Investigating the attentional effects of acute aerobic exercise and crossmodal processing on the modulation of frontoparietal interactions

by

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Author's Declaration

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Statements of Contributions

I hereby attest that my contribution to the material presented in this thesis included sole-authorship of: Chapters 1, 2, 4-6. My contribution to Chapter 3 included: participant recruitment, data collection, statistical analysis, all figure illustrations, as well as co-authorship writing the published journal article.

Abstract

The sense of touch commences when afferent sensory signals from the periphery ascend via the spinal cord to the cortex. At the cortical level, incoming peripheral signals are susceptible to neuronal modulation at the primary somatosensory cortex; the principle region responsible for tactile perception. This modulation is largely influenced by two attentional mechanisms: 1) Bottom-up attention whereby salient stimuli automatically capture attention; and/or, 2) Top-down or selective attention, whereby relevant sensory signals are voluntarily selected for in-depth cognitive processing, while irrelevant signals are ignored. Selective attention to both task-relevant stimuli as well as to crossmodal sensory interactions can facilitate neuronal responses at very early stages in modality-specific sensory regions. Efforts to understand the mechanisms underlying top-down attention suggest that the prefrontal cortex (PFC) has a critical role in the modulation of modality-specific regions by gating or suppressing irrelevant sensory information. Recent evidence suggests that an acute bout of moderate intensity aerobic exercise upregulates PFC excitability thereby facilitating cognitive tasks requiring top-down attentional control, particularly in older populations. However, the specific contribution of each sensory system during attentional processing and, importantly, how these interact with the required behavioural motor goals remains unclear. It is also unclear whether acute bouts of moderate intensity aerobic exercise modulate cortical regions downstream from the PFC, such as the somatosensory cortex. This thesis will aim to address these questions in order to gain a better understanding of the neural mechanisms underlying somatosensory processing, and whether aerobic exercise can be used as a plausible intervention strategy for sensory processing impairments that are often associated with normal aging.

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List of Abbreviations

ACC Anterior cingulate cortex

ANOVA Analysis of variance

BDNF Brain derived neurotrophic factor

BOLD Blood oxygen level dependent

CFT Cardiovascular fitness training

cTBS Continuous theta burst stimulation

DLPFC Dorsolateral prefrontal cortex

EEG Electroencephalography

ERN Error-related negativity

ERP Event-related potential

fMRI Functional magnetic resonance imaging

fNIRS Funtional near-infrared resonance spectroscophy

HRmax Heart rate max

IGF-1 Insulin growth factor 1

MEG Magnetoencephalography

PET Positron emission topography

PFC Prefrontal cortex

RA Rapidly adapting

RAH Reticular activating hypofrontality

RAS Reticular activating system

SA Slowly Adapting

SEF Somatosensory evoked field

SEP Somatosensory evoked potential

SI Primary somatosensory cortex

SII Secondary somatosensory cortex

TPJ Temporal parietal junction

TRN Thalamic reticular nucleus

VEGF-1 Vascular endothialial growth factor 1

VPL Ventral posterior lateral thalamus

V0$_2$max Maximal oxygen uptake

Chapter 1 – Introduction

1.1 Overview of thesis proposal

Chapter 1 outlines the general objectives of the thesis, followed by a review of relevant literature pertaining to the anatomy and physiology of somatosensory cortex, the sensory-gating role of the prefrontal cortex in modulating task-relevant sensory information in modality-specific sensory regions, and how aerobic exercise influences attention-related cortical activity during sensory processing. Chapters 2-5 detail the rationale, hypotheses, methods, results, discussion, and conclusions of the research studies to the thesis. Chapter 6 includes a general discussion of the findings of the thesis, its limitations, and future directions for study.

1.2 General objective of thesis

The general objective of this thesis is to probe the sensory-gating role of the prefrontal cortex (PFC) to examine the neural mechanisms underlying top-down attentional control on modality-specific somatosensory cortex. On a larger scale, investigating factors that up-regulate or enhance neuronal activity in the PFC is critical for gaining a better understanding of the well-documented impairments in cognitive control and sensory processing often observed in elderly populations. Research in animal models and patients with focal lesions in the PFC have provided compelling evidence for the sensory-gating role of the PFC in the suppression of task-irrelevant sensory information (Jacobson et al., 1935; Skinner and Yingling, 1976; Yingling and Skinner, 1976; Yamaguchi and Knight, 1990; Chao and Knight, 1998; Knight et al., 1999). In all of these studies, PFC damage resulted in the disinhibition of distractor stimuli in a range of sensorimotor and cognitive processes. These findings provide support for the "distractibility hypothesis of

PFC function", first proposed in 1942 by Malmo, and later again by Bartus and Levere in 1977. As stated by Knight et al. (1999), this hypothesis implies that the PFC exerts "selective and parallel inhibition and excitation control to remote brain regions during a variety of behaviours". Notably, inhibitory control impairments such as: inhibiting proponent responses that are no longer task relevant and ignoring distractor stimuli in the environment are among the most consistently reported in older adults (Rabbitt, 1965; Kausler and Hakami, 1982; Hasher and Zacks, 1988; Yamaguchi and Knight, 1990; Fabiani et al., 2006; Reuter-Lorenz and Park, 2010; Bolton and Staines, 2012). Neuroimaging data has shown that with increasing age, atrophy of frontal lobe regions is disproportionately greater relative to other brains areas (Haug and Eggers, 1991), with the greatest shrinkage occurring in medial temporal areas of the frontal lobe (Raz, 2000). Collectively, these findings suggest that the distractibility hypothesis of PFC function may also explain inhibitory control impairments seen in elderly populations.

Studies investigating multimodal integration suggest that top-down attentional control is critical for driving modulation of early stages of cortical processing during a sensory to motor integration task (Dionne et al., 2010, 2013). Moreover, growing evidence suggests that acute bouts of aerobic exercise selectively enhance neuronal excitability in frontal lobe regions, thereby facilitating cognitive performance in tasks involving executive functions (Hillman et al., 2004; Hatta et al., 2005; Themanson et al., 2006; Hillman et al., 2008, 2009; Kamijo et al., 2010; Yanagisawa et al., 2010). Although crossmodal integration or aerobic exercise are not the only factors that seem to influence PFC excitability, the studies presented in this thesis seek to investigate whether enhanced attentional control, mediated likely via the PFC, will enhance somatosensory ERPs generated over modality-specific and multimodal cortices during selective attentional processing of tactile information. The interaction of vision and touch is of particular interest since information from these modalities is often used to guide motor behaviour. Effects of vision on somatosensory event-related potential (ERP) components suggest that vision may modulate excitability in SI (as inferred by modulation of somatosensory ERP components) during a tactile acuity task, and that this modulation is associated with an improvement in acuity (Taylor-Clarke et al., 2002). It is known that stimulus relevance and selective attention can modulate early stages of somatosensory processing (Dionne et al., 2010, 2013). The purpose of this thesis is to further explore somatosensory processing by investigating whether factors such as bottom-up sensory-sensory interactions, behavioural context, or aerobic exercise, also modulate neuronal responses in modality-specific SI.

1.3 Background research

1.3.1 Functional organization of somatosensory cortex

The somatosensory cortex is the brain region responsible for processing somatic signals related to the body (i.e. touch, temperature, pain, position). Somatosensory information is represented in multiple brain regions, but the primary and secondary somatosensory cortices (SI and SII) are the principal regions for tactile perception (Johansen-Berg et al., 2000). SI is located caudal to the central sulcus in the postcentral gyrus of the parietal lobe, while SII is found in the most lateral portion adjacent to the Sylvian fissure. SI is arranged in a somatotopically organized map with feet and face representations lying most medial and lateral, respectively. Four functionally and anatomically distinct Brodmann areas comprise SI: 3a, 3b, 1 and 2, with area 3a located anterior and area 2 located to posterior along the postcentral gyrus. Somatosensory processing occurs when peripheral inputs from the dorsal column-medial lemniscal system reach Brodmann areas via thalamic sensory nuclei. The majority of thalamic fibres terminate in areas 3a and 3b, while surrounding cells send small projections to areas 1 and 2. Independent thalamocortical inputs generated by cutaneous afferents are received by areas 3b and 1. Proprioceptive inputs from peripheral muscle and joint afferents are received by areas 3a and 2. The input to 3b is primarily thalamocortical, however input from 3b to areas 1 and 2 consist of thalamocortical and cortico-cortical projections. Lesion studies in primate have shown that damage to: area 1 impairs texture discrimination, area 2 impairs contour recognition, while global somatic deficits are produced following damage to area 3b since it is the main pathway for cutaneous input to areas 1 and 2 (Randolph and Semmes, 1974; Carlson, 1981). Furthermore, the removal of neural connections in the hand area of SI resulted in abolished SII activation, while removal of SII regions had no effect on SI neuronal responses following stimulation to the hand. Each Brodmann area in SI is extensively interconnected so that processing in adjacent, higher-order sensory regions, including SII, can refine the information of a single sensory modality.

SII (also known as the parietal operculum) receives thalamocortical and cortico-cortical projections from thalamic somatosensory nuclei and post-central somatosensory areas, respectively. Somatotopic mapping of the body surface is less precise in SII and lesions in this area tend to produce more complex somatosensory disorders than lesions of SI (Garcha and Ettlinger, 1978). This is in line with the role of SII in executing higher-order somatosensory functions including tactile discrimination, memory and learning, as well as, somatosensory engagement of the motor system at the cortical level (Burton et al., 1997;

Mima et al., 1998; Johansen-Berg et al., 2000; Fujiwara et al., 2002). Studies indicate bilateral SII activation during somatosensory stimulation, although larger SII responses are typically found in regions contralateral to stimulation (Johansen-Berg et al., 2000; Nelson et al., 2004). However, several studies have demonstrated that SI cortical activity is also modulated by higher-order processes including selective attention (Meyer et al., 1991; Johansen-Berg et al., 2000; Popovich et al., 2010; Roland, 2012).

Higher-order sensory areas also send refined output information to multimodal association areas that, in turn, have the capability to integrate sensory information from multiple sensory modalities and co-ordinate goal-oriented behavioural responses. The posterior parietal cortex (Brodmann areas 5, 7), is considered to be a multimodal association area that receives input from SI and sends projections to the motor areas of the frontal lobe. Area 5 integrates tactile information from the skin's mechanoreceptors of both hands with proprioceptive signals from underlying muscles and joints. Area 7 receives and integrates tactile and visual proprioceptive inputs. Thus, the PPC is believed to have an important role in sensory integration and in the guidance and execution of motor actions.

1.3.2 Cortical somatosensory processing of tactile information

The somatosensory cortex, SI in particular, receives a wide range of somatic signals from different peripheral receptors including: mechanoreceptors for touch, vibration and/or pressure, thermoreceptors for thermal sensations, and nociceptors for pain. Humans possess four types of cutaneous afferent fibers which are classified based on how they adapt to constant skin indentation (Vallbo and Johansson, 1984). Slowly-adapting

(SA) fibers are associated with Merkel cells and Ruffini receptor endings, which during constant skin indentation and increased indentation, exhibit sustained discharge and increased firing rates, respectively. Rapidly-adapting (RA) fibers are associated with Meissner and Pacinian mechanoreceptors, which exhibit robust neuronal responses to the onset and offset of indentation. Notably, each of these fibres selectively responds to different spatiotemporal features of the stimulus (Talbot et al., 1968; Mountcastle et al., 1972).

Before the brain can process somatic signals received at one of these receptors, peripheral input must travel via afferent nerve fibres to dorsal root ganglion neurons in the dorsal root of spinal nerves. At the level of the spinal cord is where sensory pathways to the cortex diverge such that touch and proprioceptive inputs are transmitted via refined large diameter axons, while small axons send information regarding temperature and pain. Due to the potentially harmful nature of sensory information regarding temperature and pain, these peripheral signals follow a different, more direct pathway to the cortex. The sense of touch commences when peripheral signals carrying information about tactile stimuli impinge on the body's surface via mechanoreceptors of the skin. These signals are transmitted via central axons of dorsal root ganglion cells that convey information about the properties of mechanical contact (i.e. place, mode, intensity), before they enter the ipsilateral dorsal columns of the spinal cord, and travel to dorsal column nuclei of the medulla via the dorsal-column medial lemniscus pathway. At the medulla, somatosensory signals synapse onto secondary sensory neurons, which cross-over or decussate, to the contralateral side of the medulla before projecting to and terminating at, the ventral posterior lateral (VPL) region of the thalamus. VPL thalamic neurons receiving these inputs then send projections to somatosensory regions, whereby the most thalamic input terminates in Brodmann areas 3a and 3b, which in turn project to 1 and 2. The VPL thalamic neurons also send some sparse but direct projections to areas 1 and 2.

SI is functionally organized with neuronal columns specified for peripheral stimulation mode and location, thereby ensuring that the integrity of somatic signals is maintained as peripheral input travels from receptor to cortex (Mountcastle, 1997). In order to optimize neuronal efficiency, intracortical projections connect functionally related columns. SI neurons exhibit similar firing rates to cutaneous afferents thus can also be classified as rapidly or slowly adapting mechanoreceptors (Talbot et al., 1968; Mountcastle et al., 1972). A separate somatotopic representation of body form is associated with each of the four somatosensory areas, whereby a direct relationship between peripheral innervation density and cortical representation exists. As sensory information progresses through SI (i.e. area 3b to 1), modality and spatial specificity shifts to a more universal convergence of information to inform higher order processing. Once SI processes thalamocortical input, it sends cortico-cortical projections to posterior parietal, temporal, and frontal lobes (Kandel et al., 1991).

1.3.3 Task-relevant selective attention modulations in somatosensory cortex

Two cognitive processes can mediate attention. Bottom-up attention refers to when salient stimuli automatically capture attention. Top-down or selective attention describes when relevant sensory signals are selected for further in-depth cognitive processing, while irrelevant signals are ignored. Neurophysiological primate studies provide evidence that selective attention to somatosensory information enhances neurophysiological responses in modality-specific somatosensory cortical regions. Hsiao et al. (1993) trained monkeys to perform separate tactile and visual discrimination tasks. In the tactile task, rewards were delivered only after the monkey correctly identified whether a letter displayed on a monitor matched the pattern of an embossed letter rotated against their fingertip. In the visual task, the same tactile pattern was delivered to the fingertip, but rewards were delivered only after the monkey correctly identified when one of three light-emitting diode displays dimmed. Results showed that neuronal responses elicited during the tactile versus visual discrimination task only produced increased SI firing rates, while both increased and decreased firing rates were observed in SII (Hsiao et al., 1993). Similarly, Chapman et al. (1994) found that performance of a tactile discrimination task increased neuronal responses in the SI of monkey cortex. Nelson et al. (1991), recorded vibratory stimulus-related responses from monkey SI while the animal performed either a: 1) movement task, whereby vibratory stimuli acted as a go-cue for wrist movement, or 2) no-movement task, whereby the same vibratory stimuli required no movement. Deep receptive field neurons located in Brodmann areas 3a, 3b, and 1, and cutaneous receptive fields in area 3b of the SI, showed enhanced firing rates during the movement task relative to the no-movement task (Nelson et al., 1991).

Additional studies investigating attentional effects in SI using tactile stimuli, have failed to report such an association (Hyvärinen et al., 1980; Poranen and Hyvärinen, 1982; Hämäläinen et al., 2002). Differences in the nature of the task used to examine SI attentional effects may be responsible for these oppositional findings. For example, in a functional magnetic resonance imaging (fMRI) study by Nelson et al. (2004), both attentional demand requirements and the physical characteristics of the tactile stimuli were manipulated. During the attend condition, participants detected slight variations in the stimulus amplitude of the tactile stimuli, while in the ignore condition, trains of similar tactile stimuli were ignored. Due to the variations in attentional demand and stimulus attributes, it is possible that the greater habituation effects observed in SI during ignore versus attend conditions may have inflated the activation differences between the conditions. Conversely, a fMRI study by Hamalainen et al. (2002), found no attentional effects in SI using an oddball paradigm comprised of ignore and attend conditions, but during the ignore condition, tactile stimuli were passively ignored and no further task was given. Johansen-Berg and Lloyd (2000) argue that it is difficult to control attentional focus when no distractor stimuli are used in ignore conditions to ensure disengagement from the tactile stimuli. Thus, the lack of SI attentional effects found in this study may be a result of the passive nature of the ignore condition.

Human neuroimaging studies, using Positron Emission Tomography (PET), or fMRI, have shown that somatosensory discrimination tasks increased regional blood flow in SI and SII regions during task-relevant versus irrelevant stimuli (Roland, 1981; Meyer et al., 1991; Pardo et al., 1991; Burton et al., 1999; Johansen-Berg et al., 2000; Nelson et al., 2004; Sterr et al., 2007). Using fMRI, Nelson et al. (2004), reported a significant increase in percent signal change and activation volume in SI with attention, while Johansen-Berg et al. (2000) and Staines et al. (2002), reported increased brain activity, as measured by the blood oxygenated level dependent (BOLD) signal changes in SI and SII of equal magnitude, during attended versus unattended tactile conditions. Decreased SI activity has been observed when attention is guided towards a different spatial location of the body (Drevets et al. 1995), or to a different sensory modality (Haxby et al., 1994; Kawashima et al., 1995;

Fiez et al., 1996). Yet, some neuroimaging studies have failed to report any attentional effects in SI (Backes et al., 2000; Hoechstetter et al., 2000; Hämäläinen et al., 2002), or have reported diminished attention-related SI activation compared to that generated in SII (Mima et al., 1998; Fujiwara et al., 2002; Chen et al., 2008). It is likely that these opposing findings are due to differences in the characteristics of the tactile stimuli employed or in the attentional demand of the task. Another possibility for these discrepant findings may be that the neuroimaging technique used may not be sensitive enough to detect discrete changes in neuronal modulation. Thus, techniques equipped with exquisite temporal resolution, such as electroencephalography (EEG) and magnetoencephalography (MEG) may be better-suited to understanding the neural mechanisms underlying attentional effects in modality-specific cortices.

Attention-related enhancements of SI activity using these techniques are well-documented, with reports of increased modulation occurring at early components of somatosensory evoked potentials (SEPs) (Desmedt et al., 1983; Desmedt and Tomberg, 1989; Josiassen et al., 1990; Garcia-Larrea and Lukaszewicz, 1995), somatosensory evoked fields (SEFs) (Iguchi et al., 2001, 2002) , and somatosensory event-related potentials (ERPs) (Michie, 1984; Michie et al., 1987; Staines et al., 2002; Schaefer et al., 2005; Schubert et al., 2008). Robust evidence suggests SI plays a central role in gating sensory information at early stages of somatosensory perception by amplifying neural signals conveying task-relevant tactile information and suppressing task-irrelevant distractor stimuli (Meyer et al., 1991; Staines et al., 2002; Nelson et al., 2004; ; Sterr et al., 2007; Dionne et al., 2013; Popovich and Staines, 2014). By contrast, SII is believed to be involved in higher-order somatosensory processes including: identifying and/or comparing stimulus attributes (i.e. roughness, length, shape) (Ledberg et al., 1995; Hadjikhani and Roland, 1998; Burton et al., 1999), and sensorimotor integrations (Huttunen et al., 1996; Binkofski et al., 1999). Overall, attentional effects in SI suggest that top-down control processes, such as task-relevancy, can influence cortical modulation in modality-specific somatosensory cortices.

Crossmodal integration of sensory information also facilitates attentional modulation in modality-specific sensory cortices. Functional imaging studies performed in monkey auditory cortex have shown distinct regions receptive to the presentation of visual plus auditory stimulation, and somatosensory plus auditory stimulation (Kayser et al., 2005, 2007). Lakatos et al. (2007) found that simultaneous presentation of somatosensory and auditory stimuli versus auditory stimuli alone enhanced neuronal responses in auditory cortex (Lakatos et al., 2007). Ghazanfar et al. (2005), found increased activity in auditory cortex when auditory and visual stimuli were presented together, as well as some auditory cells that responded only to visual stimuli (Ghazanfar et al., 2005). Similar effects have also been reported in the somatosensory cortex, whereby SI neurons showed increased firing in response to visual stimuli previously paired with tactile stimuli (Zhou and Fuster, 2000). Functional MRI studies have found enhancements in modality-specific BOLD responses, due to the mere presence of stimuli from another sensory modality (Calvert et al., 1997; Calvert, 2001; Foxe et al., 2002; Macaluso et al., 2000, 2002; Lehmann et al., 2006; Pekkola et al., 2006; Schürmann et al., 2006; Meehan and Staines, 2009). However, in a study using a continuous motor-tracking task, it was shown that the presence of crossmodal (visual and tactile) stimuli produced differential modulation in contralateral SI when tactile information was relevant versus irrelevant. Here, a greater increase in SI volume relative to the rest condition was found when the vibrotactile stimulus was task-irrelevant compared to the increase in volume when the same stimulus was task-relevant (Meehan and Staines, 2007). The authors offered several possible explanations for their findings, one of which concluded that the behavioural requirements of the crossmodal task may determine the nature of SI modulation, and in this case, the continuous motor-tracking demands and presence of a crossmodal distractor may have been mitigating factors for the observed SI suppression.

Other studies have shown crossmodal enhancement in modality-specific sensory cortex only occurs when both stimuli events are relevant for behaviour (Dionne et al., 2010, 2013). For example, in an fMRI study by Dionne et al. (2010), relevant unimodal (visual or tactile) and crossmodal stimuli (visual+tactile) were randomly presented and participants were instructed to summate both stimuli by squeezing a pressure-sensitive bulb. Prior to the experiment, subjects completed a brief sensorimotor training session, whereby, learned associations between the amplitude of visual and vibrotactile stimuli were established so that graded motor response representing the perceived amplitude of the stimuli could be performed. Results revealed a common network of activation in frontal-parietal regions across all conditions, regardless of stimulus modality. Enhanced BOLD responses were elicited in SI during crossmodal versus unimodal interactions, suggesting that combining visual-tactile information relevant for behaviour enhances modality-specific excitability in SI (Dionne et al., 2010). Several studies using multisensory integration tasks have shown increased BOLD activity in higher-order frontal and parietal cortical regions including the: dorsolateral prefrontal cortex (DLPFC), temporal parietal junction, superior temporal sulcus, and intraparietal sulcus (McDonald et al., 2000; Calvert, 2001; Downar et al., 2001; Beauchamp et al., 2004, 2008). It is believed that the DLPFC is particularly involved in top-down modulation of crossmodal interactions.

EEG studies have shown that crossmodal attention facilitates early stages of sensory processing. Giard and Peronnet (1999), found that visual modulation for audio-visual stimuli, occurred as early as 40 ms post-stimulus onset (Giard and Peronnet, 1999), while audio-tactile modulation has been found at 50 ms (Foxe et al., 2000; Molholm et al., 2002). Kennett et al. (2001), found modulation of visual ERPs by irrelevant but spatially aligned tactile stimuli at approximately 140 ms post visual onset (Kennett et al., 2001), while McDonald et al. (2000), reported modulation of visual ERPs was possible with spatially aligned auditory stimuli (McDonald et al., 2000). Schürmann et al. (2002) reported enhancements in evoked-potentials over midline and ipsilateral electrode sites at 75 ms when visual stimuli were paired with median nerve stimulation (Schürmann et al., 2002). Lastly, in a recent EEG study using the same crossmodal stimuli and pressure-sensitive bulb paradigm (refer to Dionne et al., 2010), it was shown that task-relevant crossmodal interactions between vibrotactile and visual stimuli enhanced the P50 somatosensory event-related component, generated in SI, at contralateral parietal electrode sites. In addition, the amplitude of the P100, likely generated in SII, increased bilaterally at parietal electrode sites during presentation of crossmodal stimuli but was not sensitive to the task-relevance of the stimuli. Although, ERP studies have shown attention-related modulation of the P100 component (Desmedt et al., 1983; Josiassen et al., 1982; Michie et al., 1987; Eimer and Forster, 2003a; Schubert et al., 2006), studies investigating crossmodal effects on mid-latency components fail to report any effects on this potential (Eimer and Driver, 2000; Eimer, 2001). These studies employed oddball detection tasks with different attentional demands from those utilized by Dionne et al. (2013) whereby participants had to monitor both hands for deviant stimuli in one sensory modality while ignoring the other, and report them with a verbal response. However, the lack of P100 modulation across crossmodal paradigms suggests that the P100 is sensitive to the presence, but not the attentional relevance, of crossmodal stimuli. These results suggest that crossmodal modulation occurs at very early stages in the somatosensory processing stream if both stimuli are relevant for behaviour (Dionne et al., 2013). Collectively, these findings suggest that crossmodal processing is likely mediated by both bottom-up sensory-sensory interactions and top-down attentional mechanisms in order to allow for the selection, amplification, and integration of sensory input relevant for initiating goal-oriented responses.

1.3.4 The role of the prefrontal cortex in gating of sensory information

In 1935, Charles Jacobsen discovered what is considered today to be a landmark observation in our current understanding of the functional role of the PFC in cognitive processing. His work revealed that monkeys with bilateral frontal lobe damage, including the sulcus principalis, a region analogous to the DLPFC in humans (Rajkowska and Goldman-Rakic, 1995a,b) demonstrated severe impairments in tasks involving delayed responses. Decades later, Skinner and Yingling's work in cat models, provided the first physiological evidence of a PFC inhibitory pathway responsible for regulating the flow of sensory signals through thalamic relay nuclei. Cryogenic blockade of the cat PFC produced increased evoked response amplitudes in primary sensory cortex, while stimulation of the thalamic reticular nucleus (TRN); a "shell-like" shield that encapsulates thalamic sensory neurons, produced neural suppression in modality-specific primary cortex (Skinner and Yingling, 1976; Yingling and Skinner, 1976). The existence of a prefrontal-thalamic inhibitory system offered the first evidence that suppression of task-irrelevant or distractor input(s) can occur at very early stages of sensory processing in modality-specific cortices. It is thought that this inhibitory system is modulated via excitatory input from the PFC to the TRN, which in turn, sends inhibitory GABAergic projections to sensory relay nuclei ensuring that irrelevant sensory signals are not received or processed by modality-specific cortices (Guillery et al., 1998).

Prefrontal lesion studies further support the role of the PFC in gating of sensory information. Reports of severe cognitive impairments and/or aberrant cortical responses in patients have been found during tasks involving: selective attention, inhibitory control, lexical processing, or working memory (Knight et al., 1981; Janowsky et al. 1989a; Janowsky et al., 1989b; Yamaguchi and Knight, 1990; Richer et al., 1993; Chao and Knight, 1995, 1998; Knight et al., 1999). Work by Yamaguchi and Knight (1990) revealed that during passive median nerve stimulation, patients with focal lesions to the DLPFC, relative to controls, displayed enhanced neuronal responses in several early SEPs with known generators in postcentral, post-rolandic, and frontal areas. Yet, SEPs generated in spinal cord and brainstem areas were unaffected. The authors suggested that inhibitory modulation of sensory inputs may be governed by corticocortical PFC-parietal connections (Yamaguchi and Knight, 1990). Thus, sensory gating impairments observed in PFC patients may stem from abnormalities in either the prefrontal-thalamic or prefrontal-sensory cortex mechanism.

Delayed-match-to-sample tasks are commonly used to investigate higher-order top-down cognitive processing. In these paradigms, participants are required to indicate whether a initial "target" stimulus (S1), matches a subsequent "cue" stimulus (S2), following an arbitrary time delay. Using an auditory version of this task, Chao and Knight (1995) compared data from patients with lesions to the DLPFC, the temporal-parietal junction (TPJ), or the posterior hippocampus, to controls. Here, the silent period between S1 and S2 varied between 4 to 12.5 seconds, which was or was not interrupted by a series of distractor tones. Significant impairments in the suppression of task-irrelevant stimuli were observed in DLPFC patients at all delay times, while TPJ patients only displayed impairments at longer delay times, and patients with posterior hippocampal damage performed similarly to controls. Concluding remarks suggested that the damage to DLPFC produces an inability to suppress irrelevant information which leads to difficulties in target detection following a time delay. Lesion studies using visual inspection tasks support this notion, whereby patients with frontal damage exhibit impairments detecting visual targets embedded among distractors (Richer et al., 1993), and diminished modulation of visual event-related potentials (Knight, 1999). In healthy controls, transient inhibition to the DLPFC using continuous theta burst stimulation (cTBS), produced disinhibition of task-irrelevant stimuli at early stages of somatosensory processing (Bolton and Staines, 2012). Using EEG and a tactile discrimination task, participants were divided into one of three groups: 1) cTBS, 2) sham-cTBS, or 3) no simulation, and pre-post measures of cortical activity were collected. Participants received vibrotactile stimuli to the index and pinky fingers of the left hand and were instructed to report target stimuli on one digit only. Results revealed that in the non-attend versus attend conditions, the sham-cTBS and no stimulation groups, showed reductions in the amplitude of the P100 component, while no such effect was found in the cTBS group. These findings are in accord with those reported in patients with focal lesions in DLPFC, thus supporting the role of the DLPFC in the gating of task-irrelevant sensory input at very early stages of cortical processing.

Research suggests that task-relevant modulation in modality-specific SI is regulated by top-down control of the PFC. Using fMRI and a vibrotactile task, Staines et al. (2002) found that task-relevant somatosensory stimuli increased BOLD responses in contralateral SI and the right PFC, as well as decreased activity in ipsilateral SI regions in healthy adults. This finding is suggestive that, a frontal-parietal sensory gating mechanism, capable of regulating the flow of relevant sensory information to modality-specific somatosensory cortices, exists. A recent MEG study using the Tower of Hanoi task; a higher-order cognitive control task known from patient and imaging studies for its recruitment of frontal and prefrontal cortices (Baker et al., 1996; Dagher et al., 1999; Anderson and Douglas, 2001), further supports that task-relevant modulation of SI is regulated by frontal regions, namely the PFC (Schaefer et al., 2005). In this study, healthy participants had tactile stimuli attached to distal portions of the index (D1) and pinky (D5) fingers of both hands and in separate blocks were instructed to: 1) complete the Tower of Hanoi (ToH) task, 2) perform the ToH using the same movements but with no specific instructions, or 3) rest. Results showed that, during the ToH task, the spatial representation of D1 and D5 in SI was significantly greater upon comparison to the other two tasks, suggesting that plastic changes in SI occurred only during the higher-order cognitively demanding ToH task. Although, the nature of this experiment failed to explicitly measure PFC activity, the authors concluded that their findings supported the notion presented by Staines et al.

(2002) of a prefrontal sensory gating mechanism responsible for regulating task-relevant modulation in SI. Recent fMRI and EEG studies investigating the effects of task-relevancy during crossmodal processing, further support the idea that top-down attentional control facilitates somatosensory processing in modality-specific SI (Dionne et al., 2010, 2013).

Cognitive impairments commonly observed in healthy aging populations share striking similarities to those reported in prefrontal patient data. Behavioural findings report age-related impairments during tasks involving inhibitory control (Rabbitt, 1965; Kausler and Hakami, 1982; Hasher and Zacks, 1988; Reuter-Lorenz and Park, 2010; Bolton and Staines, 2012), and inhibiting proponent responses that are no longer task-relevant (Hasher and Zacks, 1988; Yamaguchi and Knight, 1991; Fabiani et al., 2006). Furthermore, neuroimaging data has shown that atrophy of frontal lobe regions is disproportionately greater relative to other brains areas in older adults (Haug and Eggers, 1991), with the greatest shrinkage occurring in medial temporal areas (Raz, 2000). In a fMRI study using a selective working memory task, young and older adults were required to remember images of faces and ignore scenery images or vice versa. Results showed that both groups displayed increased activation patterns during task-relevant stimuli, however, older adults, relative to younger adults, showed diminished suppression of task-irrelevant stimuli (Gazzaley et al., 2005). Gazzaley et al. (2007) replicated these results using EEG, by showing deficits in the suppression of the N170 latency shift in older adults. The N170 component is a face-sensitive visual ERP localized to posterior occipital electrodes (Bentin et al., 1996). Collectively, these results suggest that age-related inhibitory control deficits may be related to alterations in blood flow and/or neuronal response activation.

Recent EEG work by Bolton and Staines (2012), suggests that age-related impairments in top-down attentional control may explain diminished modulation at very early stages of somatosensory processing in the elderly. Using the same tactile discrimination task previously described, these authors showed that older adults, relative to their younger counterparts, showed attention-related: 1) reductions in the amplitudes of the P100 and P300 components, 2) increases in the P300 latency, and 3) behavioural impairments in target detection. Both the P100 and P300 ERP components are modulated by attentional processes (Desmedt and Robertson, 1977; Desmedt et al., 1983; Michie et al., 1987; Polich and Kok, 1995; Linden, 2005; Bolton and Staines, 2011; Dionne et al., 2013). The latency of the P300 component reflects stimulus evaluation time such that shorter latencies reflect more efficient cognitive processing (Donchin & Coles, 1988). Thus, the authors concluded that older adults showed age-related loss in the attentional processing of somatosensory information (Bolton and Staines, 2012). Extensive research suggests that various physiological, cognitive, and behavioural deficits typically observed in patients with PFC damage, are also seen in older adult populations. As a result, some aging theorists believe that age-related deficits may also be explained by the distractibility hypothesis of PFC function.

1.3.5. Aerobic exercise effects on cortical activity and cognition

A growing body of evidence suggests that a beneficial relationship between exercise and cognition exists. However, the findings suggest that the underlying mechanisms behind exercise effects on cognition are multifactorial and depend on various factors, some of which include: exercise duration (i.e. acute versus chronic), exercise intensity (i.e. light, moderate, or strenuous), cardiovascular fitness of the participants, as well as the type of psychological task used to investigate cognitive performance. How some of these factors influence cognition will be discussed in the following sections.

