was delivered in the presence of varying levels of intramodal noise. Vibrotactile stimulation was delivered via a modified speaker. Participants were instructed to rest their right index finger upon a piece of Velcro© (1 cm x 1 cm) attached to the dust cap located at the center of the speaker's diaphragm. The dust cap vibrated at varying forces by passing fluctuating current through the voice coil of the speaker via a 25 Hz sine wave with random intensity fluctuations. Vibrotactile stimulation was controlled by digitally generating waveforms that were converted to an analog signal (DAQCard 6024E, National Instruments, Austin, Texas) and then amplified (Bryston 2B-LP, Peterborough, Ontario, Canada). Variation in the amplitude of the driving voltage at the given frequency (25 Hz) led to proportionate increases in force applied by the dust cap onto the volar surface of the finger. The vibrotactile waveform varied in average frequency from 0.10 Hz – 0.50 Hz superimposed upon the underlying 25 Hz vibrations and was generated as a random combination of 4 sinusoid waveforms of varying amplitude and frequency using custom software (Labview 7.1, National Instruments, Austin, Texas).

The visual stimulus consisted of a red-circle (15 cm in diameter) presented on a flat screen monitor (SyncMaster 171s) at a distance of 68 cm. The intensity of the visual stimulus was controlled using an array of thirty different hexadecimal values for sequential shades of red. The continuous changes in the amplitude of the visual intensity were controlled by sequentially presenting each shade of red using the same Labview software that controlled the vibrotactile stimulation.

Bimodal stimulation was delivered in blocks of 150 seconds. Prior to the start of each block participants were instructed to track the amplitude of the intensity of one modality (target) while ignoring that of the other modality (distracter). Tracking was carried out by applying graded force to a pressure sensitive bulb held in their left hand.

During vibrotactile tracking (Vibrotactile) conditions participants were instructed to continuously track the amplitude of the vibrotactile stimulation on their right index finger by applying graded force to the bulb held in their left hand. During the visual tracking (Visual) conditions participants were instructed to apply graded force that followed the amplitude of the intensity of the red-circle.

In all cases noise was presented simultaneously for each modality. Tactile noise was presented by a second speaker placed to vibrate against the palmar cutaneous surface just below the metacarpo-phalangeal joint of the right index finger. Tactile noise consisted of a constant 25 Hz vibration proportional to the amplitude of the continuous vibrotactile stimulus. Visual noise was presented by placing a red square (21 cm x 21 cm) around the visual stimulus red circle. The visual noise consisted of fluctuations between two shades of red.

In addition to tracking the target modality, noise was manipulated from low to high. During vibrotactile tracking the amplitude of the constant vibrations applied to the cutaneous surface of the metacarpo-phalangeal joint was 25% (Low) or 75% (High) of the maximal amplitude of the tactile stimulus. During visual tracking noise was manipulated by changing the shade of red of the noise square between the 11th and 12th shades of red (Low) or the 11th and 16th shades of red (High). In all cases the associated distracter modality was always presented in the presence of low noise.

Finally, the temporal synchrony between the target and distracter modalities also had two levels, asynchronous and synchronous. In the former case the waveforms that drove the vibrotactile and visuospatial stimulation were either the same (Synchronous) or different (Asynchronous). Manipulations of temporal synchrony were done without the prior knowledge of the subject, in order to prevent an overt bias to one modality over the other. There were four experimental manipulations in total: 1) Low Asynchronous, 2) Low Synchronous, 3) High Asynchronous and 4) High Synchronous. Each of these experimental conditions was performed twice, once each where participants tracked the vibrotactile stimulus or the visual stimulus. There were eight experimental conditions in total (Figure 6-1).

All conditions were performed in a sound-attenuating chamber with the lights off to maximize the luminance of the visual stimulus. Participants received 70 dB whitenoise (70 dB – Stim2, Neuroscan, Compumedics USA, Ltd. Corp., Charlotte, NC) throughout the experiment to avoid vibrotactile tracking via audition.

6.3.2 Data Analyses

Behavioral tracking performance for each condition was quantified by calculating the root mean square error (RMSE) of the difference between the graded motor response and the target stimulus. In all cases the amplitude of the target stimulus was normalized to the motor response. The first and last second of tracking for each block was dropped to avoid artificial increases in RMSE associated with initial lags in participant responses. A decrease in the RMSE represents a decrease in the difference between the motor output generated and the sensory task-relevant target supplied and thus an increase in tracking performance, whereas an increased RMSE represents decreased tracking performance.

