The Electrophysiology of Human Visuomotor Integration During Memory-Guided Action

by

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ABSTRACT

The visuomotor pathways of the brain are comprised of millions of neurons and complex interconnections among them exist. In order to fully understand visuomotor processes, we need to understand the mechanisms that allow neurons within these areas and between networks to coordinate with each other. The objective of the four studies presented in this thesis was to test whether specific electrophysiological signals reflect visuomotor integration and determine which aspects of behaviour are reflected in the modulation of these signals. I measured oscillatory and ERP activity during various delayed action tasks in order to determine how the brain uses both immediate visual information and visuoperceptual memory to execute goal-directed reaching.

In the first study I addressed whether visuomotor regions might coordinate their function via theta oscillations. I determined that theta synchronization and mu desynchronization may represent broadly applicable rhythmic mechanisms for integration and visuomotor function in the human brain. In the second study, I investigated event-related potentials (ERPs) during the planning phase of actions. I found that the N170 ERP component, which is generally considered in the context of perception, is also sensitive to elements of action planning and connects visual-perceptual and action processes. In the third study, I expanded on these results and investigated how perception for action is coded over time, by manipulating the delay period of the task. As delay period between target occlusion and movement initiation increased, modulation in the N170 amplitude reflected the accuracy of the stored memory representation. Finally, in the fourth study, I investigated how the two hemispheres of the brain contribute to visuomotor processes using the N170 as a measure. Results suggest that whereas visually initiated action is left-dominant, memory-initiated action may be right-dominant.

In sum, this body of work provides further insight into the electrophysiological basis of human visuomotor function. Employment of a modifiable reaching paradigm has permitted the systematic investigation of how immediate available visual information and visuoperceptual memory informs action. I have identified two signals that can be used to assess brain activity during visuomotor behaviour in real-time.

PREFACE

This thesis is an original work by Leanna Catherine Cruikshank. Five research projects contributing to this work received ethics approval from the University of Alberta Research Ethics Board. Chapter 2 of this thesis has been published as Cruikshank, L. C., Singhal, A., Hueppelsheuser, M., & Caplan, J. B. (2012), "Theta oscillations reflect a putative neural mechanism for human sensorimotor integration", *Journal of Neurophysiology, 107*(1), 5-77. doi:10.1152/jn.00893.2010. Mark Hueppelsheuser assisted with the conceptualization of the study and Bernd Kohler assisted with the implementation of the experimental paradigm. I was responsible for acquiring and analyzing the data and drafting the manuscript. Chapter 3 of this thesis has been published as Cruikshank, L.C, Caplan, J.B., & Singhal, A. (2012), "Human electrophysiological reflections of the recruitment of perceptual processing during actions that engage memory", *Journal of Vision,* 12(6):29, 1-13. Bernd Kohler assisted with implementation of the paradigm and I was responsible for acquiring and analyzing the data and drafting the manuscript. Chapter 4 of this thesis has been published as Cruikshank, L. C., Caplan, J. B., & Singhal, A. (2014), "A perception-based ERP reveals that the magnitude of delay matters for memory-guided reaching", *Experimental Brain Research,* doi:10.1007/s00221-014-3897-x. Sylvia Romanowska assisted with data collection and I was responsible for analyzing the data and drafting the manuscript. Chapter 5 of this thesis has not been published elsewhere. Tania Shapka and Larissa Shapka assisted with data collection and I was responsible for the analysis. In conjunction with my supervisors Anthony Singhal and Jeremy Caplan, I was involved in concept formation for all chapters, interpretation of the data, and the final approval of all published manuscripts.

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Chapter 1:

General Introduction

1.0 Introduction

In order to successfully interact with one's environment, sensory-perceptual and motor systems must work together to facilitate a response. Any mechanism by which these systems influence and inform one another to produce behavior can be conceptualized as *sensorimotor integration*, and understanding such a process is crucial if we wish to understand basic cognitive brain function. In recent years, significant advances have been made regarding the processes responsible for transforming sensory-perceptual information into motor commands. Evidence derived from single cell recordings, imaging studies and neuropsychological patients has led to the identification of a 'visuomotor circuit,' which is engaged during visuomotor performance (Castiello & Begliomini, 2008). Similarly, evidence derived from animal electrophysiology has suggested that theta oscillations (3-12 Hz rhythmic brain activity) are a neural mechanism underlying integration of sensory and motor activity in rats (Bland & Oddie, 2001). In humans however, it is mu rhythm (8-16 Hz) desynchronization that is primarily implicated in sensorimotor behaviour. Oftentimes in scientific endeavors, separate areas of research and knowledge must be incorporated in order to fully understand and comprehensively explain a phenomenon. The aim of the following research is to elucidate the eletrophysiological basis of human viusomotor integration while taking into account and attempting to reconcile and connect parallel areas of research. Electrophysiological techniques may have been underused in action tasks because movement and saccades can produce artifacts that are confounded with brain activity guiding the behaviour. However, I examined brain activity that occurred just after the signal to move, but before the movement was initiated. I also included a control experiment in chapter 3 to rule out visual evoked potentials to the offset of a stimulus. In the experiments presented in this thesis, both rhythmic mechanisms of visuomotor integration (oscillations) and event-related potential (ERP) components, which likely reflect time-limited mechanisms of integration, were examined. By manipulating the visual availability of a target during movement initiation in a reaching paradigm, I investigated how these two measures operate within components of the visuomotor circuit.

1.1 Dorsal and Ventral Streams

The brain has the ability to perceive the world around us and to produce skilled, and elaborate movements with astonishing precision and fluidity. Even a common task of identifying and grasping an object, requires that the brain perform countless computations with minimal time and ease. How is it that the brain transforms visual information into motor commands, and what is the interaction between sensory-perceptual processes and motor output? Researchers have been interested in this subject for years, and recent advances have provided considerable insight into this particular question.

In 1982, Ungerleider & Mishkin identified two separate visual processing streams, a dorsal and a ventral, which were proposed to mediate the spatial information and distinguishing properties of objects, respectively (Ungerleider & Mishkin, 1982). It was suggested that the dorsal stream was responsible for enabling the subject to spatially locate an object, whereas the ventral stream enabled the subject to determine what the object of interest was. The dissociation of visual streams into 'what' vs. 'where' pathways was then reinterpreted and revised in 1992. Based on emerging evidence from various lines of research, Milner and Goodale proposed that a 'division of labor' exists between dorsal and ventral pathways, rather than a purely sensory distinction. Their claim is that the two streams, dorsal and ventral, are responsible for action and perception, respectively. They have suggested that the ventral stream is responsible for constructing perceptual representations of the world, while the dorsal is specialized for the visual control of actions (Goodale & Milner, 1992). This distinction between ‘vision-for-action’ and ‘vision-for-perception’ is well founded, and these streams have important implications for the types of actions we perform on a regular basis. However, not everyone fully agrees with the two-stream hypothesis or that an absolute functional dichotomy between dorsal and ventral streams exists (Schenk & McIntosh, 2010).

1.2 Visually Guided and Delayed Actions

Immediate, visually guided actions are those performed when a target remains visually available for the programming of a motor plan. Conversely, delayed actions are those performed when the target has been removed from view, or is no longer visually available. For example, if an individual looks at his/her coffee cup while reaching for it, he/she is performing an immediate, visually guided action. Conversely, if an individual turns away from the coffee cup prior to reaching for it, he/she is performing a delayed action. According to the dual visual stream model (Goodale & Milner, 1992), the cortical circuitry subserving visually guided and delayed action planning differs, given that a previously formed percept must inform the motor plan for a delayed action, rather than directly accessible visual information (Goodale, 1998). Immediate, visually guided reaching can be performed relying solely on dorsal stream activation, as this area is specialized for the visual control of action. Delayed reaching, however, is thought to require integration of the ventral stream (Westwood & Goodale, 2003), which is responsible for the identification of objects and the construction of perceptual representations (Goodale & Milner, 1992). The perception-action model suggests that delayed action planning requires a shift from dorsal to ventral activation in order for previously stored representations to inform the motor plan (Westwood & Goodale, 2003). Converging neuropsychological, neuroimaging, and kinematic studies support this theory, as follows:

Visual-form agnosia patient D.F. has bilateral ventral stream damage and an intact dorsal stream. She is able to accurately scale her grip in order to grasp objects, yet when asked to either verbally or manually indicate the size, shape, and orientation of the objects, she is at a loss (Milner, Dijkerman, Pisella et al., 2001; Goodale, Milner, Jakobson et al., 1991). Furthermore, if a delay is introduced in the grasping task and she is to pantomime the action in the absence of the target object (i.e. she is now to perform a delayed action opposed to an immediate one), the task becomes impossible (Goodale , Jakobson & Keillor, 1994). These findings lend support to the idea that visual perceptual information is indeed processed and represented within the ventral stream, and that reactivation of stored representations is likely required for the planning of delayed actions. Studies conducted on unimpaired populations also support this idea. For example, various behavioural studies indicate that whereas the action system is resistant to pictorial illusions under visually guided conditions, this is not the case when a delay is introduced. Rather, erroneously perceived perceptual information appears to influence behaviour when a delay is introduced (Hu & Goodale, 2000; Westwood, Dubrowski, Carnahan et al., 2000, Westwood, McEachern & Roy, 2001; Ganel, Tanzer & Goodale, 2008). These findings suggest that the planning of delayed actions engages previously stored perceptual mechanisms within the ventral stream.

Kinematic studies have also suggested that ventral stream processes are recruited during delayed action planning and that previously stored perceptual information is reactivated. Presumably, the dorsal and ventral streams operate on different time scales. The dorsal stream is able to carry out fast visuomotor computations, and is thus sufficient for performing immediate, visually guided actions (Goodale et al, 1994). However, information in this pathway is suggested to decay very quickly. Thus, when a target disappears from view, as is the case with delayed action, the ventral stream is thought to recruit and incorporate perceptual information with the programming of the motor plan (Goodale et al., 1994; Singhal et al., 2007). Accordingly, delayed hand actions have been shown to be slower, and less accurate than immediate, visually guided actions.

Finally, functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS) studies have revealed specific regions within the ventral stream that are likely involved in delayed action planning. Due to the fact that delayed actions rely on the recall of target features, perceptual memory processes are thought to be involved to a certain extent (Goodale & Milner, 1992; Klatzky, Pellegrino, McCloskey et al., 1993). One study has shown that if perceptual memory is engaged while performing delayed, compared to immediate actions, interference tends to be greater, presumably due to the overlap in task demands or shared resources (Singhal, Culham, Chinellato et al., 2007). Thus, perceptual information that is reactivated for delayed action planning needs to be stored or represented somewhere for brief periods of time. The lateral occipital cortex (LOC) is a ventral stream area associated with object recognition and perception (Grill-Spector, Kourtzi & Kanwisher, 2001) and studies have shown that it is activated not only during initial form perception, but also as the percept of an object endures (Ferber, Humphrey & Vilis, 2003). Interestingly, the LOC displays bilateral damage in patient D.F. (James, Culham, Humphrey et al., 2003) and neuroimaging studies have shown that it is involved in the online control of delayed actions (Singhal, Kaufman, Valyear et al., 2006; Singhal et al., 2013). Similarly, virtual lesioning of LOC using TMS has also revealed its involvement in delayed, but not immediate grasping (Cohen, Cross, Tunik et al., 2009).

It is important to note however, that in addition to ventral stream areas, studies have also reported reactivation of dorsal stream, parietal neurons during delayed action planning. Neurons in the anterior intraparietal (AIP) area, that were shown to be selective for shape information, remained active in monkeys during the delay period of a memory-guided hand manipulation task (Murata, A., Gallese, V., Masakazu, K. et al, 1996). Similarly, neuroimaging has also revealed activation of AIP during the maintenance phase of delayed reaching and grasping (Singhal et al., 2006). One problem in addressing the question of whether different neural mechanisms subserve immediate and delayed actions in humans is that it is difficult to directly compare the two action types using neuroimaging techniques. The primary reason for this is that delayed and immediate trials require differences in timing, and in the case of fMRI with immediate actions, it would be difficult to distinguish between activation associated with target presentation from activation associated with action. Thus, electrophysiological techniques provide a strong advantage for studying sensorimotor processes, as these methods provide excellent temporal resolution.

1.3 Electroencephalography (EEG)

The non-human animal and human brain both produce electromagnetic activity that we are able to record (Niedermeyer & Lopes da Silva, 2005). We may assess the activity of a single cell, or a population of neurons with electrophysiological techniques. In animals, action potentials and membrane fluctuations can be measured using intracellular and extracellular recordings (Kandel, Schwartz & Jessell, 2000). In humans, it is much more difficult to perform single cell recordings and instead, electroencephalography (EEG) is used to measure the summed, synchronous activity of a population of neurons (Bear, Connors, & Paradiso, 2006). This can be done either intra-cranially using depth electrodes or non-invasively with scalp EEG.

Scalp EEG is a useful tool for understanding the neural processes and mechanisms that are involved in sensorimotor behavior.

1.4. Event-Related Potentials

There are several ways of examining the electrical activity produced by the brain. Small deflections in the ongoing EEG can occur in response to internally or externally generated events, known as event-related potentials (ERPs; Kandel, Schwartz & Jessell, 2000). They are a subset of the EEG activity and can be decomposed into various *components,* which are associated with different processes in the brain (Luck, 2005). One particular ERP component (the N170) has been associated with perceptual processes and in Chapter 3, I examined this component during the action-planning phase of movements in order to better understand the interplay between sensory-perceptual processing and motor output.

1.4.1 The N170

The N170 is an ERP component associated with perceptual processing. It was first described in the context of face perception, when researchers determined that a negative deflection occurring 170 ms post-stimulus was larger for faces than for other objects (Bentin et al., 1966). This component responds more negatively to faces compared to other object categories, reflects the structural encoding of faces (Eimer, 2011; Wronka & Walentowska, 2011), and displays sensitivity to emotional facial expression (Batty & Taylor, 2006; Eimer & Holmes, 2002). Since its discovery however, the N170 has been implicated in more general perceptual processing, and object classification (Sreenivasan, Katz & Jha, 2007), which is likely a necessary component of delayed action. The N170 has also been found to have a source in the lateral occipital cortex (LOC; Rossion et al., 2003), a ventral stream area involved in the representation and perception of objects (Ferber, Humphrey, & Vilis, 2003). While largely considered a perceptual brain wave, the N170 had never been previously considered in action studies. Ventral visual stream processes that the waveform is typically associated with, however, are the same perceptual processes necessarily engaged during delayed action planning. It follows then that characteristics of the N170 extend to these behaviours as well.

In Chapter 3 I sought to determine whether the N170's role in perception would extend to action, essentially linking the two processes. I tested the hypothesis that the N170 reflects ventral stream processing, predicting that N170 amplitude should be larger for delayed than for immediate, visually initiated reaching. Participants were auditorily cued to reach towards target dots presented on a touch-sensitive monitor (see fig 3-01). I analyzed event-related potentials (ERPs) during the action-planning phase of trials. Confirming my prediction, the N170 response was larger during the planning phase of the delayed action condition than the immediate condition (see fig 3-03). This effect was robustly observed at temporal sites bilaterally, and likely reflects regions of inferior-temporal cortex. These results suggest that the N170 is a marker of activity within ventral stream areas during the planning of delayed action. This is the first such study to seek instantaneous electrophysiological markers of immediate versus delayed actions and to directly compare the action types in humans.

1. 5 Oscillations

While ERPs index brain activity that occurs in response to discrete events, the entire EEG signal holds information about the multitude of ongoing processes occurring in the brain. Neuronal oscillations are rhythmic brain activity that is produced as the result of neurons firing in a synchronized manner (Bear, Connors, & Paradiso, 2006). Rhythmic fluctuations in voltage occur ubiquitously throughout the central nervous system, and oscillatory activity can emerge at various levels of neuronal organization in the brain (Buzsaki, 2006). Intrinsic properties of individual nerve cells can give rise to rhythmic patterns of action potentials and subthreshold membrane potential deviations (Kandel, Schwartz & Jessell, 2000). As well, localized groups of neurons and larger, disparate neuronal ensembles may produce rhythmic firing patterns through the coupling of excitatory and inhibitory local and long-range synaptic connections (Buzsaki, 2006). The brain's ability to generate rhythmic activity at increasingly complex levels of organization has led to theories postulating the functional significance of brain rhythms. Over the past few decades, investigations into how rhythmic activity is generated at both the cellular and network level have increased. Rhythms that typically occur in the adult human brain are delta (1-3 Hz), theta (4-8 Hz), alpha (8-16 Hz), beta (16-30 Hz), and gamma (30 Hz >; Niedermeyer & Lopes da Silva, 2005). Like ERP components, rhythmic activity within these frequency bands has been correlated with different aspects of behavior, and two rhythms in particular have been specifically implicated in sensorimotor processes in humans and animals.