1.3.5.1. Chronic aerobic exercise effects on cognition

It is thought that aerobic exercise training over an extended period of time (i.e. chronic interventions) produces neurophysiological alterations in brain physiology. Non-human studies have allowed researchers to examine the underlying neural and cellular mechanisms influenced by exercise training (Hillman et al., 2008). Several rodent studies have reliably shown that exercise training increases cell proliferation and survival in the dentate gyrus of the hippocampus, an area involved in learning and memory processes (Van Praag et al., 1999; Brown et al., 2003). Exercise-induced cell proliferation has also been shown to promote angiogenesis in the motor cortex (Swain et al., 2003), cerebellum (Black et al., 1990), and striatum (Ding et al., 2004), which may be dependent on the up-regulation and release of molecules such as: vascular endothialial growth factor (VEGF); important for blood vessel formation and development, insulin growth factor 1 (IGF-1); a regulator of VEGF and important for blood vessel formation, or brain derived neurotrophic factor (BDNF); a long-term potentiation neural transmission signal needed for memory formation (Cotman and Berchtold, 2002; Cotman et al., 2007). Rhyu et al. (2010) investigated the effects of aerobic exercise training on cortical vascularity and cognitive functions in primates. In this study, adult female monkeys were divided into either an exercise group (trained to run on a treadmill for 1 hour/day, 5 days/week, for 5 months) or a sedentary group (sat on an immobile treadmill), and then performed the Wisconsin General Testing Apparatus during the 5th week of training. Groups were further delineated into age-related populations (mature versus young) to investigate whether age influenced any cognitive benefits associated with exercise training. A subset from the exercise group also performed a 3 month sedentary period following exercise training, in order to examine the longevity of any exercise-induced benefits on cortical vascularisation. Results showed that the exercise group learned the cognitive task significantly quicker than the sedentary group regardless of age. However, at the end of exercise training, only the mature monkey exercise group showed increased cortical vasculature in the motor cortex and these effects did not persist after the 3 month sedentary period. These findings suggest that aerobic exercise training increased learning across all ages, as well as the blood flow in the cerebral cortex of mature monkeys, but that these effects were contingent on exercise maintenance (Rhyu et al., 2010). In summary, animal research has shown that chronic exercise training induces beneficial effects on cognitive function by promoting neurogenesis and synaptic plasticity in various brain regions. These studies may help researchers understand the neural and cellular mechanisms that moderate the relationship between aerobic exercise training and cognitive function in humans (Hillman et al., 2008).

Novel findings in human research have provided convincing evidence that aerobic chronic exercise induces neurophysiology alterations in brain activity and cognitive performance, particularly in older adults. Results of a meta-analysis of aggregated longitudinal data from 1966-2001, showed that older adults who engaged in physical fitness training programs significantly improved cognitive performance, especially, on tasks requiring cognitive control (Colcombe and Kramer, 2003). Colcombe et al. (2004) used fMRI to examine the effects of cardiovascular fitness training (CFT) on cortical circuitry in older adults using a modified version of the flanker task. In the first cross-sectional study, participants were divided into high fit and low fit groups, based on their current levels of cardiorespiratory fitness (i.e. VO_2 max uptake assessment), and received no CFT intervention. Results indicated that the older adults in the high fit group showed significantly less activation of the ACC, greater recruitment of attention-related cortical areas including the middle frontal gyrus and inferior parietal lobules, and less behavioural conflict, relative to the low fit group. The second study involved a randomized 6-month clinical intervention wherein participants were assigned into either a CFT group (i.e. 45 minutes of aerobic exercise performed 3 times/week) or a control group (i.e. 45 minutes of stretching/toning exercises performed 3 times/week). Imaging scans were collected one week pre- and post- intervention. Results replicated and extended those reported in the first study with the CFT group showing less ACC activation, greater recruitment of attention-related cortices, and less behavioural conflict overall (Colcombe et al., 2004). Thus, maintaining higher levels of physical fitness may induce beneficial changes in the neural circuitry of the brain by recruiting areas involved in selective attention (i.e. medial temporal lobes, inferior parietal lobe), while reducing the demand on areas involved in conflict interference (i.e. ACC activation), in order to make behavioural performance more efficient. Another study by Colcombe et al. (2003), reported significantly less grey matter loss in the frontal, parietal, and temporal lobes and significantly less tissue loss in anterior and posterior white matter pathway tracts in high fit older adults relative to low fit older adults, using a high resolution voxel-based morphometric analysis approach.

Unlike acute exercise effects, chronic exercise effects on cognition are not limited to PFC regions involved in executive control processes. Erikson et al. (2011) found a 2% increase in hippocampal volume in older, sedentary adults who participated in a one year moderate intensity aerobic exercise training program. Increased hippocampal volumes were also related to improvements in spatial memory and increased levels of serum BDNF. Furthermore, recent work by Chapman et al. (2013) found that even a 12 week aerobic exercise training program increased resting cerebral blood flow in the hippocampus and was associated with improved memory performance in sedentary older adults, suggesting that shorter term aerobic exercise facilitates brain health in sedentary adults.

1.3.5.2. Acute effects of aerobic exercise on cognition

Cognitive neuroimaging studies have reliably shown that regions of the frontal lobes, specifically the PFC and ACC, are involved in mediating executive control processes including: selective attention, inhibitory control, decision-making, and error monitoring (Miller and Cohen, 2001). Notably, studies investigating the effects of acute aerobic exercise on cognition report enhanced neuronal responses particularly in these brain regions and performance improvements on tasks requiring executive control (Ekkekakis, 2009; Hillman et al., 2009; Yanagisawa et al., 2010; Endo et al., 2013). However, these results seem to be dependent on exercise intensity prescribed. Using a go/nogo task, Kamijo and colleagues (2004) showed variable modulation of the P300 component depending on aerobic exercise intensity prescribed, whereby P300 amplitudes: increased following moderate intensity exercise, decreased following hard intensity exercise, and showed no change following light intensity exercise. Similar results were found using a version of the Erikson flanker task, whereby P300 amplitudes increased after light and moderate intensity aerobic exercise and decreased following strenuous exercise. Additional findings revealed decreased reaction times and P300 latencies to incongruent trials across all exercise intensities (Kamijo, Nishihira, Higashiura, & Kuroiwa, 2007). The

P300 component is generated over fronto-central electrodes sites in response to task-relevant target stimuli (Pfefferbaum et al., 1985). The amplitude of the P300 is thought to reflect the amount of attentional resources devoted to a given task, while the latency reflects stimulus evaluation (Donchin and Coles, 1988). Thus, these studies suggest that acute bouts of moderate intensity aerobic exercise facilitated attentional processing in healthy young adults. Based on these and various other studies (Levitt and Gutin, 1971; Sjöberg, 1975; Chmura et al., 1994; Grego et al., 2004; Kamijo et al., 2004), it is proposed that improvements in cognitive performance immediately after acute exercise follow the Yerkes and Dodson inverted U-shape arousal model, whereby when arousal states increase with physical exertion, cognitive performance improves to an optimal point after which further increases in physical exertion cause decreased arousal levels resulting in decrements in performance (Tomporowski, 2003a).

Acute exercise studies using moderate intensity exercise protocols have shown enhancements in neuronal profiles, particularly of the P300 component (Nakamura et al., 1999; Hillman et al., 2009; Hillman et al., 2003). However, recently, Yanagaisawa et al. (2010) used functional near infra-red spectroscopy (fNIRS) and the Stroop task to compare cortical activation patterns pre versus post an acute bout of moderate exercise in healthy young adults. Functional NIRS is a non-invasive neuroimaging technique with excellent spatial resolution that measures changes in cerebral blood flow (i.e. hemodynamic response) related to neural activity in the brain. Participants were randomly assigned into either an exercise group (15 minutes of recumbent biking) or a control group (15 minutes of rest) and then completed the Stroop task. To examine exercise-related PFC activation imaging scans were collected before and after the bout of aerobic exercise or rest period.

Results showed decreases in reaction time and increases in Stroop-interference-related cortical activation post training in the exercise group, relative to the control group. In particular, the left DLPFC showed greater activation in the exercise group post training. These results suggest that the left DLPFC may be the brain region responsible for improved behavioural performance post exercise training (Yanagisawa et al., 2010).

1.3.5.3. The impact of cardiovascular fitness on cognition

EEG work examining the relationship between cardiovascular fitness and cognitive control suggest that maintaining cardiovascular health throughout the lifespan plays the critical role in producing beneficial neurophysiological changes in the brain. For instance, Themanson and Hillman (2006) used the Eriksen flanker task and a cardiovascular fitness paradigm to investigate differences in the amplitude of the error-related negativity (ERN) component in high fit versus low fit individuals. The ERN is a negative peak generated in the ACC that occurs 50-100 ms following an erroneous response and is associated with error detection and monitoring. Neuroelectric (i.e. ERN amplitudes) and behavioural (i.e. response speed, accuracy, post-error slowing) indices of action monitoring were assessed following a 30 minute acute bout of treadmill exercise or following 30 minutes of rest in healthy young adults. Participants were divided into higher fit and lower fit groups based on assessment of individual cardiorespiratory fitness levels using a graded maximal exercise (i.e. respiratory exchange ratio and 30s averages for maximal oxygen uptake; VO). Results indicated that higher-fit adults showed reduced ERN amplitudes and increased post-error slowing compared to lower-fit adults. Notably, the acute exercise session was not related to any of the dependent measures. A follow-up EEG study by Themanson et al. (2008) investigated the relationships between fitness and neuroelectric and behavioural indices of action monitoring in conjunction with task instructions emphasizing either speed or accuracy. They hypothesized that "a strengthening of the relationships between ERN amplitudes and post-error behaviour (accuracy, reaction time) with fitness when accuracy was stressed (compared with when speed was stressed) would indicate that higher fitness increases one's ability to flexibly modulate the recruitment and interpretation of cognitive control in response to salient task parameters". Results showed that higher fit individuals exhibited greater ERN amplitudes and post-error accuracy, relative to their less fit counterparts, during tasks emphasizing accuracy, as well as greater modulation of these indices across task instruction conditions (Themanson et al., 2008). In light of these findings, the authors concluded that higher cardiovascular fitness, and not acute bouts of aerobic exercise per se, may promote more efficient neural processing during tasks that involve error monitoring by enhancing cognitive flexibility and top-down attentional control (Themanson and Hillman, 2006; Themanson et al., 2008).

Collectively, these neurophysiological findings are provocative, and suggest that a beneficial relationship between exercise and cognition exists, but the underlying mechanisms producing the effects depend on the type exercise intervention used. In general, cognitive benefits following acute aerobic exercise seem to be greatest in frontal lobe regions involved in top-down attentional control (Kamijo et al., 2004; Kamijo et al., 2007; Hillman et al., 2009; Yanagisawa et al., 2010), while chronic exercise effects influence various regions some of which include the: PFC (Colcombe and Kramer, 2003; Colcombe et al., 2004;), hippocampus (Van Praag et al., 1999; Brown et al., 2003), and motor cortex (Rhyu et al., 2010; Swain et al., 2003). These findings may be particularly relevant for older adults since advancing age is associated with structural deterioration particularly in frontal lobe and hippocampal regions resulting in attentional and working memory deficits (Hasher and Zacks, 1988; Reuter-Lorenz and Park, 2010; Bolton and Staines, 2012).

1.4 Specific research objectives

1.4.1. Research Objective 1

To examine the relative contributions of visual priming (bottom-up sensory input) and task-relevance (top-down attention) on influencing early somatosensory cortical responses, namely the P50 somatosensory ERP generated in SI.

Research has shown that crossmodal interactions across sensory modalities can influence SI excitability, even if only one modality is task-relevant (Meehan and Staines, 2007). However, recent fMRI findings suggest that simultaneous presentation of crossmodal visual and tactile stimuli enhance SI and PFC excitability when both stimuli are task-relevant (Dionne et al., 2010), while EEG findings using the same paradigm imply that these crossmodal effects occur as early as 50 ms post-stimulus onset over SI regions (Dionne et al., 2013). Collectively, these results suggest that crossmodal interactions may occur via bottom-up sensory-sensory interactions and top-town attentional processes. Research Objective 1 sought to determine the relative contributions of visual information and attentional relevance on modulating modality-specific SI activity. Using EEG, it was hypothesized that if bottom up and top-down mechanisms influence early somatosensory ERPs in contralateral SI, then the amplitude of the P50 component generated over SI regions should be greatest for relevant crossmodal (visual+tactile) interactions with a brief temporal delay between stimulus onsets and smallest for the irrelevant unimodal (tactile-tactile/visual-visual) conditions. To test whether bottom-up mechanisms influence crossmodal modulation of the P50 component, we manipulated the temporal onsets of visual and tactile events in two crossmodal conditions. In one condition, visual stimuli preceded tactile stimuli by 100 msec to examine whether the presentation of relevant visual information prior to tactile information influenced crossmodal modulation of the P50 component. In another condition, tactile stimuli preceded visual stimuli by 100 msec which acted as a control to the previously described condition since the onset of the P50 component would have already occurred prior to the presentation of visual information, thus P50 modulation in this condition would not be influenced by the presentation of task-relevant visual stimuli.

1.4.2 Research Objective 2

To examine the relative contributions of visual priming, attentional relevance and task-specific sensory-motor requirements to the enhancement of somatosensory cortical responses.

Findings from Study 1 imply that SI excitability is modulated by both top-down attentional mechanisms and bottom-up sensory-sensory interactions by showing that the amplitude of the P50 component was significantly greater during crossmodal (visual+tactile) interactions where task-relevant visual information preceded tactile information (Popovich and Staines, 2014). Yet, modulation of the P50 is thought to be mediated by the degree of attentional demand required by the type of task employed, such that tasks with greater attentional demand are more successful in driving P50 modulation (Schubert et al., 2008). The purpose of Research Objective 2 was to follow-up the findings of Study 1 as well as to determine the influence of task-relevant sensory-motor requirements on modulating the P50 component. Based on the results of the first study in this thesis, it was hypothesized that SI activity would be sensitive to the temporal order of task-relevant crossmodal (visual-tactile) stimuli and that the degree of modulation would depend on the difficulty of the associated motor task demands. Specifically, it was hypothesized that modulation of the P50 component would be greatest during relevant crossmodal (visual+tactile) interactions where visual information preceded tactile information (100 ms delay), and participants were required to produce a force-graded motor response representing the summation of both stimulus amplitudes versus a button press representing the detection of the presence of both stimuli.

1.4.3 Research Objective 3 & 4

To examine if increases in PFC activity, following an acute bout of moderate intensity aerobic exercise, would enhance attention-based modulation of tactile ERPs generated at early and later stages of somatosensory processing in healthy young and older adults.

Research suggests that aerobic exercise enhances neuronal activity, particularly in frontal lobe regions, and improves cognitive performance during higher-order attentionally demanding tasks (Colcombe et al., 2004; Hatta et al., 2005; Themanson and Hillman, 2006; Themanson et al., 2008; Kamijo et al., 2009; Pontifex et al., 2009; Yanagisawa et al., 2010). Yet, few studies have administered cognitive tests designed to elicit neuronal activity downstream from the PFC in modality-specific sensory regions. This poses an important limitation to the current understanding of the relationship between exercise and cognitive function since the circuitry of the PFC is complex, with corticocortical and thalamocortical connections with parietal cortices, making it an important structure for modulating modality-specific cortical regions via attentional mechanisms. Research Objectives 3 and 4 sought to determine whether the attention-related exercise effects would modulate neuronal activity in somatosensory regions downstream from the PFC during a tactile discrimination task across different age groups (i.e. young and older adults). It was hypothesized that an acute bout of moderate intensity exercise preceding performance of the tactile odd-ball discrimination task would increase PFC excitability resulting in more efficient sensory-gating of irrelevant versus relevant tactile information. More efficient sensory-gating would be reflected by greater suppression of unattended, task-irrelevant tactile information and/or greater enhancement of attended, task-relevant tactile information following exercise in young and older adults as well as performance improvements particularly in the elderly population.

Chapter 2 - Study 1: The attentional relevance and temporal dynamics of visual-tactile crossmodal interactions differentially influence early stages of somatosensory processing.

Adapted from: Popovich C. & Staines WR. (2014). The attentional relevance and temporal dynamics of visual-tactile crossmodal interactions differentially influence early stages of somatosensory processing. *Brain and Behaviour, 4* (2), 247-260.

2.1 Overview

Crossmodal interactions between relevant visual and tactile inputs can enhance attentional modulation at early stages in somatosensory cortices to achieve goal-oriented behaviors. However, the specific contribution of each sensory system during attentional processing remains unclear. We used EEG to investigate the effects of visual priming and attentional relevance in modulating somatosensory cortical responses. Healthy adults performed a sensory integration task that required scaled motor responses dependent on the amplitudes of tactile and visual stimuli. Participants completed an attentional paradigm comprised of 5 conditions that presented sequential or concurrent pairs of discrete stimuli with random amplitude variations: 1) tactile-tactile (TT), 2) visual-visual (VV), 3) visual-tactile simultaneous (SIM), 4) tactile-visual delay (TVd), and 5) visual-tactile delay (VTd), each with a 100 ms temporal delay between stimulus onsets. Attention was directed to crossmodal conditions and graded motor responses representing the summation of the 2 stimulus amplitudes were made. Results of somatosensory ERPs showed that the modality-specific components (P50, P100) were sensitive to i) the temporal dynamics of crossmodal interactions, and ii) the relevance of these sensory signals for behaviour.

2.2 Introduction

It is well-known that attention can modulate neurophysiological responses in modality-specific cortices including: visual (Motter, 1993; Gazzaley et al., 2007; Andersen et al., 2008), auditory (Woldorff et al., 1993; Jäncke et al., 1999; Petkov et al., 2004), and somatosensory cortices (Josiassen et al., 1990; Hsiao et al., 1993; Johansen-Berg et al., 2000; Staines et al., 2002). However, recent investigations have begun to examine whether attention influences neural responses across sensory modalities when sensory input from more than one modality is present. Behavioral studies have shown that crossmodal input can also improve performance as indexed by faster reaction times (Hershenson, 1962; Gielen et al., 1983), improved detection of weak stimuli (Frens and Van Opstal, 1995; Driver and Spence, 1998; McDonald et al., 2000), and improved sensory-perception of illusory effects such as the ventriloquist or McGurk illusions (Howard and Templeton, 1966; McGurk and MacDonald, 1976). Human and animal studies have shown that the mere presence of additional sensory input even when it is irrelevant for performance of a task can enhance neural excitability in the attended sensory modality (Calvert et al., 1997; Macaluso et al., 2000; Calvert, 2001; Foxe et al., 2002; Kayser et al., 2005; Pekkola et al., 2006; Lehmann et al., 2006; Kayser et al., 2007; Lakatos et al., 2007; Meehan and Staines, 2009), suggesting that interactions between modality-specific cortical representations exist. By contrast, other studies have shown crossmodal enhancement in modality-specific sensory cortex occurs only when both stimuli events are relevant for behavior (Dionne et al., 2010, 2013). These findings suggest that crossmodal processing is likely governed by both bottom-up sensory-sensory interactions and top-down attentional mechanisms in order to allow for the selection, amplification, and integration of sensory input relevant for initiating goal-oriented responses. Bottom-up interactions can occur when salient stimuli from an unattended sensory modality influence neural excitability in the attended modality, while top-down processing occurs when attention is voluntarily directed toward relevant stimuli in the presence of environmental distracters. However, while both these attentional mechanisms can modulate neural responses in modality-specific sensory cortex, it remains unclear how these attentional mechanisms interact during sensory processing of crossmodal stimuli.

Neurophysiological research in the primary auditory cortex of monkeys has provided evidence that sensory-to-sensory interactions exist. Recent studies have shown that neural responses in regionally distinct areas of the primary auditory cortex are enhanced when visual and/or tactile stimuli are paired with auditory stimuli (Kayser et al., 2005, 2007). Lakatos et al. (2007) showed that presentation of somatosensory stimuli increased auditory neural responses when the two stimuli were simultaneously combined versus when the auditory stimulus was presented in isolation. Furthermore, Bizley et al. (2007) reported a 15% neuronal increase in the ferret primary auditory cortex following simultaneous presentation of visuo-auditory stimuli (Bizley et al., 2007).

Neuroimaging studies in humans complement the sensory-to-sensory interactions reported in animal findings by showing that the presence of crossmodal input can modulate neural excitability in modality-specific sensory cortices. For example, several functional magnetic resonance imaging (fMRI) studies have reported increased blood oxygenation level-dependent (BOLD) responses in modality-specific cortices due to the mere presence of stimuli from another modality. These interactions have been found between: visual and auditory cortices (Calvert et al., 1997; Calvert, 2001; Lehmann et al., 2006; Pekkola et al., 2006), auditory and somatosensory cortices (Foxe et al., 2002; Schürmann et al., 2006), as well as visual and somatosensory cortices (Macaluso et al., 2000, 2002). However, a recent fMRI study investigated crossmodal effects on BOLD responses generated in the primary somatosensory cortex (SI) when both stimuli were relevant for guiding a motor response. Here, relevant unimodal (visual or tactile) and crossmodal stimuli (simultaneous visual + tactile) were presented and participants were required to summate both stimuli by squeezing a pressure-sensitive bulb. In order to ensure that stimulus associations were successfully learned prior to testing, participants completed a brief sensorimotor training session that required them to judge the amplitude of visual and vibrotactile stimuli and make a graded motor response representing the perceived amplitude of the stimuli. Results showed that the greatest BOLD responses were elicited in SI during crossmodal versus unimodal interactions suggesting that combining visual-tactile information relevant for behavior enhances modality-specific excitability in SI (Dionne et al., 2010). In a follow-up study, Dionne et al. (2013); used electroencephalography (EEG) and the same sensory-to-motor task to investigate the time course of crossmodal effects in SI. Results showed that crossmodal interactions between vibrotactile and visual stimuli enhanced the amplitude of the somatosensory P50 component, generated in SI, at contralateral parietal electrode sites only when both stimuli were task-relevant. By contrast, the amplitude of the P100, likely generated in SII, increased bilaterally at parietal electrode sites during presentation of crossmodal stimuli but was not sensitive to the task-relevance of the stimuli. These findings suggest that crossmodal modulation occurs at very early stages in the somatosensory processing stream if both stimuli are relevant for behavior (Dionne et al., 2013).

Several other EEG studies support the finding that crossmodal stimuli can modulate neural excitability at very early stages of sensory processing. For example, Giard and Peronnet (1999) found that visual modulation for audio-visual stimuli, occurred as early as 40-msec post stimulus onset, while audio-tactile modulation has been found at 50 msec (Foxe et al., 2000; Molholm et al., 2002). Kennett et al. (2001) found modulation of visual event-related potentials (ERPs) by irrelevant but spatially aligned tactile stimuli at approximately 140-msec post visual onset, while McDonald et al. (2000) reported modulation of visual ERPs was possible with spatially aligned auditory stimuli. In summary, crossmodal interactions can improve behavioral performance and enhance neural excitability at early stages in modality-specific cortices to achieve goal-oriented behaviors (Dionne et al., 2010, 2013). However, the specific contribution of each sensory system during attentional processing in modality-specific sensory cortices remains unclear. In this study, we manipulated the attentional relevance and temporal onsets of visual and tactile stimuli to examine whether both top-down and bottom-up mechanisms can modulate early stages of somatosensory processing.

The specific aim of this study was to explore the relative contributions of visual priming (bottom-up sensory input) and task-relevance (top-down attention) on influencing early somatosensory cortical responses, namely the P50 somatosensory ERP generated in SI. We hypothesized that somatosensory activity would be modulated based on the temporal onset and stimulus order of task-relevant crossmodal (visual-tactile) events. To test whether bottom-up sensory-sensory interactions influence crossmodal modulation of the P50 component, we manipulated the temporal onsets of visual and tactile events in two crossmodal conditions. In one condition, visual stimuli preceded tactile stimuli by

100 msec to examine whether the presentation of relevant visual information prior to tactile information influenced crossmodal modulation of the P50 component. In the other condition, tactile stimuli preceded visual stimuli by 100 msec. This condition acted as a control to the previously described condition since the onset of the P50 component would have already occurred prior to the presentation of visual information, thus P50 modulation in this case would not be influenced by the presentation of task-relevant visual stimuli. If bottom-up and top-down mechanisms influence early somatosensory ERPs in contralateral SI, then the P50 amplitude should be greatest for relevant crossmodal interactions where visual information preceded tactile information and smallest for the irrelevant unimodal interactions.

2.3 Methods

2.3.1. Participants

EEG was collected from 20 self-reported right-handed healthy participants (mean age = 26, 10 males). Five subjects were excluded due to either excessive artifacts found during inspection of the raw EEG collection, or the absence of clearly defined somatosensory ERPs of interest (i.e., P50 and/or P100 components). The final sample consisted of 15 healthy participants (mean age = 27.5, 7 men). Experimental procedures were approved by the University of Waterloo Office of Research Ethics. All subjects provided informed written consent.

2.3.2. Behavioural task

The behavioral paradigm consisted of five conditions that presented pairs of discrete visual and/or tactile stimuli with random amplitude variations. Stimuli were always presented in pairs, either sequentially (unimodal conditions) or simultaneously (crossmodal conditions): (1) tactile-tactile (TT; 500 msec each, 30-msec interstimulus interval [ISI]), (2) visual-visual (VV; 500 msec each, 30-msec ISI), (3) visual-tactile simultaneous (SIM; 1000 msec concurrent), (4) visual-tactile with a 100-msec temporal delay between stimulus onsets (visual-tactile delay, [VTd]; 500 msec each, visual presented first), and (5) tactile-visual with a 100-msec temporal delay between stimuli (tactile-visual delay, [TVd], tactile presented first) (refer to Fig. 2.1 A–D). Participants were instructed to only attend to the crossmodal stimuli (i.e., TT/VV conditions were ignored), judge the amplitude of the two stimuli, and then make a graded motor response representing the sum of these amplitudes by squeezing a pressure-sensitive bulb with their right hand (Fig. 2.1E). Prior to the EEG collection, participants underwent a 5-min training session with visual feedback in a sound attenuated booth to learn the relationship between the amplitudes of the stimuli and the corresponding force required to apply to the bulb. During training, a horizontal target bar appeared on the computer monitor and subjects were instructed to squeeze the pressure-sensitive bulb with enough force to raise another visual horizontal bar to the same level as the target bar. At the same time, as subjects applied force to the bulb with their right hand the vibrotactile device vibrated against the volar surface of their left index finger with corresponding changes in amplitude. In other words, as they squeezed harder on the bulb the amplitude of the vibration increased proportionately. Subjects were instructed to pay attention to these changes in amplitude as they related to the force they were applying to the bulb. This training allowed subjects to become familiar with the relationship between the vibrotactile stimulus amplitude and the corresponding force applied to the bulb. To control for force related trial to trial differences, stimulus amplitudes were scaled such that no single stimulus required a squeeze of more than 25% of an individual's maximum force, thus the response for adding two stimuli was never more than 50% of an individual's maximum force. Stimuli were always presented in pairs, either unimodally (two visual or two tactile) presented sequentially, or crossmodally (one visual and one tactile), presented simultaneously or with a 100-msec temporal offset between each stimuli.

2.3.3. Experimental design

During the experiment, participants sat comfortably in a sound attenuated booth and were instructed to visually fixate on the computer monitor, rest the volar surface of their left index finger gently on the vibrotactile device, and hold the pressure-sensitive response bulb in their right hand (Fig. 2.1F). Participants were instructed to attend only to crossmodal interactions, judge the amplitude of both the visually presented horizontal bars and the vibrotactile stimuli, and produce force graded motor responses using the pressure-sensitive bulb that represented the summation of both stimulus amplitudes. Stimuli were presented for 1 sec after which participants were required to make their motor response immediately following presentation of the crossmodal stimuli during a 2.5 sec window prior to the start of the next trial, for a total of 3.5 sec per trial. Each condition was randomized and performed in six blocks of 120 trials with each block lasting approximately 5 min. The order of the conditions was counterbalanced across each block and all subjects performed the same six blocks in sequential order.

2.3.4. Stimuli

Visual stimuli consisted of a centrally presented horizontal bar (6 cm wide), which raised to varying heights on a computer monitor positioned 50 cm in front of the subject and represented different visual amplitudes. Vibrotactile stimuli consisted of discrete vibrations delivered by a custom made vibrotactile device applied to the volar surface of the left index finger. Vibrotactile stimulation was controlled by converting digitally generated waveforms to an analog signal (DAQCard 6024E; National Instruments, Austin, TX) and then amplifying the signal (Bryston 2BLP, Peterborough, Ontario, Canada) using a custom program written in LabVIEW (version 8.5; National Instruments). Varying the amplitude of the driving voltage to the vibrotactile device produced proportional changes in vibration of the device on the finger. The amplitude of each discrete vibration was constant within a trial and varied randomly between trials. The average stimulus amplitude across all trials including a tactile stimulus did not differ between the experimental conditions. The frequency of the vibration was held constant at 25 Hz. Participants received 70 db whitenoise (Stim2; Neuroscan, Compumedics USA, Charlotte, NC) throughout the training session and the experiment to prevent auditory perception of the vibrotactile stimulus.

2.3.5. Data acquisition & recording parameters

EEG data were recorded from 64 electrode sites (64-channel Quick-Cap, Neuroscan, Compumedics USA) in accordance with the international 10–20 system for electrode placement, and referenced to the linked mastoids (impedance <5 kOhms). EEG data were amplified (20,000×), filtered (DC-200 Hz), and digitized at 512 Hz (Neuroscan 4.3, Compumedics USA) before being saved for subsequent analysis. Individual traces were visually inspected for artifacts (i.e., blinks, eye movements, or muscle contractions) and any contaminated epochs were eliminated before averaging. On average a minimum of at least 80 trials per condition were analyzed for each participant.

Event-related potentials were averaged to the onset of each stimulus relative to a 100-msec pre-stimulus baseline. Somatosensory ERPs were measured from individual participant averages for each task condition. Mean ERP amplitudes and latencies were computed for each subject within specified time windows selected around the post stimulus latencies of early somatosensory ERP components: P50 (40–70 msec), P100 (90–125 msec). Figures 2.2 and 2.4 illustrate the distribution of these potentials over parietal electrode sites. Figure 2.3 illustrates the voltage distribution across the scalp at the latency of the P50. On the basis of these topographies, the amplitude of each potential was measured from pre-selected electrode sites corresponding to scalp locations showing maximal voltage during the corresponding latency window. Thus, the P50 component was measured from sites centered around CP4 (C4, CP4, P4), roughly overlying right sensory-motor cortex and contralateral to the vibrotactile stimulus. The P100 is typically observed bilaterally at parietal electrode sites thus amplitude and latency of this component was measured from P3, PZ, and P4. All amplitudes were measured as raw voltage relative to the pre-stimulus baseline.

2.3.6. Data analysis

To test the hypothesis that the temporal onset and stimulus order of task-relevant crossmodal (visual-tactile) events would contribute to the modulation of early modality-specific somatosensory ERPs, a one-way repeated measures analysis of variance (ANOVA) with condition as a factor was carried out on the amplitude and latency of the P50 component at electrode sites C4, CP4, and P4 (regions contralateral to vibrotactile stimulation). These ANOVAs were followed by a *priori* contrasts performed to test the hypothesis that modulation of the P50 would be greatest for the task-relevant crossmodal visual-tactile task with a 100-msec temporal delay between stimulus onsets (VTd) and smallest for the irrelevant unimodal tactile-tactile (TT) task. Our statistical approach to the P100 component had to exclude analysis of the VTd condition since the 100-msec temporal delay between the visual and tactile stimuli produced an interaction with the visual ERPs over the time window (90–125 msec) chosen for the P100 peak amplitude. A one-way repeated measures ANOVA with condition as a factor was also computed on the amplitude and latency of the P100 at electrodes sites P4, PZ, and P3. Tukey's post hoc tests were carried out on any main effects to investigate whether relevant crossmodal conditions would be associated with greater amplitudes compared to the irrelevant unimodal conditions.

Behavioural data were analyzed by summing the amplitudes of the two target stimuli and comparing this to the amplitude of the response, i.e. the force applied to the pressure-sensitive bulb. The percent difference between the summed target stimulus amplitude and the actual response amplitude was calculated and a repeated measures ANOVA was conducted to assess statistical differences across the experimental conditions.

2.4 Results

2.4.1. The P50 component

All subjects demonstrated a clear P50 component (mean latency 53 ± SE 2 msec) in response to vibrotactile stimuli presented to the left index finger. Figure 2.2 shows the grand averaged waveforms for all conditions at electrode sites C4, CP4, and P4 approximately overlying contralateral somatosensory cortex (centered at CP4). Scalp topography maps representing group averaged data were created by averaging neural responses generated over the 30 msec time window (40–70 msec) centered around the P50 peak to observe task-specific differences in cortical modulation (refer to Fig. 2.3). As illustrated in Figure 2.2, all conditions including vibrotactile stimuli (i.e., TT, SIM, TVd, VTd) elicited robust neural activity in somatosensory regions contralateral to stimulation. Notably, the VTd condition also elicited robust activation in modality-specific visual cortex, while the VV condition showed minimal activation overall. Statistical results using a one-way repeated measures ANOVA showed a main effect of condition on the modulation of the P50 amplitude at electrode CP4 ($F_{3,42} = 2.81$, $P = 0.05$) as well as a trend toward significance for electrode P4 ($F_{3,42} = 2.49$, $P = 0.07$), but no effect at electrode C4 ($F_{3,42} = 1.53$, $P = 0.22$). *A priori* contrasts showed that modulation of the P50 amplitude was greater in the VTd condition compared to the TT condition for all three electrode sites (C4 ($F_{1,14} = 4.44$, $P = 0.041$; CP4 ($F_{1,14} = 8.20$, $P = 0.007$); P4 ($F_{1,14} = 6.20$, $P = 0.017$)). It was also shown that P50 amplitude was significantly greater in the VTd versus the TVd condition at electrode P4 ($F_{1,14} = 4.87$, $P = 0.033$) with a strong trend toward significance for the same effect at CP4 ($F_{1,14} = 3.37$, $P = 0.07$) (refer to Fig. 2.5A). Analysis of the P50 latency using a one-way repeated measures ANOVA revealed a main effect of conditions at electrodes CP4 ($F_{3,42} = 3.08$, $P = 0.04$) and P4 ($F_{3,42} = 3.52$, $P = 0.02$). Tukey's post hoc analysis on these electrodes both showed that the latency of the P50 amplitude occurred earlier in the VTd condition than the TT condition (VTd mean latency = 50 msec versus TT mean latency = 57 msec). No main effect of condition was found at electrode C4($F_{3,42} = 2.19$, $P = 0.1$).