Tracking performance was analyzed separately for vibrotactile tracking and visual tracking using 2 (Low/High) x 2 (Asynchronous/Synchronous) ANOVAs. Post-hoc analyses were performed where appropriate.

6.3 Results

A 2 (Low/High) x 2 (Asynchronous/Synchronous) ANOVA on the RMSE values for vibrotactile tracking revealed a significant main effect of Noise [$F(1,4) = 39.93$, $p < 0.00005$, mean (±SEM), High = 0.236 (0.04), Low = 0.191 (0.03)]. There was also a moderate trend for a main effect of Synchrony [$F(1,12) = 3.85$, $p < 0.07$, Asynchronous = 0.225 (0.04), Synchronous = 0.202 (0.03)] as well as a strong trend for a Noise x Synchrony interaction [$F(1,4) = 4.34$, $p < 0.06$] (Figure 6-2A). An inspection of the interaction shown in Figure 6-2A reveals that these effects can be attributed to improved tracking performance during vibrotactile tracking in the presence of high tactile noise when the visual distracter is synchronous compared to asynchronous but no change when there is low tactile noise.

The corresponding analyses for visual tracking revealed a moderate trend for a Noise x Synchrony interaction [$F(1,12) = 3.60$, $p < 0.08$] (Figure 6-2B). An inspection of Figure 6-2B shows that the apparent interaction can be attributed to a slight decrease in tracking performance during visual tracking in the presence of low visual noise when the vibrotactile stimulus was synchronous as opposed to asynchronous. In contrast, there appears to be no change or a slight decrease in tracking performance in the presence of a synchronous vibrotactile distracter when there is high intramodal visual noise.