1.5.1 The Theta Rhythm

Electroencephalographic recordings from the hippocampus of animals reliably display a robust, large amplitude oscillation occurring at a frequency of 3-12 Hz. This rhythm was termed the 'theta rhythm' in 1944 by Walter & Dovey and has been investigated by researchers for decades (Buzsaki, 2006). However, controversy remains regarding the cognitive function of theta oscillations. Over the years, theta oscillations have been implicated in various animal behaviors, including spatial, motor, and cognitive tasks. Specifically, research has implicated rodent theta oscillations in locomotion, exploratory behavior, neural coding of place, memory, and long-term potentiation LTP. However, an alternative function of theta oscillations underlying sensorimotor integration has been proposed. The theta model of sensorimotor integration posits that the sensory and motor systems are linked and update one another through continual feedback (Bland, 1986). It remained unclear however, whether this model could be extended to humans. Cortical theta has been observed in humans and studies addressing the function of human theta have also documented its involvement during a variety of tasks (Mitchell et al., 2008). However, a weakness of the human studies has been a lack of task specificity. The paradigms that have been employed require such complex behavior on the part of the subject that it is difficult to determine a functional role for theta. Thus, a more targeted approach is required, and theta needs to be examined more systematically.

1.5.1.1 Hippocampal Theta in Non-Humans

1.5.1.1.1 Motor Behavior

Hippocampal theta oscillations have been extensively studied in animals and are one of the most researched and well documented brain rhythms in Neuroscience. Many early studies associated theta oscillations with voluntary motor behavior. In 1966, Yoshi et al. discovered that theta activity occurred when dogs were walking, but not while they were eating. Vanderwolf (1969) corroborated these findings and suggested that theta was the “electrical sign for organizing and initiating higher voluntary motor acts.” He found that in rats gross voluntary motor acts such as walking, rearing, and jumping, were accompanied by hippocampal theta, whereas more automatic behaviors (e.g. licking, blinking, scratching, chewing) were accompanied by irregular activity. The results of Yoshi et al. were interpreted to mean that walking was a voluntary motor act, whereas eating was more automatic. Furthermore, Vanderwolf (1969) determined that the frequency and amplitude of theta co-varied with the speed and magnitude of the movement, respectively. For example, smaller movements, such as postural adjustments were accompanied by smaller amplitude and lower mean frequency theta. Other experiments have demonstrated the same phenomena. For example, wheel-running experiments involving rats have demonstrated that theta frequency is systematically related to the speed of movement initiation (Oddie et al., 1996; Shin & Talnov, 2001). A jump avoidance task, in which rats were trained to avoid a foot shock by jumping out of boxes of variable height, also demonstrated that as the magnitude of a movement increases, so does the amplitude of theta (Bland et al., 2006). Stimulation and lesion studies have also implicated the hippocampus in motor behavior and it is thought that the EEG rhythms produced by a particular area are reflective of that region's function (Bland, 1986). Furthermore, phase relationships between the theta cycle and motor behaviors have been found (Buno & Velluti, 1977; Komisaruk, 1970), suggesting a possible role for theta in the timing of motor responses.

1.5.1.1.2 Exploration/ Spatial Navigation

While hippocampal theta does seem to play a role in locomotion or motor behavior, some researchers contend that this rhythm is more closely tied to 'exploratory' behavior (Buzsaki, 2005). For example, it has been discovered that the theta rhythm is present in both cats and rats during sniffing behavior (Grastyan et al., 1966; Routtenberg & Kramis, 1968). This type of behavior, while seemingly automatic, is presumably crucially involved in spatial exploration and navigation for certain animals. Many experimenters have demonstrated that the phase of the theta rhythm correlates with 'sniffing' and 'whisking' motor output (Macrides et al., 1982, Komisaruk, 1970). Other behaviors conceived of as ‘exploratory’ involve orienting, and rapid eye movement (REM) sleep, both of which are associated with the presence of theta activity (Kahana et al., 2001).

Closely related to exploration and movement, are the concepts of spatial navigation and place coding. Particular pyramidal cells located in the hippocampus respond preferentially when an animal enters what is called the place field of that cell. Interestingly, the theta rhythm is tied closely to the firing of these cells. The firing of the place cell is not constant with the phase of the ongoing theta cycle, but rather, changes systematically. As a rat traverses a place field the firing of these cells occurs at a progressively earlier phase of the ongoing theta cycle (O’Keefe & Reece, 1993). This is called theta phase precession, and this phase of firing information has proven useful for reconstructing a rat’s position in space (Jensen & Lisman, 2000). Theta oscillations in this context are thought then, to represent the neural coding of place. Similarly, if the theta rhythm is disrupted in the hippocampus, performance on spatial tasks is also impaired (O’Keefe & Conway, 1980; Sutherland & Rodriguez, 1989).

1.5.1.1.3 Learning & Memory

Investigative and exploratory behaviors promote the learning of and memory for novel environments. It follows then, that other theories regarding the function of theta oscillations have involved learning and memory processes, a somewhat broader category of behaviors. Indeed, there is support for these theories as well. One of the most compelling studies in this area has demonstrated that the amount of theta activity in the hippocampal EEG can predict a rabbit’s learning rate in an eye blink conditioning task (Berry & Thompson, 1978). A related study examined conditioning trials only in the explicit presence or absence of spontaneous theta.

Training was administered during either situation and results indicated that animals learned significantly faster when given theta-contingent training as opposed to nontheta-contingent training (Griffin et al., 2004). Furthermore, lesioning and drug manipulation studies have shown that disruption of the theta rhythm can also disrupt conditioned learning (Berry & Thompson, 1979; Winson, 1978). These studies suggest that not only is theta involved in behavioral learning, but it may also underlie synaptic plasticity.

Evidence for theta's involvement in synaptic plasticity and cellular changes associated with learning have been documented, both in vivo and in vitro. In 1986 Larson et al. found that by electrically stimulating axons in the hippocampus with theta pattern frequencies, long-term potentiation (LTP) could be effectively induced. Later it was discovered that the timing, rather than the frequency of the stimulation is what determines the synaptic modification. The phase of the theta wave at which stimulation is delivered determines the type of plasticity that is induced (Orr et al., 2001). If stimulation is delivered at the peak of the theta cycle, LTP is induced (Pavlides, 1988; Holscher et al., 1997), whereas if it is delivered at the trough, long-term depression (LTD) occurs (Huerta & Lisman, 1996).

1.5.1.2 The Theta Model of Sensorimotor Integration

In both animal and human studies, the function of theta oscillations has been hotly debated. Theories ranging from the control of movement, to exploration and navigation, and learning and memory have been discussed. However, virtually every conceivable behavior has been associated with theta activity at one point or another (Buzsaki, 2005). A more general function of theta has been proposed, and that is to integrate sensory and motor information (Bland, 1986). If we consider all of the behaviors that non-human theta has been previously associated with, integration of sensory and motor information in order to perform that particular behavior is consistently necessary. We have a great deal of knowledge as to how the sensory system works, and similar knowledge regarding the motor system. However, how the two systems communicate with one another and interact has remained elusive.

The theta model of sensorimotor integration was derived from earlier animal studies that documented the involvement of theta during voluntary motor behaviors. Studies conducted by Vanderwolf et al., provided some of the first evidence that the hippocampus was associated with voluntary motor behaviors and that theta oscillations may underlie their initiation. While this was interesting and suggested a correlation between theta and movement, more rigorous experimentation was needed in which variables were manipulated. In an interesting set of experiments, Black et al (1972), operantly conditioned dogs to either move or remain immobile. Stimuli were presented to the animals indicating which behavior was to be expressed in order to avoid a shock. It was found that hippocampal theta only occurred during the movement condition. In order to eliminate the possibility that theta was the result of proprioceptive feedback from the muscles, the dogs were then paralyzed with galamine. Again, the theta rhythm was only present during conditions in which the stimuli indicating movement was presented. However, in direct opposition to these studies, were documentations of theta occurring during alert immobility and anesthesia (Maclean et al., 1956; Klemm, 1971; Harper, 1971).

It was Kramis et al (1975) who first proposed the existence of two types of theta in both the rabbit and the rat, and this idea has formed the basis for the theta model of sensorimotor integration. Different types of theta have been differentiated according to when they occur and their pharmacologic responsiveness. Lower frequencies of theta have been associated with movement-related immobility and can be abolished by administration of atropine-sulfate, whereas higher frequencies of theta have been associated with voluntary movement and are atropine-resistant. Type 1 theta is the movement related theta, originally described by Vanderwolf (1969) as the electrical signal for initiating voluntary movement. Type 2 theta is the immobility related theta, which occurs in the absence of movement (Bland, 2007). The sensorimotor integration model asserts that components of the neural circuitry underlying production of theta oscillations provide voluntary motor systems with continually updated feedback relative to sensory conditions. Thus, it is assumed that any time Type 1 theta is present, Type 2 theta is also present obligatorily. Presumably, in order to initiate and express a movement, that movement must also be continually updated. This model (Bland, 2007) suggests that the theta rhythm is a potential neural mechanism underlying integration in rats. However, it remains undetermined whether this model can be extended to humans. A major problem with the human studies thus far was the lack of systematic investigation into the function of theta. Many correlational studies have been reported (Mitchell et al., 2008), but in order to draw stronger connections between the animal and human studies, similar paradigms need to be employed, and more structured hypothesis-testing needs to occur.

1.5.1.3 Cortical Theta in Humans

1.5.1.3.1 Frontal-Midline Theta

While the theta rhythm is robust in the hippocampus of animals, the theta band rhythm is more difficult to examine using human subjects and its existence in the adult EEG has been debated (Niedermeyer & Lopes da Silva, 2005). Nevertheless, many researchers have documented cortical rhythmic activity occurring over the frontal midline region of the scalp in the 4-8 Hz range. This rhythm has been described as frontal midline theta and researchers have been interested in determining its functional significance and whether or not it is related to the hippocampal theta rhythm (Mitchell et al., 2008). Even more so than hippocampal theta, the behavioral correlates of frontal midline theta are controversial. Frontal midline theta has been implicated in a variety of behaviors, many of which overlap with correlates of hippocampal theta, and others which do not.

Frontal midline theta has been proposed to be involved in mental functions, attention, and effort. For example, Mundy-Castle (1957) documented theta's involvement during mental arithmetic tasks. Similarly, frontal midline theta has been documented during variants of mathematical sequencing tests (Ishihara & Yoshi, 1967) and mirror drawing tasks with varying grades of difficulty (Mizuki et al., 1982). Nakashima & Sato (1993) determined a relationship between frontal midline theta and level of concentration during simple reaction tasks. In this paradigm, subjects were presented with both a warning signal and a signal to respond. Results indicated that frontal midline theta appeared between the warning and the signal to respond, which was interpreted to suggest concentration as a function of theta. Frontal midline theta has also been documented during periods of meditation (Banquet, 1973), and long-term meditators have been shown to display increased theta power as compared to short-term meditators (Aftanas & Golocheikine, 2001). As well, frontal midline theta has been reported in air traffic controllers during simulated air traffic control tasks. Higher difficulty situations were shown to result in increased frontal midline theta (Brookings et al., 1996). Flight simulation tasks in which the task was more difficult have also reported increases in frontal midline theta (Smith et al., 2001). Like hippocampal theta, frontal midline theta has also been suggested to play a role in memory processes. For example, increases in theta power have been observed with increasing memory demands on both the *n*-back task and the Sternberg working memory task (Jensen & Tesche, 2002; Gevins et al., 1997; Onton et al., 2005; Krause et al., 2000). In both paradigms, subjects are required to simultaneously encode, maintain, and retrieve information. However, differences between encoding and retrieval have also been associated with the theta rhythm. In a study by Klimesch et al. (2001), greater theta synchronization over frontal regions was demonstrated during retrieval compared to encoding during a recognition task. In other memory studies, it has been shown that theta increases during the encoding phase and that it is related to successful retrieval later on (Sederberg et al., 2003; Caplan & Glaholt, 2007). Furthermore, it has been suggested that modulations of theta oscillatory activity are associated with retrieval of information from long-term memory. Specifically, Gruber et al (2008) have proposed that familiarity is reflected in the gamma band while recollection is reflected in the theta band.

1.5.1.3.2 Intracranial Recordings

Most of the literature on frontal midline theta has been conducted using electroencephalographic scalp recordings, which represent summed synchronous activity of local field potentials. This has been in contrast to the previously mentioned animal studies, which have examined both local field potentials (LFPs) and single unit recordings from a specific area of the brain, the hippocampus. A great technique for bridging this gap between the two levels of analyses is intracranial EEG recordings (iEEG; Kahana et al., 2001). While intracranial recordings still record local field activity, an advantage of this procedure is that the source of the underlying rhythm can be determined more precisely, as the problem of volume conduction is minimized. In the rat brain the hippocampus is so large that the opposite problem occurs and it is difficult to determine alternate potential sources that could be generating a rhythm. In humans however, muscle artifacts, including eye movement artifacts, can be avoided with intracranial recording. On the other hand, iEEG recordings are generally obtained from epileptic patients who are undergoing clinical procedures to locate the foci of their seizures. Thus, it is important to note that these studies may not generalize to healthy populations, and that electrode recordings are often restricted to specific sites (Caplan et al., 2001). Nevertheless, many intracranial studies have provided insight into the human theta rhythm.

Theta has also been implicated in a number of tasks involving spatial navigation, and the learning of spatial information. These findings resonate with the hippocampal theta studies, which have also implicated theta oscillations in similar behaviors. Kahana et al. (1999) examined theta activity in relation to maze learning in a population of epileptic patients, using iEEG recordings. During learning of the maze, theta activity was the predominant rhythm that was recorded. Furthermore, theta oscillations occurred more frequently during complex mazes and during recall trials as opposed to learning trials. In 2003, Caplan et al employed a virtual taxi driver task while recording iEEG. Participants were required to alternately 'search' for passengers at random and unknown locations, or 'goal-seek' learnable, fixed target locations. It was demonstrated in this study that theta oscillations occurred during both sets of behaviors, but in particular, were present during virtual movement as opposed to stillness. In 2005, Ekstrom et al performed a similar experiment and recorded from the hippocampus and neocortex. They found that theta increased during virtual movement, and that hippocampal and cortical theta correlated with one another. Because theta was observed during virtual movement and searching (behaviors associated with coordinated sensory and motor activities), these findings are supportive of the theta model of sensorimotor integration in humans.

Given that cortical theta has been observed in humans during complex cognition, I sought to determine whether the theta model of sensorimotor integration could be extended to humans in

Chapter 2. I measured oscillatory EEG activity during visually guided and delayed goal-directed reaching (see fig 2-01), for which sensorimotor networks differ— ventral stream areas are recruited in delayed, but not visually initiated actions. I found that theta oscillations were more prevalent during movement initiation and execution, consistent with a sensorimotor function of theta. Furthermore, theta was significantly more prevalent at temporal sites in delayed, than visually guided reaching during action-planning (see fig 2-05), suggesting that theta is present within the relevant sensorimotor network. The results suggest that theta synchronization may represent broadly applicable rhythmic mechanisms for integration and sensorimotor function in the brain.

1.5.2 The Mu Rhythm

Also known as the rolandic or central rhythm, mu activity was first reported in the 1950s (Chatrian, Petersen, & Lazarte, 1959; Gastaut & Bert, 1954). Initially, it was believed that this rhythm occurred infrequently, and only in a small percentage of the population (Koshino & Isaki, 1986). With advances in technology however, like the use of independent component analysis (ICA), today it is accepted that the mu rhythm occurs in most all healthy adults (Makeig et al., 2002).