2.4.2. The P100 component

The P100 component was present in all conditions with vibrotactile stimulation. However, we omitted analysis of the VTd condition since the fixed temporal delay of 100 ms between the visual and tactile stimuli created an interaction whereby the visual ERPs overlapped the specified time window of 90–125 msec centered around the P100 peak amplitude. As seen in Figure 2.4, the grand averaged P100 waveforms (mean latency 118 ± 4 msec) for the remaining three conditions (SIM, TVd, TT) displayed a bilateral distribution at parietal sites and maximal amplitude at electrode site PZ. Results showed a main effect of condition observed at electrode sites P4 ($F_{2,28} = 7.95$, $P = 0.002$), PZ ($F_{2,28} = 5.97$,$P = 0.007$), and P3 ($F_{2,28} = 10.73$, $P < 0.001$). Tukey's post hoc tests showed that for each electrode site, the amplitude of the P100 was larger in the SIM compared to the TVd task ($P < 0.05$) and the TT task ($P < 0.05$, Fig. 2.5B). A main effect of condition was found for the P100 latency at electrode P4 using separate one-way repeated measures ANOVA ($F_{2,28} = 3.64$, $P = 0.04$). However, Tukey's post hoc analysis revealed no statistically significant differences between conditions. Furthermore, no main effect of condition was found for electrodes PZ ($F_{2,28} = 1.02$, $P = 0.37$) or P3 ($F_{2,28} = 0.36$, $P = 0.7$).

2.4.3. Behavioral Data

Figure 2.6 shows the behavioral means and standard error bars for each task-relevant crossmodal condition: SIM (mean = 92, SE = 3.3), VTd (mean = 83, SE = 2.9), TVd (mean = 98, SE = 3.4). A one-way repeated measures ANOVA was performed on the error differences represented as a percent score across all conditions and showed that there was a main effect of condition ($F_{2,16} = 8.45$, $P = 0.003$). Post hoc Tukey's test showed that performance in the VTd condition was significantly different than the TVd task.

Participants tended to produce lesser force than the ideal target in the VTd condition. There were no other differences between conditions.

2.5 Discussion

In this study, we used EEG and crossmodal stimuli (visual + vibrotactile) to examine the roles of visual information and attentional relevance in modulating early cortical responses generated in SI. To test the influence of bottom-up sensory-sensory interactions and top-down attentional processes on early modality-specific cortical responses, we devised a novel experimental protocol that manipulated the temporal onsets of task-relevant crossmodal (visual + tactile) interactions. In one condition, visual stimuli preceded the onset of tactile stimuli by 100 msec (i.e., VTd), in order to observe the influence of the visual modality on the P50 component generated in SI. In another condition, tactile stimuli preceded the onset of visual stimuli by 100 msec (i.e., TVd), in which case, the P50 would have been elicited prior to the onset of visual information and modulation would not reflect crossmodal effects. We hypothesized that both bottom-up interactions and top-down attentional mechanisms influence early somatosensory ERPs, whereby, modulation (mainly of the P50 component) would be greatest for the relevant crossmodal condition where visual events occurred 100 msec prior to tactile events (VTd), and smallest, for irrelevant tactile unimodal condition (TT). Our results confirmed our hypotheses by showing that early somatosensory ERPs, namely the P50 and P100 components were sensitive to (i) the temporal dynamics of crossmodal interactions, and (ii) the relevance of these sensory signals for behavior. Specifically, modulation of the P50 amplitude depended on the temporal onset of crossmodal stimuli with the greatest effects seen when visual events preceded tactile events (VTd condition), followed by similar modulation between the other crossmodal conditions (SIM and TVd), and lastly the smallest modulation was seen for the irrelevant unimodal tactile condition (TT). As expected, there was no P50 modulation for the unimodal visual condition (VV) since no tactile events occurred and no behavioral response was required.

It is of particular importance to highlight the differences in P50 modulation between the crossmodal conditions. In crossmodal conditions with a 100 msec temporal delay between the onset of visual and tactile stimuli (VTd and TVd conditions), we showed that P50 modulation was greater in the VTd condition relative to the TVd condition. This finding was expected since in the TVd condition, the P50 component would have already occurred before presentation of the visual information. Our topographic maps (Fig. 2.3) complement our P50 results by showing that only conditions including vibrotactile stimulation (i.e., TT, SIM, TVd, VTd) elicited neural activation in somatosensory regions contralateral to stimulation, while the VV condition showed minimal activation overall. However, a prominent difference in neural activity specific to the VTd condition was revealed, whereby robust neural activation was elicited not only in somatosensory cortex but in visual areas as well. These results imply that presentation of relevant visual information for upcoming movement modulates somatosensory processing as early as SI. Moreover, the lack of SI activity seen in the VV condition implies that the activation of the visual cortex during the VTd condition was not simply due to volume conduction via additional sensory input, but instead, was specific to the task-relevance of the visual information in performing goal-oriented behavior. Lastly, the amplitude of the P100 component was enhanced during the SIM condition and suppressed during the TVd condition and TT condition. This finding suggests that enhancement of the P100 component depended on the attentional relevance and temporal alignment of visual-tactile events. Overall, this study shows that early somatosensory ERPs generated in modality-specific cortical regions are modulated by both bottom-up sensory interactions between visual and somatosensory modalities and top-down attentional influences. Thus, both the attentional requirement and the neural networks that control modality-specific sensory processing are necessary for crossmodal interactions to occur (Dionne et al., 2013).

The P50 component is a somatosensory ERP observed maximally in parietal cortices near the post-central sulcus contralateral to tactile stimulation, and typically varies in latency between 40 and 60 msec post stimulus onset (Desmedt et al., 1983). It can be elicited via somatosensory stimuli (tactile, vibratory, peripheral nerve stimulation) in most subjects whereby changes in the amplitude of the response are believed to reflect changes in SI excitability (Allison et al., 1989; Zhu et al., 2007). However, the precise role of the P50 component in processing somatosensory information remains elusive. It has been suggested that the P50 component reflects a preattentional inhibitory filter mechanism critical for sensory gating of irrelevant stimuli, and the integrity of higher order functions (Freedman et al., 1987, 1991; Jerger et al., 1992; White and Yee, 2006). Studies in patient populations support this theory with findings showing diminished P50 gating in neurological illnesses associated with inhibitory control deficits including: Alzheimer's dementia (Thomas et al., 2010), posttraumatic stress disorder (Karl et al., 2006), schizophrenia (Adler et al., 1982; Patterson et al., 2008), and bipolar I disorder (Schulze et al., 2007; Lijffijt et al., 2009). However, Schubert et al. (2008) suggested that the modulation of the P50 is dependent on the attentional demands of a task, such that tasks with higher degrees of difficulty are more successful in driving facilitation of the P50 amplitude. If this supposition is true, then enhancement of P50 component may instead reflect cognitive strategies applied during perceptual stages of sensory processing whereby relevant sensory signals are amplified via thalamo-cortical gating mechanisms (Yingling and Skinner, 1976; Desmedt and Tomberg, 1989; Brunia, 1993), before they can be relayed to higher order association cortices for further processing.

The P100 component has a relatively broad scalp distribution and is thought to be generated in bilateral secondary somatosensory cortex (SII) (Hari et al., 1983, 1984; Mima et al., 1998; Zhu et al., 2007). Bilateral activation is typically maximal over contralateral posterior parietal electrode sites and somewhat less robust at ipsilateral sites (Desmedt and Robertson, 1977; Desmedt and Tomberg, 1989; Hämäläinen et al., 1990). The P100 is similar to the P50 component, in that it is elicited by tactile and vibratory stimuli (Goff et al., 1977), and is modulated by attention (Desmedt et al., 1983; Michie, 1984; Michie et al., 1987; Josiassen et al., 1990; Eimer and Forster, 2003a/b; Kida et al., 2004; Schubert et al., 2006). Selective attention studies have reported increased P100 amplitudes in attended versus unattended tactile stimuli with effects being greater than earlier ERP responses generated in SI (Desmedt et al., 1983; Josiassen et al., 1990; Bolton and Staines, 2011). Overall, attention influences both the P50 and P100 amplitudes, but modulatory changes may be related to differences in experimental paradigms used and/or psychological factors (Desmedt and Robertson, 1977; Goff et al., 1977).

2.5.1. Attentional modulation in somatosensory cortex

Studies investigating the effects of sustained tactile-spatial attention have shown that attention to task-relevant versus irrelevant spatial locations enhances processing of tactile stimuli and modulates somatosensory cortex (SI and SII) (Desmedt and Robertson, 1977; Michie, 1984; Michie et al., 1987). Several functional neuroimaging studies have found that sustained spatial attention to one hand versus the other during bilateral tactile stimulation enhances hemodynamic responses within contralateral SI and sensorimotor regions (Macaluso et al., 2000; Meador et al., 2002). A positron emission tomography (PET) study reported that the anticipation of tactile stimulation can increase activity in contralateral SI even in the absence of any stimuli (Roland, 1981). Furthermore, EEG investigations comparing somatosensory ERPs elicited by tactile stimulation applied to the hands, have reported that attending to the location of tactile stimulation modulates both early and late somatosensory ERPs (N80, P100, N140) with increased amplitudes for the attended versus unattended tactile location (Desmedt and Robertson, 1977; Michie, 1984; Michie et al., 1987; García-Larrea et al., 1995). However, SI responses as early as 45–50 msec post stimulus onset have been reported using an attentional vigilance task (Zopf et al., 2004). Notably, a recent study using simultaneous EEG and fMRI recordings found that sustained spatial attention during bilateral tactile stimulation (Braille) modulated early somatosensory ERPs (P50, N80, P100, and the long latency potential (LLP)) as well as increased BOLD signals in SI, SII, the inferior parietal lobe and frontal areas. Correlation results showed that attentional modulation of SI was found to be positively correlated with attentional effects for the P50 and the LLP components (Schubert et al., 2006). The LLP component has multiple neural generators from broadly distributed locations, and is often seen as a sustained positivity occurring approximately 200–500 msec post stimulus (Michie et al., 1987; Hämäläinen et al., 1990). The precise role of this later positivity remains unclear; however, several attention-based tactile ERP studies have implied that the LLP may share functional similarities to the P300 component, such that increases in the LLP amplitude is thought to reflect the amount of attentional resources devoted to a given task (Desmedt and Robertson, 1977; Michie et al., 1987; Desmedt and Tomberg, 1989). These findings imply that sustained tactile attention modulates neural activity generated in SI at both early and later stages of tactile processing (Schubert et al., 2008).

2.5.2. Crossmodal input modulates somatosensory cortex

It is well-documented that attention modulates modality-specific sensory cortex, however, little is known about how multiple sensory inputs across modalities are integrated for purposeful goal-oriented behaviors. Recently, researchers have begun to investigate how attention operates across sensory modalities with examination focused on the crossmodal links between touch and vision. Eimer and Driver (2000) used a tactile-spatial attention task whereby participants were required to attend and respond to target stimuli presented to the primary modality (touch) while ignoring distractor stimuli presented at the unattended hand and stimuli shown in the task-irrelevant modality (vision). Results showed enhanced somatosensory ERPs to tactile stimuli presented at the attended locations and increased modulation of early visual ERPs elicited by irrelevant visual stimuli presented at task-relevant tactile locations. These findings suggest that sustained attention to one modality can influence neural excitability in another spatially congruent modality (Eimer and Driver, 2000). In a behavioral study, it was reported that visualization of the finger improved acuity judgments of tactile gratings applied to the fingertip (Taylor-Clarke et al., 2004), while a separate EEG study showed modulation of somatosensory ERPs as early as 80 msec post-stimulus when participants viewed stimulation of their own arm (Taylor-Clarke et al., 2002). In another EEG study, Meehan and Staines (2009) examined crossmodal effects on somatosensory evoked potentials elicited via median nerve stimuli. Results showed that enhancement of P50 amplitude was greatest when crossmodal stimuli (visual + vibrotactile) were presented in spatiotemporal alignment but attention was directed only to vibrotactile events. These results suggest that the presence of visual information that is spatiotemporally congruent to relevant tactile information enhanced the amplitude of the P50 component. However, it was uncertain if participants were aware that crossmodal events were synchronous, therefore, alterations in cognitive strategy to perform the task are unknown (Meehan and Staines, 2009). Lastly, Dionne et al. (2013) showed that the amplitude of P50 was sensitive to simultaneous presentation of crossmodal stimuli, but only when both crossmodal events were relevant for behavior, and not when one event was irrelevant (i.e., when participants only responded to one modality). Specifically, the presence of visual stimuli, alone, did not enhance the P50 amplitude, suggesting that modulation of this component is mediated by top-down sensory gating mechanisms. Results also showed that enhancement of P100 amplitudes were greatest during simultaneous presentation of crossmodal (visual + vibrotactile) stimuli relevant for behavior versus task-irrelevant unimodal stimuli. Despite these P100 results and the findings reported in this study, crossmodal effects on this component are variable, and seem to depend on the spatial location of attention. For example, studies using EEG and sensory oddball tasks have investigated crossmodal links in spatial attention between vision and touch. In tactile manipulations, participants responded to tactile 'oddball' targets at attended spatial locations (primary modality) while ignoring visual stimuli (secondary modality). Results showed that attended, relative to unattended tactile stimuli, enhanced the negativity of the somatosensory N140 component, but failed to produce attentional effects at earlier stages of somatosensory processing (Eimer and Driver 2000). However, recent work by Jones and Forster (2013) showed that engaging in a visual task while performing an exogenous tactile attention task diminished cortical modulation at early stages of somatosensory processing. Here, subjects either performed a tactile exogenous attention task while either just watching a visual stream of letters (single task), or were required to perform the tactile task and detect targets within the visual stream (dual task). ERP results showed diminished modulation of the N80 and P100 somatosensory components during the dual task suggesting that early stages of somatosensory processing are sensitive to crossmodality effects (Jones and Forster, 2013). Plausible explanations for the inconsistent crossmodal effects on early stages of somatosensory processing may be differences in the attentional tasks employed (i.e., crossmodal sensory integration task versus tactile spatial attention task), and/or in the attentional demands required between studies (i.e., graded force response representing the summation of visual and tactile stimuli with the hand versus vocal response made when target stimuli were presented at attended spatial locations) (Eimer and Driver, 2000; Eimer, 2001; Dionne et al., 2013; Jones and Forster, 2013).

Crossmodal interactions between relevant sensory inputs can facilitate perceptual processing in modality-specific sensory cortex to achieve goal-oriented behaviors. Studies have shown that the presence of an additional (but task-irrelevant) modality can enhance neural excitability in the attended modality (Calvert et al., 1997; Macaluso et al., 2000; Calvert, 2001; Foxe et al., 2002; Kayser et al., 2005; Pekkola et al., 2006; Lehmann et al., 2006; Schürmann et al., 2006; Kasyer et al., 2007; Lakatos et al., 2007; Meehan and Staines, 2009), suggesting that attention within one modality can modulate neural excitability (to some extent) in another sensory modality. Furthermore, recent neuroimaging studies have found that relevant crossmodal stimulation (i.e., tactile and visual sensory input) increases neurophysiological responses in SI relative to unimodal stimulation (i.e., either visual or tactile sensory input) (Dionne et al., 2010, 2013). Taken together, these studies suggest that both bottom-up (i.e., the presence of an additional sensory modality) and top-down attentional mechanisms (i.e., task-relevance) work together to process and integrate relevant sensory signals for successful execution of goal-oriented behaviors. However, the neural mechanisms underpinning the contribution of each sensory system during crossmodal attentional processing remains unclear. In this study, we examined the relative contribution of visual information in modulating early somatosensory ERPs by manipulating the temporal parameters of relevant visual-tactile interactions. Results showed that modulation of the P50 component varied based on the temporal delay between relevant bimodal stimuli, with greatest enhancement seen when visual information occurred 100 msec prior to the onset of tactile information. In addition, the P100 component was enhanced during simultaneous bimodal interactions relevant for behavior, but not during bimodal interactions where tactile information occurred 100 msec prior to visual information, or during irrelevant unimodal interactions suggesting that the P100 component was increased only when visual-tactile events occur in temporal synchrony and require selective attention. Lastly, behavioral results revealed differences between the sensory-motor responses produced during the VTd versus the TVd conditions, such that, participants tended to under-squeeze the pressure-sensitive bulb when summating VTd stimuli. It is plausible that participants may have employed different cognitive strategies to facilitate processing of these crossmodal conditions. It certainly is possible that such modulation of these modality-specific regions would have some behavioral benefits in terms of the efficient sensorimotor transformation. However, since participants were not explicitly asked whether they used a specific strategy to aid their sensorimotor judgments, we can only speculate potential factors that may have produced the differences in behavior found in our study. There are some notable limitations in the design of the experimental paradigm used in this study which must be considered. Although the crossmodal conditions with 100-msec temporal delays between the onset of visual or tactile stimuli events (i.e., TVd and VTd), were advantageous for interpreting crossmodal effects on the P50 component, the temporal delay interfered with the timing of some early (i.e., the P100 component for the VTd condition) and all later onset ERPs (i.e., N140) beyond typical latency boundaries, thus crossmodal effects could not be discussed for these components. Second, the behavioral results of this study suggest that participants may develop different cognitive strategies in order to facilitate perceptual processing of crossmodal stimuli with temporal delays between the onsets of each stimulus. Previous studies using the same stimuli described in this study have reported no differences in behavior during unimodal (TT, VV) conditions versus simultaneous presentation of crossmodal (visual + vibrotactile) conditions, suggesting that performance accuracy was similar across all conditions (Dionne et al., 2010, 2013). Indeed, the discrepancy between these behavioral results compared to the results of this study reveal a need for future studies to investigate if a potential relationship between these early changes in neural excitability and behavioral responses exists.

Notwithstanding these limitations, the results of this study are novel and suggest that presentation of visual information relevant for upcoming sensory-guided movement can facilitate tactile processing at very early stages in SI. Our findings complement previous observations reporting that crossmodal attention effects can occur at early stages in modality-specific sensory ERP components (Eimer and Driver, 2000; Taylor-Clarke et al., 2002; Dionne et al., 2013). Notably, this study extends the current literature by showing that crossmodal modulation of early somatosensory ERPs is facilitated by bottom-up sensory interactions between visual-tactile cortical associations and top-down sensory gating mechanisms. Overall, this research offers novel and important information about how the brain merges sensory input from multiple modalities in order to execute goal-oriented behaviors.

2.6 Conclusions

Modulation of the P50 amplitude depended on the temporal onset of crossmodal stimuli with the greatest facilitation seen when visual events primed tactile events (VTd condition), followed by similar modulation between the other crossmodal conditions (SIM and TVd), and lastly the smallest modulation was seen for the irrelevant unimodal tactile condition (TT). The amplitude of the P100 component was enhanced during the SIM condition and suppressed during the TVd condition and TT condition. This finding suggests that facilitation of the P100 component depended on the attentional relevance and temporal alignment of visual-tactile events. Overall, this study showed that early somatosensory ERPs generated in modality-specific cortical regions are modulated by both bottom-up sensory interactions between visual and somatosensory modalities and top-down attentional influences.

2.7 Figures

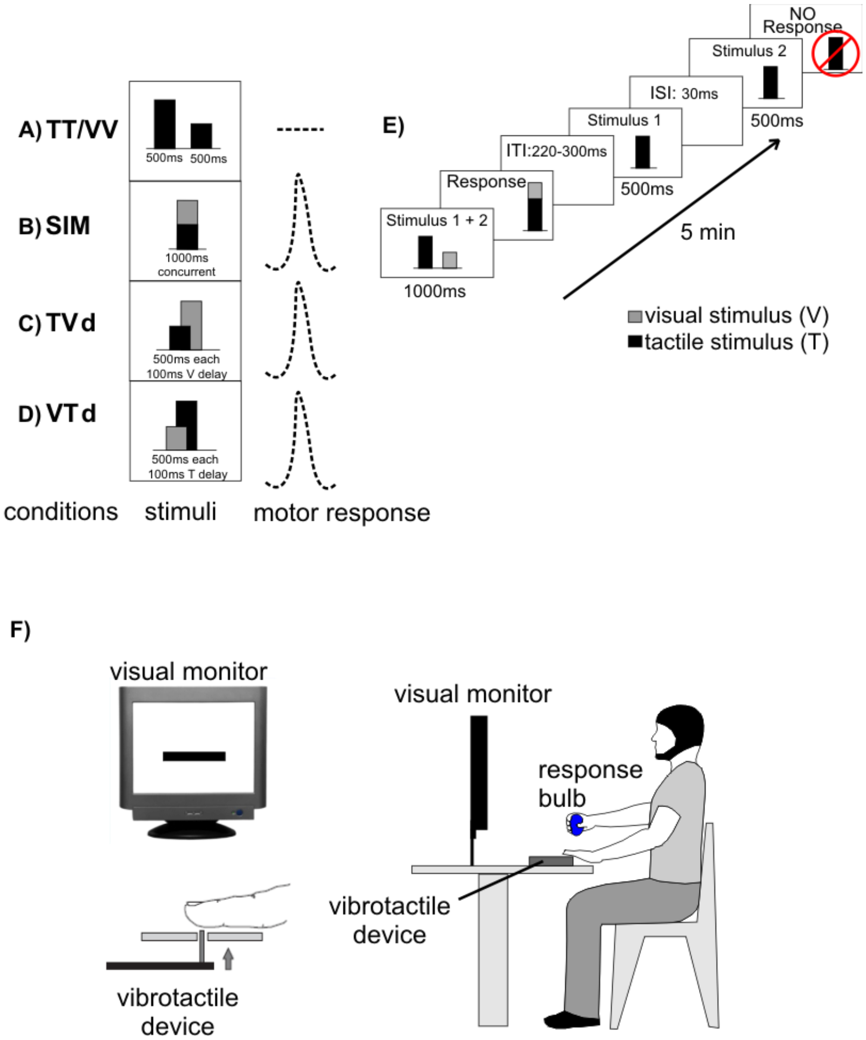

Figure 2.1. Experimental paradigm

A) shows the unimodal conditions (VV, TT), B) shows the crossmodal condition with simultaneously presented visual-tactile stimuli, C) shows the crossmodal condition where tactile stimuli are presented 100ms before visual stimuli (TVd), D) shows the crossmodal condition where visual stimuli are presented 100ms before tactile stimuli (VTd) between visual-tactile condition (VT). Participants were required to ignore all unimodal conditions and only respond to the crossmodal conditions. To depict the behavioural task, the columns are intended to represent examples the temporal onset and amplitudes of stimulus events amplitudes while the dotted trace is a schematic of the corresponding force applied to the squeeze-bulb when making the motor response to those stimuli. E) shows an example a bimodal simultaneous condition (SIM) and a unimodal tactile-tactile condition (TT). F) Subjects were to attend only to bimodal conditions and make a graded motor response with a pressure bulb representing the summation of each stimuli. (ITI; Intertrial interval, ISI; Interstimulus interval).

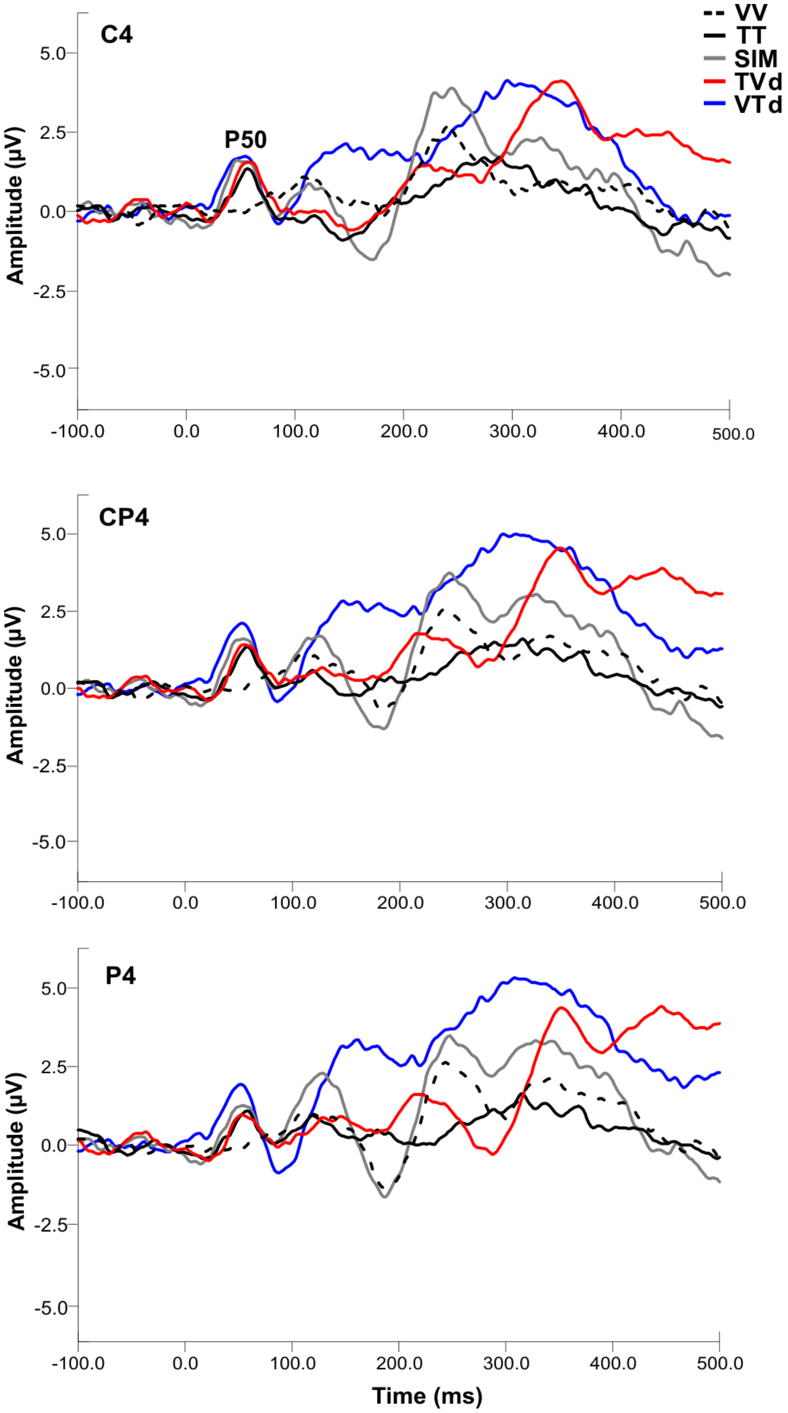

Figure 2.2. Grand averaged P50 waveforms

Grand average waveforms all for conditions are shown for parietal electrode sites contralateral to vibrotactile stimulation (C4, CP4, P4). The P50 ERP component is labeled on the trace for electrode site C4. Black and light gray solid traces show VTd, SIM, dark gray dotted traces show TVd conditions, while gray and black dashed traces show TT and VV conditions, respectively.

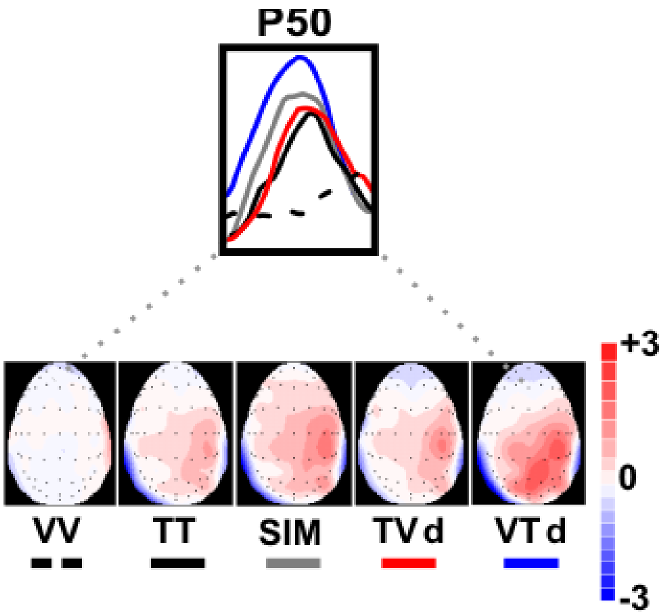

Figure 2.3. P50 scalp topography maps

Inset shows modulation of the P50 ERP waveforms in response to bimodal and unimodal conditions. The P50 ERP component is labelled on the trace for electrode site CP4. Solid black and light gray traces show VTd and SIM conditions, dotted dark gray traces show TVd conditions, while gray and black dashed traces show TT and VV conditions, respectively. Below images show group averaged data of peak areas of cortical activity generated over a 30 ms time window (40-70ms) centered around the P50 ERP peak. All values are in microvolts (uV).

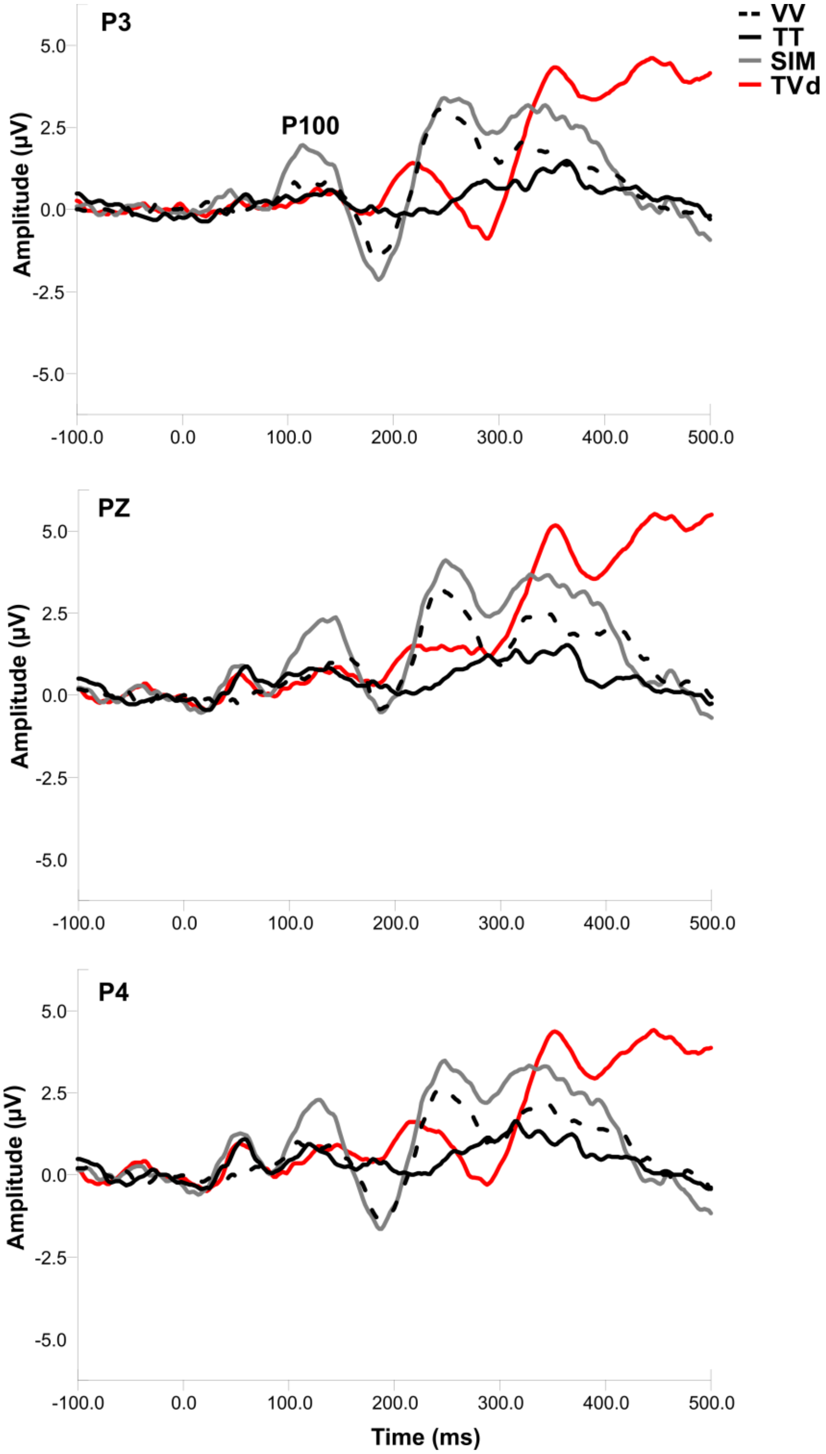

Figure 2.4. Grand averaged P100 waveforms

Grand average P100 waveforms are shown for parietal electrode sites (P3, PZ, P4) for SIM, TVd, and TT conditions. The P100 ERP component is labelled on the trace for electrode site P3. Solid light and dotted dark grey traces show SIM, TVd conditions, respectively, while dashed light grey traces show the TT condition.

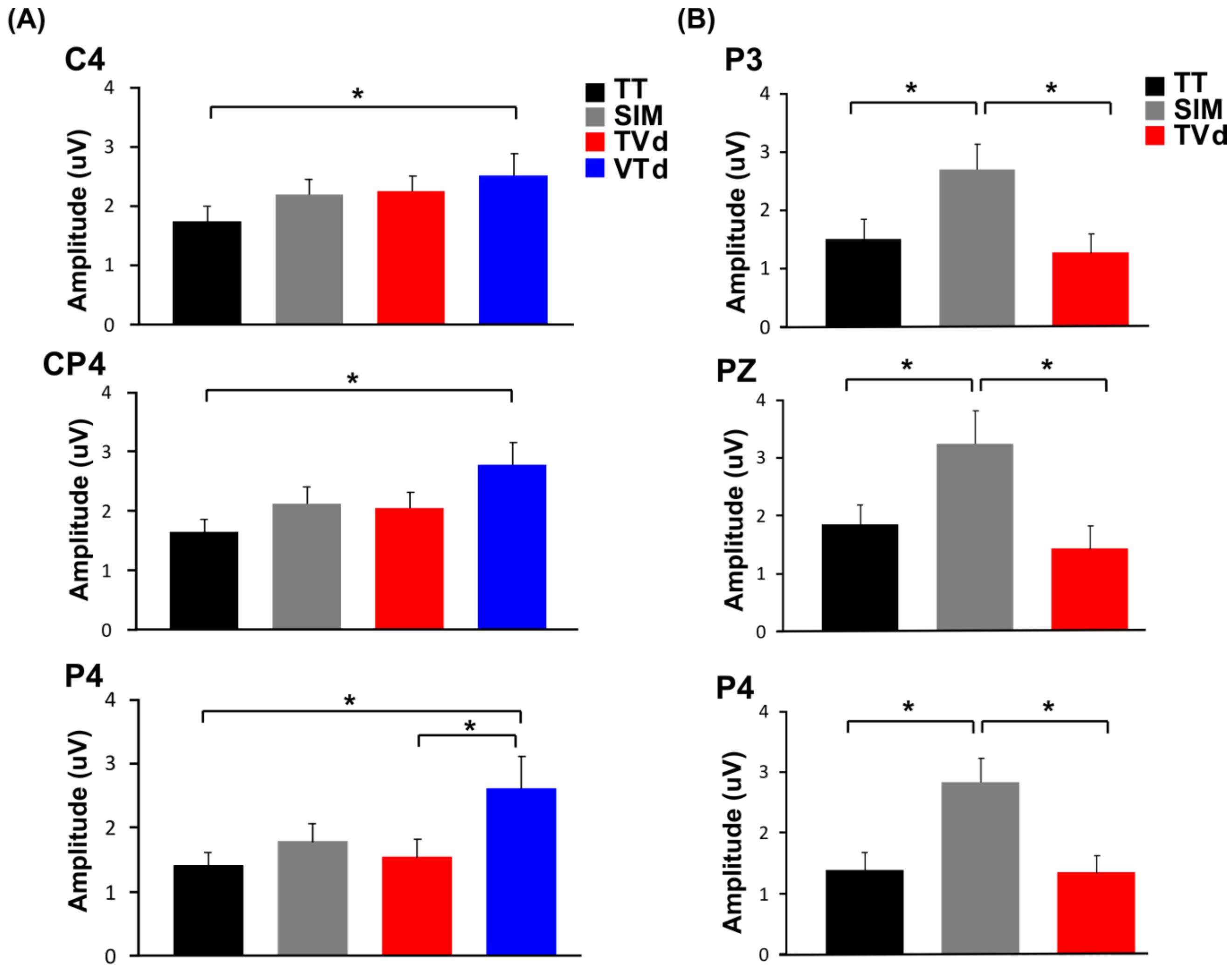

Figure 2.5. Group ERP means

Group means for A) P50 and B) P100 ERP components. Solid black bars represent group data for the crossmodal condition where presentation of visual stimuli preceded tactile stimuli (VTd), dark gray bars with dotted lines represent group data for the crossmodal condition where presentation of tactile stimuli preceded visual stimuli (TVd), solid light gray bars represent group data for the crossmodal condition where visual+tactile stimuli were presented simultaneously (SIM), dashed light gray bars represent group data for the unimodal tactile condition (TT). Error bars show SEM, * denotes significance p<0.05. (A) Mean P50 amplitude measured at CP4, (B) depicts the mean P100 amplitude at PZ, respectively.