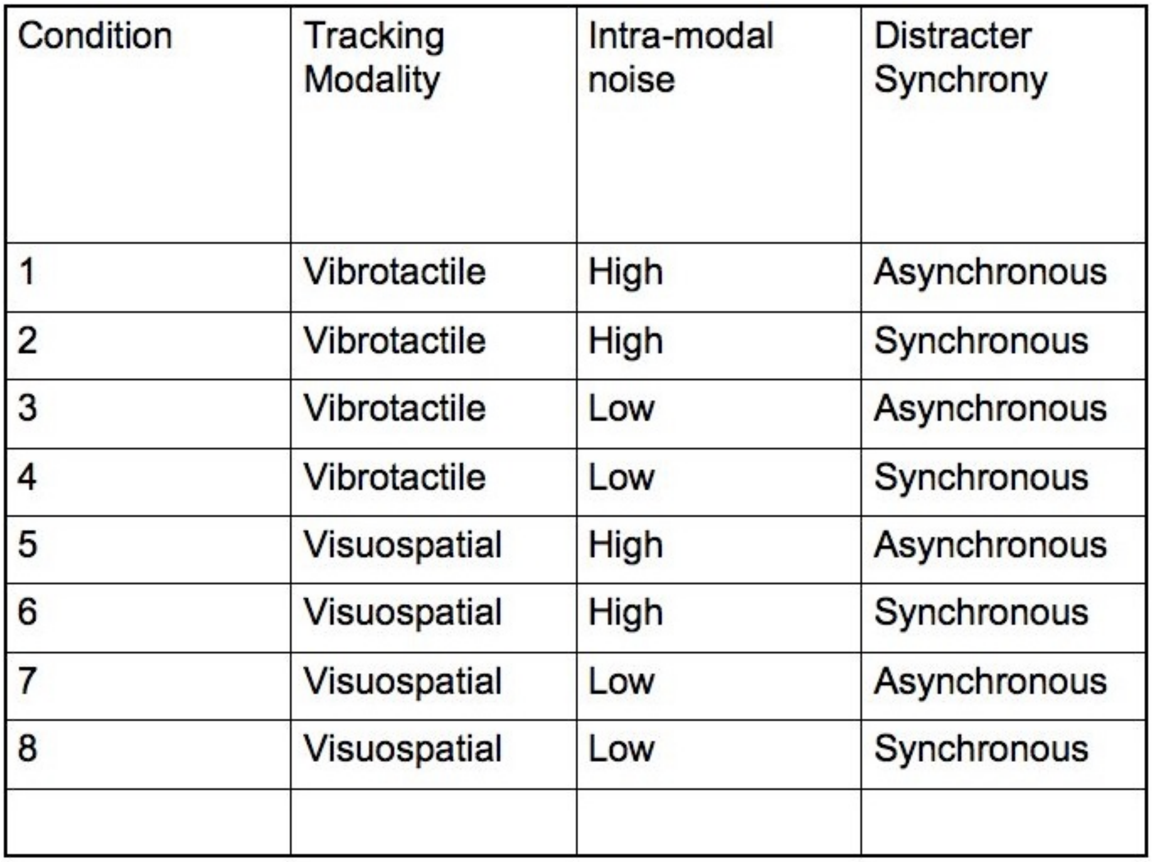
6.4 Discussion

The present study assessed the salience of a synchronous distracter modality during continuous sensorimotor transformations in the presence of varying levels of noise. It was observed that tracking performance increased when a vibrotactile target with a low signal to noise ratio was presented with a simultaneous visual distracter that mirrored the random fluctuations in intensity to be tracked. In contrast, the opposite was true during visual tracking where a concurrently presented synchronous vibrotactile distracter was associated with a decrease in tracking performance when presented with a visual tracking target obscured by higher levels of visual noise.

Increased performance during vibrotactile tracking when intermodal conflict is alleviated by changing the visual distracter is supported by the phenomenon of “visual capture” during movement planning where an irrelevant mirror representation of the left arm has effects upon reaching movements with the occluded right arm (Holmes et al., 2004). It has also been shown that multimodal representations are mediated by the modality that has the greatest signal to noise ratio (Ernst & Banks, 2002). However, what is unique about the current study is that unlike previous studies the visual distracter was explicitly deemed irrelevant to the current task. Therefore, an interesting question arises as to why changing the distracter to reflect the same pattern of changes as the vibrotactile target improved behavior. There are two possibilities 1) participants integrated the two modalities due to the involuntary nature of sensory convergence or 2) the synchronous pattern of the visual distracter made it easier to ignore (cognitive load effects). Load effects can likely be ruled out as if processing of the visual distracter was an issue then it would be expected that there would have been an increase in tracking performance under low intramodal noise in addition to the increase in tracking performance observed during high intramodal noise. With respect to the former possibility it is likely that the similarities in the temporal properties of the spatially related stimuli resulted in multisensory convergence. If this convergence was unconscious then it is likely that the visual stimulus (that had a higher intramodal signal to noise ratio) dominated the conscious percept. If this convergence resulted in conscious perception then it is possible that participants switched attention between the vibrotactile and visual distracter alternately attending to both.

In contrast to vibrotactile tracking, changing the vibrotactile distracter to mimic the random changes in the visual modality resulted in a decrease in tracking performance when the visual target was associated with high visual noise. Again there are two possibilities that may explain this effect 1) visual dominance interacted with multisensory convergence, 2) distraction was greatest when participants had a synchronous vibrotactile distracter. The former would be associated with differential abilities to detect signal from noise for the visuospatial and vibrotactile stimuli. Therefore, the presence of a synchronous vibrotactile distracter resulted in maladaptive integration because of involuntary integration of a noisier vibrotactile representation that converged on the multisensory neurons due to the similarities in their physical properties. This effect would be similar to the McGurk (McGurk & MacDonald, 1976) and ventriloquist (Radeau & Bertelson, 1974) effects. The latter may be associated with lower signal detection but is associated with conscious perception of the similarities between the two modalities. In this case participants realized the two modalities were similar but switching attention between them to ensure that they were still acting in a similar manner penalized participants since the distracter was harder to track in the first place. In both cases the effects observed are likely enhanced by the lack of an effect of the visual intramodal noise manipulation as it appears that the signal to noise was not affected during visual tracking in the presence of high noise.

The current study demonstrates that the effect of a task-irrelevant distracter is dependent not only upon its similarities with the relevant modality but also upon the ability to detect changes within that modality. During a continuous sensorimotor transformation it appears that a concurrent and identically changing visual stimulus can enhance tracking performance while the effects of a similar vibrotactile distracter are only beneficial when the visual stimulus is extensively degraded.



Condition	Tracking Modality	Intra-modal noise	Distracter Synchrony
1	Vibrotactile	High	Asynchronous
2	Vibrotactile	High	Synchronous
3	Vibrotactile	Low	Asynchronous
4	Vibrotactile	Low	Synchronous
5	Visuospatial	High	Asynchronous
6	Visuospatial	High	Synchronous
7	Visuospatial	Low	Asynchronous
8	Visuospatial	Low	Synchronous

Figure 6-1: A layout of the eight conditions used in this study depicting the tracking modality, the level of noise and distracter synchrony. See text for details.