1.5.2.1 Mu During Sensorimotor Behavior

To date, the mu oscillation has been the chief rhythm associated with human sensorimotor function. Though it occurs within the same frequency band as alpha (8-16 Hz), mu is both topographically and functionally distinct. Alpha activity is reported to occur over posterior occipital areas during resting wakefulness, while mu is present over the motor cortex and is strongly related to its functions (Niedermeyer & Lopes da Silva, 2005). Displaying a pattern opposite to what we expect of theta, mu activity is present during periods of stillness and desynchronizes with movement. Because of its presence during inactivity, mu has been conceived of as an 'idling' brain state. Synchronization of mu is thought to reflect inactivation of cortical areas while its desynchronization reflects cortical activation (Pfurtscheller, Stancak, & Neuper, 1996). Consistent with this, Pfurtscheller et al. (1997) reported enhancement of the mu rhythm in the motor cortical hand area during foot movement, for which activation of the hand area is unnecessary. Researchers today are becoming more and more interested however, in the relationship between mu activation and suppression patterns and whether and how they might relate to differential aspects of sensorimotor behavior (Pineda, 2005).

In Chapter 2, I tested the hypothesis that mu suppression is a sensorimotor phenomenon and not just a motor phenomenon. I examined mu activity during visually guided and delayed actions, which rely on different amounts of sensory-perceptual based neural activity. Using a goal-directed reaching paradigm (see figure 2-01), participants were auditorily cued to reach towards target dots appearing on a touchscreen while EEG activity was recorded. Mu activity was present prior to movement and desynchronized during the movement, replicating the classic behavioral dependence of mu (Niedermeyer & Lopes da Silva, 2005). However, mu activity was more desynchronized during delayed reaching (see figure 2-05). These results suggest that mu desychronization reflects sensorimotor and not just motor processes.

1.6 Conclusion

The overarching purpose of this research programme was to investigate which electrophysiological signals reflect sensorimotor integration and test which aspects of behaviour are reflected in the modulation of these signals. In order to address these issues, I incorporated what is known about human visuomotor integration with what is known about animal sensorimotor integrative processes. Results of the following studies broaden our understanding of how rhythmic and non-rhythmic brain activity produces effective sensorimotor behaviour.

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Chapter 2:

Theta Oscillations Reflect a Putative Neural Mechanism for Human Sensorimotor Integration

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2.0 Introduction:

Electroencephalographic recordings from the hippocampus of many animals reliably display a robust, large amplitude oscillation with frequency 3–12 Hz. These theta oscillations have been implicated in various animal behaviors, including locomotion (Black & Young, 1972; Buno & Velluti, 1977; Komisaruk, 1970; Vanderwolf, 1969; Yoshii, Shimokochi, Miyamoto, & Ito, 1966), exploratory behavior (Buzsaki, 2005; Grastyan, Karmos, Vereczkey, & Kellenyi, 1966; Kahana, Seelig, & Madsen, 2001; Macrides, Eichenbaum, & Forbes, 1982; Routtenberg & Kramis, 1968), neural coding of place (Jensen & Lisman, 2000; O'Keefe & Conway, 1978; O'Keefe & Recce, 1993; Sutherland & Rodriguez, 1989; Yamaguchi et al., 2007), and memory (Berry & Thompson, 1978; Berry & Thompson, 1979; Griffin, Asaka, Darling, & Berry, 2004; Winson, 1978). As well, theta oscillations have been implicated in modulating synaptic plasticity (long-term potentiation, LTP, and long-term depression, LTD; Holscher, Anwyl, & Rowan, 1997; Huerta & Lisman, 1996; Larson, Wong, & Lynch, 1986; Orr, Rao, Houston, McNaughton, & Barnes, 2001; Pavlides, Greenstein, Grudman, & Winson, 1988). However, Bland (1986) proposed an alternative (but compatible with the learning function) view of the general function of theta oscillations: to integrate sensory and motor information during sensorimotor behavior (Bland, 2009; Bland & Oddie, 2001). Bland's theta sensorimotor integration model posits that theta oscillations function like a carrier wave, which the sensory and motor systems use to inform and update one another, and coordinate their activity (Bland, Declerck, Jackson, Glasgow, & Oddie, 2007). The model was developed to explain integration in rats and it is not clear whether and how the model might apply to the human brain.

The theta rhythm is more difficult to study in human subjects, as it is not as robust as in the hippocampus of animals. Characteristics of theta activity in the adult EEG are even still debated

(Mitchell, McNaughton, Flanagan, & Kirk, 2008; Niedermeyer & Lopes da Silva, 2005). Nevertheless, many researchers have documented large-amplitude rhythmic activity occurring symmetrically over the frontal region of the scalp in the 4–8 Hz range, termed frontal midline theta. Researchers have been interested in determining its significance and whether or not it is related to the hippocampal theta rhythm, without clear resolution (Mitchell, McNaughton, Flanagan, & Kirk, 2008). Given this controversy, it is perhaps not surprising that the behavioral correlates of human cortical theta activity remain unclear. Cortical theta activity has been implicated in a variety of behaviors, many of which overlap with correlates of rat hippocampal theta, and others which do not. For example, cortical theta activity has been proposed to be involved in mental functions, attention, and concentrated effort (Aftanas & Golocheikine, 2001; Banquet, 1973; Brookings, Wilson, & Swain, 1996; Ishihara & Yoshii, 1967; Mizuki, Takii, Tanaka, Tanaka, & Inanaga, 1982; Mundy-Castle, 1957; Nakashima & Sato, 1993; Smith, Gevins, Brown, Karnik, & Du, 2001), memory processes (Gevins, Smith, McEvoy, & Yu, 1997; Gruber, Tsivilis, Giabbiconi, & Muller, 2008; Jensen & Tesche, 2002; Klimesch et al., 2001; Krause et al., 2000; Onton, Delorme, & Makeig, 2005; Sederberg, Kahana, Howard, Donner, & Madsen, 2003), learning and spatial navigation (Caplan, Madsen, Raghavachari, & Kahana, 2001; Caplan et al., 2003; de Araujo, Baffa, & Wakai, 2002; Ekstrom et al., 2005; Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999; Kahana, Seelig, & Madsen, 2001), and has been proposed to underlie sensorimotor integration in analogy with Bland's model (Caplan et al., 2003). One reason for the lack of clarity about the relevance of human theta activity may be a lack of task specificity. Many of the paradigms that have been employed require such complex, multifaceted behavior on the part of the participant (e.g. mental arithmetic, meditation etc.) that it is difficult to pinpoint a potential functional role for theta activity. Human cortical theta activity needs to be examined more systematically, and our aim was to directly test the hypothesis that this rhythm is involved in sensorimotor integrative processes, motivated by Bland's model of theta activity in the rat. Theta activity could be the expression of the neural phenomenon that itself guides state-dependent neural and information processing in a given area.

Cortical theta activity has seldom been reported before in purely sensorimotor tasks (Perfetti et al., 2010; Pfurtscheller, Brunner, Schlogl, & Lopes da Silva, 2006; Tombini et al., 2009). More commonly, the large-amplitude mu rhythm appears robustly during human sensorimotor function. This rhythm has a fundamental frequency around 10 Hz and is often thought to represent an idling state of the brain, present during periods of stillness and desynchronizing with movement (Niedermeyer & Lopes da Silva, 2005). The mu and human cortical theta rhythms that have been documented are nearby in frequency (8–12 Hz and 4–8 Hz, respectively) as well as recording site on the head (central lateral and frontal bilateral sites, respectively). If Bland's proposal that theta activity reflects sensorimotor integration is applicable to humans, we would expect theta activity to synchronize most during movement initiation and execution times— precisely when we know the mu rhythm desynchronizes. Because of the concurrent fluctuation of two closely related rhythms, we speculated that theta activity during sensorimotor tasks may have been previously overlooked by researchers primarily interested in mu activity.

To test whether Bland's theta sensorimotor integration model extends to humans we employed a sensorimotor reaching task, in which subjects were auditorily cued to reach toward target dots appearing on a touchscreen. We directly compared the amount of theta activity that was present during the preparatory (PREP), movement initiation (INIT), and movement execution (MOVE) phases for two different kinds of reaching. The reaching conditions were designed to manipulate the contribution of the ventral visuomotor stream by controlling the visibility of the target at different stages of the reach. Previous research has demonstrated that when a target object is in full view for the duration of a movement, the real-time visual image is able to guide the action to completion. Such ‘visually guided’ actions are known to depend on mechanisms residing in the parietal cortex of the dorsal stream. If however, immediate visual information is unavailable at the time a response is initiated, a perceptual memory of the target’s characteristics must be used to initiate the action instead. These types of actions still engage dorsal structures (Murata, Gallese, Kaseda, & Sakata, 1996), but according to the influential perception-action model of Goodale & Milner (1992), they also critically depend on perceptual mechanisms residing in the ventral stream. Behavioral and neuroimaging evidence suggests that even when occlusion of a target coincides with a response cue, or occurs shortly beforehand, ventral stream mechanisms are necessarily recruited (Armstrong & Singhal, 2011; Singhal, Culham, Chinellato et al., 2007; Singhal, Kaufman, Valyear et al., 2006; Westwood & Goodale, 2003). In the current study, the target disappeared at either the end of the participants’ reaction time (condition 1) or the beginning (condition 2), thereby altering the contribution of the ventral stream at the response initiation phase. While the target did not endure throughout execution of the movements (neither condition was “visually guided”), the dorsal stream should still be engaged, as a persistent target is a sufficient but not necessary criterion for the stream’s activation. On the other hand, ventral stream neural activity should differ between the two conditions, as recruitment of perceptual mechanisms should update and modify the motor plan at different stages of the response. We reasoned that if theta oscillations reflect the coordinatation of activity in sensory-processing and motor-production areas, theta activity should be adaptable, and present within sensory and motor regions that are required for a given task. Thus, we hypothesized that the pattern of observed theta activity, reflecting these changing sensorimotor networks, should differ between conditions, particularly at electrodes overlying the ventral visual stream. Our chief hypothesis was that theta oscillations reflect sensorimotor integration in general, leading to the prediction that theta activity would be present during movement, coinciding with the mu rhythm desynchronizing. Our second hypothesis was that there should be greater theta activity over ventral-stream areas when the visual target is occluded at the beginning (condition 2), rather than the end (condition 1) of the behavioral reaction time.

2.1 Methods

2.1.1 Participants

Twenty-seven (20 female, 7 male) right-handed undergraduate students, aged 18–25 (mean 21, SD=1.86) received payment for participating in this study. One participant's data was excluded from analyses due to persistent EMG contamination. All participants had normal or corrected-to-normal vision, and normal hearing. Written informed consent was obtained prior to the experiment and the methods were approved by the University of Alberta's ethical review board.

2.1.2 Procedure

The study was conducted in a darkened, electrically shielded, and sound-attenuated chamber. At the start of the experiment, participants were seated in front of a 430.4 mm x 270.3 mm touchscreen. At the beginning of each session, the touchscreen was re-calibrated by the participant being tested to ensure that accuracy measures remained reliable across subjects. Based on average distance from the screen, the vertical and horizontal visual angles of the touchscreen were 33.78 and 46.82, respectively. The vertical and horizontal visual angles of the stimuli were 1.98 and 1.13, respectively.

Our task required that participants reach towards and touch 9 mm x 14 mm black dots displayed on a touchscreen using E-Prime presentation software version 1.2 (Psychology Software Tools). The participant depressed a button to begin a trial. 1 second after the button was depressed, a target appeared on the screen in a random location. An 800 Hz, 64 dB (SPL) tone sounded 1-3 s after the target appeared. The participant was instructed to continue holding down the button until he/she heard the tone, and then to touch the target as quickly and accurately as possible. In condition 1, the target disappeared as soon as the button was released (i.e., with movement onset). After 1 s, if the participant had not yet initiated a movement, the target disappeared. In condition 2, the target disappeared simultaneously with the tone (Figure 1). Similar timing has been previously used (Armstrong & Singhal, 2011; Singhal Culham, Chinellato et al., 2007; Westwood & Goodale, 2003), and in our task the target disappeared in both conditions so that trials were made as similar as possible. By manipulating whether the target was available on the retina during movement onset, we were able to manipulate the network required to perform the task in a way that was imperceptible to participants (Westwood & Goodale, 2003, Singhal, Culham, Chinellato et al., 2007). After participants made contact with the screen, they were to return their finger to the response button, which advanced the next trial. Prior to testing, 4 practice trials were administered to ensure that participants understood the task. Condition 1 and condition 2 trials were presented in random order with the restriction that a particular condition did not occur more than 5 times consecutively. A total of 360 test trials (180 per condition) were included in a session and participants were given a break period for a self-determined length of time, every 120 trials.

2.1.3 Behavioral Analyses

For each condition, reaction time (RT), movement time (MT) and touch position were recorded. RT was defined as the time it took to initiate a movement in response to the beep, by lifting one's finger and releasing the response button, whereas MT was defined as the time it took to fully execute a movement, from release of the response button to contact with the touchscreen. Trials were considered to be accurate if the participant responded within 8 mm of the center of the target. Trials were excluded from analyses if RTs were ≤ 150 ms or ≥ 800 ms or MTs were ≤ 200 or ≥ 2000 ms. On average, 3% of trials were removed. Statistical analyses were carried out using Matlab 7.1 (The Mathworks) and SPSS version 18.0.

2.1.4 EEG Recordings and Preprocessing

EEG was recorded using a high-density 256-channel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR) and impedances were typically kept below 50 k. Voltage was sampled at 250 Hz and initially referenced to the vertex electrode (Cz). Signal was preprocessed using EEGlab 7.1.4 (Delorme & Makeig, 2004), running under Matlab 7.1 (The Mathworks). Signal was bandpass filtered from 0.5-50 Hz and was re-referenced to a common average. The dimensionality of the data was first reduced using Principal Component Analyses (PCA), keeping 150 components. Independent Component Analysis (ICA) was then performed to detect and remove artifacts from the data. Those components accounting for stereotyped artifacts, including eye blinks, eye movements, and muscle movements, were identified and removed from the data. Artifactual components were determined by visual inspection of the spectral characteristics, time courses, and spatial topographies of all components.

2.1.5 Oscillation Detection: Electrophysiological Analysis

The EEG signal was analyzed for oscillations using the wavelet-based oscillation detection method, BOSC (Better OSCillation detection, for further details, see Caplan, Madsen, Raghavachari, & Kahana, 2001; Whitten, Hughes, Dickson, & Caplan, 2011). One disadvantage of traditional spectral analyses is its sensitivity to non-rhythmic signals, possibly accounting for some of the lack of functional specificity of the neuronal dynamics underlying human theta oscillations (Mitchell, McNaughton, Flanagan, & Kirk, 2008). Transient artifacts may occasionally contribute to sharp increases in the power spectrum for a particular signal. To classify a signal segment as rhythmic, we wanted to ensure that sustained oscillations were occurring, and not simply increases in power (Caplan, Madsen, Raghavachari, & Kahana, 2001). In applying this method, signals were only classified as rhythmic if they exceeded a particular power threshold for a given frequency and a particular duration threshold. In calculating the power threshold for a given frequency, the BOSC method allows us to exclude from oscillation detection 95% of the background, "colored noise" spectrum, which is characteristic of all EEG signals. This ensures that oscillatory activity normally occurring by chance for a given frequency is taken into consideration (Caplan, Madsen, Raghavachari, & Kahana, 2001). Additionally, by setting a duration threshold of 2 cycles, we can be confident that the detected signal is rhythmically sustained. The proportion of BOSC-detected oscillations ($P_{episode}$) occurring at different frequencies was calculated to determine whether theta activity was present during this task. Analysis was confined to frontal, left and right motor, parietal, left temporal, and right temporal electrode clusters (Figure 2), regions that we expected could take part in the sensorimotor network. Each cluster was comprised of seven adjacent electrodes, which centered around an electrode corresponding to the traditional 10–20 system. The frontal cluster was centered on Fz, a frontal midline site where cortical theta activity has been previously reported.