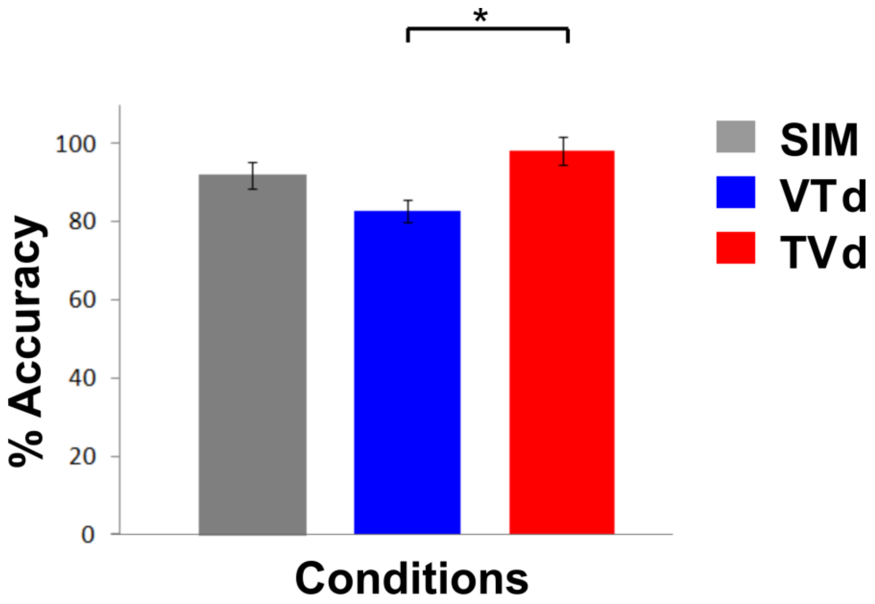

Figure 2.6. Behavioural performance

The solid light gray bar graph represents group data for the visual + tactile simultaneous condition (SIM), the dotted dark gray bar graph represents group data for the condition where tactile stimuli were presented 100ms before visual stimuli (TVd), and the solid black bar graph represents group data for the condition where visual stimuli are presented 100ms before tactile stimuli (VTd) between visual-tactile condition (VT). Error bars show SEM.

Chapter 3 - Study 2: Early modality-specific somatosensory cortical regions are modulated by attended visual stimuli; interaction of vision, touch, and behavioural intent.

Adapted from:

Staines WR, Popovich C, Legon JK, Adams MS. (2014). Early modality-specific somatosensory cortical regions are modulated attended visual stimuli; interaction of vision, touch, and behavioural intent. *Frontiers in Psychology, 5(*351), 1-11.

3.1 Overview

Crossmodal interactions between relevant visual and tactile inputs can facilitate attentional modulation at early stages in somatosensory cortices to achieve goal-oriented behaviours. However, the specific contribution of each sensory system during attentional processing and importantly, how these interact with required a behavioural motor goal remains unclear. Electroencephalography was used to test the hypothesis that activity from modality-specific somatosensory cortical regions would be enhanced with task-relevant crossmodal stimuli (visual+tactile), and that the degree of modulation would depend on the difficulty of the associated sensory-motor task demands. Tactile stimuli were discrete vibrations to the index finger and visual stimuli were horizontal bars on a computer screen, both with random amplitudes. Streams of unimodal (tactile) and crossmodal (visual+tactile) stimuli were randomly presented and participants were instructed to attend to one type of stimulus (unimodal or crossmodal). Responses involved either an indication of the presence of an attended stimulus (detect), or the integration and summations of two stimulus amplitudes using a pressure-sensitive ball (grade). Force-amplitude associations were learned in a training session with no performance feedback while ERPs were time-locked to tactile stimuli and extracted for early modality-specific components (P50 and P100). Results showed enhancement of the P50 during the presentation of attended, crossmodal stimuli. This was maximal when the motor requirements involved integration of the two stimuli in the grade task and when the visual stimulus occurred before (100 ms) the tactile stimulus. These results suggest that visual information relevant for movement modulates somatosensory processing as early as SI and that the motor behavioural context influences this likely through interactions of top-down attentional and motor preparatory systems with more bottom-up crossmodal influences.

3.2 Introduction

Selective attention is often classified as a top-down cognitive process whereby attentional resources are voluntarily directed towards sensory stimuli relevant for goal-oriented behaviour. Neurologically, animal and human studies have shown that selective attention enhances neuronal responses in corresponding modality-specific regions of the brain (Josiassen et al., 1990; Hsiao et al., 1993; Motter, 1993; Woldorff et al., 1993; Jäncke et al., 1999; Johansen-Berg et al., 2000; Staines et al., 2002; Petkov et al., 2004; Gazzaley et al., 2007; Andersen et al., 2008). However, the presence of salient sensory stimuli in the environment can also capture attentional resources; a process referred to as bottom-up attention. Neuroimaging studies have reported that the presentation of a task-relevant stimulus when paired with another task-irrelevant stimulus from a different sensory modality also enhances neuronal responses in the attended modality (Calvert et al., 1997; Macaluso et al., 2000; Calvert, 2001; Macaluso and Driver, 2001; Molholm et al., 2002; Lehmann et al., 2006; Pekkola et al., 2006; Schürmann et al., 2006; Meehan and Staines, 2007, 2009). Animal work by Zhou and Fuster (1997) has shown that neurons in SI fire in response to visual stimuli that has been previously paired with tactile stimuli. Moreover, recent investigations have shown that neuronal responses in modality-specific cortex are enhanced when the crossmodal stimuli are task-relevant for behaviour. For example, previous neuroimaging studies by Dionne et al. (2010, 2013), showed that simultaneous presentation of relevant visual and tactile stimuli increased neuronal activity in modality-specific SI within 50 ms post stimulus onset. Popovich and Staines (2014) compliment these top-down crossmodal effects on SI, and extend them by showing that presentation of relevant visual stimuli 100 ms prior to the onset of tactile stimuli produced the greatest P50 facilitation, suggesting that meaningful vision can exert modulatory effects on modality-specific SI activity. Taken together, these studies imply that crossmodal processing is likely governed by both bottom-up sensory-sensory interactions and top-down attentional mechanisms in order to allow for the selection, amplification, and integration of sensory input relevant for initiating goal-oriented responses. However, while both these attentional mechanisms can modulate neural responses in modality-specific sensory cortex, it is unclear how these attentional mechanisms interact during sensory processing of crossmodal stimuli.

Excitability of somatosensory cortex is modulated by the relevance of stimuli to behavior, with the goal of facilitating the extraction of relevant sensory information for further cortical processing. The modulation of somatosensory information during movement provides evidence that the primary somatosensory cortex (SI) is sensitive to the relevance of somatosensory stimuli to behavior. Inhibition of afferent information ascending to the cortex is seen when somatosensory evoked potentials (SEPs) to passive somatosensory stimuli are attenuated during movement, a phenomenon often called movement-related gating (Cheron and Borenstein, 1991; Chapman, 1994; Brooke, 2004), this gating effect is lifted, at least partially, when the stimuli are made relevant to the performance of a task (Staines et al., 1997, 2000).

In a non-gating context, recent findings using event-related potentials (ERPs) provide evidence that task-relevance of stimuli facilitates crossmodal modulation of early and mid-latency somatosensory-specific ERP components, namely the P50, a positive potential peaking at approximately 50 ms after presentation and generated in the primary somatosensory cortex (Hämäläinen et al., 1990), as well as the P100 and N140 (Dionne et al., 2013; Popovich and Staines, 2014) generated in secondary somatosensory cortex (Mima et al., 1998; Frot and Mauguière, 1999; Gu, 2002). These results are novel as crossmodal effects on the somatosensory P50 have not been previously reported, and even attentional modulation of this potential is not consistently observed (Desmedt and Robertson, 1977; Michie et al., 1987; Eimer and Forster, 2003a/b; Zopf et al., 2004; Schubert et al., 2008). Part of the difficulty in reconciling the inconsistent reports of P50 modulation can be attributed to a lack of clarity in what it represents. Although the P50 is typically thought to reflect S1 excitability, early reports have suggested that the latency of this potential makes it unlikely to reflect processing of the evoking stimulus, but instead is more likely to represent the application of cognitive strategies to stimulus processing (Desmedt and Tomberg, 1989). If this is the case, then modulation of the P50 could be highly dependent on elements of the task that contribute to the strategy used by the subject, which could account for the lack of consensus on modulation of this potential across different tasks and paradigms. Early interactions have also been shown between auditory and somatosensory cortices in tasks with simultaneous stimulus presentation (Foxe et al., 2000). Further, Foxe and Simpson (2002) showed that early modality-specific visual cortex is active as early as 56 ms after stimulus onset with evidence of dorsolateral frontal cortex by 80 ms. Neuroimaging studies in humans complement the sensory-to-sensory interactions reported above by showing that the presence of crossmodal input can modulate neural excitability in modality- specific sensory cortices. Several functional magnetic resonance imaging studies have reported increased blood oxygenation level dependent (BOLD) responses in modality-specific cortices due to the mere presence of stimuli from another modality. These interactions have been found between: visual and auditory cortices (Calvert et al., 1997; Calvert, 2001; Lehmann et al., 2006; Pekkola et al., 2006), auditory and somatosensory cortices (Foxe et al., 2002; Schürmann et al., 2006), as well as visual and somatosensory cortices (Macaluso et al., 2000, 2002). In addition, Dionne et al. (2010) investigated crossmodal effects on BOLD responses generated in SI when both stimuli were relevant for guiding a motor response. Here, relevant unimodal (visual or tactile) and crossmodal stimuli (simultaneous visual + tactile) were presented and participants squeezed a pressure-sensitive bulb with a force that was dependent on the summation of both stimuli. Results showed that the greatest BOLD responses were elicited inS1during crossmodal versus unimodal interactions suggesting that combining visual-tactile (VT) information relevant for behavior enhances modality-specific excitability in S1 (Dionne et al., 2010).

The objective of the current study was to investigate the role of specific task requirements in mediating the previously observed crossmodal modulation of early modality-specific somatosensory cortical responses, represented by the P50. Importantly, this crossmodal modulation occurred when both the visual and tactile target stimuli were attended to and necessary for an impending motor task. The current study investigates the role of the motor requirements of the impending task. Based on the findings of Dionne et al. (2010, 2013) and Popovich and Staines (2014), it was hypothesized that activity from modality-specific somatosensory cortical regions would be enhanced with task-relevant crossmodal (visual-vibrotactile) stimuli and that the degree of modulation would depend on the difficulty of the associated motor task demands (i.e. sensory-motor integration task or detection task). Specifically, it was hypothesized that crossmodal enhancement of the amplitude of the P50 component would be greatest when the onset of relevant visual information occurred prior to the onset of tactile information and required a sensory-motor integration response, and smallest during the detection of unimodal (tactile) stimuli.

3.3. Methods

3.3.1 Participants

EEG was collected from 10 healthy self-reported right-handed participants (mean age=24 years, 5 males). All participants provided informed written consent and the experimental procedure was approved by the University of Waterloo Office of Research Ethics.

3.3.2. Behavioural task

The behavioural task consisted of 3 conditions that presented pseudo-randomized pairs of discrete tactile or visual and tactile stimuli with random amplitude variations. Stimuli were always presented in pairs, either sequentially (unimodal conditions) or simultaneously (crossmodal conditions): 1) tactile-tactile (TT; 500 ms each, 30 ms ISI), 2) visual-tactile simultaneous (SIM; 1000 ms concurrent), 3) visual-tactile with a 100 ms temporal delay between stimulus onsets (VTd; 500 ms each). Streams of unimodal (tactile) and crossmodal (visual-tactile) stimuli were presented in each block. In separate blocks, participants were verbally instructed to attend to one type of stimulus interaction (i.e. unimodal or crossmodal) and produce a motor response which represented either the: i) indication of the presence of an attended stimulus (detect), or (ii) integration and summation of 2 stimulus amplitudes (grade). In this way, attentional and motor response state was established prior to each experimental block. In each motor task condition, participants were required to make their response using a pressure-sensitive ball in order to keep the relative nature of the motor response similar across conditions. Stimuli were presented for 1 second after which participants were required to make their motor response immediately following presentation of the crossmodal stimuli during a 2.5 second window prior to the start of the next trial, for a total of approximately 5 seconds per trial. Crossmodal grade and detect conditions were randomly presented in 5 blocks of 90 stimulus events each (30 each of TT, SIM, and VTd), totaling 10 blocks of 900 stimulus events in total, with each block lasting approximately 6 min. Unimodal grade and detect conditions occurred in two blocks of 150 stimulus events each for a total of four blocks of 600 stimulus events in total (refer to Fig. 3.1.).

Prior to the EEG collection participants underwent a 5-minute training session with visual feedback to learn the relationship between the amplitudes of the stimuli and the corresponding force required to apply to the bulb. During training, a horizontal target bar appeared on the visual display and subjects were instructed to squeeze the pressure-sensitive bulb with enough force to raise another visual horizontal bar to the same level as the target bar. At the same time, as subjects applied force to the bulb with their right hand the vibrotactile device vibrated against the volar surface of their left index finger with corresponding changes in amplitude, i.e. as they squeezed harder on the bulb the amplitude of the vibration increased proportionately. Subjects were instructed to pay attention to these changes in amplitude as they related to the force they were applying to the bulb. This training allowed subjects to become familiar with the relationship between the vibrotactile stimulus amplitude and the corresponding force applied to the bulb. To control for force-related trial-to-trial differences, stimulus amplitudes were scaled such that no single stimulus required a squeeze of more than 25% of an individual's maximum force, thus the response for adding two stimuli was never more than 50% of an individual's maximum force. Stimuli were always presented in pairs, either unimodally (two tactile), presented sequentially or crossmodally (one visual and one tactile), presented simultaneously or with a 100ms temporal offset between each stimuli.

3.3.3. Stimuli

Visual stimuli consisted of a centrally-presented horizontal bar (6 cm wide) at varying heights representing different amplitudes. Visual stimuli were displayed on a computer monitor positioned 50 cm in front of the subject. Vibrotactile stimuli consisted of discrete vibrations delivered by a custom-made vibrotactile device applied to the volar surface of the left index finger. Vibrotactile stimulation was controlled by converting digitally generated waveforms to an analog signal (DAQCard 6024E, National Instruments, Austin, Texas) and then amplifying the signal (Bryston 2B-LP, Peterborough, Ontario) using a custom program written in LabVIEW (version 8.5, National Instruments, Austin, Texas). Varying the amplitude of the driving voltage to the vibrotactile device produced proportional changes in vibration of the device on the finger. The amplitude of each discrete vibration was constant within a trial and varied randomly between trials. The average stimulus amplitude across all trials including a tactile stimulus did not differ between the experimental conditions. The frequency of the vibration was held constant at 25 Hz. Participants received 70 dB whitenoise (Stim2, Neuroscan, Compumedics USA, Charlotte NC) throughout the experiment to prevent auditory perception of the vibrotactile stimulus.

3.3.4. Data acquisition & recording parameters

EEG data was recorded from 32 electrode sites (64 channel Quick-Cap, Neuroscan, Compumedics USA) in accordance with the international 10-20 system for electrode placement, and referenced to the linked mastoids (impedance <5 kohms). EEG data were amplified (20 000x), filtered (DC-200 Hz) and digitized at 500 Hz (Neuroscan 4.3, Compumedics USA) before being saved for subsequent analysis. Individual traces were band-pass filtered (1-30Hz) and visually inspected for artifacts (i.e. blinks, eye movements, or muscle contractions). Any contaminated epochs were eliminated before averaging. Event-related potentials were averaged to the onset of each stimulus relative to a 100 ms pre-stimulus baseline. Somatosensory ERPs were measured from individual participant averages for each task condition. Mean ERP amplitudes and latencies were computed for each subject within specified time windows centered around the post stimulus latency of somatosensory P50 component (40-70ms). Figure 3.2 illustrates the distribution of these potentials. Amplitude and latency of the P50 component was measured from C4, CP4, and P4 electrode sites, located over right sensory-motor and parietal cortex, contralateral to the vibrotactile stimulus. All P50 amplitudes were measured as raw voltage relative to the pre-stimulus baseline.

3.3.5. Data analysis

A repeated measures ANOVA was carried out on P50 amplitudes with the following within subject factors: motor task (two levels: detect, grade), attended modality (two levels: unimodal, crossmodal) and stimulus type (three levels: TT, SIM, VTd). Tukey's *post hoc* tests were carried out following a main effect of stimulus type. Our statistical approach was restricted to the P50 component since the constant 100 ms temporal delay between the visual and tactile stimuli in the VTd condition produced an interaction with the visual ERPs over the time windows used to quantify any later somatosensory components (i.e. the P100 and N140). Previous work using the same temporal delay between the visual and tactile stimuli as used here showed that the distribution of visual-locked ERPs spread to the central-parietal electrodes that overlap the time of the P100 but not the P50 (Popovich and Staines, 2014).

Behavioural data were analyzed for each motor requirement (i.e. detect and grade tasks). For the detection task, the number of hits and misses were counted. For the grade task, behavioural analysis was conducted by summing the amplitudes of the two target stimuli and comparing this to the amplitude of the response, i.e. the force applied to the bulb. The percent difference between the summed target stimulus amplitude and the actual response amplitude was then calculated. Paired *t*-tests were used to assess statistical differences between unimodal and crossmodal stimuli for each task.

3.4. Results

3.4.1. Early ERP components (P50)

ERP analyses was focused on the P50 because the constant 100 ms temporal delay between the visual and tactile stimuli in the VTd condition produced an interaction with the visual ERPs over the time window (90–125ms) chosen for the P100 peak amplitude. All subjects demonstrated a clear P50 component in response to vibrotactile stimuli presented to the left index finger. Figure 3.2 shows the grand averaged waveforms for the VTd stimuli in all conditions at electrode site CP4 approximately overlying the contralateral somatosensory cortex. Ignore VTd represents ERPs to VTd stimuli (time locked to the tactile stimulus) when participants were responding to unimodal (TT) stimuli. Scalp topography maps representing group averaged data were created by averaging neural responses generated over the 30 ms time window (40–70ms) centered around the P50 peak to observe task-specific differences in cortical modulation (Figure 3.3). As illustrated in Figure 3.2, all conditions including vibrotactile stimuli elicited robust neural activity over somatosensory regions contralateral to stimulation. Notably, the VTd conditions also elicited robust activation over modality- specific visual cortex. Statistical results showed a main effect of the stimulus type ($F_{2,99} = 11.1$, $p < 0.0001$) and the *post hoc* Tukey's test revealed that the P50 amplitude was largest in the VTd conditions where the visual stimulus preceded the tactile stimulus by 100 ms compared to both the simultaneous (VT/SIM) or unimodal tactile (TT) conditions at electrode CP4 ($p < 0.05$). Figure 3.2 shows P50 amplitudes for the Grade and Detect tasks for both VTd and TT stimulation. P50 amplitude was maximal in the condition where participants graded their force to the crossmodal stimuli and the visual stimulus preceded the stimulus by 100 ms.

3.4.2. Behavioral data

Paired *t*-tests were carried out on the behavioral data for each task to test whether the unimodal task differed from the crossmodal task. Figure 3.5 shows response percent accuracy scores for each motor task. The percentage scores exceeding 100% accuracy in the grade conditions signifies that participant's tended to over-squeeze the pressure bulb when attention was directed towards either unimodal stimuli (TT Grade) or simultaneously presented crossmodal stimuli (SIM Grade). Statistical results showed that participant performance in the graded task was significantly more accurate in the VTd compared to the unimodal task ($p = 0.02$). No other significant differences were found for any of the other task conditions (Figure 3.5).

3.5. Discussion

This study set out to probe the role of behavioral task requirements in mediating crossmodal modulation of early modality-specific somatosensory cortical processing represented by early ERP components. The greater purpose was to provide insight into what the somatosensory P50 may represent by testing the hypothesis that it would be sensitive to changes in task set despite identical stimulus parameters. It was predicted that P50 modulation would be sensitive to task demands, specifically, that crossmodal modulation would be maximal in the grade task, when the relationship between stimulus attributes and motor response was greatest. More importantly this condition required cortical networks involved in motor preparation and selective attention to both be active. In addition, it was hypothesized that having the visual target information onset slightly earlier, allowing sufficient processing time for the potential interaction between the sensory modalities, would enhance such crossmodal modulation. Overall, the hypotheses were supported by the data. Responses from modality-specific somatosensory cortex (SI) were greatest when the required motor task was dependent on extracting stimulus details in order to accurately carry out the execution of the specific movement. Such a task involves attention directed to the sensory target modalities as well as preparation in the cortical motor areas. This enhancement of the modality-specific cortical response was further enhanced when the temporal arrangement of the crossmodal stimuli allowed for interaction between the visual and somatosensory modalities.

3.5.1. Early modality-specific effects

In the present study, crossmodal modulation of the P50 was replicated as in previous studies when the behavioral task required a graded motor response linked to the amplitude of the stimuli. Yet this modulation was not observed when the task requirements were changed despite the stimuli being identical. This finding provides fairly compelling evidence that crossmodal effects on the P50 are mediated by the demands of the task. The detection and graded tasks represent varying requirements to extract sensory information in order to make the appropriate motor response, with the detection task being the least demanding and the graded task the most demanding. In support of this argument, the behavioral data show that the detection task was performed with near perfect accuracy, whereas the graded task was associated with less accurate performance, which would suggest it was the most difficult to perform. When the conditions were altered such that the visual stimulus was available prior to the tactile target there was an association between behavioral performance and the excitability of early somatosensory responses. As shown in Figure 3.4, performance in the VTd grade task was significantly more accurate than in the unimodal task while the P50 amplitude was significantly enhanced relative to the others.

Considering all these findings together, some interesting possibilities arise about what the somatosensory P50 might represent. The lack of crossmodal effects in the detection and discrimination tasks argues strongly against the idea of a global crossmodal facilitation in response to visual and tactile stimuli. The finding that crossmodal effects only emerge under specific task requirements suggests that this potential is likely to reflect cognitive strategies being applied to the processing of the sensory inputs at an early stage, as was suggested by Desmedt and Tomberg (1989) in their discussion of what they termed the cognitive P40, which showed a similar topographical distribution to the P50 recorded in this experiment. A study by Schubert et al. (2008) provides support for this idea and suggests that early sensory-specific modulations are associated with more demanding tasks. Such enhancements are presumably mediated via reciprocal thalamocortical networks that act to bias processing towards selected inputs (Yingling and Skinner, 1976; Brunia, 1993).

It is important to note that in all cases the somatosensory ERPs are time-locked to the onset of the tactile stimuli. In addition, in the case when the visual stimulus precedes the tactile stimulus by 100 ms (VT Grade) shown in Figure 3.2 (red trace) there is some indication of alpha-like activity. The absence of this in the ERPs time-locked to the unimodal, tactile stimulus in the same block, suggests that this was not inherent to the task. In addition, the presentation of visual information prior to tactile stimuli did not permit observation of crossmodal effects on the P100 component since the constant 100 ms temporal delay between the visual and tactile stimuli in the VTd condition produced an interaction with the visual ERPs over the time windows used to quantify later components (i.e. P100 and N140). The P100 is bilaterally distributed over parietal electrode sites and is thought to be generated in bilateral SII (Mima et al., 1998; Gu, 2002). Several studies report sensitivity of this potential to effects of attention (Josiassen et al., 1982; Desmedt et al., 1983; Michie et al., 1987; Eimer and Forster, 2003a/b; Kida et al., 2004; Schubert et al., 2006), and functional imaging studies show modulation of SII when attention is directed towards TT stimuli (Meyer et al., 1991; Johansen-Berg et al., 2000; Staines et al., 2002; Nelson et al., 2004). While the effects of attention on the P100 appear fairly consistent, studies investigating crossmodal influences on mid-latency components are mixed. Studies employing an oddball detection task that required subjects to monitor both hands for deviant stimuli in one modality while ignoring the other and reporting detections with a verbal response also failed to find crossmodal effects on this potential (Eimer and Driver, 2000; Eimer, 2001). Dionne et al. (2013) reported that the P100 was sensitive to the presence of crossmodal stimuli but not to the task- relevance of those stimuli during the performance of a graded motor task, yet that same effect was not observed in the current study. However, there are differences in the design of these two experiments that may account for this discrepancy. In the current study the stimuli received by participants were intermixed pairs of either tactile (TT) or visual and tactile (VT) stimuli, and they were required to attend to either the unimodal (TT) or crossmodal (VT) events, essentially a crossmodal oddball task with varying motor requirements. In the previous experiment, pairs of crossmodal or unimodal stimuli were presented in different blocks while participants performed the same task.

3.6. Conclusion

Crossmodal effects on early somatosensory cortical processing, represented by the P50 component, depends on the engagement of the attentional system and on the specific requirements of the behavioral task, suggesting this component may reflect the application of cognitive strategies to sensory processing and extraction of relevant features. There may be functional interaction of systems responsible for attention, multimodal sensory integration and motor preparation that contribute to modulation of modality-specific somatosensory cortex.

3.7. Figures

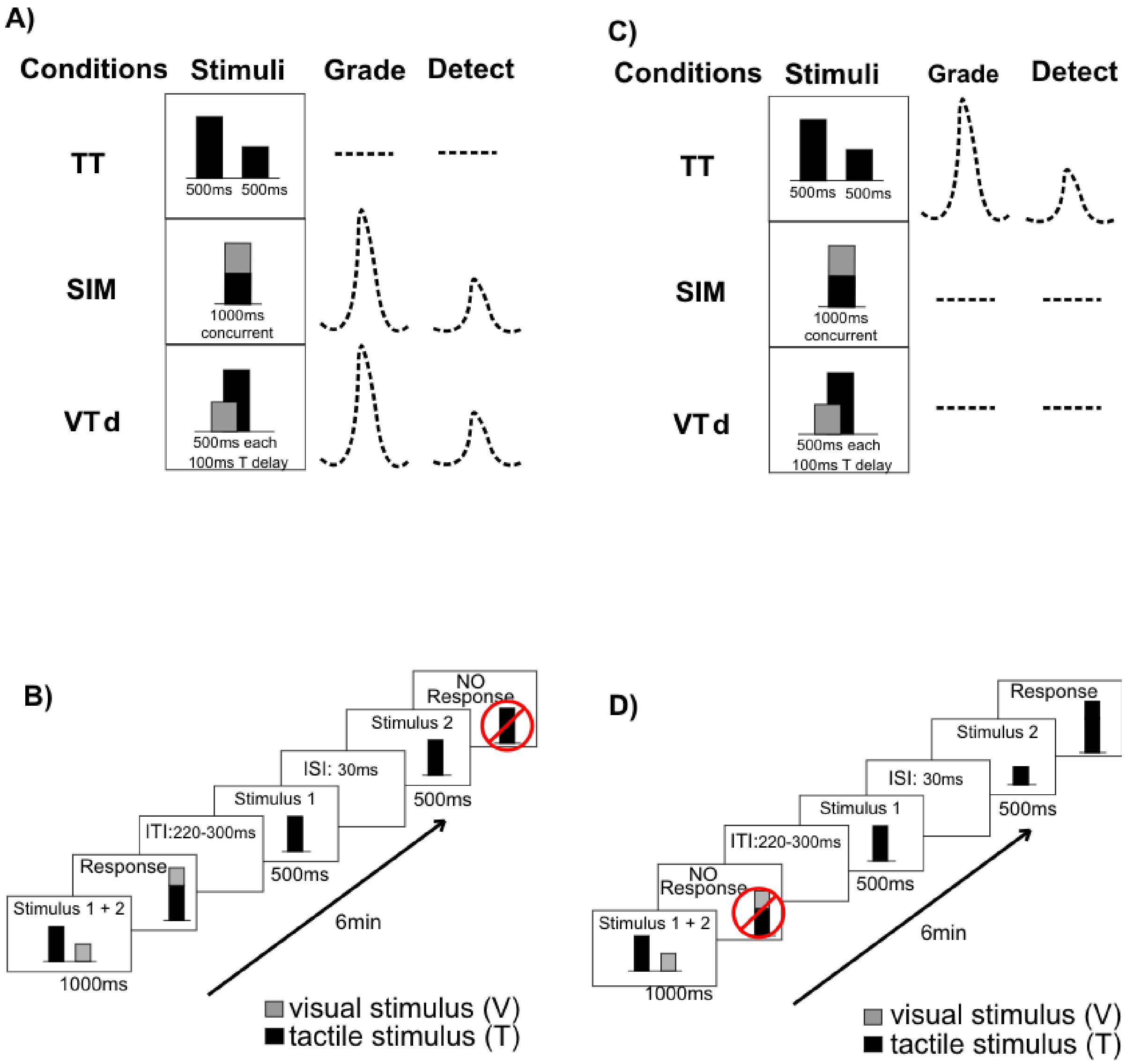

Figure 3.1. Experimental paradigm

(A) and **(B)** illustrate the task blocks in which participants attended and responded to crossmodal visual-tactile stimuli. Responses were either scaled to the summed amplitudes of the two stimuli (Grade) or simply indicated the presence of the attended stimuli (Detect). **(C)** and **(D)** illustrate the presentation of the same stimuli; however, in these blocks participants attended and responded to the unimodal tactile stimuli. Each block of trials lasted approximately 6 min.

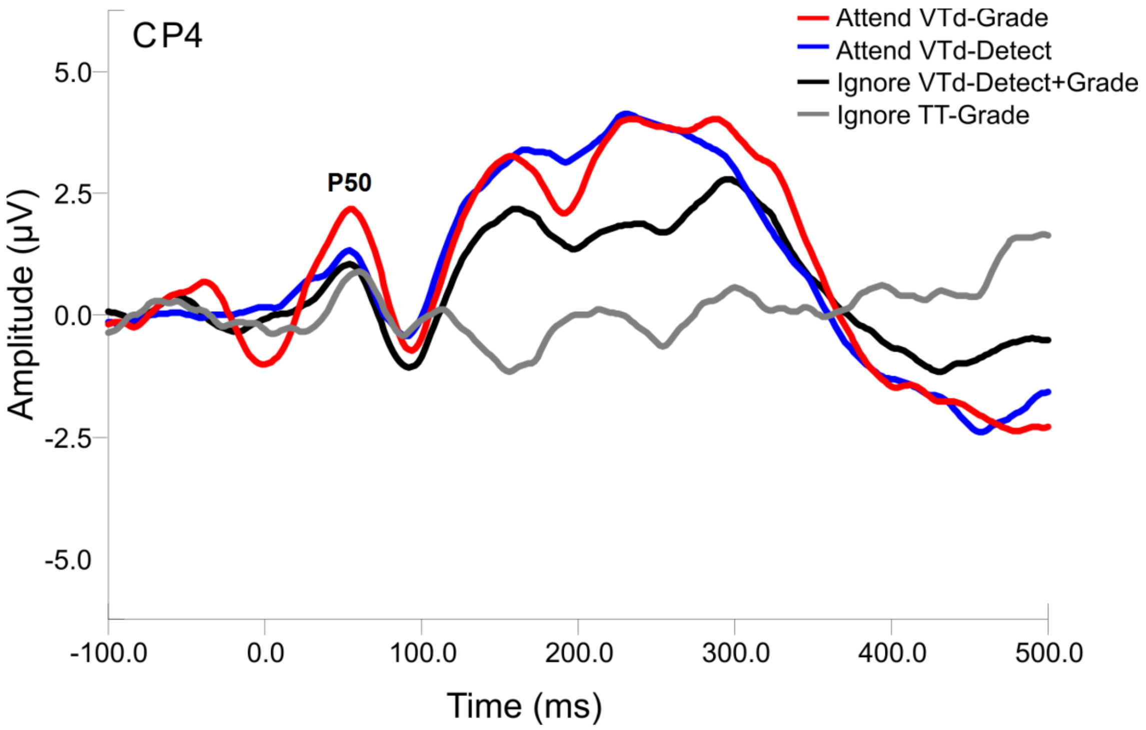

Figure 3.2. Grand averaged P50 waveforms

Grand average waveforms for the crossmodal VTd conditions at electrode CP4. The P50 ERP component is labeled on the trace for electrode site CP4. Red, blue, and black traces show VTd stimuli in the detect, grade or when attention was directed to the unimodal stimuli (Ignore VTd), respectively. The gray trace shows the ERP time-locked to the TT stimuli when participants were responding to the crossmodal stimuli in the Grade response condition (Ignore TT-Grade).