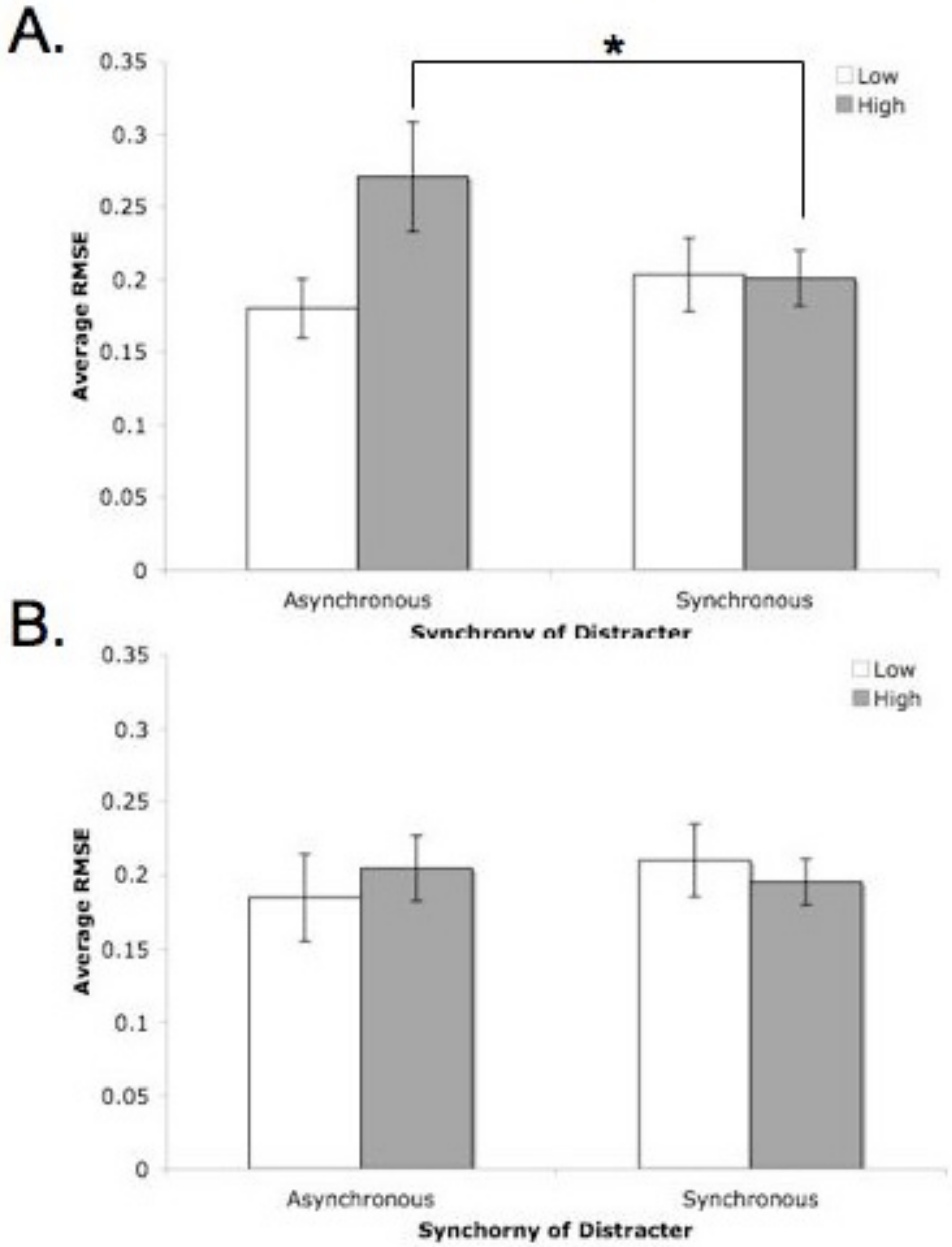


Figure 6-2: A plot of the mean RMSE values demonstrating the interaction between intramodal noise and temporal synchrony during (A) vibrotactile and (B) visual tracking. Bars indicate SEM. * denotes $p < 0.05$.