The left motor cluster was centered on C3, a site where mu is commonly reported, and which is contralateral to participants' right-handed movements. The right motor cluster was centered on C4. The parietal (dorsal) cluster centered on Pz, and the left and right temporal (ventral) clusters on T5 and T6, respectively. We differentiated times of sensory processing, movement initiation, and movement execution by comparing oscillations during periods of 1 s before the auditory cue to move (PREP), between the auditory cue and when participants lifted their fingers from the response button (INIT), and between when participants lifted their finger from the response button and made contact with the touchscreen (MOVE). Frequency bands were defined as the following: theta: 4–8 Hz, mu: 8–16 Hz, and frequencies within a band were collapsed by averaging the proportion of oscillations present within that particular bandwidth. $P_{episode}$ values were corrected for non-normality with a log (odds ratio) transform. Then, $P_{episode}$ values within each band were averaged together, across individual electrodes within a cluster, and compared using repeated-measures ANOVAs. Greenhouse-Geisser correction was used to correct for non-sphericity where appropriate.

2.2 Results:

2.2.1 Behavioral Measures

Average movement time (MT), accuracy, and reaction time (RT) were compared between the two conditions using two-tailed, paired-samples t-tests. One participant was excluded from the accuracy analysis due to a touchscreen calibration error. Average MT was significantly longer in condition 2, compared to condition 1 (534.7 ms vs. 528.6 ms; $t(25)=-3.16$, $p<0.01$) and mean accuracy was also lower in condition 2 (74% vs 79%; $t(25)=4.62$, $p<0.01$). These results replicate previous findings that actions requiring more perception-based information are slower and less accurate because they may rely on the recall of target features (Goodale, Jakobson, & Keillor, 1994), which is likely less precise than using directly visually available information. Finally, response initiation times were faster in condition 2 than condition 1 (261.0 ms vs. 277.7 ms; $t(25)=12.75$, $p <0.01$).

2.2.2 Theta Oscillations

The time-frequency plots averaged across subjects are shown in Figure 3 and single-trial raw traces for a representative subject are shown in Figure 4. The average $P_{episode}$ (amount of time occupied by oscillations as a function of frequency) across subjects for each phase and condition is plotted in Figure 5. We first analyzed average $P_{episode}$ within the theta band. For each electrode cluster, we conducted 23 repeated-measures ANOVAs with factors reaching type (condition 1/condition 2), and phase (PREP/ INIT/ MOVE). A summary of results is presented in Table 1.

2.2.2.1 Frontal Region

The first region examined was the frontal electrode cluster, as the majority of human theta activity has been reported over frontal-midline sites. We hypothesized that frontal-midline theta activity reflects executive, or supervisory functions that could apply to a broad range of tasks, including many tasks that have not involved sensorimotor integration in the past. We asked whether frontal-midline theta activity was present during this basic goal-directed reaching task. If theta activity applies to sensorimotor behavior as well, there should be more theta activity at this region during INIT and MOVE than PREP. There should also be no significant difference between the reaching types, as processes associated with the frontal lobe (executive functioning, attention etc.) should be comparable between both types of reach. Consistent with this prediction, there was a main effect of phase [F(1.88, 47.10)=40.20, p<0.01], which was explained by posthoc pairwise comparisons as INIT > MOVE > PREP (see Figures 5 and 6a). All phases were significantly different from one another (p<0.01). The main effect of reaching type and interaction did not reach significance.

2.2.2.2 Motor Region

Because the task is sensorimotor in nature, integration of motor circuitry is necessary; thus, we expected to see theta modulation at motor region clusters (centered around C3, which is contralateral to the right-handed movement behavior, and C4). These electrodes may also be sensitive to activity in neighboring somatosensory cortex due to proprioceptive feedback during the reach. Because this region should be sensitive to motor (or proprioceptive) nodes of the sensorimotor network, we hypothesized that there should be more theta activity in this region during INIT and MOVE than PREP. Further, because the movements being made in the two conditions are quite similar (basic pointing), we expected very similar levels of theta activity between conditions. Similar to the frontal region, there was a main effect of phase [F(1.80, 45.10)=28.16, p<0.01], which was explained by posthoc pairwise comparisons as INIT > MOVE > PREP (see Figure 5). Again, all phases were significantly different from one another (p<0.01; Figures 6c and 6d). The main effect of reaching type and interaction were not significant.

2.2.2.3 Ventral Stream Regions

The left and right temporal electrode clusters were chosen to be locations we expected to see differences in reaching type, as these areas should be sensitive to ventral stream activity. Based on suggestions that the ventral stream is recruited to a greater extent in condition 2 (see

Introduction), we predicted that theta activity should be greater over ventral sites for this type of reaching. Both left and right temporal clusters were included because although participants are making right-handed movements, stimuli are presented in both visual hemifields. We hypothesized that there should be more theta activity in these regions during INIT than the other two phases, as the necessary perceptual information should be drawn on at this time. Motor planning will have begun prior to the INIT phase— the appearance of the target during PREP will initiate a series of sensory-transformations and activate cortical sensorimotor networks (Gordon, Ghilardi, & Ghez, 1994; Kettner, Schwartz, & Georgopoulos, 1988; Messier & Kalaska, 1997; Soechting & Flanders, 1989a; Soechting & Flanders, 1989b). However, the motor plan will be further updated and modified at the time of INIT, and ventral stream mechanisms will likely be engaged earlier in condition 2 than condition 1. At both clusters, there was a main effect of phase [left temporal: $F(1.73, 43.29)=30.65$, $p<0.01$, right temporal: $F(1.77, 44.23)=26.34$, $p<0.01$]. Similar to the frontal and motor clusters, the main effect for each was explained by posthoc pairwise comparisons as INIT > MOVE > PREP (see Figure 5). All phases were significantly different from one another ($p<0.01$; Figures 6e and 6f). A main effect of reaching type was not significant. However, the two-way interaction between phase and reaching type was significant at the left temporal region only [$F(1.65, 41.36)=4.49$, $p<0.05$]. Posthoc paired samples t-tests revealed that theta activity was significantly greater for condition 2 reaching during the initiation phase at this site [$t(25)=-2.16$, $p<0.05$; Figure 6e]. To our knowledge, this is the first study to provide electrophysiological evidence that ventral stream areas are necessarily recruited during reaching tasks requiring perception-based information, corroborating previous behavioral and neuroimaging findings.

It is important to consider, however, an alternative explanation of the result. A sequence of evoked potentials induced by the tone stimulus, each of which is not ‘in principle’ part of a rhythm, might happen to be evoked with approximately theta-period timing, and this type of pattern could be interpreted as reflecting either a rhythm, or a rhythmic sequence of discrete, non-repeating events. This difference is similar to a commonly made distinction between “evoked” (phase-locked to stimuli) versus “induced” (not phase-locked to stimuli) oscillatory activity (Basar-Eroglu, Struber, Schurmann, Stadler, & Basar, 1996). Thus, we sought to determine whether BOSC-detected oscillations in the event-related potential (ERP), which is reflective of evoked activity (whether rhythmic or not), could completely account for the BOSC-detected oscillations in the original raw trials (a combination of induced and evoked activity). If the reported rhythms could not be entirely explained by the portion of the signal observable in the ERP, then the activity could quite confidently be interpreted as truly rhythmic. In essence, it would be the brain producing the rhythmicity, not the timing of the task, nor an approximately rhythmic and coincidental sequence of evoked (non-rhythmic) potentials (but note: what follows conservatively eliminates any contribution from truly evoked oscillations as well).

We first computed the event-related potential (ERP). EEG was segmented into 20-s epochs, time-locked to the auditory cue to move (epochs extended 10 s prior to the tone to 10 s after). The long window ensured that this cross-check analysis could accommodate the variable duration times of the INIT phase. Trials were averaged together and baseline corrected relative to pre-stimulus activity (–100–0 ms). We then calculated the spectrogram of the ERP and divided each cell of this matrix by each cell of the initially computed trial-by-trial time-frequency matrix of $P_{episode}$ values. This estimates how large the oscillation would have been on each trial if evoked potentials were the sole contributor to our result. The $P_{episode}$ values in the theta band for the ‘estimated evoked’ signal (which were matched to the trial-by-trial durations of the INIT phase) were then subtracted from the initial theta-band $P_{episode}$ values for each trial. We truncated the subtracted $P_{episode}$ values at zero to avoid negative numbers. Difference values were then compared between condition 1 and condition 2 with a paired-samples t-test to determine whether a difference between reaching type remained. After conservatively removing any detected oscillations that could be due to evoked activity, the same difference was obtained: there was more theta activity in condition 2 than condition 1, and the significance was improved [$t(181)=-5.33$, $p<10^{-6}$]. Thus, the central result cannot be explained away as being entirely due to effects that are observable in the ERP. This includes phase-locked oscillations as well as discrete evoked potentials that happen to arise in an approximately rhythmic pattern.

2.2.2.4 Dorsal Stream Region

We considered the parietal electrode cluster (located near the dorsal stream) a control region to determine whether the topography of theta activity changes as the set of regions within the sensorimotor network changes. Condition 1 and 2 reaching are both reliant on the dorsal stream (Franz, Hesse, & Kollath, 2009; Hesse & Franz, 2009; Murata, Gallese, Kaseda, & Sakata, 1996); thus, theta activity should not differ between conditions at this site, as both types of reaching rely on its activation. The ANOVA revealed a main effect of phase [$F(1.58, 39.58)=32.31$, $p<0.01$] which was explained by posthoc pairwise comparisons as INIT > MOVE > PREP (see Figure 5). All phases were significantly different from one another ($P<0.01$; Figure 6b). The main effect of reaching type and interaction did not reach significance.

2.2.2.5 Theta Activity as a function of Region

Because frontal-midline theta is the main topographic pattern of theta activity that has been reported, we wanted to evaluate our hypothesis that it is largest in amplitude at anterior sites, potentially explaining why it has received more attention than theta oscillations with different topographies. Thus, we collapsed $P_{episode}$ across condition and reaching type and conducted a one-way ANOVA with the within-subjects factor region [5]. There was indeed a significant main effect [$F(3.21,80.16)=9.89$, $p<0.01$], with the greatest proportion of theta activity present at the frontal cluster, consistent with the bulk of human EEG-recorded theta having been reported here. Posthoc pairwise comparisons t-tests revealed that the frontal cluster differed significantly from the left temporal and parietal areas ($p<0.05$); the other comparisons were not significant.

2.2.3 Mu Oscillatory Activity

We also analyzed the average $P_{episode}$ within the mu band to determine whether the paradigm was as successful as previous sensorimotor studies at eliciting mu desynchronization. We conducted a 23 repeated-measures ANOVA with factors reaching type and phase at the left and right motor clusters, which is where we expected to see the greatest mu activity. We hypothesized that mu activity should desynchronize the most in this region during MOVE, when the reaches are being executed. Furthermore, if mu activity reflects principally an idling state there should be no difference between reach type, as mu desynchronization should simply reflect an override of that state in both conditions. However, if neural synchrony in the mu band has a more functional purpose, then differences between the conditions may be evident. In support of the latter conjecture, there was a main effect of phase for both left [$F(1.25, 31.17)=49.64$, $p<0.01$] and right [$F(1.57, 39.30)=39.14$, $p<0.01$] regions, explained by posthoc pairwise comparisons as INIT > PREP > MOVE. However, only during the MOVE phase was mu activity significantly less than either INIT or PREP ($p<0.01$) at both left and right regions; INIT and PREP phases were not significantly different from one another (Figures 6c and 6d). There was no main effect of reach type at either region, and the two-way interaction at the right motor region was not significant. The two-way interaction between reach type and phase was significant at the left region [$F(1.70, 42.49)=3.77$, $p<0.05$]. Posthoc paired-samples t-tests revealed that mu activity was significantly lower during MOVE for condition 2 [$t(25)=2.26$, $p<0.05$; Figure 6c].

2.3 Discussion

The aim of this study was to test whether the sensorimotor integration model of theta activity extends to humans. Results reveal that rhythmic theta-band activity synchronizes in humans while mu activity desynchronizes during sensorimotor behavior. Theta activity increased significantly during initiation (INIT) and movement (MOVE) relative to preparation (PREP), and reached its greatest proportions during the initiation phase. At the left ventral site during initiation, theta activity was significantly greater for condition 2 than condition 1. Mu activity on the other hand, decreased significantly during movement, replicating the standard mu-rhythm pattern, yet was lower in presence in condition 2. These results suggest that network-specific theta synchronization in conjunction with mu desynchronization may represent broadly applicable rhythmic mechanisms for integration, including sensorimotor function, in the human brain.

2.3.1 Theta Activity and Sensorimotor Function

While EEG studies have rarely reported cortical theta-band activity during purely sensorimotor tasks, our results are consistent with those that have analyzed theta-band power, finding increased theta-band power during the planning phase of a catching task (Tombini et al., 2009), during the planning and execution phases of a choice-reaction task (Perfetti et al., 2010) and, intracranially, during motor imagery for sensorimotor planning (Hinterberger et al., 2008. Our results are also consistent with local field potential (LFP) recordings in monkeys, which found increased theta-band activity over motor cortex during movement planning and execution (Rickert et al., 2005; Mehring et al., 2003). In the present study, the BOSC method allowed us to confidently claim that the signal in the theta band is in fact rhythmic, in turn suggesting that these recent theta-band findings may also have included rhythmic theta oscillations. Taken together, results suggest that Bland's theta-based sensorimotor integration model can be extended both to non-human primate and human neocortical regions that presumably participate in the sensorimotor network.

2.3.2 Bland's Theta Sensorimotor Integration Model Revisited

Bland's model derives from earlier animal studies of hippocampal theta activity during gross voluntary motor behaviors, but not more automatic behaviors (Black & Young, 1972; Vanderwolf, 1969; Yoshii, Shimokochi, Miyamoto, & Ito, 1966). Our results reveal that theta activity in humans is also associated with voluntary motor behavior that is not restricted to learning and memory relevant function. Relative to baseline (preparation), theta activity increased significantly in our task during initiation and movement, providing strong support for the suggestion that human cortical theta activity may be physiologically and functionally related to hippocampal theta activity in animals (Mitchell, McNaughton, Flanagan, & Kirk, 2008). Furthermore, Bland's model was motivated by observations that two types of theta activity occur during sensorimotor behavior. Type 1 is the originally described, movement-related theta activity that has a higher frequency, whereas Type 2 is immobility-related theta activity that occurs in the absence of movement at a lower frequency (Bland, Declerck, Jackson, Glasgow, & Oddie, 2007). While a substantial shift in frequency is not readily apparent in the $P_{episode}$ plots (although visual inspection of Figure 5 suggests that peak frequency might depend to some degree on electrode location), theta activity does change systematically across the three phases of the task, just as Type 2 theta activity transitions to Type 1 during movement onset in animals.

The present paradigm successfully elicited theta activity in the absence of any “higher” cognitive or memory demands, and results are consistent with Bland’s model of hippocampal theta activity indexing a functional mechanism for sensorimotor integration (Bland, 1986; Bland & Oddie, 2001; Bland, Declerck, Jackson, Glasgow, & Oddie, 2007). A more general view of the role of theta oscillations may be that they facilitate precisely timed coordination amongst brain regions, which may or may not include the hippocampus (Burgess & Gruzelier, 1997; Jensen & Tesche, 2002; Klimesch et al., 2001; Payne & Kounios, 2009; Womelsdorf, Vinck, Leung, & Everling, 2010).

It is important to note however, that these results do allow for alternative interpretations. Namely, theta oscillations may not be a mechanism, but rather a by-product of a neurophysiological state conducive to sensorimotor integration. Whether any oscillatory signal has a mechanistic function should be included as a caveat to all oscillation research, as it is possible that rhythms are epiphenomena that reflect a change in the state of the network. Thus, while our results do not provide unequivocal evidence that theta oscillations are a central mechanism of sensorimotor integration, our results offer support for a hypothesis derived from a model that does assume this (Bland, 1986).

2.3.3 Theta Activity within the Relevant Sensorimotor Network: Condition 1 vs. Condition 2

The most compelling evidence for theta activity's involvement in sensorimotor integration is that the topography of theta activity changes as the cortical circuitry required to execute a behavior changes. Frontal and motor electrodes did not display differences in the amount of theta activity between condition 1 and condition 2 reaching, which is understandable given that both regions would be expected to contribute to sensorimotor integration to a similar degree in both conditions. Likewise, the parietal region did not display differences in the amount of theta activity between conditions, consistent with evidence that both types of reaching rely on the dorsal stream (Franz, Hesse, & Kollath, 2009). During the initiation phase, theta activity was greater for condition 2 at the left temporal region (located near ventral stream areas), corroborating behavioral, neuropsychological and neuroimaging reports that perceptual brain mechanisms in the ventral stream are recruited when planning perceptually driven hand actions (Armstrong & Singhal, 2011; James, Culham, Humphrey, Milner, & Goodale, 2003; Goodale, Milner, Jakobson, & Carey, 1991; Milner et al., 2001; Singhal, Kaufman, Valyear et al., 2006; Cohen, Cross, Tunik, Grafton, & Culham, 2009). Thus, as the sensorimotor network shifts to include ventral regions, theta activity increases at the ventral site, during the phase when perceptual mechanisms are recruited.