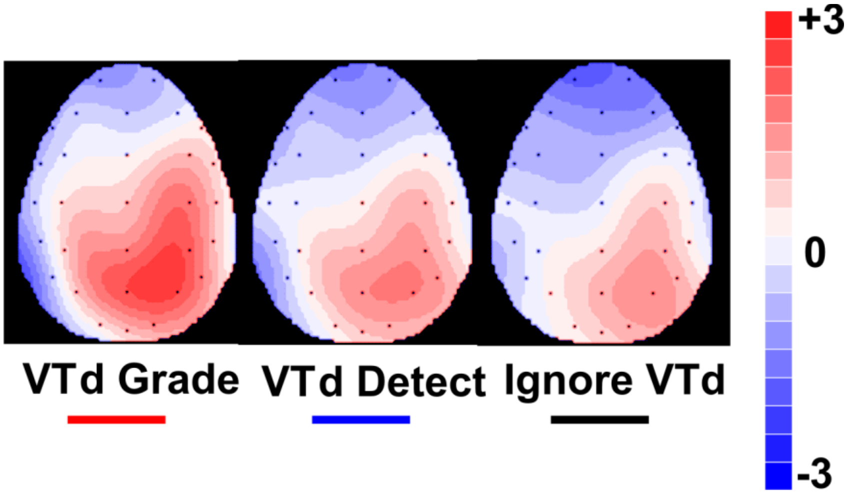

Figure 3.3. P50 scalp topography maps

Inset shows modulation of the P50 ERP waveforms in response to conditions in 1A. Images show group averaged data of peak areas of cortical activity generated over a 30 ms time window (40–70 ms) centered around the P50 ERP peak. All values are in microvolts (μV).

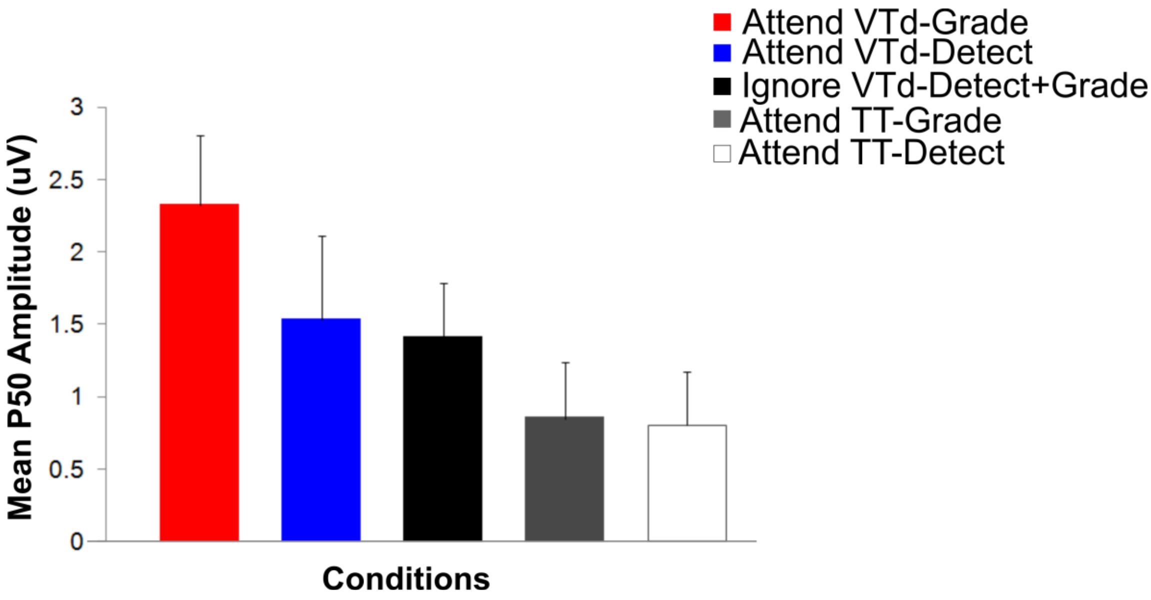

Figure 3.4. Group means for P50 amplitudes

P50 mean amplitudes measured at CP4 for the Grade and Detect tasks for both VTd and TT stimulation. P50 amplitude was maximal in the condition where participants graded their force to the crossmodal stimuli and the visual stimulus preceded the tactile stimulus by 100 ms (Attend VTd-Grade; red bar). Red and blue bars represent group data for the crossmodal visual + tactile conditions (VTd) in which subjects graded their force for the response (Grade) or indicated detection of the target stimulus (Detect). The black bar represents the same VTd condition during blocks where attention was directed to the unimodal (TT) stimuli (grey/white bars). Error bars show SEM.

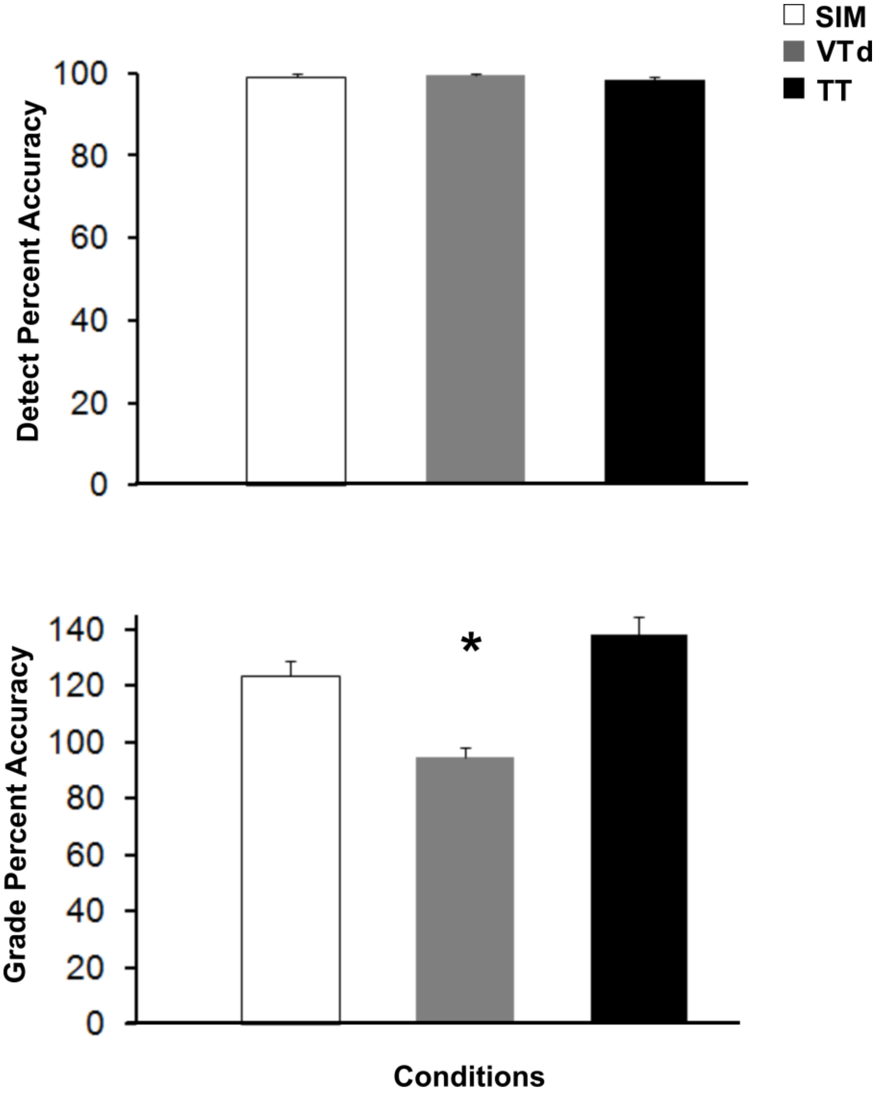

Figure 3.5. Behavioural performance

Performance is shown for the crossmodal visual + tactile task condition where the stimuli were presented simultaneously (VT, white bars) or with a 100 ms delay (VTd, gray bars). Black bars represent group data for the unimodal tactile condition (TT). Error bars show SEM, * denotes significance $p < 0.05$.

Chapter 4 - Study 3: Acute aerobic exercise enhances attentional modulation of somatosensory event-related potentials during a tactile discrimination task

Adapted from:

Popovich C. and Staines WR. (2015). Acute aerobic exercise enhances attentional modulation of somatosensory event-related potentials during a tactile discrimination task. *Behavioural Brain Research, 281,* 267-75.

4.1. Overview

Neuroimaging research has shown that acute bouts of moderate intensity aerobic exercise can enhance attention-based neuronal activity in frontal brain regions, namely in the PFC, as well as improve cognitive performance. The circuitry of the PFC is complex with extensive reciprocal corticocortical connections, yet it remains unclear if enhanced PFC activity following exercise can also assist cognitive processing in modality-specific sensory cortices. To test this, we used a tactile discrimination task to compare tactile event-related potentials (ERPs) prior to and following an acute bout of moderate intensity aerobic exercise. We hypothesized that exercise preceding performance of task would increase PFC excitability resulting in more efficient sensory-gating of irrelevant/non-attended and enhancement of relevant/attended sensory information, respectively. Participants received vibrotactile stimulation to the second and fifth digit on the left hand and reported target stimuli on one digit only. ERP amplitudes for the P50, P100, N140 and long latency positivity (LLP) were quantified for attended and non-attended trials at FC4, C4, CP4 and P4 while P300 amplitudes were quantified in response to attended target stimuli at electrodes CZ, CPZ and PZ. Results showed no effect of attention on the P50, however, both P100 and LLP amplitudes were significantly greater during attended, task-relevant trials, while the N140 was enhanced for non-attended, task-irrelevant stimuli.

Moreover, unattended N140 amplitudes over parietal sites were significantly greater post versus pre-exercise, while modulation of LLP varied with greater unattended amplitudes post exercise over frontal sites and greater attended amplitudes post exercise over parietal sites. These results suggest that a single session of moderate intensity aerobic exercise facilitated the sensory-gating of task-irrelevant tactile stimuli so that relevant sensory signals could be enhanced at later stages of somatosensory processing.

4.2. Introduction

Selective attention is commonly referred to as a higher-order executive process that requires conscious allocation of cognitive resources towards relevant information in the presence of environmental distracters. Attention-related neuroimaging studies have shown that attending to task-relevant sensory information can activate a widespread neural network consisting of cortical and subcortical structures (Corbetta, 1998; Hopfinger et al., 2000), as well as enhance neuronal responses in modality-specific sensory cortices (Motter, 1993; Petkov et al., 2004; Popovich and Staines, 2014). It is thought that attentional control is mediated by the prefrontal cortex (PFC) which operates as an inhibitory-control filtering mechanism, suppressing irrelevant sensory information so that relevant sensory signals can be amplified and passed on for further processing in modality-specific brain regions(Skinner and Yingling, 1976; Yingling and Skinner, 1976). Indeed, neuroimaging findings in healthy adults have shown attention-related neuronal enhancement of task-relevant tactile stimuli in frontal and modality-specific somatosensory regions (Staines et al., 2002; Dionne et al., 2010), while studies in patients with focal frontal lobe lesions have found that PFC damage produces disinhibition of distractor stimuli during a range of sensorimotor and cognitive processes (Knight et al., 1999). Furthermore, a recent imaging study in healthy young adults showed that transient disruption to neuronal activity in dorsolateral PFC via continuous theta burst stimulation (cTBS), produced disinhibition of task-irrelevant stimuli at early and later stages of somatosensory processing during a tactile discrimination task (Bolton and Staines, 2011). A follow-up study in PFC patients using the same tactile discrimination task showed similar aberrations in the neuronal profile of some of the same early and late somatosensory ERPs found following cTBS to the dorsolateral PFC (Bolton and Staines, 2014). Collectively, these studies support the notion that the PFC has a critical role in mediating attentional control over incoming sensory information by suppressing irrelevant sensory signals so that attended task-relevant information may be amplified in modality-specific sensory regions.

Notably, a growing body of evidence suggests that a single bout of acute aerobic exercise improves cognitive performance and produces neurophysiological changes, particularly in frontal lobe regions, during tasks requiring selective attention (Ekkekakis, 2009; Yanagisawa et al., 2010; Endo et al., 2013). Moreover, studies examining acute exercise-induced effects on cognition report that the greatest increases in neuronal activity are found in frontal regions following moderate bouts of aerobic exercise when tasks requiring higher-order attentional control are utilized (Kamijo et al., 2004, 2007; Hillman et al., 2009; Kamijo et al., 2009). These exercise effects on attentional processing support the inverted U-shape arousal hypothesis first proposed by Yerkes and Dodson (1908), which states that as arousal states increase with physical exertion, cognitive performance improves to an optimal point after which further increases in physical exertion cause decreased arousal levels resulting in decrements in performance (Tomporowski, 2003). However, the majority of human neuroimaging studies have employed psychological tasks tailored to examine the effects of exercise on PFC function (i.e. the Erikson Flanker, Stroop, or go/nogo tasks). As a result, it remains unclear if acute aerobic exercise modulates cortical activity downstream from the PFC in modality-specific sensory regions. Investigating the effects of aerobic exercise on frontoparietal interactions is an important avenue of the exercise and cognition research to pursue since the circuitry of the PFC is complex with reciprocal corticocortical and thalamocortical connections involved in modulating modality-specific sensory regions via attentional mechanisms. Determining whether acute bouts of aerobic exercise can improve attentional regulation over modality-specific sensory cortices provides an additional perspective regarding how exercise may transiently improve cognitive function perhaps via more efficient modulation between corticocortical networks. Notably, an EEG study performed in soccer athletes and non-athletes using a lower limb somatosensory stimulation oddball task showed that the athletic group demonstrated increased P300 amplitudes and decreased latencies over central-parietal electrode sites compared to the non-athletic group (Iwadate et al., 2005). These findings imply that long-term physical activity that requires selective attention and skilled motor responses may induce plastic changes in somatosensory processing during the execution of goal-oriented behaviours (Iwadate et al., 2005). However, no exercise intervention was implemented in this study, thus a causal link between the effects of exercise on somatosensory processing cannot be determined.

The purpose of the present study was to use EEG and a well-established tactile discrimination task to examine whether an acute bout of moderate intensity aerobic exercise, would enhance attention-based modulation of somatosensory ERPs generated at early and later stages of somatosensory processing in healthy young adults. Based on the findings of Bolton and Staines (2011), our first hypothesis was that early and later somatosensory ERPs would be modulated by attentional relevance (Bolton and Staines, 2011). Specifically, we hypothesized that an acute bout of moderate intensity aerobic exercise preceding performance of a tactile discrimination task would result in more efficient sensory-gating of irrelevant/non-attended and enhancement of relevant/attended sensory information. Therefore, improvements in sensory-gating would be observed as increased neural suppression of task-irrelevant stimuli and enhancement of relevant sensory information post- relative to pre-exercise.

2. Methods.

2.1. Participants

EEG was collected from 16 healthy participants (aged 21-28, 6 males). One participant was excluded due to the absence of clearly defined somatosensory event-related potentials of interest (i.e. P50, P100, N140, LLP components). The final sample consisted of 9 females and 6 males (mean age = 25.2 years). Participants were self-reported right-handed individuals with no medical history of any major neurological illness, and no heart or blood pressure conditions that could be exacerbated with aerobic exercise. Each participant provided informed consent and confirmed that they were physically able to engage in 20 minutes of moderate intensity aerobic activity on a recumbent bicycle. Experimental procedures were approved by the University Of Waterloo Office Of Research Ethics.

2.2. Behavioural Task

Subjects were seated in a sound-attenuating booth (Industrial Acoustics, 120A, NY), facing a blank computer screen and instructed to look directly ahead throughout testing. Tactile stimuli were delivered via 2 blunt plastic probes contacting the fingertips of the second and fifth digits on the left hand as depicted in Figure 4.1. These probes (approximately 1 cm diameter) were vibrated using piezo-electric actuators at a rate of 25 Hz for 125 ms during each stimulus.

Vibrotactile stimulation was delivered by digitally generated waveforms converted to an analog signal (DAQCard 6024E, National Instruments, Austin, TX, USA) and then amplified (Bryston 2B-LP, Peterborough, ON, Canada). The amplitude of vibration was set so that minimal values (i.e. small amplitude targets) exceeded sensory threshold for all subjects. These stimuli were presented randomly to each finger (but never simultaneously) with random interstimulus intervals in the range of 500–1500 ms. An oddball paradigm was employed whereby 17% of the trials for each finger consisted of the deviant stimulus. These deviant stimuli represented the targets to which attention was paid and the amplitude of these targets was set to 25% the standard (non-target) amplitude (i.e. deviant stimuli, 105% of perceptual threshold; standard stimuli, 120% perceptual threshold). The two experimental conditions required subjects to either (a) attend to the second digit (Attend D2; Attend Index) on the left hand while ignoring all stimuli delivered to the fifth digit, or (b) attend to the fifth digit (Attend D5; Ignore Index) on the left hand while ignoring all stimuli to the second digit. Subjects reported target stimuli on the attended finger by pressing a button with the right hand. Subjects were instructed to gently rest their hand on the probes to ensure consistent hand pressure throughout testing. Headphones delivering white noise were worn throughout the experiment to block sound from the vibration device. Trials requiring attention to either D2 or D5 were randomly presented to subjects in 3 min blocks followed by a rest period of approximately 1 min. There were a total of 6 testing blocks with 3 blocks attending to D2 and 3 blocks attending to D5. Approximately 600 standard (non-target) stimuli were applied to each digit over the entire experiment with each testing block consisting of approximately 100 standard and 20 target stimuli.

2.3. Exercise protocol

Upon task completion, participants were seated comfortably on a cycle ergometer while a measure of their resting heart rate was taken using a Polar heart rate monitor. Participants were instructed to begin pedaling on the ergometer to reach their target heart rate (60% of age-predicted maximum heart rate; [220-age] x 0.60), and maintain this exercise intensity for the remainder of the 20 minute aerobic session. For each participant, the ergometer resistance level was always set to its minimum value (level 1). To ensure that participants adhered to the exercise protocol, frequent heart rate monitor checks were recorded, as well as two self-reported measures of the participant's perceived rating of exertion were recorded after 10 and 20 minutes of exercise using the 10 point Borg Scale. After the exercise session, participants were seated back into the sound proof booth where electrode impedances were checked to ensure that all recorded sites were below 5 kohms and a final heart rate measure was recorded to ensure that participants' heart rates were within 10% their original resting heart rate (approximately 5 minute duration). Participants were then instructed to repeat the tactile discrimination task again.

2.4. Recording and analysis

EEG data was recorded from 32 electrode sites according to the international 10-20 system for electrode placement and referenced to bilateral mastoids. All channel recordings had impedance values below 5kohms. EEG data were amplified (20,000×), filtered (DC-200 Hz, 6 dB octave roll-off) and digitized (1000 Hz, SynAmps2, Scan 4.5, Compumedics Neuroscan, Charlotte, NC) before being stored for off-line analysis. Somatosensory ERPs to tactile stimuli were averaged relative to a 100 ms pre-stimulus baseline for each attention condition. Data were band-pass filtered (1–30 Hz) and trials with artefacts (i.e. eye blinks, muscle activity) were identified by visual inspection and were excluded from further analysis. Since stimulation of the fifth digit did not result in consistently clear ERP components, analysis was restricted to non-target stimuli (i.e. large amplitude vibrations) delivered to the second digit (i.e. index finger). Several somatosensory ERP components were evaluated in this study focusing on the peak amplitude for each defined ERP component. Somatosensory ERPs were measured from individual participant averages for each task condition. Mean ERP amplitudes were computed for each subject within specified time windows selected around the post stimulus latencies of each ERP component of interest: P50 (40-70 ms), P100 (85-125 ms), N140 (125-165 ms), LLP (175-250 ms), and the P300 (300-600 ms). Clearly defined components and peaks were required for inclusion. Separate two-way ANOVAs with factors attention (Attend index, Ignore index) and time (Pre-Exercise, Post-Exercise) were calculated for each component of interest at the electrode sites as follows: P50 (C4, CP4), P100 (P4, CPZ, P3), N140 (FC4, CP4, P4), LLP (FC4, CP4, P4) and P300 (FCZ, CZ, CPZ). Pre-planned contrasts were performed to test the hypotheses that ERP modulation would show greater suppression of task-irrelevant distractor stimuli (i.e. Ignore Index conditions) and greater enhancement of task-relevant stimuli (Attend Index conditions), post-exercise relative to pre-exercise.

The P50 ERP component has been shown to be generated in the primary somatosensory cortex (SI) (Schubert et al., 2008), while studies examining early somatosensory evoked potentials (SEPs) typically show more robust over central-parietal electrodes contralateral to stimulation in SI areas (Hämäläinen et al., 1990; Allison et al., 1992), thus the P50 was analyzed at electrode sites C4 and CP4 positioned over SI, contralateral to vibrotactile stimulation. We analyzed the P100 component at electrode sites P4, CPZ, and P3 since the P100 amplitude has known neural generators in bilateral secondary somatosensory cortices (SII) (Hämäläinen et al., 1990), with maximal activation typically seen in contralateral posterior parietal sites, but with enhancements also extending to ipsilateral and frontal sites (Desmedt and Robertson, 1977; Desmedt and Tomberg, 1989; Hämäläinen et al., 1990). For the later components, both the N140 and the LLP have shown increased activation in frontal regions during attentionally-demanding tasks resulting in continued engagement of modality-specific cortices (Pasternak and Greenlee, 2005), thus we analyzed these ERPs at frontoparietal electrode sites contralateral to stimulation (FC4, CP4, P4). Lastly, attention-based modulation of the P300 component typically occurs at fronto-central electrodes sites in response to task-relevant target stimuli (Pfefferbaum et al., 1985), thus for this component, we analyzed electrode sites FCZ, CZ, CPZ in response to target stimuli. Here, we time-locked and averaged somatosensory ERPs to the target stimuli (i.e. smaller vibrations) delivered to the index finger during the Attend Index conditions only, and a one-tailed paired t-test was performed to test whether exercise would increase attention-based modulation of this somatosensory ERP.

Behavioural performance was evaluated by determining the number of targets hit relative to the overall number of targets that were presented for each subject. This success rate was expressed as a percentage and compared using a two-way repeated measures ANOVA with factors attention (Attend Index, Ignore Index), and time (Pre-Exercise, Post-Exercise). The significance level was set at $p \leq 0.05$ for all comparisons.

3. Results.

3.1. Early ERP components: P50 & P100

Figure 4.2 shows waveforms at electrode sites contralateral to vibrotactile stimulation (i.e. FC4, CP4, and P4) with the components of interest specified (i.e. the P50, P100, N140, and LLP). Results for the P50 amplitude revealed no main effects or significant interaction at any of the electrode sites analyzed. Results for the P100 component showed a main effect of attention whereby P100 amplitudes were enhanced by task-relevant stimuli (i.e. Attend Index) compared to task-irrelevant stimuli (i.e. Ignore Index) (P4: $F_{1,14} = 14.0$, p=0.001; CPZ: $F_{1,14} = 6.73$, p=0.02; P3: $F_{1,14} = 9.38$, p=0.01). However, no other P100 results reached statistical significance (refer to Figure 4.4A).

3.2. Later ERP components: N140, LLP, & P300

A main effect of attention was found for the N140 component at all electrode sites analyzed whereby N140 amplitudes were increased during task-irrelevant conditions (i.e. when tactile stimuli were delivered to the index and attention was directed towards another spatial location (i.e. Ignore Index condition) (FC4: $F_{1,14} = 14.35$, p=0.002; CP4: $F_{1,14} = 9.58$, p=0.01; P4 $F_{1,14} = 8.49$, p=0.01). A significant attention* time interaction was also found for the N140 amplitude at P4 ($F_{1,14} = 9.96$, p=0.01), and a trend towards significance was found at CP4 ($F_{1,14} = 3.85$, p=0.07). Pre-planned contrasts at these electrode sites revealed that the amplitude of the N140 component was significantly greater post- relative to the pre-exercise session when stimuli delivered to the index finger were irrelevant (P4: $F_{1,14} = 18.46$, p=0.001; CP4: $F_{1,14} = 4.62$, p=0.05) (refer to Figure 4.4B).

A main effect of attention was found for the LLP component at all electrode sites measured whereby LLP amplitudes were enhanced by task-relevant stimuli (i.e. Attend Index) compared to task-irrelevant stimuli (i.e. Ignore Index) (FC4: $F_{1,14} = 5.67$, $p=0.03$; CP4: $F_{1,14} = 11.45$, $p=0.01$; P4: $F_{1,14} = 10.23$, $p=0.01$). Significant attention*time interactions were also found at all electrode sites analyzed for the LLP component (FC4: $F_{1,14} = 7.40$, $p=0.02$; C4: $F_{1,14} = 6.56$, $p=0.02$; CP4: $F_{1,14} = 8.11$, $p=0.01$; P4: $F_{1,14} = 5.02$, $p=0.04$). Pre-planned contrasts also showed that at electrodes CP4 and P4, the LLP amplitude was enhanced post- relative to the pre-exercise session when attention was directed towards relevant tactile stimuli (CP4: $F_{1,14} = 6.67$, $p=0.02$; P4: $F_{1,14} = 5.56$, $p=0.03$). Pre-planned contrasts revealed that at frontal electrode site FC4, the LLP amplitude was decreased post-exercise versus pre-exercise during the task-irrelevant condition ($F_{1,14} = 4.77$, $p=0.05$) (Figure 4.4C/D).

Lastly, analysis of the P300 amplitude revealed no statistical differences between the P300 amplitude when attention was directed towards relevant tactile stimuli post- versus pre-exercise at any electrode sites analyzed (FCZ: $t_{14}= 0.362$, $p > 0.05$; CZ: $t_{14}=0.35$, $p > 0.05$; CPZ: $t_{14}= 0.36$, $p > 0.05$). Results for the P300 latency also revealed no statistical differences pre- versus post-exercise during the Attend Index conditions (FCZ; $t_{14}= 0.1$, $p > 0.05$; CZ: $t_{14}=0.36$, $p > 0.05$; CPZ: $t_{14}= 0.17$, $p > 0.05$) (refer to Figure 4.3 for P300 traces).

3.3. Behavioural Results

Behavioural analysis showed a main effect of attention with success rates being higher when attention was directed towards the index finger versus away from it suggesting that participants were slightly less accurate in detecting target stimuli presented to the pinky finger ($F_{1,14} = 9.66$, $p=0.01$) (Figure 4.5).

4. Discussion.

Evidence suggests that acute aerobic exercise selectively up-regulates excitability in frontal lobe regions, thereby promoting greater top-down attentional control during executive functioning tasks (Ekkekakis, 2009; Yanagisawa et al., 2010; Endo et al., 2013). However, the effects of acute exercise in cortical areas downstream from the PFC in modality-specific cortices are not well understood. This study examined how an acute bout of moderate intensity aerobic exercise modulated neuronal activity in somatosensory cortices using a tactile discrimination task. Our ERP results, particularly for the LLP component, suggest that an acute bout of moderate intensity aerobic exercise facilitated the sensory-gating role of the PFC by suppressing neuronal responses to unattended, task-irrelevant stimuli at frontal regions and amplifying attended, task-relevant signals at modality-specific somatosensory regions contralateral to stimulation. Furthermore, our N140 results suggest that an acute bout of moderate intensity aerobic exercise may improve selective attentional processing by enhancing involuntary shifts of attention by showing greater enhancement of the N140 component to task-irrelevant stimuli post- relative to the pre-exercise session. Our findings are in line with current literature examining the inverted U-shape relationship between aerobic exercise and cognitive function by demonstrating that a single bout of moderate intensity exercise modulates frontoparietal interactions during a tactile discrimination task and facilitates selective attentional processing of tactile information in healthy young adults.

4.1. Neural mechanisms of attention-based modulation in somatosensory cortices

The P100 component is modulated by vibrotactile stimulation (Goff et al., 1977) and attentional processes (Desmedt et al., 1983; Josiassen et al., 1990; Eimer and Forster, 2003b), but it is thought to have bilateral neural generators in SII regions (Gu, 2002; Mima et al., 1998). Selective attention studies have reported increased P100 amplitudes to attended versus unattended tactile stimuli with effects being greater than earlier ERP responses generated in SI (Desmedt et al., 1983; Josiassen et al., 1990; Bolton and Staines, 2011, 2012), but these effects may also be task-specific and/or due to inter-individual differences in P100 modulation (Goff et al., 1977).

Using the same tactile discrimination task as reported in this study, Bolton and Staines (2011) revealed no modulation of the P50 component, but increased P100 amplitudes to task-relevant versus task-irrelevant stimuli. It was also found that transient disruption to the dorsolateral PFC via cTBS produced disinhibition of the P100 component to task-irrelevant stimuli, suggesting that this region plays an important role in the gating of task-irrelevant tactile information during selective attentional processing (Bolton and Staines, 2011). Our results were similar to previous findings using the same task, in that there was no attention-related modulation of the P50 component, but the P100 amplitude was enhanced to attended, task-relevant versus unattended, task-irrelevant tactile stimuli (Bolton and Staines, 2011). Failure to drive modulation of the P50 component using tactile stimulation paradigms is not uncommon, and task-difficulty may be an important factor required for driving modulation at early stages of somatosensory processing (Schubert et al., 2008). Based on previous work using the same tactile paradigm (Bolton and Staines, 2011, 2012, 2014), it seems likely that the cognitive demand of this particular task may not be sufficient for driving attentional modulation of the most primary measures of somatosensory processing. There were also no exercise-related changes in the modulation of the P100 amplitude when attention was directed towards the index finger (i.e. no differences Attend Index Pre-Exercise versus Post-Exercise).

The N140 component has been observed over frontal electrode sites contralateral to stimulation and along midline and ipsilateral sites (Desmedt and Tomberg, 1989), but is thought to have bilateral generators in SII regions with the hemisphere contralateral to stimulation online earlier (Frot and Mauguière, 1999). Although the neural generators of this ERP are not well understood, Allison et al. (1992) suggested that bilateral activation of the frontal lobes may generate the frontal N140 component. The frontal N140 may also reflect PFC activation and reciprocal neural communication with posterior and subcortical structures (Desmedt and Tomberg, 1989). If this supposition is true, then the N140 component would be an important electrocortical marker of PFC activation during situations when relevant sensory information must be maintained and retrieved to execute behavioural goals (Allison et al., 1992; Desmedt and Tomberg, 1989). However, unlike earlier modality-specific ERPs, modulation of the N140 component involves activation of multimodal cortical generators, thus making direct inferences about how attention modulates this component is somewhat nebulous. Several EEG studies investigating attentional modulation of the N140 component have found that the presentation of transient stimuli at a to-be-ignored spatial location can involuntarily direct attention towards that unattended, task-irrelevant side (Kida et al., 2004a, 2004b, 2006; Adler et al., 2009). Kida et al. (2004b, 2006) compared the influence of deviant stimuli on attentional modulation of the P100 and N140 somatosensory evoked potential when deviants were embedded in an oddball task to when they were presented in isolation. Subjects were instructed to either count the number of deviants presented, press a button indicating the detection of deviants (active attention tasks), or to ignore all tactile events and read a book (passive attention task). Results showed that attentional enhancement of N140, but not the P100, was greater when deviants were presented in isolation versus when they were embedded in an oddball sequence which was not the case for the

P100 component. The authors concluded that isolated deviants capture more attentional resources relative to when they are embedded in an oddball discrimination task. Adler et al. (2009) complemented these findings by showing that N140 enhancement was greatest for distracter stimuli presented to the to-be-ignored spatial location but only when the discrimination task involving the to-be-attended finger was relatively easy. It was suggested that the presentation of distracter stimuli at an unattended spatial location can involuntarily pull attention towards that body location under low, but not high, cognitive load demands. Similarly, Bolton and Staines (2011, 2012) found enhanced N140 amplitudes to task-irrelevant versus relevant tactile stimuli presented to the index finger using the same tactile discrimination task adopted in this study and surmised that their findings may relate to the interpretation proposed by Adler and colleagues (Adler et al., 2009). In our study, we showed consistent results for the N140 component across sensorimotor electrode sites contralateral to vibrotactile stimulation (i.e. CP4, P4), whereby the N140 amplitude was statistically greater post-exercise relative to pre-exercise, when attention was directed away from the index finger and towards another spatial location (i.e. Ignore Index). These findings suggest that the ability to involuntarily shift attention towards task-irrelevant tactile stimuli was more efficient following a single bout of acute moderate intensity aerobic exercise. More efficient involuntary shifts in attention towards and away from distracter stimuli in the environment may have, in turn, facilitated sensory processing of task-relevant stimuli observed at later stages of somatosensory processing.

The LLP has multiple neural generators from broadly distributed locations, and is often seen as a sustained positivity occurring approximately 200-500 ms post-stimulus (Hämäläinen et al., 1990). Several tactile ERP studies have reported variable attention-related effects on LLP modulation (Desmedt and Tomberg, 1989; Eimer and Forster, 2003b; Bolton and Staines, 2011, 2012). These discrepancies are likely due to differences in attentional requirements or demands of the task employed. The precise role of this later positivity remains unclear; however, several attention-based tactile ERP studies have implied that the LLP may share functional similarities to the P300 component (Desmedt and Robertson, 1977; Desmedt and Tomberg, 1989). The P300 component is typically observed during higher-order cognitive functions and is thought to have roles in selective attention and resource allocation, whereby the P300 amplitude is proportional to the amount of attentional resources engaged in processing a given stimulus (Donchin and Coles, 1988). EEG studies in healthy young and older adults using the same tactile discrimination task have reported increased LLP amplitudes during attended, task-relevant stimuli compared to non-attended, irrelevant tactile stimuli (Bolton and Staines, 2011, 2012). Notably, ERP data from PFC patients using the same tactile paradigm revealed aberrations, particularly, in the neuronal profile of the LLP component, with increased amplitudes elicited by task-irrelevant tactile stimuli (Bolton and Staines, 2014). This finding along with cTBS work by the same authors suggests that the PFC plays an integral role in sensory gating of early (i.e. P100) and later (LLP) stages of somatosensory processing in order to ensure that relevant sensory signals are amplified in sensory-specific cortices (Bolton and Staines, 2011; 2014). In our study, the amplitude of the LLP was suppressed at contralateral frontal and ipsilateral centroparietal sites, post- relative to pre-exercise, during the task-irrelevant condition, and was enhanced over modality-specific somatosensory cortices contralateral to stimulation. If the LLP arises from frontal generators and shares functional similarities with the P300 component, then our results suggest that an acute bout of moderate intensity exercise may have facilitated the sensory gating role of frontal networks by suppressing irrelevant sensory signals so that relevant tactile information could be passed on and amplified in modality-specific somatosensory cortex.