CHAPTER 7 – General Discussion

The general purpose of the experiments of this thesis was to investigate how sensorimotor requirements interact with attentional modulation of sensory processing associated with competing bimodal stimulation.

In the first two studies (Chapter 2 and 3) participants were presented with simultaneous vibrotactile and visuospatial stimuli and asked to track random fluctuations in one modality while ignoring those from the other. Continuous tracking of the vibrotactile stimulus resulted in decreased activation in S1 compared to when the same vibrotactile stimulus was a distracter during visual tracking. Attending to a vibrotactile stimulus is generally associated with a facilitation of it sensory representation compared to when it is to be ignored (Macaluso, Frith, & Driver, 2002a; Shomstein & Yantis, 2004; Staines et al., 2002). This novel result was replicated in the second study.

In contrast, the spatial relationship (Chapter 2) and the temporal synchrony (Chapter 3) between the two modalities was not reflected at the level of S1 but instead was reflected in various cortical areas despite changes in vibrotactile tracking performance associated with temporal synchrony.

In the third study (Chapter 4), SEPs were employed during a similar continuous tracking paradigm. SEPs were employed to investigate intermodal effects during the early stages of sensory processing. SEPs offer alternative information to fMRI providing additional insights that may be important to the interpretation of results. In the former greater temporal resolution allows for the observation of individual stages of sensory processing while in the latter changes in activation represent an aggregate of all sensory processing in a particular location. SEPs revealed early modulation of sensory processing associated with spatial relationship and temporal synchrony but not the simple modality effects observed in the fMRI studies. Behaviorally, the changes in SEPs appeared to correlate with changes in behavior associated with manipulating spatial relationship and temporal synchrony.

The differential results between the fMRI studies in Chapters 2 and 3 and the SEP study in Chapter 4 may be attributable to differences in what is measured by each technique. As mentioned one difference between the two techniques is the temporal resolution of each method. It is possible that lower temporal resolution of fMRI

(Chapters 2 and 3) may have masked sensitivity of S1 to these changes due to the summation of temporal processing steps, that include initial sensory, as well as feedback, processing. In contrast, the greater temporal resolution of SEPs (Chapter 3) minimizes the role of feedback processing and thus may have under-represented the associated effects of tracking modality.

In addition to the differences in temporal resolution there is also a difference in the dependent measure of each technique. In the case of fMRI changes in BOLD response index changes in cortical activation that are directly related to the physical presentation of the vibrotactile stimulus to the right index finger. However, measures of cortical activation as indexed by SEPs are directly related to the stimulus delivered to the median nerve rather than that to the right index finger. While the median nerve stimulus acts as a probe of the state of the sensory processing pathway for the vibrotactile stimulus, the cortical representation also includes additional sensory representations recruited by the median nerve stimulus.

Another difference between the fMRI studies in Chapters 2 and 3 and the SEP study in Chapter 4 is the change experimental design. In the case of the latter the physical limitations imposed by the scanning environment meant that there was a physical dissociation between the location of the vibrotactile and visuospatial stimuli. Although the spatial experimental manipulation attempted to reduce this dissociation the visuospatial stimulus may not have been perceived to be in peripersonal space. This was not the case in the SEP study as the visual LED was presented directly in peripersonal space. This difference may have been crucial to the effects observed as it has been shown that multisensory interactions involving spatial relationship and temporal synchrony are maximal when a visual stimulus is in peripersonal space, likely due to overlapping receptive fields (Farne, Pavani, Meneghello, & Ladavas, 2000; Maravita, Husain, Clarke, & Driver, 2001; Mattingley, Driver, Beschin, & Robertson, 1997).

Finally, the different sensorimotor transformations inherent to the visuospatial stimulus used in Chapters 2 and 3 and the visual intensity-based used in Chapter 4 may have also contributed to the differential effects. The differences in the sensorimotor relationship of the visual stimulus and the vibrotactile stimulus (an intensity based stimulus itself) may have resulted in greater spatial/temporal interactions with a similar intensity based visual stimulus while the visuospatial stimulus may have favored modality based differences.

In the fourth study (Chapter 5), paired-pulse TMS was delivered over the right index finger representation in S1 (the representation contralateral to the vibrotactile stimulus) during a task requiring continuous sensorimotor tracking or discrete sensorimotor responses in the presence of vibrotactile/visuospatial bimodal stimulation. It was observed that differential states of S1 cortical excitability associated with the motor requirements of the task interacted with the effects of presenting a CS prior to the TS.