2.3.4 Has Theta Activity Been Previously Overshadowed in Sensorimotor Tasks?

To our knowledge, theta activity has only recently been reported in human sensorimotor tasks and may have been previously overlooked. The timecourses of these rhythms were visualized within the time-frequency spectrogram (Figure 3) as well as the raw trace (Figure 4):

approximately 500 ms before the auditory cue to move, mu rhythmic activity dominates the signal, giving way to theta oscillations at the onset of the movement. As mentioned in the Introduction, we suggest that the visual impact of the mu rhythm may have garnered researchers' attention, and theta activity may not have been as easily observed. Motivated by Bland's model however, we identified both human theta and mu activity in a sensorimotor task with little or no demand on learning.

Just as mu activity may have previously overshadowed frontal-midline theta activity, frontal-midline theta activity (even in memory and higher cognitive studies) may have overshadowed more posterior theta activity. Task-dependent theta activity at posterior locations may be harder to see if it is invoked at more transient times within experimental tasks, and a difference in source, therefore, might be easiest to see when comparing closely related tasks that vary in their underlying sensorimotor networks, as is the case here.

2.3.5 Theta Activity and Integration

A role for theta activity in sensorimotor integration may seem somewhat removed from alternate theories of frontal-midline theta activity indexing cognitive (Aftanas & Golocheikine, 2001; Banquet, 1973; Brookings, Wilson, & Swain, 1996; Ishihara & Yoshii, 1967; Mitchell, McNaughton, Flanagan, & Kirk, 2008; Mizuki, Takii, Tanaka, Tanaka, & Inanaga, 1982; Mundy-Castle, 1957; Smith, Gevins, Brown, Karnik, & Du, 2001) learning and memory processes (Caplan & Glaholt, 2007; Gevins, Smith, McEvoy, & Yu, 1997; Jensen & Tesche, 2002; Krause et al., 2000; Onton, Delorme, & Makeig, 2005). However, for arguably *all* reported behavioral correlates of theta activity (both animal and human), integration of information in various brain regions is demanded. Theta oscillations may reflect a mechanism for integration more generally, beyond the domain of sensorimotor behaviors, and serve to coordinate brain activity in a range of tasks for which integration is crucial. This includes learning and memory tasks at one end of the spectrum, and sensorimotor tasks at the other. While these functions may not be cleanly dissociable in practice, theories of theta activity in memory tend to be connected to findings that suggest theta activity has a local action; phase-coding sequential information and windowing LTP/LTD. In contrast, theories of an integrative significance for theta activity implicate long-range coordination and do not require memory or learning. Results of the present study challenge theories pertaining *only* to learning, memory, and cognitive functions, and it is plausible that the two roles co-exist.

Theta activity may also reflect a refinement of sensorimotor and other behaviors. Animal research has shown that while disruption of the hippocampal theta rhythm may sometimes abolish sensorimotor behaviors (Bland & Vanderwolf, 1972), it can also impair performance on goal-directed tasks, (Cornwell, Johnson, Holroyd, Carver, & Grillon, 2008; Hasselmo, Hay, Ilyn, & Gorchetchnikov, 2002; Winson, 1978), and greatly reduce the rate and the extent to which conditioned associations are learned (Berry & Thompson, 1979; Griffin, Asaka, Darling, & Berry, 2004; Seager, Johnson, Chabot, Asaka, & Berry, 2002). LFP research has also shown that theta activity in the motor cortex of monkeys correlates with intended movement direction (Rickert et al., 2005), which suggests theta activity may optimize performance by coding precise task details. In humans, increased theta power was found to correlate with improved performance on a repetitive catching task (Tombini et al., 2009), lending further support to this theory.

2.3.6 Mu and Sensorimotor Function

The mu rhythm has been the chief rhythm implicated in sensorimotor function

(Niedermeyer & Lopes da Silva, 2005), and our results are consistent with literature demonstrating bilateral mu desynchronization during movement. However, mu activity desynchronized more during condition 2 than condition 1 reaching, over the left motor region. While mu desynchronization reflects activation of specific motor areas during movement (Pfurtscheller, Neuper, Andrew, & Edlinger, 1997), it may also be sensitive to additional task demands (Pineda, 2005). Our results demonstrate that mu suppression is a sensorimotor, and not just motor phenomenon, as sensory input influenced the degree of desynchronization. Results are also consistent with the theory of mu activity as an analogue of the mirror neuron system (Altschuler et al., 1997; Rizzolatti & Craighero, 2004), a proposed mechanism for perception-action coupling. Because mu desynchronization occurs even when actions are observed or imagined (Pfurtscheller, Brunner, Schlogl, & Lopes da Silva, 2006; Woodruff & Maaske, 2010), additional desynchronization in condition 2 may reflect a combined effect of both motor cortical activation, and recruitment of perceptual mechanisms that are likely similarly engaged during motor imagery or imagined movement.

2.3.7 Higher-frequency rhythms

Although this study focused on low-frequency rhythms (theta and mu), higher-frequency oscillations in the beta and gamma ranges have also been implicated in non-human and human sensorimotor behavior (Donoghue, Sanes, Hatsopoulos, & Gaal, 1998; Engel & Fries, 2010; Fukuda, Juhasz, Hoechstetter, Sood, & Asano, 2010; Mehring et al., 2003; Murthy & Fetz, 1992; Neuper & Pfurtscheller, 2001; Perfetti et al., 2010; Schalk et al., 2008; Szurhaj & Derambure, 2006; Tzagarakis, Ince, Leuthold, & Pellizzer, 2010; Wilson et al., 2010; Zhang, Chen, Bressler, & Ding, 2008; Zhuang, Truccolo, Vargas-Irwin, & Donoghue, 2010). Thus, a full model of the role of rhythmic activity in sensorimotor integration will need to address how multiple frequencies contribute differentially to behavior.

2.3.8 Conclusion

Theta oscillations synchronized while the mu rhythm desychronized during a purely sensorimotor task. Both theta and mu activity responded to changes in the underlying sensorimotor network, suggesting a connection between animal and human electrophysiology. These findings support the notion that theta activity reflects underlying sensorimotor activities, whereas mu activity likely reflects levels of cortical activation during a sensorimotor task. If theta activity is a mechanism of not only sensorimotor integration, but of integration more generally, this may explain the broad range of complex cognitive tasks previously known to induce theta rhythms.

Figure 2-01

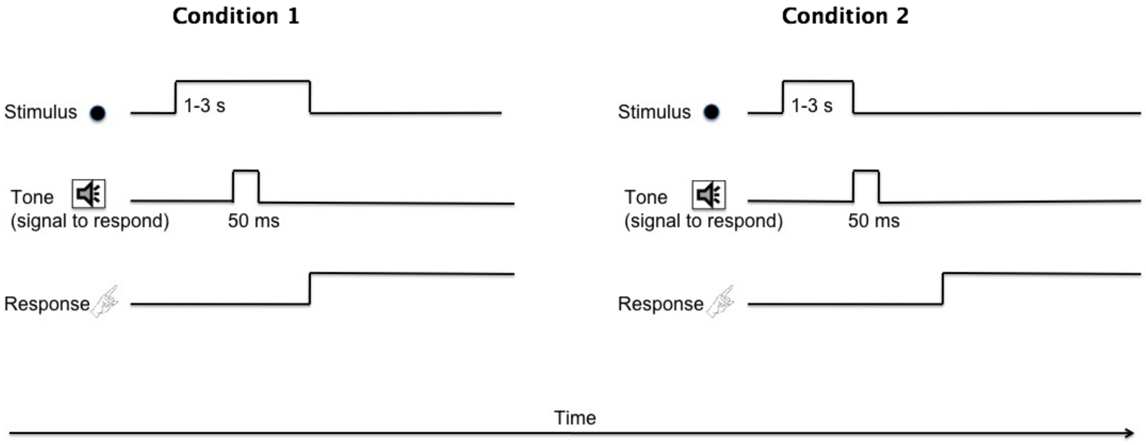

Condition 1
Condition 2
Stimulus
1-3 s
Tone
(signal to respond)
50 ms
Response
Stimulus
1-3 s
Tone
(signal to respond)
50 ms
Response
Time

Figure 2-01 Caption:

Schematic of the behavioral procedure. One hundred eighty trials of each condition were presented to participants within a session. In condition 1, the tone sounds and the stimulus disappears when the participant lifts his/her finger from the response box. In condition 2, the tone sounds simultaneously with the disappearance of the target.

Figure 2-02

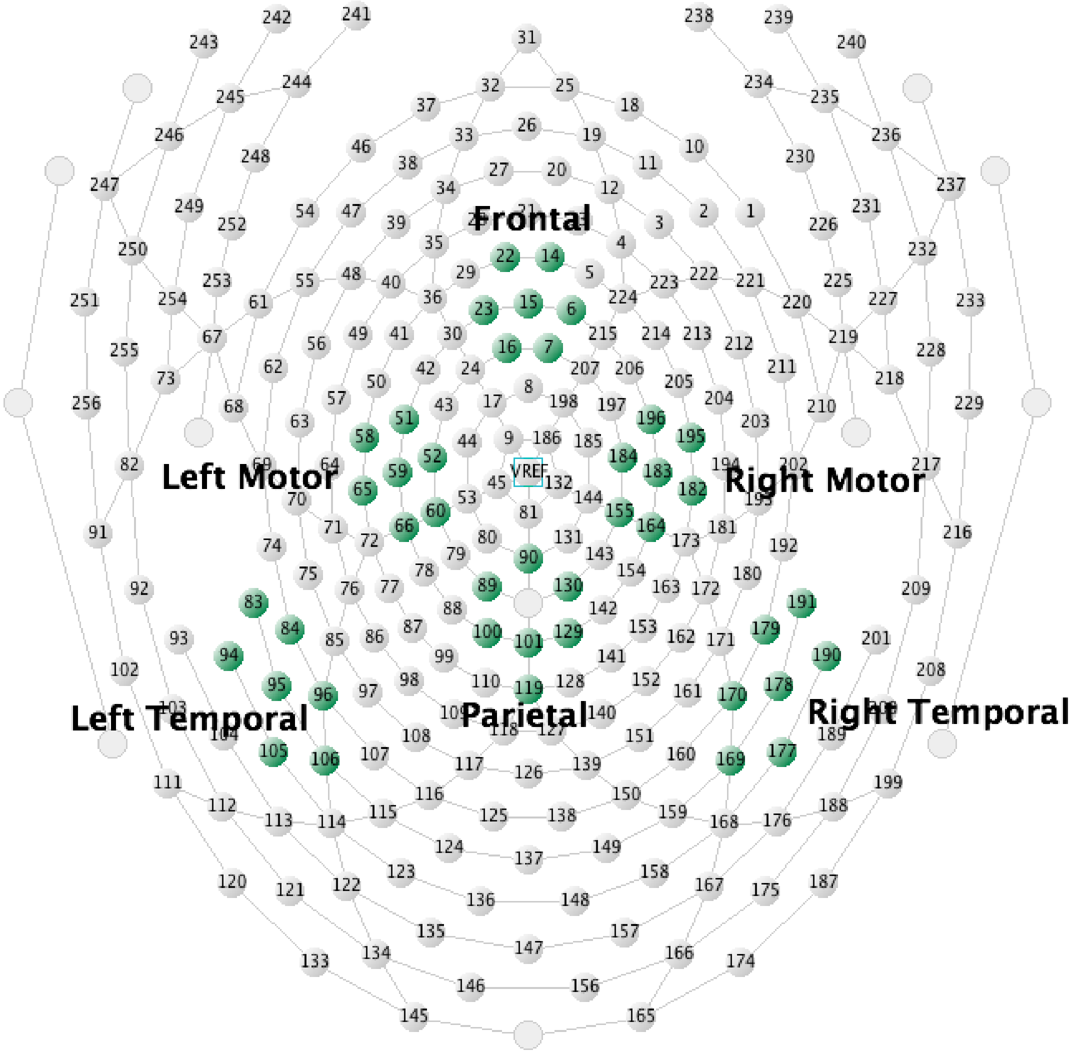
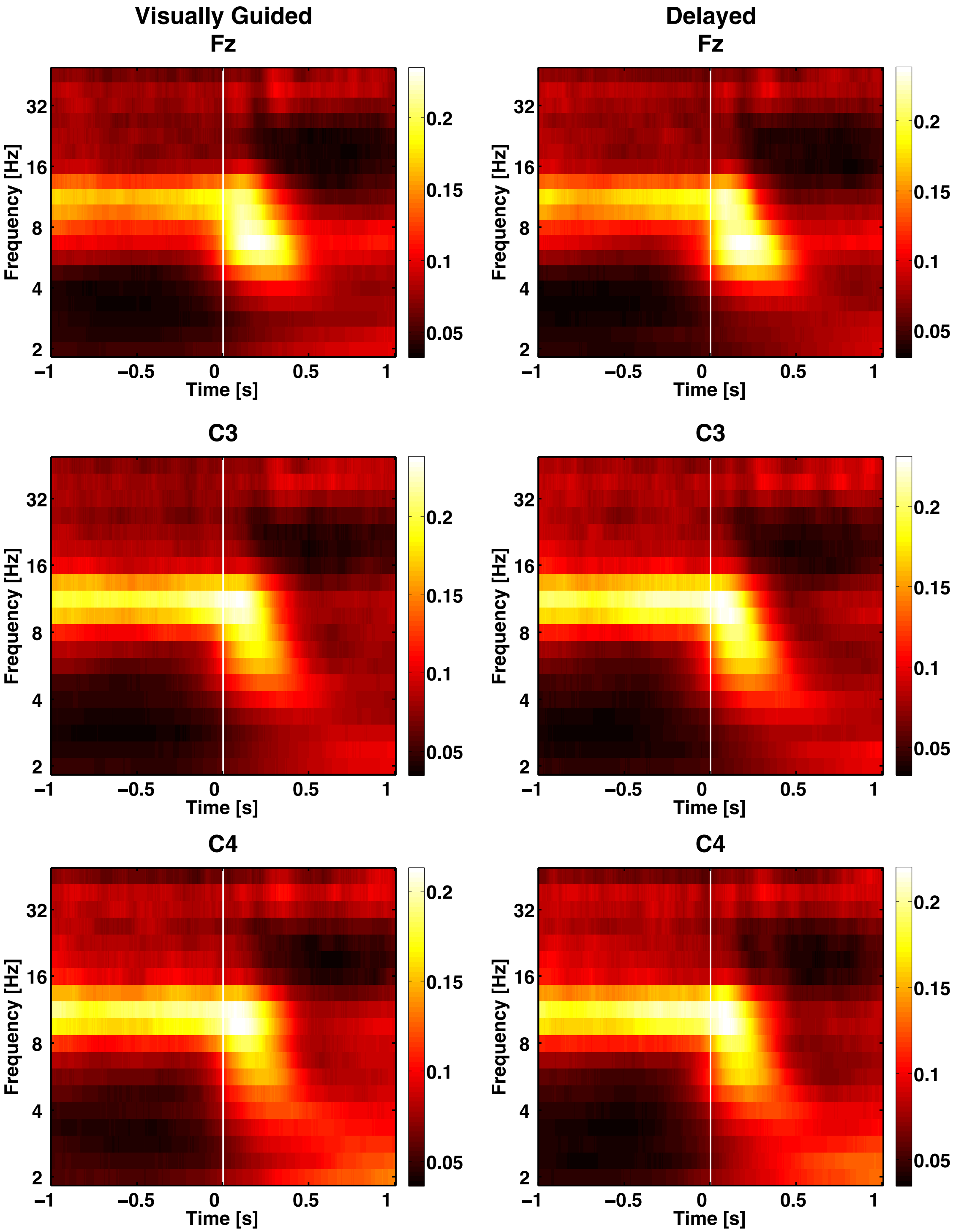

Frontal
Left Motor
Right Motor
VREF
Left Temporal
Parietal
Right Temporal

Figure 2-02 Caption:

Sensor layout and analysis clusters (shown in green). Oscillations within the mu and theta bands were analyzed at the frontal, motor, temporal (ventral), and parietal (dorsal) electrode clusters.