4.2. Exercise-related benefits on cognition

Acute aerobic exercise has been shown to induce neuromodulatory changes in PFC activity and improve cognitive performance during tasks requiring higher-order attentional control (Ekkekakis, 2009; Yanagisawa et al., 2010; Endo et al., 2013). Our study supports this idea and provides novel information about the effects of exercise on cortical areas downstream from the PFC. Our most interesting results occurred for the N140 and LLP components, whereby an acute bout of moderate intensity aerobic exercise potentially assisted involuntary shifts of attention towards and away from distractors in the environment so that relevant sensory signals could be enhanced at later stages of sensory processing over modality-specific somatosensory cortices. These findings suggest that an acute bout of moderate intensity aerobic exercise in healthy young adults facilitated selective attentional processing of somatosensory information.

In the present study, an acute bout of moderate intensity exercise did not drive significant modulation of early somatosensory ERPs of interest (i.e. the P50/P100 components), nor of the later P300 component. EEG studies have shown that the amplitudes of these earlier somatosensory ERPs are typically enhanced when attention is directed towards task-relevant sensory information (Eimer and Forster, 2003b; Schubert et al., 2008; Bolton and Staines, 2011, 2012; Popovich and Staines, 2014). However, failure to drive modulation of the P50 component is not uncommon in tactile literature and seems to be heavily dependent on the attentional demand of the cognitive task used (Schubert et al., 2008). Previous findings using the same tactile discrimination task as reported here have also failed to drive attention-related P50 modulation (Bolton and Staines, 2011, 2012). Thus, we have reason to infer that our chosen task may not be attentionally demanding enough to drive modulation at the most primary stage of somatosensory processing. Our behavioural results further support this supposition since participants performed the task with success rates of approximately 80%, suggesting that the attentional task was relatively easy. Furthermore, the absence of exercise-induced modulation of the P300 component may also be a result of the tactile discrimination task used. The majority of studies reporting exercise-induced effects on the P300 component in healthy young adults have used attentional tasks including: the flanker, the Stroop, or a go/nogo inhibitory control task (Kamijo et al., 2004, 2007; Hillman et al., 2009; Kamijo et al., 2009). These tasks reliably elicit P300 responses, while previous studies using sensory oddball tasks report mixed exercise-induced effects on the P300 component (Polich and Lardon, 1997; Nakamura et al., 1999; Yagi et al., 1999; Grego et al., 2004). The observation that P300 amplitudes were reduced post-exercise relative to pre-exercise in our healthy young adults is contrary to most exercise studies using attentional tasks requiring greater cognitive demand (Kamijo et al., 2004, 2007; Hillman et al., 2009; Kamijo et al., 2009) and the argument could be made that learning or practice effect may account for this result. However, behavioural results suggest that no change in cognitive performance across exercise sessions, thus we have reason to believe that the reduction in P300 amplitude post-exercise is not a reflection of practice or learning effects. Instead, it is plausible that this sensory oddball task may not be an advantageous paradigm for examining exercise-related effects on the P300 component in healthy young adults. Lastly, the absence of discernible ERPs from stimulation of the fifth digit hindered our ability to examine whether exercise-induced attentional effects would extend to a different spatial location of the same hand. However, this absence of neuronal modulation following vibrotactile stimulation of this digit is not unusual. The main purpose of this condition was to direct attention to a different spatial location than the index finger and in this way served as an attentional control. Previous work using the same task also failed to elicit discernible ERPs from the fifth digit (Bolton and Staines, 2011, 2012, 2014), while a recent fMRI study reported an absence in the hemodynamic responsiveness, particularly, of the fifth digit to vibrotactile stimulation, suggesting that there may be digit-specific differences in the activation of neuronal responses (Schweizer et al., 2008). Furthermore, electrophysiology recordings in owl and squirrel monkeys have shown that the neuronal representation of the fifth digit in area 3b of SI is the smallest when compared to the remaining four digits (Merzenich et al., 1987).

5. Conclusion

Our results suggest that an acute bout of moderate intensity aerobic exercise facilitated selective attentional processing of somatosensory information by improving: i) the efficiency of involuntary attentional shifts towards task-irrelevant environmental distracters over modality-specific somatosensory regions, and ii) attentional control of somatosensory input at later stages of sensory processing over frontoparietal regions. These findings imply that an acute bout of moderate intensity exercise is also capable of influencing attentional regulation of somatosensory information perhaps via enhanced top-down attentional control over modality-specific somatosensory cortices. Future studies will use TMS neuroimaging techniques better suited to examining the direct effect of exercise on modulating frontoparietal interactions.

4.7 Figures

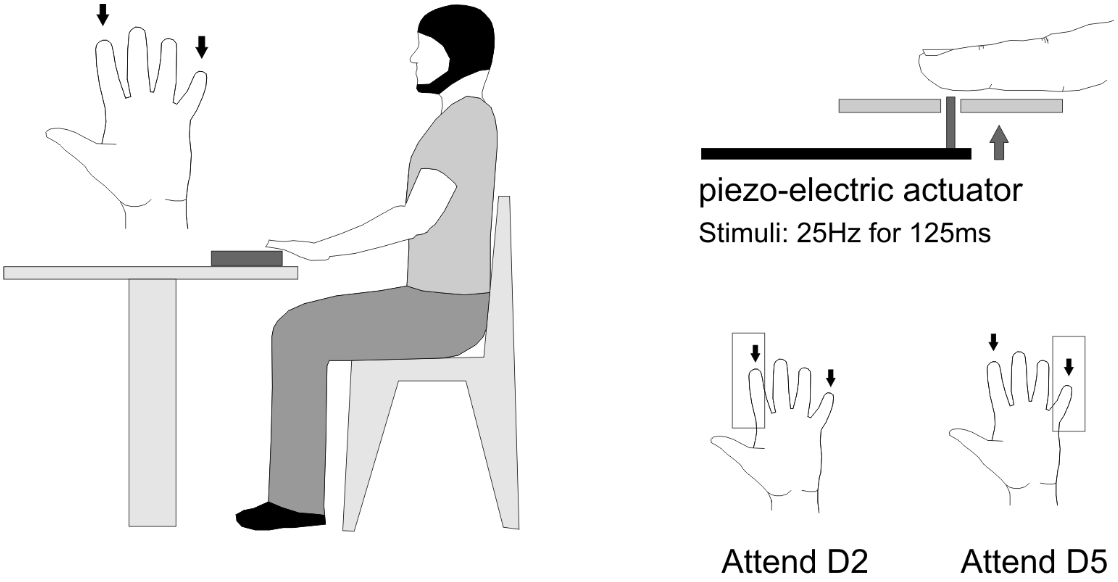

Figure 4.1. Experimental paradigm

This figure depicts how participants received vibrotactile stimulation to their second digit (D2) on the left hand, or (b) attend to the fifth digit (D5) on the left hand. Subjects reported target stimuli on the attended finger by pressing a button with the right hand. Subjects were instructed to gently rest their hand on the probes to ensure consistent hand pressure throughout testing. Headphones were worn throughout the experiment to deliver white noise and block sound from the vibration device. Trials requiring attention to either D2 or D5 were randomly presented to subjects in 3min blocks followed by a rest period of approximately 1 minute. There were a total of 6 testing blocks with 3 blocks attending to D2 and 3 blocks attending to D5, both prior to and following an acute aerobic exercise session, respectively.

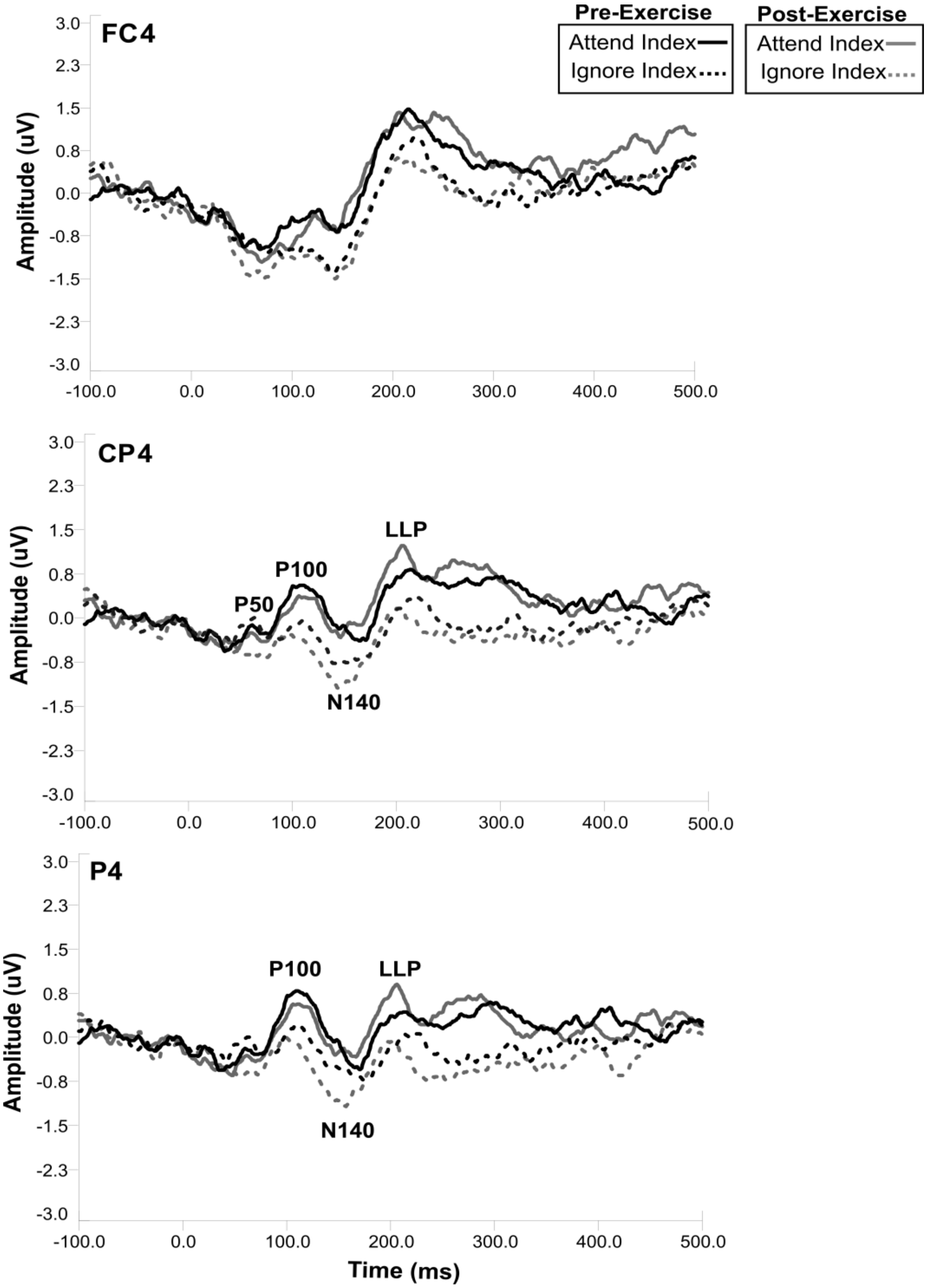

Figure 4.2. Grand averaged waveforms

Grand average waveforms all for conditions are shown for parietal electrode sites contralateral to vibrotactile stimulation (C4, CP4, P4). The P100, N140, and LLP ERP components are labeled on the trace for each electrode site. Black solid and dashed traces show Attend D2 and Attend D5 conditions, respectively, prior to exercise. Grey solid and dashed traces show Attend D2 and Attend D5 conditions, respectively, following exercise.

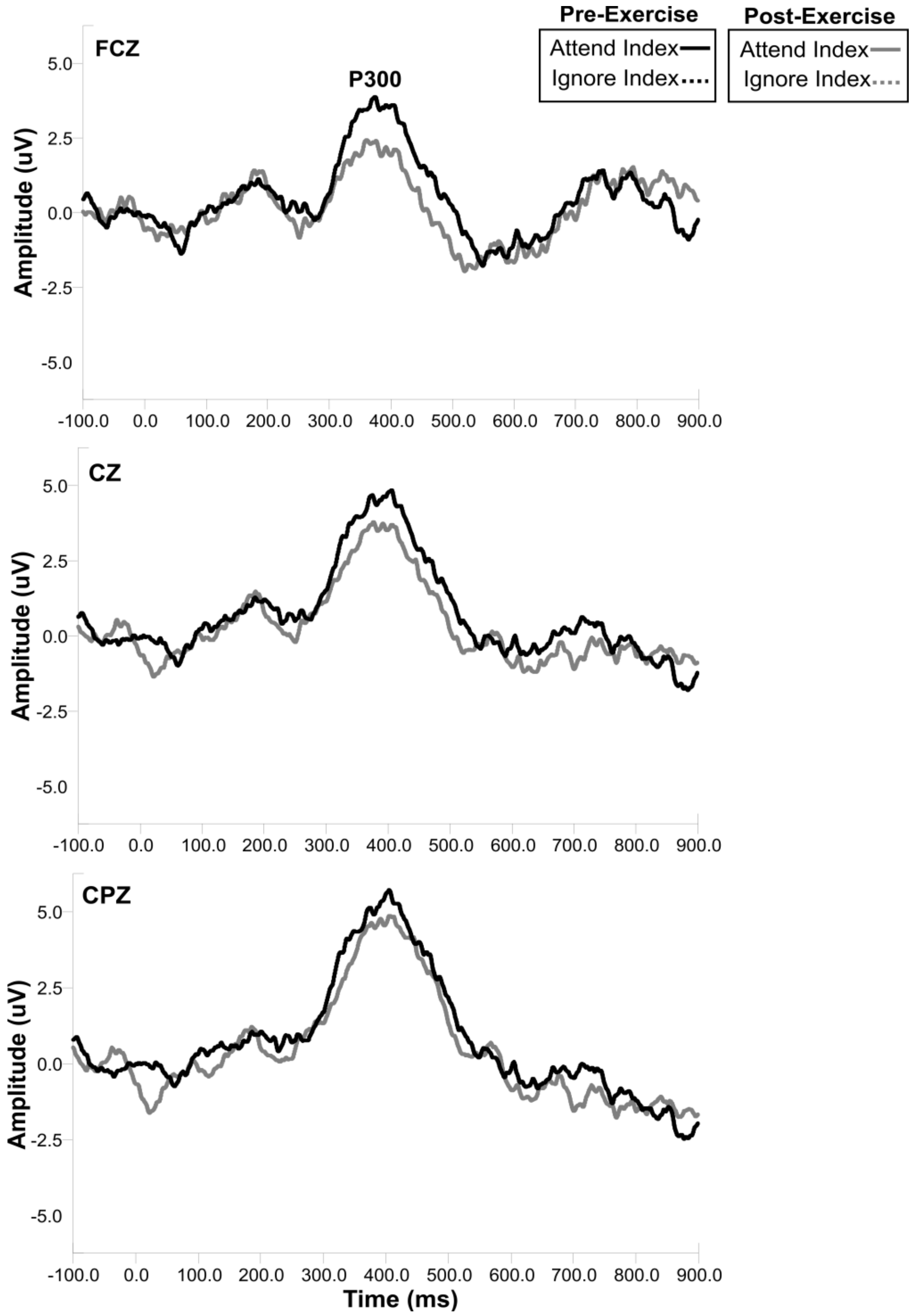

Figure 4.3. Grand averaged P300 waveforms

Grand average waveforms all for conditions are shown for centroparietal electrode sites (FCZ, CZ, CPZ). Black solid and dashed traces show Attend D2 and Attend D5 conditions, respectively, prior to exercise. Grey solid and dashed traces show Attend D2 and Attend D5 conditions, respectively, following exercise.

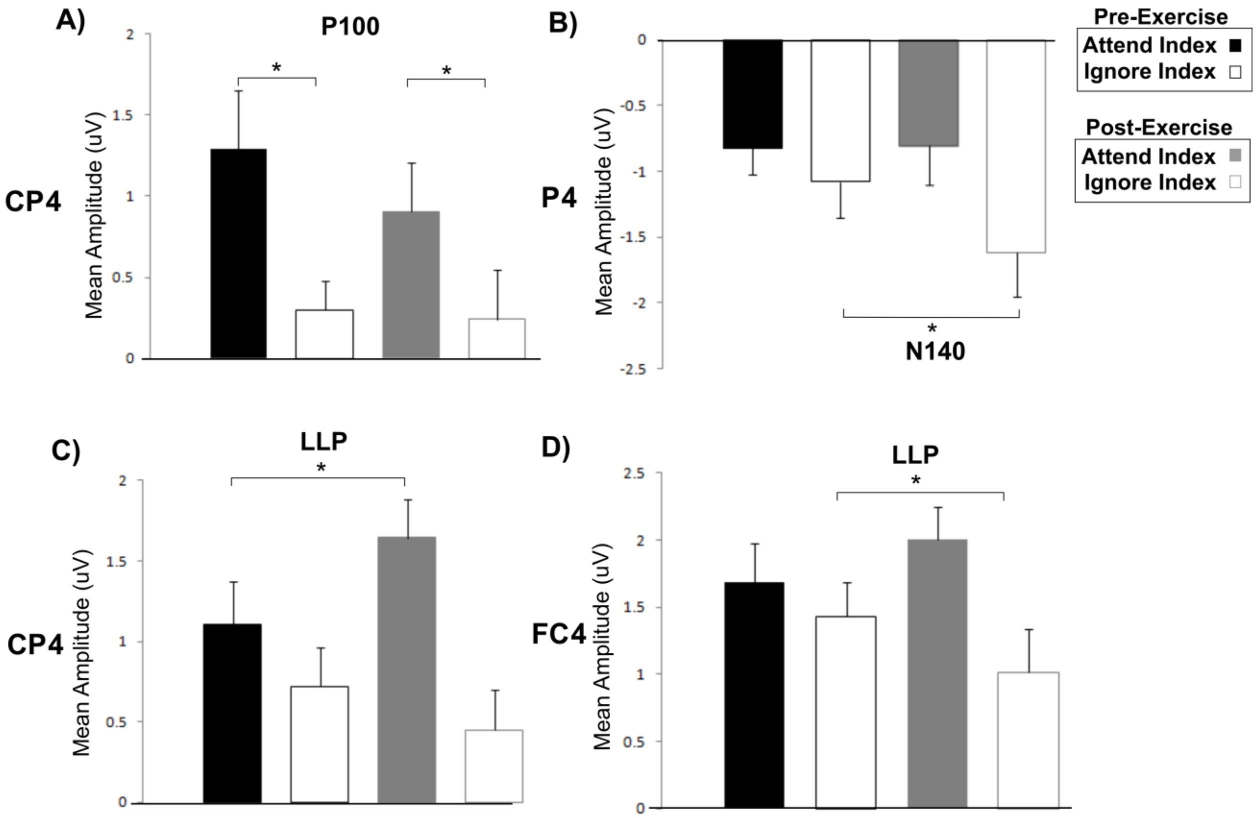

Figure 4.4. Group ERP means

Group means for A) P100, B) N140, and C) LLP ERP components at electrodes C4, CP4, and PZ. Black solid and dashed bars represent group data for the Attend D2 and the Attend D5 condition prior to exercise, respectively. Grey solid and dashed bars represent group data for the Attend D2 and the Attend D5 condition following exercise, respectively. Error bars show SEM, * denotes significance $p<0.05$.

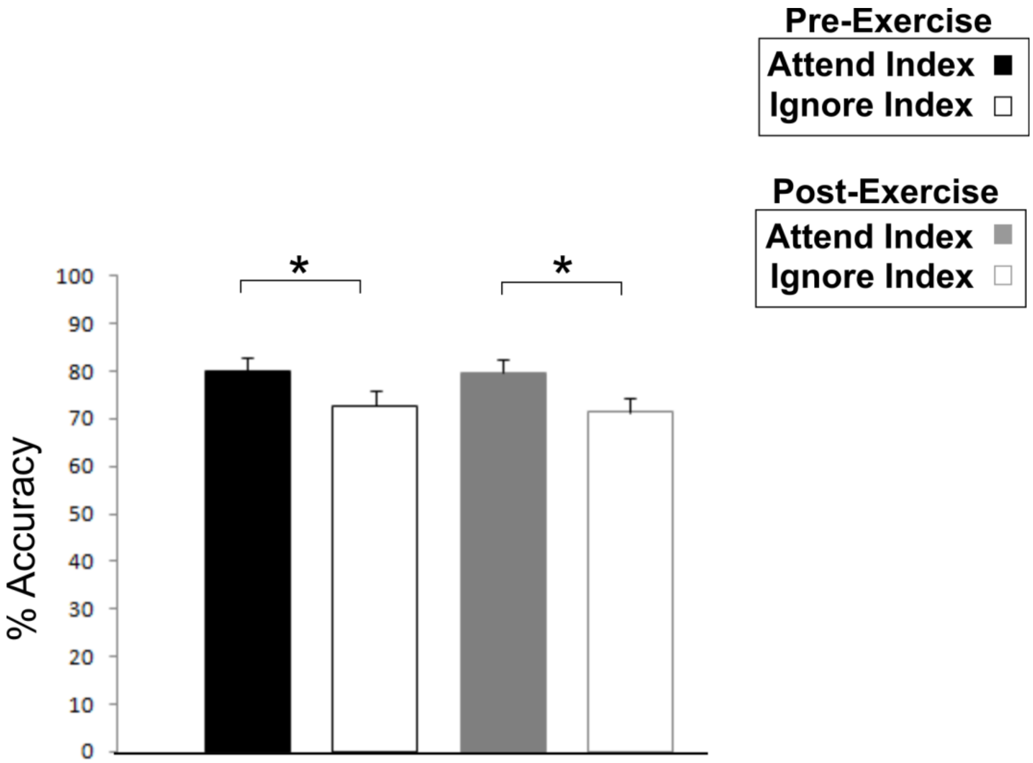

Figure 4.5. Behavioural performance

Behavioural performance was evaluated by determining the number of targets hit relative to the overall number of targets that were presented for each subject, and this success rate was expressed as a percentage. Black solid and dashed bars represent group data for the Attend D2 and the Attend D5 condition prior to exercise, respectively. Grey solid and dashed bars represent group data for the Attend D2 and the Attend D5 condition following exercise, respectively. Error bars show SEM, * denotes significance $p<0.05$.

Chapter 5 - Study 4: Acute aerobic exercise enhances attentional processing of task-relevant tactile stimuli in older adults.

5.1 Overview

Neuroimaging data in older adults has shown that atrophy of frontal lobe regions is disproportionately greater relative to other brains areas. The frontal lobes have a well-established role in various executive function tasks, thus discovering strategies that work to preserve the integrity of this brain region are imperative for ensuring that the quality of life in elderly populations is maintained across the life span. Neuroimaging research has revealed that acute bouts of moderate intensity aerobic exercise can enhance cortical activity, specifically in frontal lobe areas, during executive functioning. However, findings from Study 3 revealed that in healthy young adults, an acute bout of moderate intensity aerobic exercise modulated neuronal activity overlying frontoparietal regions during performance of a tactile discrimination task. Using the identical paradigm, the following study examined if exercise-induced increases in PFC activity would enhance attention-based modulation of tactile ERPs during somatosensory processing in healthy older adults. We hypothesized that exercise preceding performance of the odd-ball task would increase PFC activity thereby enhancing ERPs to attended tactile stimuli and suppressing those to unattended stimuli. Results showed increased amplitudes of the P100, LLP, and P3a/b components, as well as a decreased P3b latency to attended versus unattended stimuli post exercise. These findings suggest that exercise enhances neural responses to and cognitive processing of task-relevant information at frontocentral and centroparietal electrode sites in healthy older adults.

5.2 Introduction

Aging is associated with various physiological, cognitive, and behavioural deficits. Cross-sectional and longitudinal studies have shown variability in the onset of age-related impairments in tasks involving perceptual, cognitive, and motor functions, with some deficits seen early, while others appear in later adulthood (Schaie, 2000; Park et al., 2002). However, age-related decrements in brain structure and function do not occur uniformly. Aging studies have shown that older adults typically demonstrate difficulties ignoring task-irrelevant stimuli (Rabbitt, 1965; Kausler and Hakami, 1982), and inhibiting proponent responses that are no longer task-relevant (Hasher and Zacks, 1988; Yamaguchi and Knight, 1991; Fabiani et al., 2006). Neuroimaging data in older adults has shown that atrophy in frontal lobe regions is disproportionately greater relative to other brain areas (Haug and Eggers, 1991), with the greatest shrinkage occurring in medial temporal areas (Raz, 2000). The frontal lobes have a well-established role in ensuring successful completion of executive control functions (i.e. selective attention, interference or conflict control, error monitoring, or task coordination) (Kramer et al., 1999, 2000; DiGirolamo et al., 2001). Specifically, it is thought the PFC reflects a sensory-gating system responsible for suppressing task-irrelevant distracter stimuli so that relevant sensory signals may be enhanced in modality-specific sensory cortices. Animal research has provided compelling neurophysiological evidence in support of this theory, with reports that the PFC is responsible for producing a net inhibitory influence onto cortical and subcortical structures in: dorsal column nuclei (Ghez and Pisa, 1972), thalamic structures (Tsumoto et al., 1975), and primary somatosensory cortices (Chapin and Woodward, 1981; Yamamoto et al., 1988). Moreover, studies in frontal lobe lesion patients have shown significant deficits in the ability to ignore environmental distracters and suppress neural activity in response to task-irrelevant sensory information (Knight et al., 1999). Recent work by Bolton and Staines (2011) supports these findings by reporting that transient disruption of the dorsolateral prefrontal cortex (DLPFC), using transcranial magnetic stimulation (TMS), produced disinhibition of the P100 somatosensory component to task-irrelevant distractor stimuli in healthy young adults. Follow-up work by the same authors extended these cTBS findings by showing similar sensory-gating impairments in older adult and prefrontal patient populations (Bolton and Staines, 2012, 2014), thereby supporting previous findings that older adults show similar sensory-gating impairments as those reported in frontal lobe lesion patients (Alain and Woods, 1999; Golob et al., 2001; Fabiani et al., 2006). Given these results, it is not surprising then, that the cognitive impairments observed in elderly populations are greatest for higher-order executive functioning tasks dependent on PFC function (Kramer et al., 1994).

Novel findings in neuroscience research have provided convincing evidence that aerobic exercise induces neurophysiology alterations in brain activity and cognitive performance, particularly in older adults. Findings of a recent meta-analysis of aggregated longitudinal data from 1966-2001, showed that older adults who engaged in aerobic exercise significantly improved cognitive performance especially on tasks requiring executive control (Colcombe and Kramer, 2003). Functional MRI results have found greater task-related activity in prefrontal and parietal brain regions during inhibitory control processes in high-fit or aerobically trained older adults when compared with low-fit or nonaerobic controls (Colcombe et al., 2004). Additional work by Colcombe and colleagues also found that older adults, with higher levels of aerobic fitness, displayed significantly less grey matter loss in frontal, parietal, and temporal lobes, as well as significantly less tissue loss in anterior and posterior white matter pathway tracts relative to their lower fit counterparts (Colcombe et al., 2003, 2006). Aerobic exercise also has proven to enhance specific ERPs, namely the P300 component and the error-related-negativity (ERN), in both young and older adults (Hatta et al., 2005; Themanson and Hillman, 2006; Themanson et al., 2008; Hillman et al., 2009; Pontifex et al., 2009; Kamijo et al., 2010). These results suggest that individuals with higher levels of aerobic fitness employ greater top-down attentional control during tasks involving error processing (Themanson and Hillman, 2006).

It is hypothesized that exercise-induced effects on cognition support the inverted U-shape arousal hypothesis first proposed by Yerkes and Dodson (1908), which states that as arousal states increase with physical exertion, cognitive performance improves to an optimal point after which further increases in physical exertion cause decreased arousal levels resulting in decrements in performance (Tomporowski, 2003). Behavioural and neuroimaging studies investigating the impact of exercise intensity on cognition support this model by reporting performance improvements following moderate exercise intensities relative to low and high intensities (Kamijo et al., 2004, 2007, 2009). In fact, these studies have reported minimal to no cognitive improvements following low exercise intensities and decrements in performance following strenuous intensities, suggesting that moderate levels of aerobic exercise may be the optimal aerobic prescription for cognitive function.

One limitation to the current findings on the relationship between exercise and cognition is that the majority of psychological tasks used to investigate exercise-induced effects on cognition are all considered to be classical measures of frontal lobe function (i.e. the Erikson Flanker, Stroop, or Go/Nogo tasks). Thus, it is perhaps not surprising that the exercise-induced enhancements in neuronal activity are primarily observed in PFC regions. However, the circuitry of the PFC is complex with extensive and reciprocal corticocortical connections, making it an important structure for modulating modality-specific cortical regions via attentional mechanisms. These neuroanatomical connections are particularly relevant for studies examining the relationship between exercise and cognition in older adults since atrophy of PFC regions likely governs the sensory-gating impairments observed in modality-specific sensory regions (Bolton and Staines, 2012). Despite this, few studies have administered cognitive tests designed to elicit neuronal activity downstream from the PFC in modality-specific sensory regions. Using EEG and a lower limb somatosensory oddball task, Iwadate et al. (2005) showed that soccer athletes demonstrated increased P300 amplitudes and decreased latencies over central-parietal electrode sites compared to the non-athletic group, suggesting that long-term physical activity requiring selective attention and skilled motor responses, induces neuroplastic changes in modality-specific somatosensory regions during goal-oriented behaviours (Iwadate et al., 2005). Moreover, Popovich and Staines (2014) found that an acute bout of moderate intensity aerobic exercise facilitated the sensory-gating role of the PFC by suppressing neuronal responses to unattended, task-irrelevant stimuli at frontal regions and amplifying attended, task-relevant signals at modality-specific somatosensory regions contralateral to stimulation. These findings may be particularly relevant in older adults for improving the inhibitory control impairments observed during attentional processing of sensory information (Hasher and Zacks, 1988; Reuter-Lorenz and Park, 2010; Bolton and Staines, 2011).

In this study, we used EEG and the same tactile discrimination task used by Bolton and Staines (2011, 2012, 2014) and Popovich and Staines (2014), to examine if increases in PFC activity, following an acute bout of moderate intensity aerobic exercise, would enhance attention-based modulation of somatosensory ERPs generated at early and later stages of somatosensory processing in healthy older adults. Based on the findings of Popovich and Staines (2014), our first hypothesis was that early and later somatosensory ERPs would be modulated by attentional relevance. Specifically, we hypothesized that an acute bout of moderate intensity aerobic exercise preceding performance of a tactile discrimination task would result in either more efficient sensory-gating of irrelevant/non-attended and/or enhancement of relevant/attended sensory information. Therefore, improvements in attentional regulation would be observed as increased neural suppression of task-irrelevant stimuli and enhancement of relevant sensory information post-exercise relative to pre-exercise.

5.3. Methods.

5.3.1. Participants

EEG was collected from 16 healthy participants (aged 58-68, 3 males). Three participants were excluded: one due to the absence of clearly defined somatosensory event-related potentials of interest (i.e. P50, P100, N140, LLP components), the second did not meet the inclusion criterion, and the third demonstrated poor performance of the discrimination task. Thirteen participants comprised the final sample (10 females and 3 males, mean age = 63 years). Participants were self-reported right-handed individuals with no medical history of any major neurological illness, and no heart or blood pressure conditions that could be exacerbated with aerobic exercise. Each participant provided informed consent and was pre-screened using the Physical Activity Readiness Questionnaire (PAR-Q) to ensure that they were physically able to engage in 20 minutes of moderate intensity aerobic activity on a recumbent bicycle. Prior to collection, each participant completed a cognitive assessment using the Montreal Cognitive Assessment questionnaire (MoCA), and a physical activity assessment using the General Practice Physical Activity questionnaire (GPPAQ). Experimental procedures were approved by the University Of Waterloo Office Of Research Ethics.

5.3.2. Behavioural task

Subjects were seated in a sound-attenuating booth (Industrial Acoustics, 120A, NY), facing a blank computer screen and instructed to look directly ahead throughout testing. Tactile stimuli were delivered via 2 blunt plastic probes contacting the fingertips of the second and fifth digits on the left hand as depicted in Figure 5.1. These probes (approximately 1 cm diameter) were vibrated using piezo-electric actuators at a rate of 25 Hz for 125 ms during each stimulus. Vibrotactile stimulation was delivered by digitally generated waveforms converted to an analog signal (DAQCard 6024E, National Instruments, Austin, TX, USA) and then amplified (Bryston 2B-LP, Peterborough, ON, Canada). The amplitude of vibration was set so that minimal values (i.e. small amplitude targets) exceeded sensory threshold for all subjects. These stimuli were presented randomly to each finger (but never simultaneously) with random interstimulus intervals in the range of 500–1500 ms. An oddball paradigm was employed whereby 17% of the trials for each finger consisted of the deviant stimulus. These deviant stimuli represented the targets to which attention was paid and the amplitude of these targets was set to 25% the standard (non-target) amplitude. The two experimental conditions required subjects to either (a) attend to the second digit (D2; Attend Index) on the left hand, or (b) attend to the fifth digit (D5; Ignore Index) on the left hand. Subjects reported target stimuli on the attended finger by pressing a button with the right hand. Subjects were instructed to gently rest their hand on the probes to ensure consistent hand pressure throughout testing. Headphones delivering white noise were worn throughout the experiment to block sound from the vibration device. Trials requiring attention to either D2 or D5 were randomly presented to subjects in 3 min blocks followed by a rest period of approximately 1 min. There were a total of 6 testing blocks with 3 blocks attending to D2 and 3 blocks attending to D5. Approximately 600 standard (non-target) stimuli were applied to each digit over the entire experiment with each testing block consisting of approximately 100 standard and 20 target stimuli.

5.3.3. Exercise protocol

Upon task completion, participants were seated comfortably on a cycle ergometer while a measure of their resting heart rate was taken using a resting Polar heart rate monitor. Participants were instructed to begin pedalling on the ergometer to reach their age-predicted target heart rate ([220-age] x 0.60), and maintain this exercise intensity for the remainder of the 20 minute aerobic session. For each participant, the ergometer resistance level was always set to its minimum value (level 1). To ensure that participants adhered to the exercise protocol, frequent heart rate monitor checks were recorded, as well as two self-reported measures of the participant's perceived rating of exertion were recorded after 10 and 20 minutes of exercise using the 10 point Borg Scale. After exercise, participants were seated back into the sound proof booth where a final heart rate measure was recorded followed by instructions to repeat the tactile discrimination task again (approximately 5 minute duration prior to post-testing).