Finally, in the fifth study (Chapter 6), the signal to noise ratio of the target modality was altered during tracking in the presence of bimodal stimulation in order to address the opposite effects of the vibrotactile and visual distracters upon tracking performance from the second study (Chapter 3) and the third study (Chapter 4) of this thesis. It was observed that decreasing the ability to detect changes in a vibrotactile stimulus by increasing tactile noise resulted in worse tracking performance, however, a concurrently presented synchronous visual distracter could reduce these deficits despite an overt instruction to ignore the visual modality. In contrast, this effect was not observed during visual tracking and may be attributable to an insensitivity of the visual stimulus to the noise manipulation. This study suggests that the effect of the distracter modality is dependent upon the ability to detect changes in the stimulus from each modality.

7.1 Influence upon sensory processing during continuous sensory-guided movement with bimodal stimulation

Attention is the mechanism by which relevant information is extracted from irrelevant information in our environment. Physiologically, the emphasis of this mechanism is to increase the signal to noise ratio, and thus provide a competitive advantage to the relevant information, by facilitating its sensory representation and/or suppressing the sensory representation of irrelevant information. However, interactions between the motor and sensory cortices of ipsilateral cortex have the potential to increase or decrease S1 activity as well (Mochizuki et al., 2004; Seyal et al., 2005). The net effect is a facilitation or suppression of sensory perception. The strength of these interactions is likely dependent upon the degree of reliance upon ipsilateral (to the sensory stimulus) M1 and S1 to task performance. It is proposed that the weighting of the vibrotactile stimulus in the contralateral (to the sensory stimulus) somatosensory cortex, during a continuous sensory-guided motor response, is susceptible to these inter-hemispheric influences. These influences interact with the intermodal modulation of sensory processing to yield a net decrease in activation, as observed in this thesis. This was observed directly in three different studies using techniques such as fMRI and TMS. In the TMS study (Chapter 5) decreased activation was reflected in a decreased susceptibility to the effects of paired-pulse TMS during a continuous sensorimotor but not discrete sensorimotor task. Interestingly, evidence from SEPs suggests that the early SEP modulation observed in Chapter 4 with the spatial and temporal manipulations demonstrate intermodal processing effects that may interact with inter-hemispheric interactions and potentially reduce this suppression or return activity in stimulus associated S1 back to baseline, improving behavioral performance. Further, it is proposed that the pattern of physiological/behavioral changes associated with the spatial and temporal experimental manipulations are associated with the relative signal to noise ratios of the two simultaneously presented modalities, with the modality that contains the highest signal to noise ratio having a greater impact upon sensory-processing of the modality that is harder to discriminate (Ernst & Banks, 2002; Hecht et al., 2008).

Based upon the assumption that intermodal interactions serve to adjust the signal to noise ratio of each modality and increase or decrease the representation of the relevant and irrelevant modalities in the final multimodal representation of an object or environment the following interpretation of intermodal interactions is proposed.

The basis of the interpretation of sensorimotor processing during bimodal stimulation suggests that integration is in part a feedforward function of the relative signal to noise ratios of the simultaneous bimodal stimuli and that the loci of modulation of the individual sensory representations is a function of the stimulus feature of interest (i.e. the relevant modality or a subset of the relevant modality defined by a spatial or temporal aspect).

Using a vibrotactile/visual example applicable to the studies of this thesis, each modality is detected by its respective peripheral sensory receptor that converts the sensory stimulus into an electrical representation. The representation of each modality is then transmitted to it respective primary sensory cortex via thalamic relay nuclei. The thalamic nuclei are the first potential site of modulation. It is proposed that the thalamic reticular nucleus modulates the transmission of sensory information by controlling the firing pattern of the thalamic relay nuclei. This control is a function of collaterals between the various modality representations in the thalamic reticular nucleus and is based upon the spatial/temporal similarities between the two simultaneously presented modalities. In addition, cognitive task demands also mediate activation of the thalamus, likely through higher order thalamic relay nuclei by adjusting the firing rates of cortical-thalamic-cortical potentials.