Figure 2-03



Visually Guided
Fz
Delayed
Fz
C3
C3
C4
C4
Frequency [Hz]
32
16
8
4
2
Time [s]
−1
−0.5
0
0.5
1
0.2
0.15
0.1
0.05

Figure 2-03 Caption:

Time-frequency plots averaged across trials at sites Fz, C3, C4, T5, T6, and Pz, 1 s before and 1 s after movement initiation (when participants lift their finger from the response box). Increased brightness is indicative of increased oscillatory activity for a particular frequency oscillation. Movement initiation occurs at time 0 and is indicated with a white bar, and touchscreen contact is made at time 1. At all electrodes, for both condition 1 and condition 2 reaching, 8- to 16-Hz mu oscillatory activity is present before the movement and desynchronizes with movement. Alternately, 4- to 8-Hz theta oscillatory activity synchronizes just before movement initiation and continues throughout movement execution.

Figure 2-04

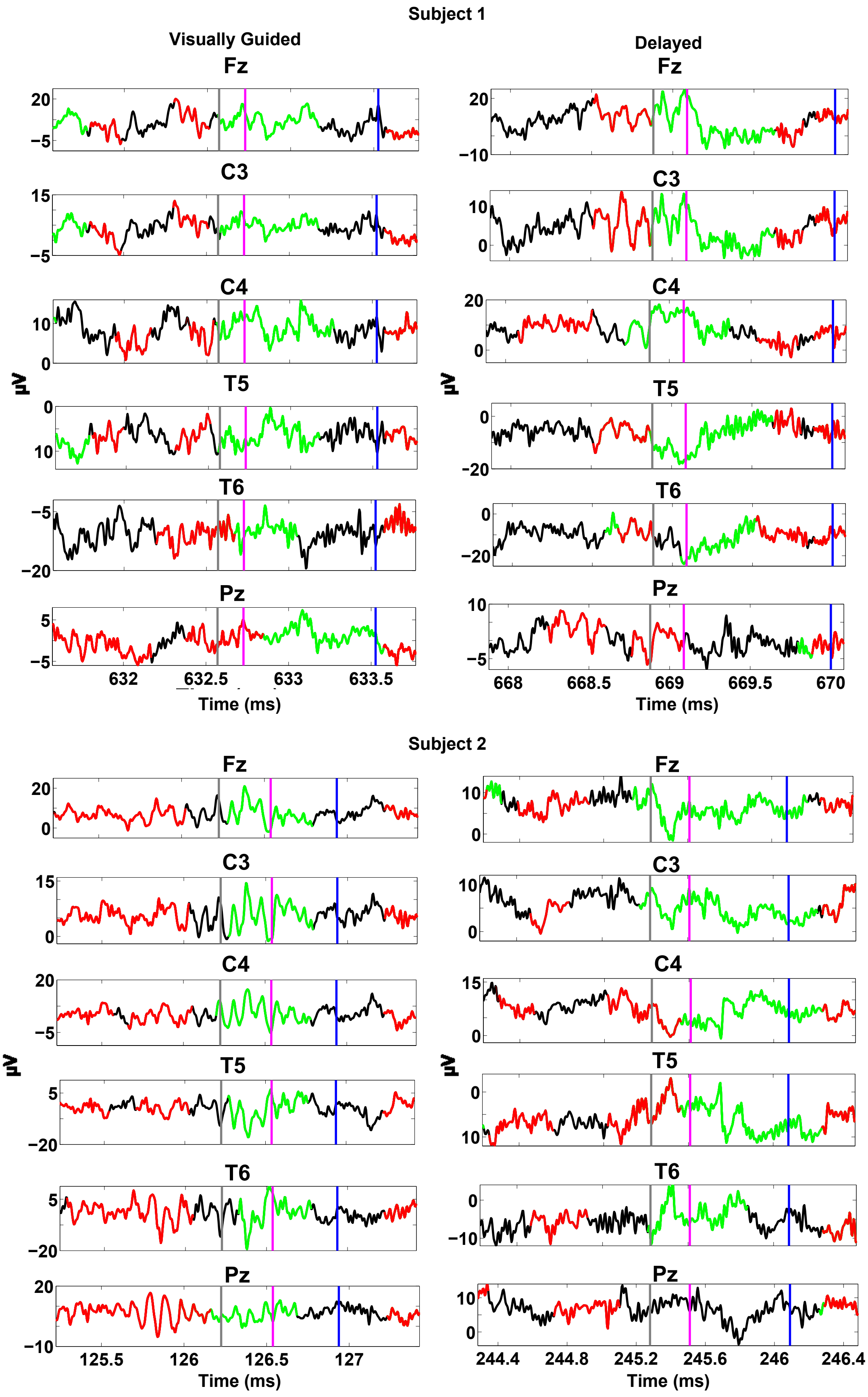

Subject 1
Visually Guided
Delayed
Fz
C3
C4
T5
T6
Pz
μV
20
−5
15
−5
10
0
0
10
−5
−20
5
−5
632
632.5
633
633.5
Time (ms)
20
−10
10
0
20
0
0
−20
0
−20
10
−5
668
668.5
669
669.5
670
Time (ms)
Subject 2
Fz
C3
C4
T5
T6
Pz
μV
20
0
15
0
20
−5
5
−20
5
−20
20
−10
125.5
126
126.5
127
Time (ms)
10
0
10
0
15
0
0
10
0
−10
10
0
244.4
244.8
245.2
245.6
246
246.4
Time (ms)

Figure 2-04 Caption:

Raw traces for single-trial data at each cluster's central electrode. Conditions 1 and 2 are shown for 2 representative subjects. BOSC (Better OSCillation)-detected mu oscillations are plotted in red. This rhythm desynchronizes around the time of the auditory cue to move, which is indicated by a gray bar. BOSC-detected theta oscillations are shown in green. In contrast to the mu rhythm, this rhythm synchronizes around the time of the auditory cue to move. For every trial, the time at which the response button was released is shown in pink and the time at which touchscreen contact was made is shown in blue.

Figure 2-05

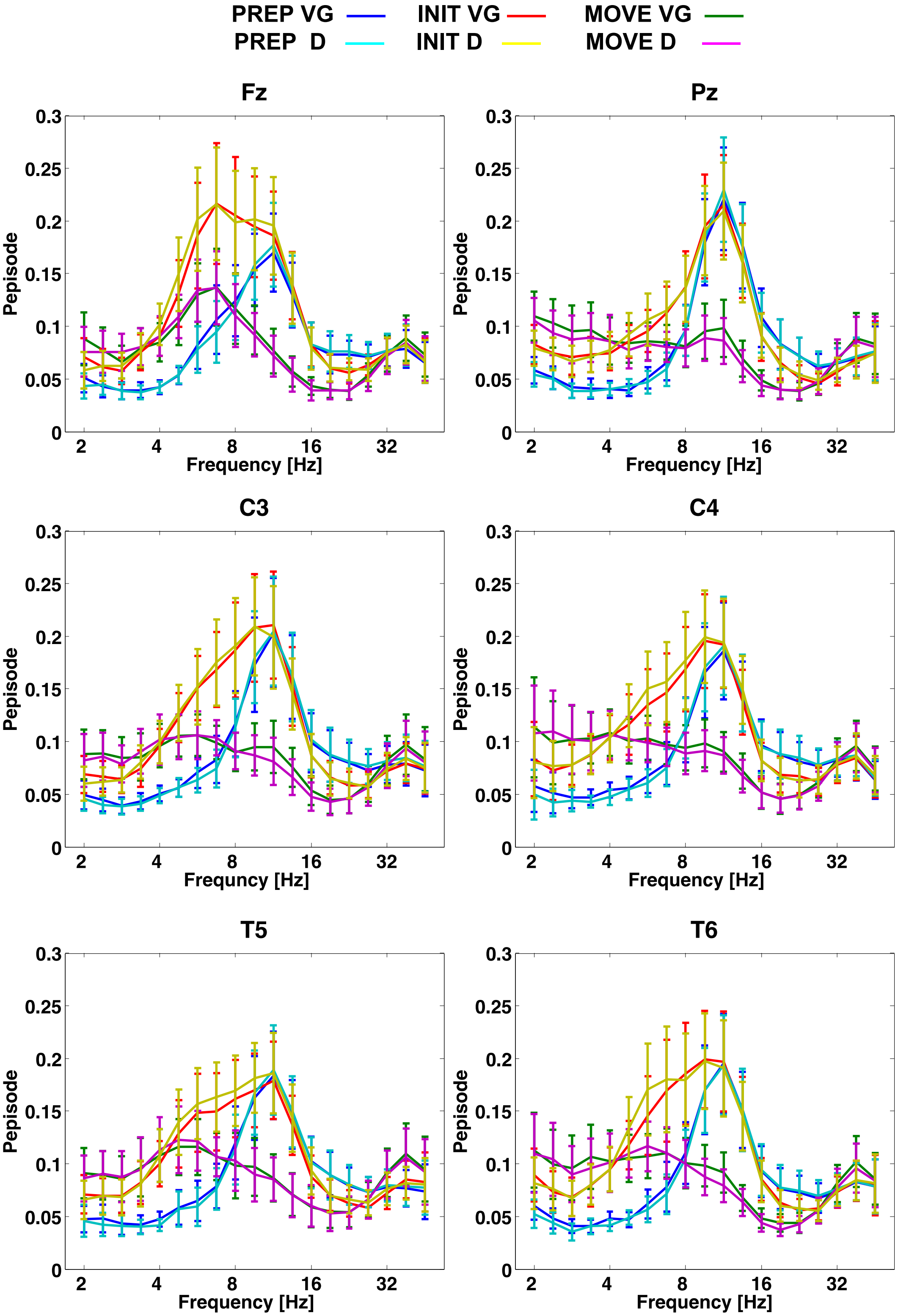

PREP VG
INIT VG
MOVE VG
PREP D
INIT D
MOVE D
Fz
Pz
C3
C4
T5
T6
Pepisode
0
0.05
0.1
0.15
0.2
0.25
0.3
2
4
8
16
32
Frequency [Hz]
Frequncy [Hz]

Figure 2-05 Caption:

Average proportion of oscillatory activity across conditions during preparatory (PREP), movement initiation (INIT), and movement execution (MOVE) phases. Error bars represent 95% confidence intervals. At electrode Fz, in both conditions (1 and 2), a strong increase in 4- to 8-Hz (theta) activity was observed during INIT and MOVE. Eight- to 13-Hz (mu) rhythmic activity at this electrode decreased during MOVE. At electrode Pz, small increases in theta were observed during INIT and MOVE, relative to PREP. Mu activity decreased during MOVE. At electrode C3, in both conditions, mu activity was observed during PREP and INIT and decreased with MOVE. Increases in theta activity happened simultaneously during INIT and MOVE. At electrode C4, in both conditions, mu activity was observed during PREP and INIT and decreased with MOVE. Increases in theta activity happened simultaneously during INIT and MOVE. At electrode T5, for both conditions, theta activity increased during INIT and MOVE, relative to PREP. During INIT, theta activity was greater during condition 2. Mu activity at this electrode decreased during MOVE. At electrode T6, for both conditions, theta activity increased during INIT and MOVE, whereas mu decreased during MOVE.

Table 2-01

Changes in Theta and Mu Oscillatory Activity for Each Condition During INIT and MOVE, Relative to PREP

	Theta						Mu					
	INIT			MOVE			INIT			MOVE		
Electrode Clusters	1	2	1/2	1	2	1/2	1	2	1/2	1	2	1/2
Frontal	↑	↑		↑	↑							
Left Motor	↑	↑		↑	↑		—	—		↓	↓	+
Right Motor	↑	↑		↑	↑		—	—		↓	↓	
Left Ventral	↑	↑	+	↑	↑							
Right Ventral	↑	↑		↑	↑							
Dorsal	↑	↑		↑	↑							

1=Condition 1 Reaching, 2=Condition 2 Reaching; (↑) = increase in oscillatory activity, (↓) = decrease in oscillatory activity, (—)= no change ($p<0.05$). (+) indicates when the synchronization or desynchronization of oscillatory activity is significantly greater for condition 2, compared to condition 1.

Figure 2-06

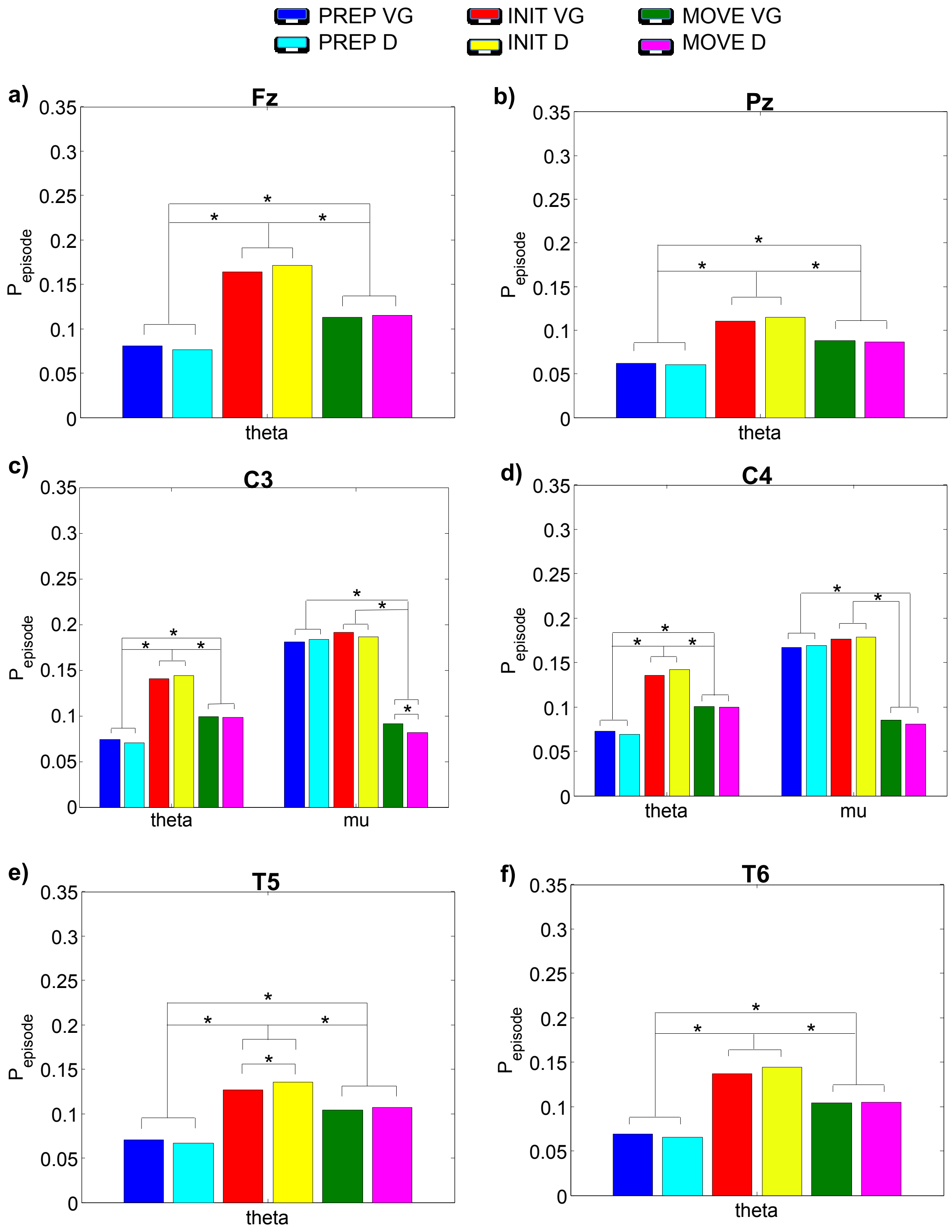

PREP VG
PREP D
INIT VG
INIT D
MOVE VG
MOVE D
a)
Fz
b)
Pz
c)
C3
d)
C4
e)
T5
f)
T6
$P_{episode}$
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
theta
mu
*

Figure 2-06 Caption:

Summary of the chief findings. Average $P_{episode}$ (amount of time occupied by oscillations as a function of frequency) is plotted as a function of condition for theta and mu bands (averaged across frequencies sampled within each band) at the respective locations analyzed (theta: Fz, Pz, C3, C4, T5, and T6; mu: C3 and C4). *$P < 0.05$.