5.3.4. Recording and analysis

EEG data was recorded from 32 electrode sites according to the international 10-20 system for electrode placement and referenced to bilateral mastoids. All channel recordings had impedance values below 5 koms. EEG data were amplified (20,000×), filtered (DC-200 Hz, 6 dB octave roll-off) and digitized (1000 Hz, SynAmps2, Scan 4.3, Compumedics Neuroscan, Charlotte, NC) before being stored for off-line analysis. Somatosensory ERPs to tactile stimuli were averaged relative to a 100 ms pre-stimulus baseline for each attention condition. Data were band-pass filtered (1–30 Hz) and trials with artefacts (i.e. eye blinks, muscle activity) were identified by visual inspection and were excluded from further analysis. Since stimulation of the fifth digit did not result in consistently clear ERP components, analysis was restricted to non-target stimuli (i.e. large amplitude vibrations) delivered to the second digit (i.e. index finger). Several somatosensory ERP components were evaluated in this study focusing on the peak amplitude for each defined ERP component. Somatosensory ERPs were measured from individual participant averages for each task condition. Mean ERP amplitudes were computed for each subject within specified time windows selected around the post stimulus latencies of each ERP component of interest: P50 (40-70 ms), P100 (85-125 ms), N140 (125-165 ms), LLP (175-250 ms), and the P300 (300-600 ms). Clearly defined components and peaks were required for inclusion. Separate two-way ANOVAs with factors attention (attend index, ignore index) and time (pre-exercise, post-exercise) were calculated for each component of interest at the electrode sites as follows: P50 (C4, CP4), P100 (P4, PZ, P3), N140 (FC4, CP4, P4), LLP (FC4, CP4, P4) and P300 (FCZ, CZ, CPZ). Based on previous findings using the same experimental paradigm (refer to Popovich and Staines, 2014), pre-planned contrasts were performed to test the hypotheses that ERP modulation would show greater suppression of task-irrelevant distractor stimuli (i.e. Ignore Index conditions) and greater enhancement of task-relevant stimuli (Attend Index conditions), post-exercise relative to pre-exercise.

The P50 ERP component has been shown to be generated in the primary somatosensory cortex (SI) (Schubert et al., 2008), while studies examining early somatosensory evoked potentials (SEPs) typically show greater neuronal responses over central-parietal electrodes contralateral to stimulation in SI areas (Hämäläinen et al., 1990; Allison et al., 1992), thus the P50 was analyzed at electrode sites C4 and CP4 positioned over SI, contralateral to vibrotactile stimulation. We analyzed the P100 component at electrode sites P4, PZ, and P3 since the P100 amplitude has known neural generators in bilateral secondary somatosensory cortices (SII) (Hämäläinen et al., 1990), with maximal activation typically seen in contralateral posterior parietal sites, but with enhancements also extending to ipsilateral and frontal sites (Desmedt and Robertson, 1977; Desmedt and Tomberg, 1989; Hämäläinen et al., 1990). For the later components, both the N140 and the LLP have shown increased activation in frontal regions during attentionally-demanding tasks resulting in continued engagement of modality-specific cortices (Pasternak and Greenlee, 2005), thus we analyzed these ERPs at electrode sites contralateral (FC4, CP4, P4). Lastly, attention-based modulation of the P300 component typically occurs at frontocentral electrodes sites in response to task-relevant target stimuli (Pfefferbaum et al., 1985). Thus for this component, we observed changes in P300 modulation across midline electrode sites FCZ, CZ, PZ in response to target stimuli. To produce P300 waveforms, we time-locked and averaged somatosensory ERPs to the target stimuli (i.e. smaller vibrations) delivered to the index finger during the Attend Index conditions only. To test the hypothesis that exercise would enhance attentional processing of task-relevant somatosensory stimuli, one-tailed paired t-tests were performed on peak P3a/b amplitudes and latencies at frontocentral electrode CZ. This electrode site was chosen because it demonstrated discernible and maximal peak amplitudes relative to electrodes FCZ and CPZ.

Behavioural performance was evaluated by determining the number of targets hit relative to the overall number of targets that were presented for each subject. This success rate was expressed as a percentage and compared using a two-way repeated measures ANOVA with factors attention (attend index, ignore index), and time (pre-exercise, post-exercise). The significance level was set at $p \leq 0.05$ for all comparisons.

5.4. Results.

5.4.1. Early ERP components: P50 & P100

Figure 5.2 shows waveforms at electrode sites contralateral to vibrotactile stimulation (i.e. FC4, CP4, and P4) with the components of interest specified (i.e. the P50, P100, N140, and LLP). Results for the P50 amplitude revealed no main effects or significant interaction at any of the electrode sites analyzed. Results for the P100 component showed a main effect of attention whereby P100 amplitudes were enhanced by task-relevant stimuli (i.e. Attend Index) compared to task-irrelevant stimuli (i.e. Ignore Index) (P4: $F_{1,12} = 33.25$, $p<0.001$; PZ: $F_{1,12} = 54.42$, $p<0.001$; P3: $F_{1,12} = 43.77$, $p<0.001$). Moreover, a significant attention* time interaction was found at electrode PZ ($F_{1,12} = 4.37$, $p=0.05$). Pre-planned contrasts revealed that the amplitude of the P100 was significantly larger post-exercise relative to pre-exercise when attention was directed towards attended, task-relevant information ($F_{1,12} = 6.48$, $p=0.03$). No other P100 results reached statistical significance (refer to Figure 5.4A).

5.4.2. Later ERP components: N140, LLP, & P300

A main effect of attention was found for the N140 component at all electrode sites analyzed whereby N140 amplitudes were increased during task-irrelevant conditions (i.e. when tactile stimuli were delivered to the index and attention was directed towards another spatial location (i.e. Ignore Index condition)) (FC4 ($F_{1,12} = 12.55$, $p=0.004$), CP4($F_{1,12} = 11.06$, $p=0.01$), and P4 ($F_{1,12} = 20.09$, $p=0.001$)). No further results for the N140 amplitude reached statistical significance.

A main effect of attention was found for the LLP component at all electrode sites measured whereby LLP amplitudes were enhanced by task-relevant stimuli (i.e. Attend Index) compared to task-irrelevant stimuli (i.e. Ignore Index) (FC4: $F_{1,12} =32.91$, $p<0.001$; CP4: $F_{1,12} =35.76$, $p<0.001$; P4: $F_{1,12} =34.78$, $p<0.001$). Significant attention*time interactions were also found at electrode sites FC4 ($F_{1,12} = 4.69$, $p=0.05$) and CP4 ($F_{1,12} = 9.42$, $p=0.01$), while a trend towards significance was found at electrode P4 ($F_{1,12} = 3.84$, $p=0.07$). Pre-planned contrasts showed that at electrode FC4 and CP4, the LLP amplitude was enhanced post-exercise relative to the pre-exercise session when attention was directed towards relevant tactile stimuli (FC4 ($F_{1,12} = 7.10$, $p=0.02$), CP4 ($F_{1,12} = 5.25$, p=0.04)). Furthermore, a trend towards significance for the LLP component was found at CP4 ($F_{1,12}$ = 4.19, p=0.06) suggesting that post- relative to pre-exercise, the LLP amplitude was suppressed when attention was directed away from the index finger (i.e. Ignore Index). (Figure 5.4C/D).

The P300 component was delineated into the P3a/b amplitudes. Amplitude results for P3a component measured over central electrode site CZ revealed a trend towards significance for the P3a component (t_{12}= 1.66, p=0.06), indicating that the P3a mean amplitude was larger post-exercise (mean = 2.88 uV) relative to pre-exercise (mean = 2.05 uV) when attention was directed towards task-relevant information. The P3b amplitude at electrode CZ was statistically greater post- versus pre-exercise when attention was directed towards task-relevant information (t_{12}= 2.07, p=0.03). Latency results revealed a marginally significant effect for the P3b component at electrode CZ (t_{12}= 1.67, p=0.06), suggesting that the onset of the P3b amplitude peak occurred earlier post-exercise relative to pre-exercise. No significant effects were found for the P3a latency (t_{12}= 0.68, p=0.26) (refer to Figure 5.3 for P300 traces).

5.4.3. Behavioural results

Behavioural analysis showed a main effect of attention with success rates being higher when attention was directed towards the index finger versus away from it ($F_{1,13}$ = 7.69, p=0.02) (Figure 5.5).

5.5. Discussion

Evidence suggests that aerobic exercise improves cognitive function on tasks involving these higher-order attentional control processes, in healthy young and older adults (Colcombe et al., 2004; Hatta et al., 2005; Themanson and Hillman, 2006; Themanson et al., 2008; Kamijo et al., 2009; Pontifex et al., 2009; Yanagisawa et al., 2010). Moreover, these exercise-induced benefits seem to be greatest in the PFC; a brain region susceptible to age-related decline (Raz, 2000). However, a limitation in our current understanding of the exercise-cognition relationship is whether exercise modulates neuronal activity in regions downstream from the PFC. Previous EEG work in healthy young adults has shown that habitual long-term physical exercise, as well as, an acute bout of moderate intensity aerobic exercise enhanced neuronal activity in modality-specific somatosensory regions during goal-oriented behaviours (Iwadate et al., 2005; Popovich and Staines, 2014). Therefore, the purpose of this study was to determine whether a single bout of moderate intensity aerobic exercise performed by older adults would modulate neuronal activity in prefrontal and somatosensory cortices using a tactile discrimination task. Based on Popovich and Staines' (2014) findings, we hypothesized that exercise preceding performance of a tactile discrimination task would result in either more efficient sensory-gating of irrelevant/non-attended and/or enhancement of relevant/attended sensory information. More efficient attentional regulation of somatosensory input would be demonstrated by increased neural suppression of task-irrelevant stimuli and enhancement of relevant sensory information post- relative to pre-exercise. Results showed increased P100 and LLP amplitudes at fronto-parietal regions contralateral to stimulation post-exercise relative to the pre-exercise session, as well as increased P3a/b amplitudes and shorter P3b latencies along midline electrode sites during attended, task-relevant conditions. Collectively, these findings support the inverted U-shape model for exercise-induced effects on cognition and suggest that a single session of moderate intensity exercise facilitated cognitive processing of attended, task-relevant tactile information in healthy older adults.

5.5.1. Exercise effects on attentional modulation of somatosensory ERPs

The P100 component is bilaterally distributed over parietal electrode sites with neural generators believed to be located in SII (Hari et al., 1983; Mima et al., 1998; Gu, 2002). It is modulated by both vibrotactile stimulation (Goff et al., 1977) and attentional processes, with amplitudes typically enhanced during attended versus unattended tactile stimuli (Desmedt et al., 1983; Michie et al., 1987; Josiassen et al., 1990; Eimer and Forster, 2003a/b; Kida et al., 2004). Despite neural generators in SII, recent cTBS work has shown that attention-based modulation of this component to task-irrelevant stimuli was significantly disinhibited following transient disruption of the dorsolateral PFC during a tactile discrimination task (Bolton and Staines, 2012). Similar results were found in separate follow-up studies performed in older adults and patients with PFC lesions using the identical tactile discrimination task, whereby in both groups, disinhibition of the P100 component over somatosensory cortices occurred during unattended, task-irrelevant tactile stimuli (Bolton and Staines, 2014). Collectively, these findings suggest that the functional integrity of the PFC is crucial for gating irrelevant sensory information so that relevant tactile inputs may be amplified in modality-specific cortices, and that age-related loss in attentional control may occur via disruption or atrophy of prefrontal brain regions. By contrast, our study showed that a single session of moderate intensity aerobic exercise in older adults significantly enhanced the amplitude of the P100 component to attended, task-relevant tactile stimuli relative to the pre-exercise session. Previous work in healthy young adults showed no statistically significant exercise-related attentional effects on the

P100 component (Popovich and Staines, 2014). These variations in P100 modulation between age groups, suggest that a single session of moderate intensity aerobic exercise was sufficient in driving modulation of early modality-specific somatosensory areas in older, but not younger adults. Although the acute exercise session enhanced task-relevant ERPs in older adults, it was not sufficient in driving modulation of the N140 component to task-irrelevant stimuli as was observed in the younger adult group (refer to Popovich and Staines, 2014). Age-related attentional differences in neuronal modulation despite similarities in behavioural performance suggest that aging may recruit alternative neural networks during sensory processing. Indeed, neuroimaging studies have shown that in some instances, older adults who perform similarly to their younger counterparts display more local neural information processing while younger adults show more distributed neural processing (Cabeza et al., 2004; Davis et al. 2008). Moreover, Heisz et al. (2014) showed that physically active older adults also engaged in more local neural information processing which was associated with improved executive function performance. The authors suggested that physical activity may help to improve aspects of cognitive function in older adults by biasing the neural system toward local information processing. Since the structure and function of PFC regions is particularly susceptible to age-related decline, it is plausible that following exercise, older adults may have engaged in more local neural information processing of attended, task-relevant information, thus modulation occurred for attended, task-relevant but not unattended, task-irrelevant tactile ERPs.

The LLP component is a broadly distributed sustained positivity with multiple neural generators that typically occurs 200-500 ms post stimulus (Michie et al., 1987; Hämäläinen et al., 1990). The precise role of the LLP remains a matter of debate since several ERP studies have shown variable attentional effects on modulation of the component (Michie et al., 1987; Desmedt and Tomberg, 1989; Eimer and Forster 2003a; Bolton and Staines, 2011, 2012, 2014). Typically, amplitude enhancements are observed during attended versus unattended stimuli, but the degree of LLP modulation seems somewhat dependent on the type of task used and the attentional demand required. Attention-related ERP studies reporting attentional effects on the LLP suggest that it is a P300-like component (Desmedt and Robertson, 1977; Michie et al., 1987; Desmedt and Tomberg, 1989), whereby increased ERP amplitudes reflect an increased amount of attentional resources engaged in processing a given stimulus (Donchin and Coles, 1988). Previous aging work in our lab has shown decreased LLP amplitudes to attended stimuli in older relative to younger adults (Bolton and Staines, 2012); a similar effect is seen upon comparison of our older adult data set to that of young adults who participated in the same experimental paradigm whereby older adults showed smaller LLP amplitudes relative to younger adults to attended stimuli (Popovich and Staines, 2014). Bolton and Staines (2014) also found a complete loss of LLP modulation in PFC patients whereby patients showed larger LLP amplitudes to unattended stimuli perhaps due to structural aberrations in PFC. These findings suggest that the integrity of the PFC: i) is a critical factor in modulating this later ERP component, and ii) may be compromised with increasing age. However, in this study an acute bout of moderate intensity exercise significantly enhanced the amplitude of the LLP component over frontoparietal regions contralateral to the vibrotactile stimulation in response to attended, task-relevant information presented to the index finger. This finding is in accord with work using the same experimental paradigm in a group of healthy young adults (Popovich and Staines, 2014), thereby supporting the notion that acute aerobic exercise enhances PFC activity, and thereby facilitates cognitive processing of sensory information across the life span.

The P300 is a large positivity occurring approximately 300-800 ms post stimulus onset and reflects attentional processing. It can further be subdivided into two distinctive subcomponents, the "P3a" and the "P3b", both of which represent different but related neural processes (Pontifex et al., 2009). The P3a component is elicited in the absence of experimental instructions by an infrequent or physically novel distracter stimulus. It has a fronto-central topographic distribution, short peak latency, and is believed to be involved in the selection of stimulus information mediated by attentional orienting (Knight, 1984; Kok, 2001), with increased amplitudes indicative of greater attentional focus (Polich, 2007). Generation of the P3b component occurs over parietal cortices during sensory oddball discrimination tasks, when participants are required to respond to infrequently presented target stimuli (Johnson, 1993). Here, the amplitude of the P3b component is driven by the allocation of attentional resources when working memory is updated (Donchin and Coles, 1988), thus the larger P3b amplitudes reflect more attentional resources devoted to stimulus processing (Polich, 1987; Polich and Heine, 1996). The peak latency of the P3b component is independent of response selection and behavioural intent (Verleger, 1997), and is believed to represent stimulus evaluation and classification speed (Kutas et al., 1977), such that earlier latencies reflect more efficient stimulus processing. ERP aging studies using multiple psychological tasks have shown that both subcomponents of the P300 are useful neuroelectric markers of cognitive decline with age-related reductions in amplitude as well as latency slowing (Anderer et al., 1996; Fjell and Walhovd, 2001; Bolton and Staines, 2012). However, moderate bouts of aerobic exercise seem to reverse the typical neuronal profile seen in older adults with increased amplitudes and/or decreased latencies observed across various tasks (Hatta et al., 2005; Kamijo et al., 2007, 2009; Pontifex et al., 2009), suggesting that exercise has a positive influence on cognitive aging. Our findings support this association by showing increased P3a/b amplitudes over central electrode sites, suggesting that greater attentional focus and more attentional resources may have occurred during attended conditions post- relative to the pre-exercise session. Furthermore, results indicated that P3b latencies may also quicker following the exercise intervention implying that cognitive processing overall was more efficient.

5.5.2. The role of aerobic fitness on cognitive decline

Normal aging causes structural alterations in several regions of the brain including: decreased grey matter volume in the prefrontal, orbitofrontal, and parietal cortices (Raz, 2000; Salat et al., 2004), decreases in the quantity and quality of white matter tracts (Sullivan et al., 2001; Ota et al., 2006), and compromised neurotransmitter availability (Kaasinen et al., 2000; Kaasinen and Rinne, 2002). As a result, these age-related changes in brain physiology are believed to be the cause of several cognitive impairments typically observed in elderly populations. Deficits in tasks involving higher-order executive functioning, particularly those involving attentional control, are among the most consistently reported in older adults. However, neuroimaging research investing the relationship between cardiovascular fitness and cognitive-decline have found that older adults who maintain a physically active lifestyle show preservation of neuroantomical structures susceptible to age-related decline as well as improved cognitive performance relative to inactive counterparts. Functional fMRI techniques have found that higher fit versus lower fit, or aerobically trained versus non-aerobically trained older adults, display structural differences in brain integrity including: less grey matter loss in frontal, temporal, and parietal cortices, and less tissue loss in the anterior and posterior white matter tracts (Colcombe et al. 2003, 2006); as well as increased activity in PFC and parietal cortices (Colcombe et al., 2004). EEG studies examining the effects of exercise on the P300 component, have reported that aerobically trained individuals, or those with higher levels of physical activity, display increased P300 amplitudes and shorter latencies relative to their sedentary counterparts (Dustman et al., 1984; Hillman et al., 2004, 2006), suggesting greater allocation of attentional resources with aerobic exercise (Polich and Lardon, 1997; McDowell et al., 2003; Hatta et al., 2005). A similar relationship between exercise and the ERN exists. The ERN is generated in the dorsal portion of the anterior cingulate cortex (ACC) following an erroneous response (Van Veen and Carter, 2002), and shares functional connectivity with the prefrontal cortex during action monitoring processes and corrective actions (Gehring and Knight, 2000). EEG studies have shown smaller ERN amplitudes and post-error slowing, following error commission in higher-fit older and younger adults, when compared to their lower-fit counterparts (Themanson and Hillman, 2006; Themanson et al., 2006). Similarly, the majority of older age participants collected in our study were classified as either being active or moderately active according to the General Practice Physical Activity Questionnaire, thus it can be deduced that our older adult population consisted of higher-fit individuals which may have been an important factor responsible for the enhanced neuroelectric profiles of ERP components to task-relevant tactile stimuli post-exercise. Taken together, these studies suggest that habitual exercise training in older adults may preserve the structural integrity of grey and white matter tracts, as well as enhance cortical activity in brain regions involved in higher-order attentional control processes.

5.5.3. Attention-related somatosensory ERPs unaffected by exercise

Similar to previous work in healthy adults using the same tactile discrimination task, we did not find any exercise-induced attentional effects on the P50 component, generated over primary somatosensory cortices (Popovich and Staines, 2014). The P50 is the earliest somatosensory ERP elicited by vibrotactile stimulation with amplitude enhancements observed during attended versus unattended conditions (Meehan and Staines, 2007; Dionne et al., 2013; Popovich and Staines, 2014; Staines et al., 2014). However, failure to drive attentional modulation of this component with tactile stimulation paradigms is not uncommon and previous work in our lab using the same tactile paradigm has consistently failed to drive attentional modulation of the P50 (Bolton and Staines, 2011, 2012, 2014; Popovich and Staines, 2014). Schubert et al. (2008) proposed that task-difficulty may be an important factor required for driving modulation in the early stages of somatosensory processing. Recent work investigating crossmodal effects on somatosensory processing support this theory with studies showing enhanced P50 amplitudes to attended, task-relevant crossmodal stimuli when participants were required to produce a force-graded response representing the summation of stimuli amplitudes (Dionne et al., 2013; Popovich and Staines, 2014; Staines et al., 2014). However, several studies using the tactile discrimination task described in this study have failed to enhance attentional modulation of the P50 component (Bolton and Staines, 2011, 2012, 2014), thus we believe that the cognitive demand of this particular task is not sufficient for driving attentional modulation of the earliest stage of somatosensory processing.

Exercise did not influence attentional modulation of the N140 component in older adults. The N140 component is observed over frontal electrode sites contralateral to stimulation and along midline and ipsilateral sites (Desmedt and Tomberg, 1989), but is thought to have bilateral generators in SII regions with the hemisphere contralateral to stimulation online earlier (Frot and Mauguière, 1999). Attention-based modulation of the N140 is variable with studies showing enhanced negative amplitude in response to attend versus unattended stimuli (Desmedt and Robertson, 1977; Desmedt and Tomberg, 1989; García-Larrea et al., 1995; Eimer and Forster, 2003a), while other studies, including several using the same tactile task used in this study, report increased N140 amplitudes to unattended, task-irrelevant versus relevant tactile stimuli (Nakata et al., 2004; Nakata et al, 2005; Bolton and Staines, 2011, 2012, 2014; Popovich and Staines, 2014). However, several EEG studies investigating attentional modulation of the N140 component have suggested that this component reflects involuntary shifts of attention since findings have shown N140 enhancement to the presentation of transient stimuli at a to-be-ignored spatial location (Kida et al., 2004, 2006; Adler et al., 2009). Popovich and Staines (2014) found exercise-induced attentional effects on the N140 amplitude over parietal regions in healthy young adults, such that the neural responses to task-irrelevant tactile stimuli were larger post- versus pre-exercise. They concluded that exercise facilitated selective attentional processing of somatosensory information by improving the efficiency of involuntary attentional shifts from task-irrelevant environmental distracters so that attended, task-relevant somatosensory input could be amplified at later multimodal stages of sensory processing. In this study, the N140 amplitude was greater during unattended versus attended conditions in older adults, although the degree of this modulation between attentional conditions was minimal. Our behavioural results showed higher success rates (i.e. accurate target detection) when attention was directed towards the index finger rather than away from it, suggesting that older adults had greater difficulty ignoring distracter stimuli delivered to the index finger when attention was directed towards their pinky finger. Participants also reported greater difficulty detecting target stimuli presented to the pinky finger versus the index finger which perhaps is the reason for the decline in behavioural performance during the Ignore Index condition. Bolton and Staines (2012) reported statistically larger negative N140 amplitudes and greater differences between attended versus unattended conditions in younger versus older adults, implying that the capacity for sensory-gating in older adults was lost at the N140. Behaviourally, older adults also exhibited lower success rates and an inability to ignore irrelevant stimuli compared to younger counterparts (Bolton and Staines, 2012). The inability to efficiently direct attention towards relevant tactile stimuli delivered to the pinky while ignoring distractor stimuli presented to the index finger may be explained by digit-specific differences in tactile acuity and cortical representation in modality-specific somatosensory cortices. For example, using fMRI, Schweizer et al. (2008) reported an absence in the hemodynamic responsiveness, particularly, of the pinky finger to vibrotactile stimulation, while Merzenich et al. (1987), found that neuronal representation of the pinky finger in area 3b of SI of owl and squirrel monkeys is the smallest when compared to the remaining four digits.

5.6. Conclusions

Our findings support and extend current literature on the relationship between exercise and cognition. Results suggest that an acute bout of moderate intensity aerobic exercise, improved attention-related modulation of tactile information at both early and later stages of somatosensory processing, in older adults. Specifically, our findings suggest that exercise facilitated selective attentional processing of task-relevant information by amplifying neuronal responses representing attended stimuli across frontoparietal and centroparietal brain regions. These results mimic some of the findings in healthy young adults using the same experimental paradigm (Popovich and Staines, 2014), but also produced provocative exercise-induced age-related differences in attentional modulation of somatosensory informative. These findings are in accord with the work by Heisz et al. (2014), by demonstrating that older adults may have engaged in more local neural processing of attended, task-relevant information while younger adults may have been more efficient at task-switching between attended and unattended stimuli following aerobic exercise. Overall, these results imply that aerobic exercise has global rather than region-specific effects on brain function, and suggest that aerobic exercise and maintaining a physically active lifestyle may offer a promising cost-efficient, non-invasive approach for improving attention-related deficits in sensory processing typically observed in elderly populations (Reuter-Lorenz and Park, 2010; Bolton and Staines, 2011, 2012).

5.7. Figures

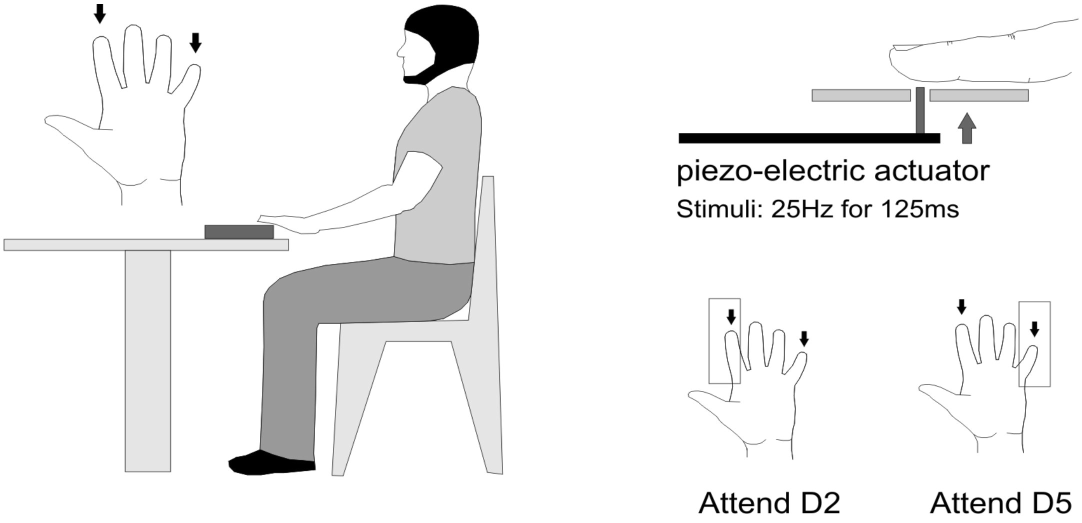

Figure 5.1. Experimental paradigm

This figure depicts how participants received vibrotactile stimulation to their second digit (D2) or the fifth digit (D5) on the left hand.

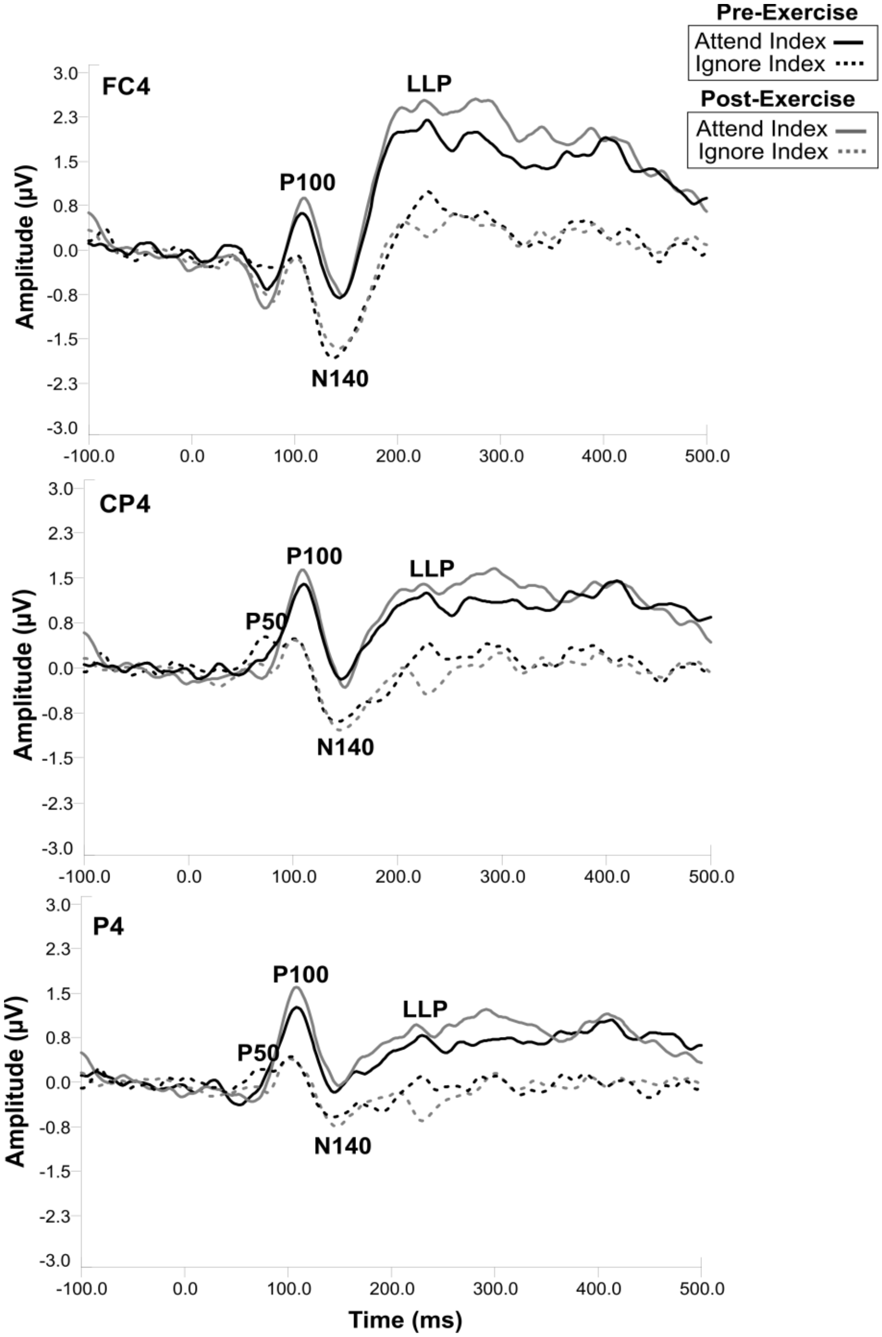

Figure 5.2. Grand averaged waveforms

Grand average waveforms all for conditions are shown for: parietal electrode sites contralateral to vibrotactile stimulation (CP4, P4) and a contralateral frontal site (FC4). (B) Tactile ERP traces of interest (P100, N140, and LLP) for electrode sites overlying frontal and somatosensory regions contralateral to stimulation. Black solid and dashed traces show Attend Index and Ignore Index conditions, respectively, prior to exercise. Grey solid and dashed traces show Attend Index and Ignore Index conditions, respectively, following exercise.

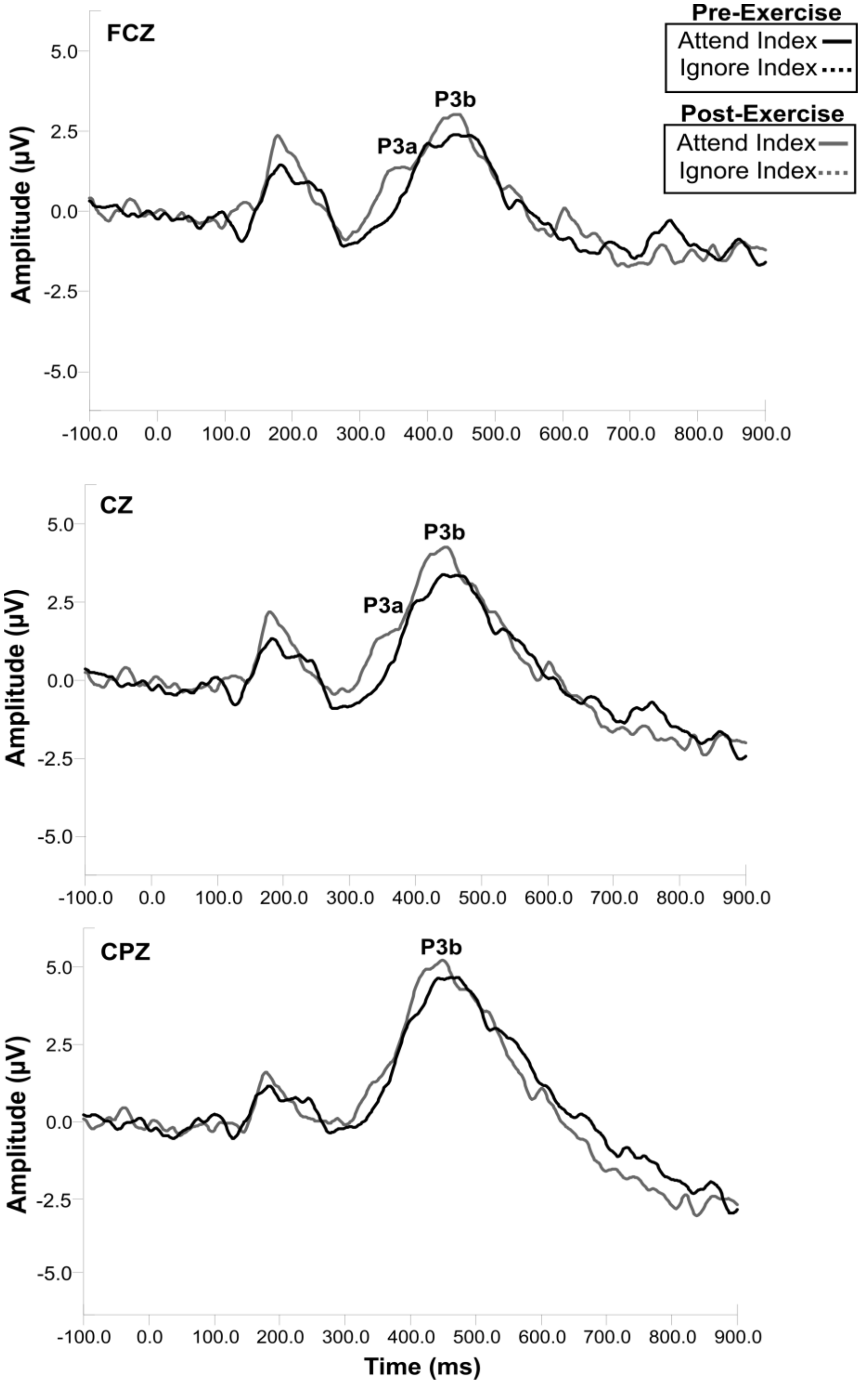

Figure 5.3. Grand averaged P300 waveforms

Grand average waveforms time-locked to target stimuli (i.e. smaller vibrations) delivered to the index finger are shown for the P300 component at midline electrodes FCZ, CZ, CPZ for all conditions. Black solid and dashed traces show Attend Index and Ignore Index conditions, respectively, prior to exercise. Grey solid and dashed traces show Attend Index and Ignore Index conditions, respectively, following exercise.