Following relay from the thalamic nuclei, sensory information is then processed in a hierarchical manner in which the receptive fields and the relation between the peripheral and central sensory representations further deviate at each stage with projections from higher processing areas feeding back to lower processing centers to restrict the flow of information based upon spatial and temporal factors, likely starting at the level of secondary cortices. Finally, in its simplest form, the simultaneous sensory information converges upon a multisensory neuron in the parietal cortex (Andersen et al., 1997) and is converted to a representation that no longer reflects one modality but the statistically optimal sum of the two modalities that have converged (Ernst & Banks, 2002). This statistically optimal integration is dependent upon the modulation of the two sensory representations with those where the signal has been suppressed dropping out or contributing a minimal amount to the multisensory representation and those where the signal is sufficiently greater than processing noise contributing the most.

In addition to the sensory modulation starting as early as primary sensory cortices, there are also inter-hemispheric interactions that are present depending upon the states of M1 and S1 in both hemispheres. Based upon the observations from Studies 1, 2 and 4 as well as previous research (Mochizuki et al., 2004; Seyal et al., 2005), it is proposed that the sensory processing of a vibrotactile stimulus is extremely susceptible to these influences, more so than visual stimuli. Somatosensory processing is proposed to be a function of a competitive balance between ipsilateral (to the somatosensory stimulation) and contralateral M1 as well as ipsilateral and contralateral S1 with task-related activation in the ipsilateral M1 and S1 cortices influencing somatosensory processing through inter-hemispheric inhibitory mechanisms. It is further hypothesized that these interactions are largest for continuous sensory-guided movements that require constant changes in motor output that must be resolved using re-afferent sensory input. The outcome is that the net effect on somatosensory processing is a sum of excitatory and inhibitory influences associated with intermodal attentional modulation and inter-hemispheric interactions, the latter of which may be of greater influence to somatosensory processing.

7.2 Limitations of thesis

There are a couple of limitations to the interpretation of the data in the current thesis relating to the measures of behavior and physiological changes associated with experimental manipulations. The first of which is the interpretation of behavioral changes as reflect by changes in RMSE. In the current thesis RMSE was used as a measure of the difference between the pattern of force changes the participant was required to make and the pattern of force changes the participant actually made. However, inherent in RMSE are a number of factors that could explain behavioral difference across conditions: 1) phase lag, 2) reaction time and 3) amplitude scaling.

Although RMS changes were used to infer changes in performance, exactly what aspect of performance was modulated and what aspect of performance correlated with the physiological changes observed (in both S1 and other cortical areas) cannot be distinguished. Although the analyses employed in this thesis attempted to minimize certain components that could be related to behavioral changes, future work should attempt to employ behavioral analyses that parse out the contributions of each factor. Failing this, future work should attempt to devise a continuous stimulus that contains explicit dependent measures of each.

In relation to the limitations of RMS, a second limitation of the current study is the absence of direct measures of momentary states of attention. During tracking of the random intensity changes it is possible that participants may have employed a strategy in which they simply detected peaks/maximums and valleys/minimums in the stimulus. In such a scenario it is possible the state of attention may have been differential in between these two points. This scenario may have resulted in the underestimation of attentional modulations and behavioral effects associated with the experimental manipulations. A possible solution to address this limitation would have been to insert abrupt changes into the continuous waveform of the modality to be tracked at random intervals between peak maximum and minimum stimulus value to determine if participants shifted attention elsewhere after altering motor output after a peak or valley.

A final limitation of the current study is the inability to directly relate the results of the studies in Chapters 2 and 3 and that in Chapter 4. This relates back to the differences in technique and experimental setup between fMRI and SEPs. Solutions to this limitation will be discussed in the next section.

7.3 Future Directions

There are a number of experiments that can be done using this continuous tracking task. The goal of this thesis was to highlight the importance of the interactions between intermodal selective mechanisms and sensorimotor requirements in understanding sensory processing. In the following sections I briefly outline three potential studies that address various issues raised in sections 7.1 and 7.2.

The first study addresses the limitation of the generalizability of results across the fMRI and SEP studies. Three aspects changed between these studies, 1) the change in the visual sensorimotor transformation, 2) the change of the visual distracter location from extrapersonal to peripersonal space and 3) the stimulus represented by each measure of physiological changes.

In a follow-up study the contribution of each of these factors to modality effects versus spatial/temporal effects could be titrated out by systematically manipulating the first and second factors while collecting SEPs. Using SEPs to index physiological changes rather than fMRI would provide consistent measures while offering greater flexibility in experimental setup.