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Chapter 3:

Human Electrophysiological Reflections of the Recruitment of Perceptual Processing During Actions that Engage Memory

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3.0 Introduction:

When individuals reach for an object in the environment, the movement characteristics of their arm and hand will often depend on whether the target object is in view or not. For example, when looking at a coffee cup while reaching for it, the real-time visual image of the cup may be used to guide the action. However, turning away from a coffee cup prior to reaching for it precludes the use of immediate visual information and a perceptual memory of the target characteristics must be used instead to guide the action. Behavioral studies have reliably shown that hand and arm kinematics vary between these action types, with the latter (memory-guided) actions tending to be slower and less accurate (Goodale, Jakobson, & Keillor, 1994). According to the influential perception-action model of Goodale & Milner (1992), visually guided actions are performed under the control of dorsal stream mechanisms in parietal cortex. However, this model also predicts that actions initiated in the absence of a visual target are influenced by mechanisms in the ventral stream, particularly those associated with inferior temporal cortex (Goodale, 1998). The perception-action model further suggests that a shift from dorsal to ventral activation is required when a target is unavailable, in order for previously stored perceptual representations to inform the motor plan (Westwood & Goodale, 2003). Converging neuropsychological, neuroimaging, and kinematic findings support this theory. For example, visual-form agnosia patient D.F., who has bilateral damage to her lateral occipital cortex (LOC) in the ventral stream, is perceptually compromised (James, Culham, Humphrey et al., 2003) but can guide her actions appropriately when the target object is in full view, presumably due to her intact dorsal stream (Milner, Dijkerman, Pisella et al., 2001; Goodale, Milner, Jakobson et al., 1991). These authors argue that D.F. is unable to correctly perform actions to disappearing targets because the damage to her ventral stream prevents perception of the object in the first place, and she cannot draw on the necessary perceptual information to act when the object is no longer in full view. Additional evidence for this perspective comes from behavioral studies that have shown that while visually guided actions are resistant to pictorial illusions, those that require previously stored perceptual representations are not. Erroneous perceptual information appears to influence behavior following a delay (Hu & Goodale, 2000; Westwood, Dubrowski, Carnahan et al., 2000; Westwood, McEachern & Roy, 2001; Ganel, Tanzer & Goodale, 2008). Furthermore, functional magnetic resonance imaging (fMRI) findings have shown that lateral occipital cortex (LOC) is re-activated in the action phase of a reaching and grasping paradigm when actions are performed without vision of a target (Singhal, Kaufman, Valyear et al., 2006), and transcranial magnetic stimulation (TMS) “virtual lesions” of LOC disrupts grasping when the object is visually unavailable, compared to when it is (Cohen, Cross, Tunik et al., 2009). Taken together, these studies suggest that when vision of a target is precluded, the motor program must rely on previously stored perceptual information in ventral stream regions.

Despite the compelling nature of the previously described studies, other findings suggest that the dorsal stream is also engaged for actions in which vision of the target is unavailable (Franz, Hesse, & Kollath, 2009; Hesse & Franz, 2009). This position is supported by monkey neurophysiology work showing sustained activity in parietal neurons across a memory delay following the presentation of a visual target, and prior to the initiation of the action toward it without vision (Murata, Gallese, Kaseda et al., 1996), a finding also supported by human fMRI data (Singhal, Kaufman, Valyear et al., 2006). One problem in addressing the extent to which different neural mechanisms subserve visually guided and perception-based actions in humans is that it is difficult to directly compare these action types using neuroimaging techniques. The primary reason for this is that the two types of action require differences in timing, and in the case of fMRI with visually guided actions it would be difficult to distinguish between LOC activation associated with target presentation from LOC activation associated with action. However, a strong advantage of the event-related potential (ERP) technique is that it provides excellent temporal resolution. Curiously, ERP is underrepresented in action-related research. Electrophysiological recordings are known be extremely sensitive to movement-related artifacts in action studies. However, this study was possible because it was focused on the response initiation phase prior to action execution, and employed strategic windows of analysis and artifact correction methods to minimize the effect of artifacts.

If perceptual processes are required for actions in which vision of the target is unavailable, a likely electrophysiological marker is the N170 ERP component. This component has been linked to perceptual processes in the ventral stream. It is elicited in response to visual stimuli and reflects the early classification of objects (Grill-Spector, Kourtzi, & Kanwisher, 2001; Rossion, Joyce, Cottrell, et al., 2003; Sreenivasan, Katz & Jha, 2007), which is likely a necessary perceptual component of perception-based actions. Moreover, the N170 likely has various neural generators, including a source in LOC (Rossion, Joyce, Cottrell, et al., 2003). Studies have also shown that the N170 is modulated by memory processes and becomes more negative in amplitude as memory requirements increase (Bankó & Vidnyánszky, 2009; Morgan, Klein, Boehm et al., 2008). This presents an additional link between the N170 and actions that cannot be guided by vision, as planning of these actions likely relies on the recall of target features, and presumably engages perceptual memory processes (Goodale & Milner, 1992; Klatzky, Pellegrino, McCloskey et al., 1993). One study has shown that if perceptual memory is engaged while performing actions to previously viewed targets, compared to those that remain visible, dual-task interference tends to be greater— likely due to the overlap in task demands or shared resources (Singhal, Culham, Chinellato et al., 2007). Additionally, it has been demonstrated that the LOC is active not only during initial form perception, but also as the percept of an object endures (Ferber, Humphrey & Vilis, 2003). This is consistent with the idea that perceptual information is stored, or maintained somewhere for brief periods of time before it is recalled during planning and execution. Since evidence suggests that the LOC is differentially activated by the perceptual memory demands associated with particular actions, we asked in the current study whether the N170 would reflect these differences. That is, would the amplitude of the N170 be larger in situations requiring more of a contribution from perceptual processes?

In short, we directly compared perception-based neural activity during the response initiation phase for two different reaching and pointing trials, which were designed to differentially manipulate the contribution of visual memory to the behavioral task. Due to the different visual memory demands, the contribution of the ventral stream likely also differed as a result of the manipulation. Moreover, since the N170 waveform likely reflects neural generators in ventral stream areas that include LOC, we tested the hypothesis that this waveform reflects motor planning processes for actions that are reliant on the ventral stream. We manipulated the visibility of a target during the response initiation phase of an instructed delayed reaching paradigm. The target was either present (condition 1) or absent (condition 2) during the response initiation phase, thereby altering the contribution of visual memory. Thus, condition 2 was predicted to recruit ventral stream resources more heavily than condition 1 during response initiation. We collected ERP data that were time-locked to the auditory cue, which signaled the participants to initiate a response. Our primary research question was as follows: Does the ERP, in response to the auditory cue for action, reflect more contribution from perceptual mechanisms in the ventral stream if the action is initiated towards a target that is no longer visible? If it does, then we would expect to observe an enhancement in the amplitude of the ERP in the post-stimulus range of the N170. We ensured that the auditory cue was identical for both conditions, and thus, we could attribute any differences in the ERP to the additional processing associated with the task requirements of each condition. If the amplitude of the ERP in the N170 latency range reflects differences between conditions, it may be that the observed effect is sensorimotor in nature, reflecting more than just sensory processing.

3.1 Methods:

3.1.1 Participants

Twenty-seven (20 female, 7 male) right-handed undergraduate students aged 18–25 (mean 21, SD=1.86) received payment for participating in this study. One participant's data was excluded from analyses due to persistent EMG contamination. All participants had normal or corrected-to-normal vision, and normal hearing. Written informed consent was obtained prior to the experiment in accordance with the University of Alberta's ethical review board, and the Declaration of Helsinki.

3.1.2 Procedure

The study, which includes the same data as reported by Cruikshank, Singhal, Hueppelsheuser & Caplan (2012) was conducted in a darkened, electrically shielded, and sound-attenuated chamber. At the start of the experiment, participants were seated in front of a 430.4 mm x 270.3 mm touchscreen that was rotated 90 so that the vertical angle was optimized for height. Participants positioned themselves so that the angle of his/her right arm could extend comfortably at a 45º angle, to reach the top of the touchscreen. The distance from the participant's nasion electrode to the monitor was taken and recorded, and measurements ranged from 35.56 to 51.82 cm (mean distance 40.39 cm from the screen). At the beginning of each session, the touchscreen was re-calibrated by the participant being tested to ensure that accuracy measures remained reliable across subjects. Based on average distance from the screen, the vertical and horizontal visual angles of the touchscreen were 33.78° and 46.82°, respectively. The vertical and horizontal visual angles of the stimuli were 1.98 and 1.13, respectively.

Our task required that participants reach towards and touch 9 mm x 14 mm black dots displayed on a touchscreen using E-Prime presentation software version 1.2 (Psychology Software Tools). The participant depressed a button to begin a trial. One second after the button was depressed, a target appeared on the screen in a random location, which the participant was told to fixate on. An 800 Hz, 64 dB (SPL) tone sounded for 50 ms 1–3 s after the target appeared. The participant was instructed to continue holding down the button until he/she heard the tone, and then to touch the target as quickly and accurately as possible. In condition 1, the target disappeared as soon as the button was released (i.e., with movement onset). After 1 s, if the participant had not yet initiated a movement, the target disappeared. In condition 2, the target disappeared simultaneously with the onset of the tone (Figure 1). After participants made contact with the screen, they were to return their finger to the response box and hold down the button, which advanced the next trial after 1 s. Prior to testing, 4 practice trials were administered to ensure that participants understood the task. Condition 1 and condition 2 trials were presented pseudo-randomly, with the restriction that a particular condition did not occur more than 5 times consecutively. A total of 360 test trials (180 per condition) were included in a session and participants were given a break period for a self-determined length of time, every 120 trials.

3.1.3 Behavioral Analyses

For each trial, reaction time (RT) and movement time (MT) were recorded. RT was defined as the time it took to initiate a movement in response to the beep, and MT was defined as the time it took to fully execute a movement, from release of the response button to contact with the touchscreen. Touch positions were recorded. Trials were considered to be accurate if the participant responded within 8 mm of the center of the target. During training, participants were required to achieve radial error accuracy and a binary measure was used for analysis. Trials were excluded from analyses if RTs were ≤ 150 ms or ≥ 800 ms or MTs were ≤ 200 or ≥ 2000 ms. The lower range of RTs was chosen based on research suggesting that auditory RTs are around 160 ms (Brebner & Welford, 1980); we did not want to include responses whereby the participant may have employed an anticipatory strategy. The upper limit was included in order to ensure that the conditions remained irrefutably separate. Because targets in condition 1 disappeared within 1 second if a participant had not responded, we wanted to ensure that any responses were made while visual information was still available. Otherwise, trials that were initially designed to rely on visual feedback during response initiation would by default, come to rely on perceptual processes instead. Thus, condition 1 trials could take on the properties of condition 2 trials by virtue of the participant's RT. By restricting MT, we also ensured that participants were indeed reaching with the hand that they were instructed to reach with, and that movements were executed in a reasonable time frame. The vast majority of RTs and MTs fell within the exclusion parameters, and < 3% of all trials were rejected based on these criteria. Statistical analyses were carried out using Matlab 7.1 (The Mathworks) and SPSS.

3.1.4 EEG Recording and Analysis

EEG was recorded using a high-density 256-channel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR), amplified at a gain of 1000 and sampled at 250 Hz. Impedances were kept below 50 k and the recording was initially referenced to the vertex electrode (Cz) before being converted to an average reference. In accordance with other studies examining the N170, we applied an offline bandpass filter of 0.5-30 Hz (Daniel & Bentin, 2010, Taylor, McCarthy, Saliba et al., 1999). Then the EEG was segmented into 600-ms epochs, time-locked to the auditory action cue (epochs extended from 100 ms prior to the tone to 500 ms after the tone). Eye blinks and eye movements were corrected for (Gratton, Coles & Donchin, 1983) and bad channels were corrected on a trial-by-trial basis using interpolated splines (Srinivasan, Nunez, Silberstein et al., 1996). Segments were rejected if they contained more than 20 bad channels and excluded from further analysis. Acceptable trials were averaged together and baseline corrected relative to pre-stimulus activity (–100 – 0 ms). On average, 159 condition-1 and 160 condition-2 trials per subject were retained. The maximum negative (N170) peak values for a given time interval were identified using a computerized statistical extraction tool (100–300 ms) and mean voltages were calculated across a window extending 1 sample in either direction of the peak's maximum. Peak latency was also quantified, based on the peak's maximal value. Analysis was confined to left temporal, right temporal, parietal, and occipital electrode clusters (Figure 2). Each cluster was comprised of seven adjacent electrodes, which were centered around an appropriate electrode corresponding to the traditional 10-20 system. Our left and right temporal clusters were centered on T5 and T6 respectively-sites where the N170 is commonly reported. Our parietal cluster was centered on Pz, and our occipital cluster was centered on Oz. Individual electrodes were averaged together for each cluster and repeated measures ANOVAs were used to compare the amplitude and latencies of the N170. The factors in the ANOVAs were reach type (condition 1/condition 2) and region (left temporal, right temporal, parietal, and occipital). Statistical analysis was conducted using SPSS version 18.0. Bonferroni corrections were also applied where appropriate and Greenhouse-Geisser corrections were made for violations of sphericity.

3. 2 Results:

3.2.1 Behavioral Results

Average MT, accuracy, and RT were compared between the two conditions using two-tailed, paired-samples t-tests. One participant was excluded from the accuracy analysis due to a touchscreen calibration error. Average MT was significantly longer in Condition 2 than Condition 1 (534.7 ms vs. 528.6 ms; $t(25)=-3.16$, $p<0.01$) and mean accuracy was also lower in Condition 2 (74% vs 79%; $t(25)=4.62$, $p<0.01$). These results replicate previous findings (Goodale, Jakobson, & Keillor, 1994) that actions requiring more perception-based information are slower and less accurate because they may rely on the recall of target features (Goodale, Jakobson, & Keillor, 1994), which is likely less precise than using directly available visual information. Finally, RTs were faster in Condition 2 than Condition 1 (261.0 ms vs. 277.7 ms; $t(25)=12.75$, $p<0.01$); a pattern opposite to the MT data. This result may describe an effect of attention on action. In condition 2, the cue to respond is paired with the visual stimulus offset, and research has shown that the disappearance of a target will attract attention. Thus, when stimulus location is relevant to a task, having a unitary target for both visual attention and goal-directed action may be advantageous (Nishimura & Yokosawa, 2010). In one study, participants were to respond to the onset or offset of a light in a two-light display. On one block of trials, both lights were initially off and the stimulus was the onset of one; in another block, both lights were initially on and the stimulus was the offset of one. Reaction times were fastest, for both onset and offset trials, when responses were directed toward the changed rather than the unchanged element (Simon, Craft, & Webster, 1971). Transient change information thus has an important perceptual effect on action, and we report similar findings.

3.2.2 ERP Results

The mean amplitudes and latencies of the N170 component measured at temporal, parietal, and occipital regions are reported in Table 1. Grand average ERPs are shown in Figure 3. We compared the amplitudes and latencies of the ERP in the latency range of the N170 component between reaching conditions 1 and 2 at temporal, parietal, and occipital regions.

A reach type [2] (condition1/condition2) X region [4] (left temporal/right temporal/parietal/occipital) repeated measures ANOVA revealed a main effect of reach type on N170 amplitude, $F(1,25)=5.61$, $p<0.05$, due to a more negative amplitude for condition 2. A main effect of region was also significant, $F(1.84, 46.10)=4.75$, $p<0.05$, although pairwise comparisons revealed no significant effects. The interaction was not significant ($p>0.1$). A lack of interaction with region indicates that the topography was not significant. However, our hypothesis would be challenged if the main effect of reach type were not observable at temporal electrodes overlying the ventral stream. Therefore, although the interaction did not reach significance, we tested these electrodes individually, as planned comparisons. While the results of the planned comparisons are not as statistically robust as an interaction, comparisons revealed that the N170 was significantly more negative at the left temporal, $t(25)=2.87$, $p<0.01$ and right temporal, $t(25)=2.79$, $p<0.05$ locations in condition 2, compared to condition 1. This difference did not reach significance at parietal or occipital locations ($p>0.1$).