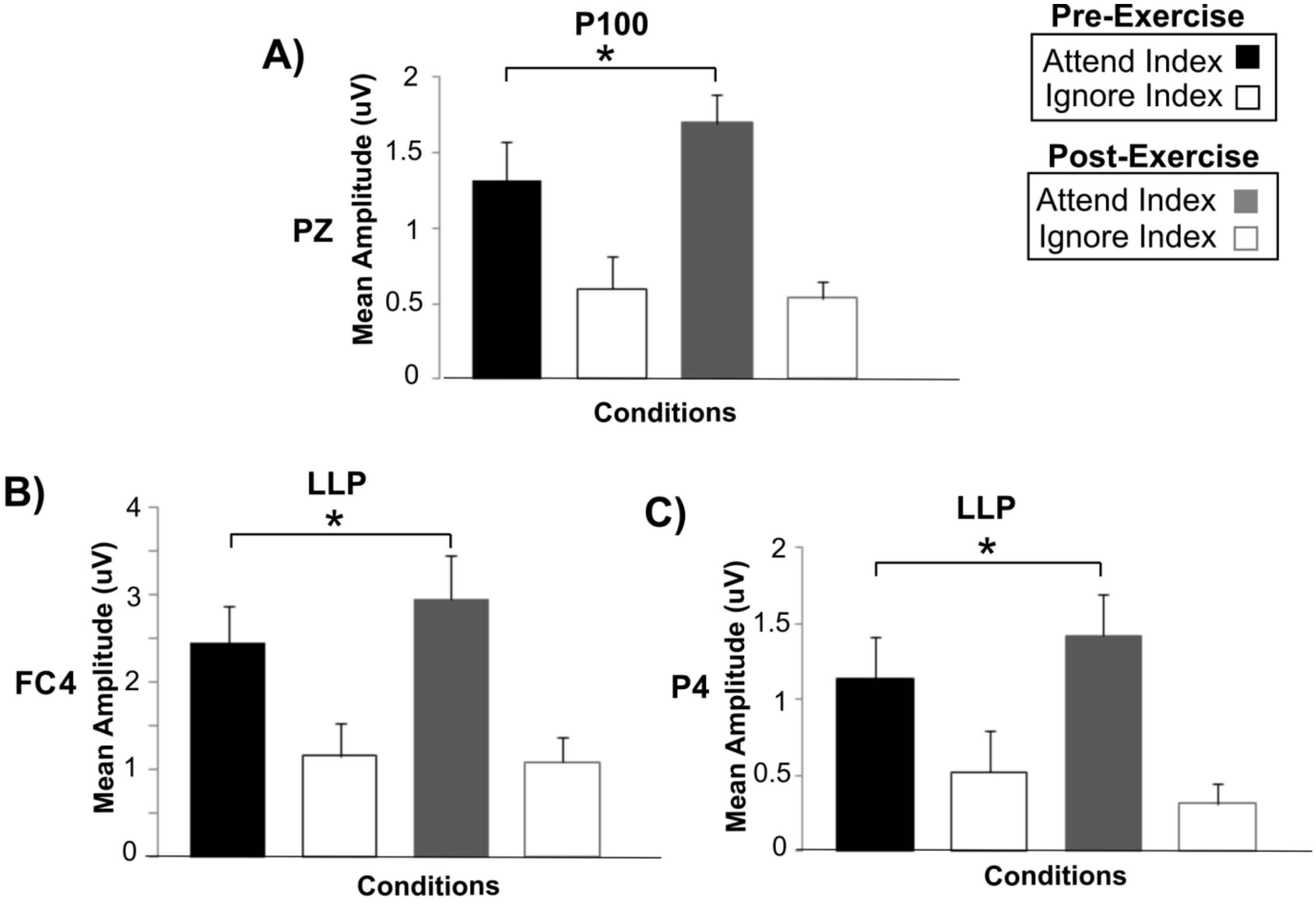

Figure 5.4. Group ERP means

Group means for A) P100, B) N140, and C/D) LLP, ERP components at electrodes of interest (FC4, CP4, P4). Black solid and outlined bars represent group data for the Attend Index and the Ignore Index condition prior to exercise, respectively. Grey solid and outlined bars represent group data for the Attend Index and the Ignore Index condition following exercise, respectively. Error bars show SEM, * denotes significance $p<0.05$.

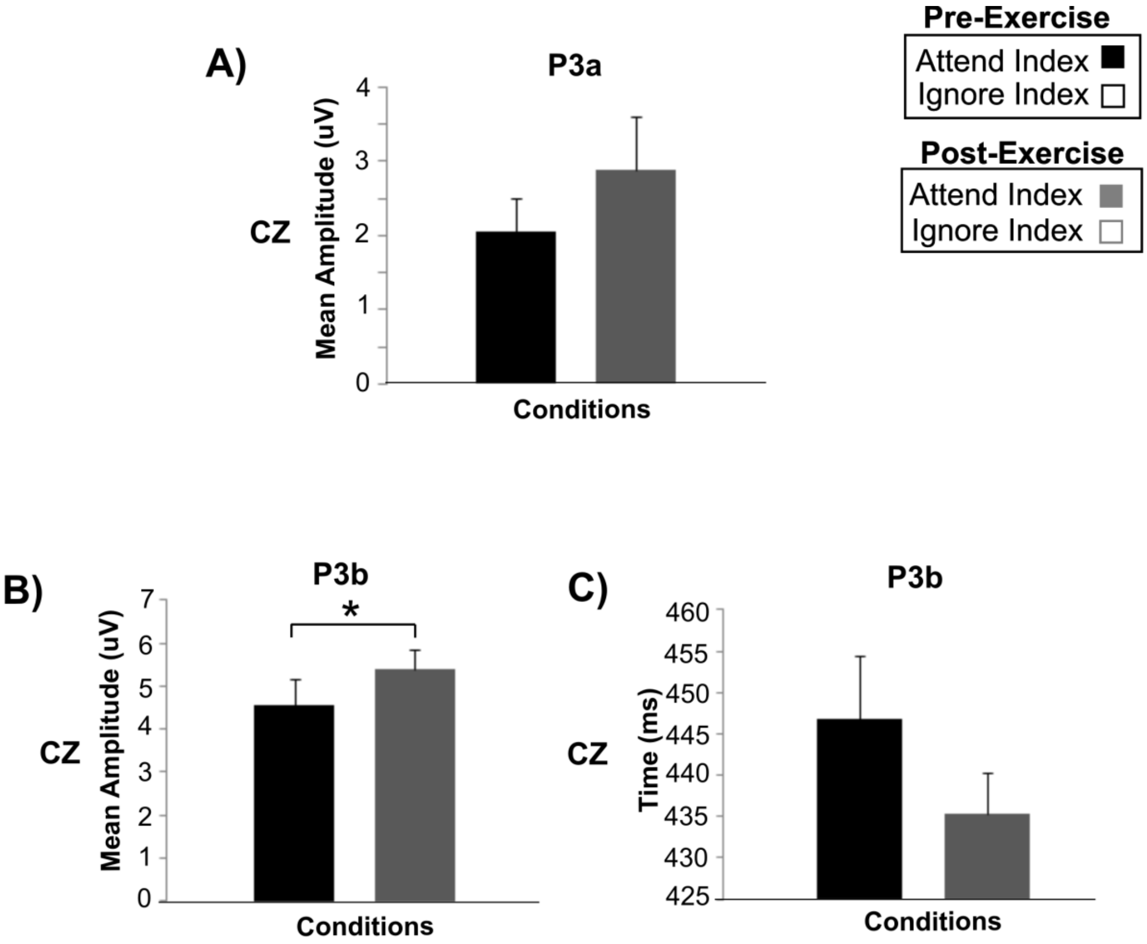

Figure 5.5. Group ERP means at frontocentral electrode CZ

Group means for A) P3a mean amplitude, B) P3b mean amplitude, and C) P3b mean latency. Black solid bars represent group data for the Attend Index condition prior to exercise. Grey solid bars represent group data for the Attend Index condition following exercise. Error bars show SEM, * denotes significance $p<0.05$.

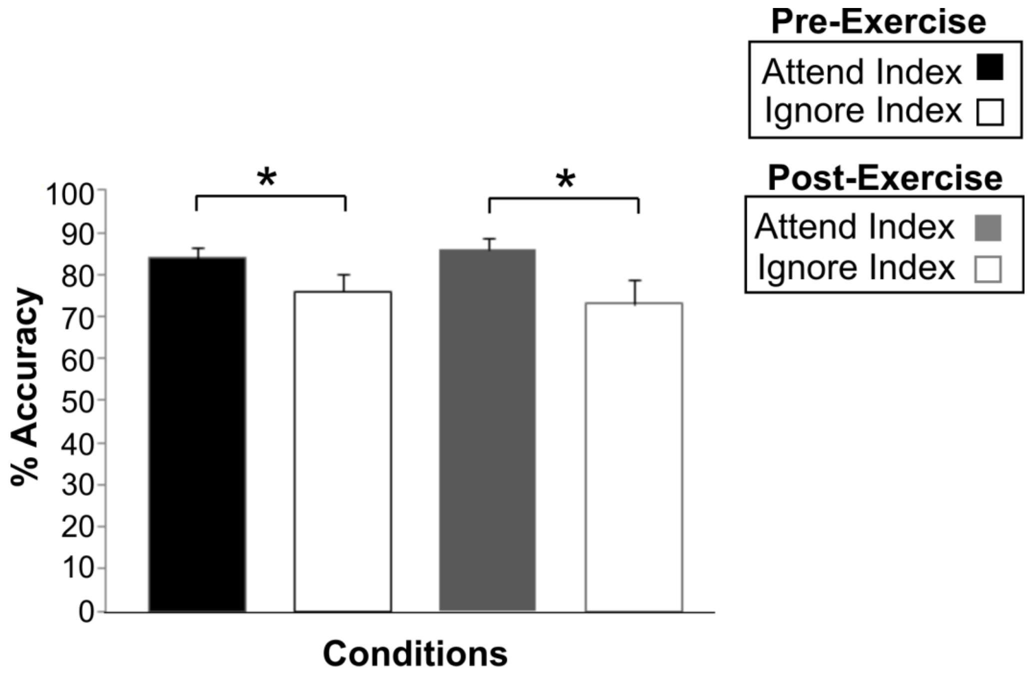

Figure 5.6. Behavioural performance

Behavioural performance was evaluated by determining the number of targets hit relative to the overall number of targets that were presented for each subject, and this success rate was expressed as a percentage. Black solid and outlined bars represent group data for the Attend Index and the Attend Index condition prior to exercise, respectively. Grey solid and outlined bars represent group data for the Attend Index and the Ignore Index condition following exercise, respectively. Error bars show SEM, * denotes significance $p<0.05$.

Chapter 6

6.1. General Discussion

The objective of this thesis was to investigate the sensory-gating role of the PFC to examine the neural mechanisms underlying top-down attentional control on modality-specific somatosensory cortex. The crossmodal findings of this thesis show that SI excitability is modulated by top-down attentional control, bottom-up sensory-sensory interactions, behavioural intent. Meanwhile, the effects of aerobic exercise on somatosensory processing suggest that acute moderate intensity exercise modulated multimodal neuronal activity generated at later stages of sensory processing in healthy young and older adults, as well as, early modality-specific SII regions in healthy older adults.

The aim of the first study was to determine the relative contributions of visual priming (bottom-up sensory input) and task-relevance (top-down attention) on influencing early somatosensory cortical responses, namely the P50 somatosensory ERP generated in SI. Previous fMRI work has shown increased neuronal activity in dorsolateral PFC and SI regions in response to attended versus unattended tactile and visual+tactile stimulation (Staines et al., 2002; Dionne et al., 2010). Moreover, EEG work showed that the amplitude of the somatosensory P50 component, generated in modality-specific SI was greatest during presentation of visual + tactile stimuli when both stimuli were relevant for upcoming motor responses (Dionne et al., 2013). Given these findings, in Study 1, we hypothesized that somatosensory activity would be modulated based on the temporal onset and stimulus order of task-relevant crossmodal (visual-tactile) events. Furthermore, we hypothesized that if bottom up and top-down mechanisms influence early somatosensory ERPs in contralateral SI, then the P50 amplitude should be greatest for relevant crossmodal (visual+tactile) interactions with a brief temporal delay between stimulus onsets and smallest for the irrelevant unimodal (tactile-tactile/visual-visual) conditions. To test whether bottom-up sensory-sensory interactions influenced SI activity, we incorporated two crossmodal conditions with variations in the temporal order of visual and tactile stimuli. In one condition, visual information preceded presentation of tactile information by 100 ms (VTd), while another condition reversed the order of the presentation of crossmodal stimuli so that tactile information preceded visual information by 100 ms (TVd). The purpose of this manipulation was to test the influence of bottom-up sensory-sensory interactions on modulation of SI activity since in the TVd condition, the P50 amplitude would have occurred prior to the onset of the visual information, thus modulatory effects elicited by this condition would not be influenced by the presentation of task-relevant visual stimuli. ERP results revealed that the P50 amplitude was greater during the attended crossmodal conditions versus unattended unimodal conditions, and greatest overall during the VTd crossmodal condition. This study provides evidence that crossmodal modulation of modality-specific SI is sensitive to both top-down attentional control and bottom-up sensory-sensory interactions.

Based on the findings of Study 1, the purpose of Study 2 was to determine if SI excitability would be modulated by behavioural intent in association with attentional relevance and the temporal onset and stimulus order of crossmodal stimuli. Specifically, it was hypothesized that crossmodal enhancement of the amplitude of the P50 component would be greatest when the onset of relevant visual information occurred prior to the onset of tactile information and required a sensory-motor integration response, and smallest during the detection of unimodal (tactile) stimuli. ERP results showed that overall, the P50 amplitude was greater during the task-relevant crossmodal condition where visual information preceded tactile information (100 ms temporal delay), and the degree of this modulation was significantly greater during the sensory-motor integration task relative to the detection task. These findings supported the results of Study 1 by confirming that top-down attentional control and bottom-up sensory-sensory interactions modulate primary stages of somatosensory processing, and extended previous work by showing that P50 modulation is also dependent on the difficulty of the associated motor task demands.

Considering the crossmodal findings that P50 modulation was greatest during attended, force-graded versus detection conditions, and the exercise findings showing an absence of attentional P50 modulation during an oddball detection task, the somatosensory P50 component may represent top-down attentional strategies applied during the processing of task-relevant information during complex, cognitively demanding tasks (Desmedt and Tomberg, 1989). EEG-fMRI work by Schubert et al. (2008) supports this notion with results showing that attention-related P50 modulation was localized to contralateral SI regions during a cognitively demanding, bilateral tactile stimulation task. The authors suggested that discrepant findings regarding attentional modulation of the early modality-specific modulations may depend on the difficulty of task demands, and our P50 results support this theory.

The objective of Study 3 and 4 sought to determine whether exercise-induced increases in PFC activity influence attention-based modulation of somatosensory ERPs in healthy young and older adults. Imaging work in humans has shown that acute bouts of moderate intensity exercise increase neuronal activity in PFC regions during attentionally demanding tasks, particularly in aging populations. Transcranial magnetic stimulation work by Bolton and Staines (2011), revealed that transient disruption to the DLPFC produced disinhibition of the P100 component generated in bilateral SII regions, while aging work by the same authors (2012) revealed an age-related reduction in attention-based modulation of somatosensory ERPs, suggests that the structural integrity of the PFC is crucial in mediating modality-specific modulations. Thus in both Study 3 and 4, we hypothesized that an acute bout of moderate intensity aerobic exercise preceding performance of a tactile discrimination task would result in more efficient sensory-gating of irrelevant/non-attended and enhancement of relevant/attended tactile information. Therefore, improvements in sensory-gating would be observed as increased neural suppression of task-irrelevant stimuli and enhancement of relevant sensory information post- relative to pre-exercise in young and older adults. ERP results for the younger adult group post- relative to pre-exercise showed greater enhancement of the N140 component to unattended/task-irrelevant stimuli over frontoparietal electrode sites, as well a reduction in the LLP amplitude over frontal sites during unattended conditions and enhancement of the LLP amplitudes over parietal sties during attended conditions. By contrast, exercise effects in older adults revealed increased: P100 amplitudes over parietal sites, LLP amplitudes over frontoparietal sites contralateral to stimulation, P3a/b amplitudes over frontocentral electrode site CZ, as well as a decreased P3b latency to attended-task-relevant tactile stimuli. There were attentional but no exercise effects on the N140 component in the older adult group such that the N140 amplitude was larger during unattended versus attended tactile stimuli. Overall, these studies confirm that acute moderate intensity aerobic exercise influences the PFC's attentional role on modality-specific somatosensory cortices, but in different ways in young and older adults. Based on our ERP findings, younger adults showed enhanced neuronal responses to unattended and attended tactile stimuli at later stages of sensory processing post-exercise versus pre-exercise (i.e. significantly greater N140 and LLP amplitudes to unattended, task-irrelevant and attended task-relevant stimuli, respectively), while older adults showed enhanced processing of attended tactile stimuli (i.e. significantly greater P100, LLP, P300 amplitudes to attended, task-relevant stimuli). Notably, behavioural performance was similar across attentional conditions and age groups (i.e. no exercise effects on performance but higher accuracy scores when attention was directed towards the index versus pinky finger). These findings are in accord with neuroimaging evidence suggesting that despite similar performance, older adults recruit different neural networks reflective of more local neural information processing than younger adults (Cabeza et al., 2002; Davis et al. 2008). Moreover, our findings also support recent research showing that older adults who were more physically active engaged in more local neural information processing (Heisz et al., 2014). However, Heisz et al. (2014) found that the shift to more local information processing in physically active older adults was associated with improved executive function performance, while no exercise-related improvements in behavioural performance were observed in our older adult group. This discrepancy may be accounted for by our use of a relatively easy cognitive task with seemingly low attentional demand as suggested by the high accuracy rates (approximately 80% accuracy for attend index conditions). Future work may seek to further explore these findings by increasing the attentional difficulty of the tactile discrimination task.

The fact that our crossmodal effects in SI and our aerobic exercise effects on modality-specific SII and multimodal cortices depended on attentional relevance suggests involvement of the dorsal fronto-parietal attention network, which has nodes in the DLPFC and posterior parietal cortex, and relies on perceptual and motor sets to bias processing towards selection of task-relevant sensory inputs. Research implies that reciprocal thalamo-cortical connections, namely between the thalamic reticular nucleus (TRN) and the PFC, are presumably responsible for attentional modulation of modality-specific sensory cortices by biasing processing towards the selection and amplification of attended, task-relevant sensory inputs (Yingling and Skinner, 1976; Brunia, 1993). The TRN is a shell-like structure that encapsulates the thalamus and is believed to act as a gatekeeper by modulating the activity of thalamocortical signals via inhibition or disinhibition of the associated sensory relay thalamic nuclei that it projects to. The state of the TRN gate determines whether or not sensory information reaches primary sensory areas for initial processing, and if so, whether the signals sent are altered or left unchanged. Zikopoulos and Barbas (2007) hypothesize that attentional regulation or sensory-gating of salient stimuli occurs via open or closed loop circuits depending of the relevance of the stimuli. In their model, an open loop circuit occurs when activation of the TRN produces disinhibition of the relevant/attended sensory thalamic nuclei and surround inhibition of the irrelevant/unattended sensory thalamic nuclei. This may be considered a potential mechanism for top down attentional processing since voluntary control of attention towards relevant stimuli in the presence of distractor stimuli is required for successful execution of goal-directed behaviours. By contrast, a closed loop circuit would only allow temporary access of salient stimuli to the cortex before increased activity from the TRN produced feedback inhibition on the associated sensory thalamic nuclei thereby shunting the flow of information to the cortex for further processing. This may occur during bottom-up attentional processing wherein unexpected salient stimuli may temporarily capture attention and interrupt ongoing cognitive processing. It is thought that the best case scenario for attentional processing of relevant versus irrelevant sensory information occurs in an open loop circuit where the TRN selectively permits the transmission of salient/relevant stimuli thereby allowing prolonged access to the cortex for optimal processing while simultaneously producing surround inhibition of the irrelevant/unattended sensory thalamic nuclei (Zikopoulos and Barbas, 2007).

The TRN and prefrontal cortex have a unique neural circuitry which is thought to facilitate attentional processing. First, the PFC has widespread connections to the TRN which extend beyond its thalamic relay nuclei (in the mediodorsal thalamus) to sensory areas thus may assist in the attentional processing of sensory information. Second, the PFC has terminations on the TRN which may enhance information transfer to other cortical regions. Lastly, the mediodorsal thalamic nucleus, which receives the majority of its input from the PFC, also has vast connectivity with the TRN making it another plausible reason why PFC activity is hypothesized to be the main driving influence on TRN activity (Zikopoulos and Barbas 2007). This connectivity between the PFC, the mediodorsal thalamic nucleus, and the TRN make it a likely candidate for efficient attentional processing of relevant sensory information transfer to primary sensory areas for further cognitive processing.

According to the attentional model proposed by Skinner and Yingling (1977), the TRN works as an ‘attentional spotlight’ that enhances and integrates relevant signals generated in the brain to allow efficient neural transmission of salient stimuli. This model proposes that attentional processing occurs via a frontothalamic mechanism whereby selective lack of TRN activation governed by the PFC, produces disinhibition on associated sensory thalamic relay nuclei, resulting in a local opening of the gate for the attended sensory modality. Given the findings of this thesis, enhancement in SI excitability likely occurred via a prefrontal-thalamic-cortical loop whereby PFC pathways to the TRN drive enhanced transmission of relevant signals and suppression of irrelevant distracters (Zikopoulos and Barbas, 2007).

However, our crossmodal findings that SI excitability was greatest during crossmodal interactions with a temporal delay between visual and tactile stimuli suggests that attended, task-relevant visual information may influence modality-specific neuronal responses generated in SI perhaps via feedforward cortico-cortical mechanisms. Anatomical evidence for such connections in primates were reported by Cappe and Barone (2005), who using retrograde tracers, found the existence of visuo-somatosensory projections originating from visual areas towards somatosensory areas 1/3b. In addition, Foxe and Scroeder (2005) have suggested that crossmodal effects may occur in a feedforward manner via visual connections influencing somatosensory cortices. Dionne et al. (2013) showed that simultaneous presentation of visual + tactile stimuli enhanced the P50 component. The authors concluded that these effects were primarily driven by a top-down attentional network, rather than from projections from visual cortex since the earliest VI response occurs within the same time window as the somatosensory P50 component at approximately 45-60 ms post stimulus-onset (Foxe and Simpson, 2002). However, simultaneous presentation of visual and tactile information does not permit investigation of the relative contribution of each sensory system in modulating the P50 component, thus it is possible that crossmodal facilitation of the P50 in this study might have also occurred in a feedforward manner. By manipulating the temporal onset of visual and tactile crossmodal interactions to better address the influence of visual priming on SI excitability, our crossmodal findings found that P50 modulation was greatest when task-relevant visual information preceded tactile information. Moreover, findings from Study 2 showed that the mere presence of visual information prior to tactile information even when it was irrelevant for behaviour enhanced P50 modulation relative to attended unimodal conditions (refer to Figures 3.2 and 3.3). These findings support the notion that while top-down attentional mechanisms influence SI excitability, it is likely that projections from visual cortex may also facilitate crossmodal modulation in modality-specific SI in a feedforward manner.

With regards to the exercise findings reported in this thesis, the reticular activating hypofrontality (RAH) model proposed by Dietrich (2011) offers a promising mechanistic explanation for the acute exercise effects on cognition. Here, it is believed that the brain has limited resource capacity whereby neuronal processing occurs on a competitive basis, such that during exercise, local increases in activation occurs for brain regions responsible for coordinated controlled bodily motion (i.e. sensorimotor cortices, autonomic nervous system, and cerebellum), while fewer resources are left available for brain functions not computing critical functions at the time. The model suggests that exercise-induced effects on cognition are a cascading, two-stage process. First, the arousing effects of aerobic exercise increase activation of the reticular-activating system (RAS) via somatosensory feedback of limb movements during exercise (Cooper, 1973; McMorris et al., 2008), which increases the production and release of several catecholamines in the brain including: dopamine, noradrenaline, and serotonin. Second, since the brain has limited capacity of available resources, during exercise the brain must shift metabolic resources to neural structures sustaining movement while disengaging higher-order functions of the PFC. Converging exercise research supports this model, with various neuroimaging studies and cerebral blood flow studies in animal models showing marked increases in activation of motor, sensory, and autonomic regions of the brain during aerobic exercise (Gross et al., 1980; Vissing et al., 1996; Holschneider et al., 2003). Furthermore, EEG studies have consistently shown that exercise is associated with increases in alpha and theta cortical rhythm activity, particularly in the frontal cortex (Petruzzello and Landers, 1994; Kubitz and Pothakos, 1997; Nybo and Nielsen, 2001). Increases in alpha activity are a well-recognized indicator of decreased brain activity (Petruzzello and Landers, 1994; Kubitz and Pothakos, 1997). Neurophysiological recordings in exercising cats found increased activity from 63 PFC neurons responsible for the control of movement during locomotion while other PFC neurons decreased their discharge rate (Criado et al., 1997). Lastly, a plethora of studies have shown that cognitive function during tasks involving higher-order executive control processes tend to be impaired when combined with an aerobic exercise session (Adam et al., 1997; Dietrich and Sparling, 2004; Hillman et al., 2007; Audiffren et al., 2009; Davranche and McMorris, 2009; Del Giorno et al., 2010). Collectively, there is compelling evidence in support for the RAH model and when taken into consideration with the sensory-gating role of the PFC, a theoretical approach to the attention-related exercise-induced findings of this thesis can be proposed. First, increased arousal via somatosensory feedback of limb movement during exercise engages the RAS to increase production and release of several monoamines in the brain. Second, during the exercise session, the CNS requires increased activation in region-specific brain structures necessary for motor control, and decreased activation in higher-order PFC regions not critically required for the execution of aerobic performance. Third, once a higher-order cognitive task is employed following exercise, a switch in the brains metabolic demand is enforced which re-engages PFC activation and the uptake of monoamines, particularly dopamine and noradrenaline. Fourth, increased monoamine uptake by the PFC exerts greater cognitive control over the TRN leading to an improved signal-to-noise ratio over incoming sensory inputs from the periphery, resulting in greater attentional regulation effects in modality-specific somatosensory cortex.

6.2. Conclusions

Findings from Studies 1 and 2 of this thesis imply that modality-specific somatosensory cortex is sensitive to the attentional relevance and temporal dynamics of crossmodal (visual+vibrotactile) stimuli, and the magnitude of SI modulation depends on the required motor response. These findings are suggestive that crossmodal modulation of SI excitability occurs via: 1) top-down mechanisms, likely mediated by the sensory-gating role of the PFC on the TRN, which allow for the enhancement of attended, task-relevant crossmodal stimuli, and 2) bottom-up sensory-sensory interactions whereby visual cortex influences somatosensory processing in a feed-forward manner.

Findings from Studies 3 and 4 of this thesis imply that aerobic exercise enhances frontoparietal interactions during a tactile discrimination task in young and older healthy adults. It is believed that the mechanisms underlying the enhancement of attention-related somatosensory ERPs are mediated by the RAH model for acute exercise effects on cognition, which exerts increased top-down attentional control over incoming sensory information.

6.3. Limitations

A prominent methodological limitation to the crossmodal studies documented in this thesis was the inability to measure whether crossmodal interactions modulated somatosensory ERPs generated at later stages of somatosensory processing (i.e. P100, N140 components). The nature of this problem stems from the crossmodal conditions with 100-msec temporal delays between the onset of visual or tactile stimuli events (i.e., TVd and VTd). Here, the temporal delays interfered with the timing of some early (i.e., the P100 component for the VTd condition) and all later onset ERPs (i.e., N140) beyond typical latency boundaries, thus crossmodal effects could not be discussed for these components. Moreover, although the 100-msec temporal delay was advantageous for investigating crossmodal effects on P50 modulation, it remains unclear if this is the optimal temporal delay for investigating the influence of visual information on SI excitability. Thorpe et al., (1996) found that the earliest cortical VI response generated during a highly demanding cognitive task was 150 msec. This finding suggests that a longer temporal delay may promote greater crossmodal effects on SI excitability.

The exercise studies in this thesis also present significant methodological limitations. Perhaps the most notable limitation was the use of the age-predicted heart rate max (HRmax) formula to set the exercise prescription parameters for our exercise session intensity. The age-predicted HRmax formula (220-age) is considered to be the most common and popular heart rate prediction formula, likely due to its simplicity and convenience, since it does not require sophisticated and/or expensive equipment for computation. However, despite its popularity, a review by Roberts and Landwehr (2002) noted that there is minimal empirical research in support of this model largely due to the large variability associated with it. Sources of this variability stem from differences in the first number chosen in the formula with equations ranging from a low of 186 to a high of 226 (Robergs and Landwehr, 2002). Moreover several formulas include an "age" modifier in the equation which also range from 0.41 to 1.07 (Robergs and Landwehr, 2002). Age variations in the population sample are another considerable limitation to using this equation with overestimations and underestimations of HRmax depending on whether the participants are younger or older adults. Lastly, exercise mode seems to have an effect on HRmax prediction formulas which are often ignored (Robergs and Landwehr, 2002).

Recently, maximal exercise tests measuring or predicting maximum oxygen consumption (VO_2 max) are considered to be the optimal standard for determining and assessing exercise prescription against which to compare other measures (Shephard et al., 1968; Bruce et al., 1973). However, research using percentage of VO_2max as an index of exercise intensity is not without its own limitations. For instance, several studies report inter-individual day-to-day variability of 4-6% in healthy individuals with no known cardiopulmonary pathology or impairment (Shephard, 1984; Jones, 1988). In addition, the possibility for fitness assessment inconsistencies also exists with regards to what VO_2 measure is actually being utilized for exercise prescription. For example, when a maximal VO_2 test is performed to determine an exercise prescription, but the criteria for VO_2max is not met, the maximal VO_2 achieved is termed a "VO_2peak" (Zeballos and Weisman, 1994).

From a clinical perspective, assessing maximal exercise performance using VO_2max is dependent on the individual's ability to attain a VO_2max without fatiguing prematurely, or being limited by musculoskeletal impairments (Noonan and Dean, 2000). Furthermore, psychological factors such as an individual's motivation level may determine the likelihood of their ability to attain their true VO_2max.

Since the purpose of the exercise studies in this thesis was not to determine what the optimal exercise prescription for modulating frontoparietal interactions, but rather, to investigate whether exercise would modulate somatosensory cortices at all, the use of prediction formula to determine a target range for modulating cortical activity proved to be sufficient for our experimental intentions.

Another possible limitation was the usage of EEG for all thesis studies, which offers exquisite temporal resolution (ms-level), but is significantly limited by its poor spatial resolution. As a result, inferences made regarding the influence of frontal cortices on somatosensory processing as a result of increase top-down attentional control, as well as those suggesting sensory-sensory interactions between visual and somatosensory cortices are merely speculative based on previous literature using high-resolution imaging techniques (Staines et al., 2002; Dionne et al., 2010).

Despite these limitations, the crossmodal and exercise findings in this thesis contribute to the mechanistic understanding of cortical and subcortical networks involved in attentional modulation of SI excitability, as well as potential factors such as behavioural intent and aerobic exercise that influence frontoparietal interactions.

6.4. Future Directions

Given the crossmodal findings that SI excitability was greatest when visual information preceded tactile information by 100 ms, the next logical question may be: is there an optimal temporal delay between visual and tactile stimuli for enhancing SI activity, and if so, what is it? Future studies may wish to further explore the temporal dynamics of visual+tactile interactions in order to establish whether a longer temporal delay results in greater P50 modulation. Such research may provide promising results further substantiating the possibility that visual cortices influence somatosensory cortices in a feedforward manner. An alternative study may seek to determine the frontal contribution of crossmodal effects on SI excitability by using an EEG-cTBS approach to transiently suppress the PFC's influence of incoming sensory input, and measure whether physiological changes in the magnitude of the P50 component as well as behavioural consequences occur.

Similarly, with regards to the exercise studies presented in this thesis, future research should investigate whether acute aerobic exercise has neuro-protective effect on the PFC using an EEG-cTBS paradigm. In other words, can engaging in a single session of moderate intensity aerobic exercise reverse transient suppression of PFC regions? Previous work by Bolton and Staines (2011) showed that cTBS to the DLPFC in healthy young adults produced disinhibition, particularly of the somatosensory P100 component, during a tactile discrimination task. Based on the exercise results shown in this thesis, it would be fascinating to see if an acute exercise session could reverse such effects. Another potential avenue of research to explore may include examining the dose-response relationship between exercise intensity and cognition using more stringent measures of fitness assessment and exercise prescription, or the effects of chronic exercise on the modulation of frontoparietal interactions. Lastly, future research using the tactile discrimination task reported in this thesis may consider slightly modifying the experimental setup, by creating stimulus competition between index fingers of separate hands rather than between the index and pinky finger of the same hand since somatosensory ERPS time-locked to tactile stimuli presented to the pinky finger did not produce discernible ERPs.

6.5. References

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