In such a study, one set of conditions would involve vibrotactile/visuospatial bimodal stimulation while a second set would involve vibrotactile/visual intensity based bimodal stimulation. It would be hypothesized that if the change in visual stimulus was responsible for the differential results using fMRI and SEPs then SEP amplitude should demonstrate a modality, but not spatial/temporal effects with vibrotactile/visuospatial bimodal stimulation. In contrast, it would be hypothesized that the vibrotactile/visual intensity bimodal stimulation would replicate the results in Chapter 4.

In addition to addressing the change in the visual stimulus the issue of peripersonal space could also be addressed by orthogonally manipulating whether visuospatial or visual intensity based bimodal stimulation presented in peripersonal or extrapersonal space.

Two interesting results from Chapter 3 were the increased activation of the inferior frontal gyrus (BA 9) during continuous tracking in the presence of bimodal conflict (Table 3-1) and the increased activation of the middle temporal gyrus (BA 19/39) with non-conflicting bimodal stimulation during vibrotactile tracking (Table 3-1 and 3-2 respectively). The inferior frontal gyrus (DLPFC) has been implicated as part of the pre-frontal cortical gating network (Staines et al., 2002) while the middle temporal gyrus (an area called the TPJ) has been linked to the extraction and integration of relevant multisensory inputs (Downar et al., 2000; Downar et al., 2001), however their exact roles during continuous sensorimotor tracking in the presence of bimodal stimulation are unknown. One hypothesis is that the DLPFC mediates the selection of the vibrotactile stimulus. Alternatively, the DLPFC may be mediating any effects associated with intramodal inter-hemispheric interactions between the two sensorimotor areas in each hemisphere. In addition, it is hypothesized that the TPJ serves to monitor the relevance of the visuospatial distracter to the ongoing sensorimotor transformation, similar to the role of the ventral circuit-breaking network proposed in visual attention (Corbetta & Shulman, 2002). The relative roles of these areas to the modulation of sensory processing could be determined using fMRI and/or using rTMS, with the former serving to observe changes in physiological response and the latter to determine behavioral/physiological changes in sensory processing associated with active disruption of each area. Differences in activation/behavior could be teased out by employing a similar set of tasks used in the current thesis in which continuous tracking is performed in the presence of bimodal stimulation. In addition to manipulating temporal synchrony, the perceptual thresholds of the vibrotactile stimulus would be altered to provide an easy/hard distinction.

There would be six conditions of interest 1) Easy Vibrotactile Tracking, No Visual Distracter, 2) Hard Vibrotactile Tracking, No Distracter, 3) Easy Vibrotactile Tracking with Conflicting Visual Distracter, 4) Hard Vibrotactile Tracking with Conflicting Distracter, 5) Easy Vibrotactile Tracking with Non-conflicting Distracter and 6) Hard Vibrotactile Tracking with Non-conflicting distracter.

If DLPFC reflects mechanisms associated with inter-hemispheric sensorimotor interactions then DLPFC activation would be greater when the vibrotactile stimulus is harder to track (activation is greater in condition 2 than condition 1) and that this relative difference is unchanged when the visual distracter is introduced (no difference between conditions 1 and 3 and conditions 2 and 4). In contrast it would be hypothesized that if TPJ is involved with monitoring the relevance of the visual distracter to the continuous sensory-guided movement then activation would increase when a non-conflicting distracter supplements a hard to track vibrotactile stimulus compared to when the same distracter supplements an easy to tracking vibrotactile stimulus (TPJ activation will be greater in condition 6 than in condition 5).

Finally, as mentioned, the long-term goal of this thesis was to understand the pathway involved with the modulation of incoming sensory information during continuous movement. In the current thesis this model was simplified to separate motor and sensory requirement across hemispheres. However, in every day life we generally move the limb with which the sensory information is associated. The prime example is the use of proprioceptive and visual information during sensory-guided movement. Therefore, a second set of experiments would investigate intermodal modulation of sensory processing during spatially related but conflicting visual and proprioceptive inputs, possibly by degrading one of these modalities to determine if modulation of sensory processing is a function of both motor requirements and intermodal attentional mechanisms. This has been investigated to a certain extent in visual-tactile cross-modal extinction paradigms but these often require discrete responses.

7.4 Conclusions

Overall, the results of this thesis provide evidence for early modulation of somatosensory processing associated with extracting vibrotactile information in the presence of a competing visual distracter. Furthermore, they illustrate the importance of motor requirements in determining the net outcome of intermodal modulation of sensory processing and offer insight into considerations that must be taken into account when developing future studies investigating intermodal interactions.

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