The N170 latency ANOVA revealed no significant effects ($p>0.1$).

3.3 Discussion

Our findings confirmed our major hypothesis that the N170 is a robust marker of increased ventral stream perceptual processes, reflected by an enhancement of the auditory ERP during the initiation phase of actions that rely more strongly on visual memory. We found that the negative evoked potential was larger in condition 2 than condition 1. However, it is important to consider an alternative explanation. That is, in condition 2, the offset of the stimulus occurs simultaneously with the auditory cue to move, whereas in condition 1, the stimulus offset coincides with the participants' initiation of a response (on average, 277.7 ms after the auditory cue). Therefore, it is conceivable that the larger negativity in condition 2 is due to an added visual evoked potential in response to the offset of the visual stimulus, which is more time-locked to the signal to move in condition 2 than condition 1, rather than the addition of a ventral-stream contribution to movement initiation.

We offer three arguments against this alternative hypothesis. First, if the N170 merely reflects the offset of the visual stimulus, we would have expected to see a similar negative deflection of equal magnitude in condition 1 trials. For condition 1, mean stimulus offset time was 261 ms, corresponding to the average participant reaction time. If the larger negativity in the N170 latency range were attributable to the combined effect of a visual offset, we would expect to see a clear negative peak occurring 455 ms post-beep (average visual offset time for condition 1 trials [261 ms] + average N170 latency for condition 1 trials at temporal electrodes [194 ms]). However, visual inspection of our ERP data reveals that this was not the case. Second, in condition 1, the visual stimulus is presented for a longer time compared to condition 2. That is, condition 2 relies on a shorter stimulus presentation time, and it does not seem likely that a shorter stimulus duration (condition 2) would elicit a larger ERP deflection in the latency range of the N170. Rather, longer stimulus duration times have been shown to elicit larger amplitude visual evoked offset responses (Morotomi & Kitajima, 1975; Wilson, 1983). Thirdly, we would expect that subtle differences in the timing of the visual offsets are more likely to be reflected in earlier sensory components recorded over occipital scalp regions (Maier, Dagnelie, Spekreijse, & van Dijk, 1987) than those in the N170 latency range over temporal areas. However, in order to directly test the alternative interpretation that our ERP effects are due to the trial pacing of our task rather than the differential contributions of perception-based processing we conducted a follow-up control study to isolate effects purely due to the trial timing (visual offset) differences between conditions 1 and 2 on the ERP we observed in the latency range of N170. A difference in ERP amplitude between conditions would suggest that the results of experiment 1 were due to an additive visual evoked potential. If there were no difference in amplitude however, this would support the interpretation that the N170 reliably reflects increased contributions of visual memory to action.

3.4 Experiment 2

Methods

3.4.1 Participants

Twelve (9 female, 3 male) right-handed undergraduate students aged 18-43 (mean 22, SD=6.92) who had not participated in experiment 1 participated in the control study. All participants had normal or corrected-to-normal vision, and normal hearing. Written informed consent was obtained prior to the experiment in accordance with the University of Alberta's ethical review board, and the Declaration of Helsinki.

3.4.2 Procedure

The experimental setup was identical to that of experiment 1, except that participants were no longer required to make reaching movements to the target. Rather, participants passively viewed the presentation of the targets while listening to the auditory tone. As in experiment 1, the tone sounded simultaneously with the disappearance of the target for condition 2 trials. In the initial study however, the disappearance of the target in condition 1 trials depended on the participants' behavioral response. Because reaching was not required in the control experiment, visual offset of the target for condition 1 trials was pre-determined using response times yoked to participants in Experiment 1. Each participant in the control study was given the same visual offset times as a randomly selected (without replacement) participant from the initial study. Rather than using mean response times or an average range of responses, yoking participant data ensured that the control group saw identical sequences of visual stimuli as participants in Experiment 1 (apart from catch trials, see below).

To ensure that participants were on task and paying attention, catch trials replaced some trials, comprising twenty percent of all trials. For these trials, the black target dot flashed to red before disappearing, requiring participants to respond manually by pressing a button. Catch trials comprised twenty percent of all trials, and there were equal numbers of condition-1 and condition-2 catch trials (i.e. the target flashed to red at the time of the auditory tone [condition-2 catch trial] or with the later stimulus offset [condition-1 catch trial]). Thus, a total of 360 test trials (288 condition 1/condition 2 trials, and 72 condition 1/condition 2 catch trials) were included in a session and participants were given a break period for a self-determined length of time, every 120 trials.

3.4.3 Behavioral and EEG Analysis

Overall accuracy was calculated by determining the percentage of correctly responded-to catch trials and correctly rejected non-catch trials. EEG recording procedures were identical to that of the initial study (see section 2.4). All catch trials were excluded from ERP analysis, and only condition 1 and condition 2 trials were compared. Only those condition 1 trials in which the visual offset occurred between 150 and 800 ms were included in the ERP analysis, to maintain consistency with the first experiment. EEG segmentation and artifact detection procedures were identical to the initial study (see section 2.4). On average, 123 condition 1 and 109 condition 2 acceptable trials per subject were retained for analysis. The maximum negative (N170) peak values were identified as before, and analysis was confined to previously defined electrode clusters (Figure 2). Individual electrodes were averaged together for each cluster and repeated measures ANOVAs were used to compare the amplitude and latencies of the N170. Statistical analysis was conducted using SPSS version 18.0. Bonferroni corrections were applied where appropriate and Greenhouse-Geisser corrections were made for violations of sphericity.

3.5 Results

3.5.1 Behavioral Results

Overall accuracy was 98% (SD=0.03%), suggesting that participants were correctly following the task procedure and remained attentive throughout the recording session.

3.5.2 ERP Results

We compared the morphology of the ERP component in the latency range of the N170 as in experiment 1 between our conditions at left and right temporal electrode sites. The mean amplitudes and latencies are reported in Table 2. Grand average ERPs are shown in Figure 4 alongside experiment 1 results at temporal electrodes, for comparison. A 2 reach type (condition1/condition2) X 2 region (left temporal/right temporal) repeated measures ANOVA revealed no main effects on N170 amplitude and no significant interactions. Similarly, the N170 latency ANOVA revealed no main effects or significant interactions ($p>0.1$).

3.6 Discussion

The absence of a difference in N170 amplitude between conditions 1 and 2 in this follow-up experiment clearly rules out the possibility that the central ERP results of experiment 1 are due to the different temporal dynamics of visual stimulus offset. Rather, based on the large body of evidence from neuropsychological patients and neurologically intact participants, it is more likely that our finding of a larger amplitude of the ERP in the latency range of the N170 during condition 2 compared to condition 1 is due to the recruitment of additional processes required for the successful completion of the task. That is, more perception-based processes required to plan the action without full visual input (Westwood & Goodale, 2003).

3.7 Conclusions

The main purpose of this study was to use ERPs to directly examine the patterns of neural activity underlying pointing actions that are initiated toward a visible target (condition 1) compared to pointing actions initiated toward a target that was previously visible (condition 2). The extant literature suggests that the second case (condition 2) likely relies on more perception based neural activity compared to the first case (condition 1). This is because the initiation of the pointing actions without a visible target (condition 2) must rely on briefly stored information about the physical characteristics of the target that was perceptually encoded prior to the action (Goodale & Milner, 1992). Our main hypothesis was that the ERP in the latency range of N170 is a good electrophysiological marker for the differences in the neural bases of the two action types in our experiment because the N170 has been previously shown to reflect perceptual processes within the ventral visual stream.

The pattern of behavioral data from this study followed other studies that have examined the nature of actions requiring perception-based information. That is, MT was increased and reach accuracy was decreased in condition 2, which compared to condition 1, engages ventral mechanisms to a greater extent. This pattern has been shown in other studies comparing visually guided actions and those for which vision of a target is precluded (Armstrong & Singhal, 2011; Klatzky, Pellegrino, McCloskey et al., 1993; Singhal et al., 2007; Westwood & Goodale, 2003); tasks which similarly differ in their reliance on the ventral stream. These findings support the idea that actions that engage the ventral stream rely on stored perceptual information, which is less accurate than real-time visual information and thus, performance to visually unavailable targets induces slowing and greater variability in the arm and hand actions (Goodale & Milner, 1992). Furthermore, our participants reported (post hoc) that they were unaware of which trial type they were engaged in, suggesting that our manipulation was successful in engaging perception and memory processes without altering performance strategy.

To our knowledge, this is the first study to use ERPs to directly compare the neural processes underlying the planning of pointing behaviors for which the putative contribution of ventral stream perceptual mechanisms differs. Results indicate that the negative evoked potential elicited by the auditory cue to move was greater in amplitude for condition 2 than condition 1 trials. Because the physical characteristics of the tone (pitch, amplitude, duration) were identical in both trial types, it does not make sense that there would be differences in amplitude between conditions due to the auditory cue alone. We argue that the brief maintenance and recall process in both conditions of our instructed delay task necessitated perceptual activity in ventral stream brain areas and these processes were reflected by the contribution of N170 range activity overlapping the ERP that was time-locked to the auditory action cue.

These results are consistent with our hypothesis that the N170 reflects ventral stream processes involved in action planning and thus is larger in amplitude for those tasks that rely more heavily on perception-based information. During a memory task, stored representations of relevant information must be recruited during recall (Goodale & Milner, 1992, Klatzky, Pellegrino, McCloskey et al., 1993). Additionally, studies have shown that the process of remembering often reactivates sensory-specific cortices that were first activated during the encoding of stimulus features (Johnson, Mitchell, Raye et al., 2007, Geng, Ruff & Driver, 2009). By directly comparing two conditions for which the contribution of the ventral stream is hypothesized to differ, we have shown that the N170 likely reflects perceptual requirements during mnemonic processing specifically linked to action. The N170 is known to have several sources in the brain, including the LOC and fusiform face area (FFA) in the temporal lobes. And while we cannot definitively conclude that our temporal electrodes are a direct index of ventral stream processing, our *a priori* hypothesis led us to predict that this area would elicit a more negative N170 during condition 2, (which presumably engages ventral mechanisms to a greater extent than condition 1), and this component would overlap with the auditory evoked potential. Our findings support previous fMRI, kinematic, and neuropsychological reports, which suggest that action planning in the absence of a visual target engages ventral stream processes (Goodale and Milner, 1992; Singhal et al., 2006; 2007). Based on the good consistency between our conclusions and previous studies, we provide converging electrophysiological support that actions towards memory-based targets demand greater contribution from ventral areas. Furthermore, our data support the idea that detailed memory representations of visual objects activate areas within the LOC (Xu & Chun, 2006), which are likely reactivated during recall (Nyberg, Habib, McIntosh, & Tulving, 2000; Wheeler, Petersen, & Buckner, 2000).

We also rule out the alternative interpretation that the stimulus offset differences contributed to the larger ERP amplitude in condition 2. In order to ensure that the offset was not contributing to the N170, experiment 2 did not require participants to make a response to the target. Therefore, there were no differences in motor planning between conditions, and thus no need for any additional recruitment of the ventral stream required to plan the action. Therefore, we were able to isolate any effects due to the varying stimulus offset timing between our conditions. Results of experiment 2 indicate that there were no differences in the N170 between condition 1 and condition 2, eliminating the possibility that there was contamination by the offset of the visual stimuli in experiment 1.

We suggest that while the ventral stream is recruited for tasks like condition 2, these types of actions likely still involve communication with parietal areas. There are hundreds of single cell studies implicating dorsal stream structures in delayed response tasks, so we would not argue for a complete dissociation between the dorsal and ventral streams. Rather, collaboration between the streams seems more plausible. Both streams should be involved somehow in the transformation of visual information into motor output and how the two streams interact may depend on the specific requirements of the task at hand (McIntosh & Schenk 2009). In our task, visual information about the hand and touchscreen are available throughout the movement, and the ventral stream may be providing allocentric spatial representations that could aid in successful reaching (Dijkerman, Milner, & Carey, 1998). Some studies have suggested that delay-related activity in the dorsal stream may also reflect inputs from the ventral stream (Toth & Assad, 2002), and offline dorsal stream activity may depend on ventral stream information. Sensorimotor transformations that occur in ventral stream areas, including coordinate transformations for object recognition and translation-invariance, likely also have implications for visuomotor control (Graf, 2006), and the output of this system may be equally important to consider.

Given the advantage of EEG's temporal resolution, we may be able to examine the time course of the communication between ventral and parieto-frontal regions, and better quantify the streams' relative contributions to different sensorimotor tasks. For example, while we have isolated and analyzed an EEG component hypothesized to reflect ventral stream processing, it is important to address a potential bias towards finding effects within temporal, versus occipital and parietal, recording sites. In theory, it is plausible that both ventral *and* dorsal streams are driven more strongly by condition 2, but that differences arise at different times for different brain areas. An electrophysiological marker of dorsal stream processing could potentially be isolated within a different temporal window of the task. However, we feel that such a possibility is difficult to test using this particular paradigm. We do not include a strictly "visually guided" condition, in which the target remains present throughout the movement. Therefore, the circuit is deprived of visual input during movement execution in both condition 1 and condition 2. Furthermore, we have not manipulated either condition to differ during the preparatory phase of the reach either. Thus, the appearance of the target should initiate planning activity in the sensorimotor system in a similar way between conditions. Perhaps a more direct test of signal differences between conditions in parietal cortex would involve an experimental paradigm in which the conditions were more strongly distinguished from one another in terms of visual feedback throughout the movement. Future studies to investigate the electrophysiological mechanisms of real-time visual feedback for guiding actions should be performed.

In sum, this study is the first to directly compare actions that are hypothesized to require differential contribution of ventral stream mechanisms using high temporal resolution ERP. Our results, taken together with previous patient data and fMRI work, support the idea that the contribution of the N170 overlapping the auditory cue ERP may be a reliable marker of increased activity within the LOC during the planning of actions which rely more heavily on perception-based information.

Figure 3-01

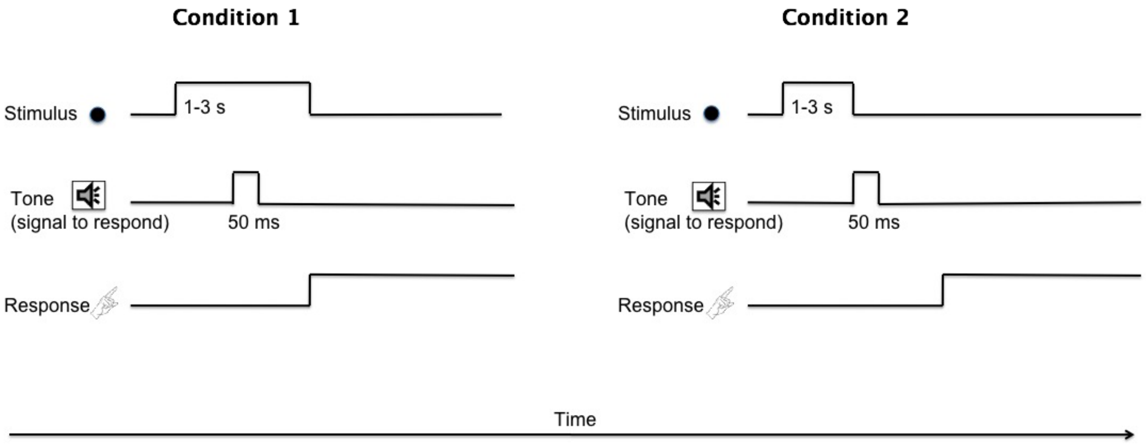

Condition 1
Condition 2
Stimulus
1-3 s
Stimulus
1-3 s
Tone
(signal to respond)
50 ms
Tone
(signal to respond)
50 ms
Response
Response
Time

Figure 3-01 Caption:

Schematic of the behavioral paradigm. 180 trials of each condition were presented to participants within a session. In condition 1(vision), the tone sounds and the stimulus disappears when the participant lifts his/her finger from the response box. In condition 2 (memory), the tone sounds simultaneously with the disappearance of the target.

Figure 3-02

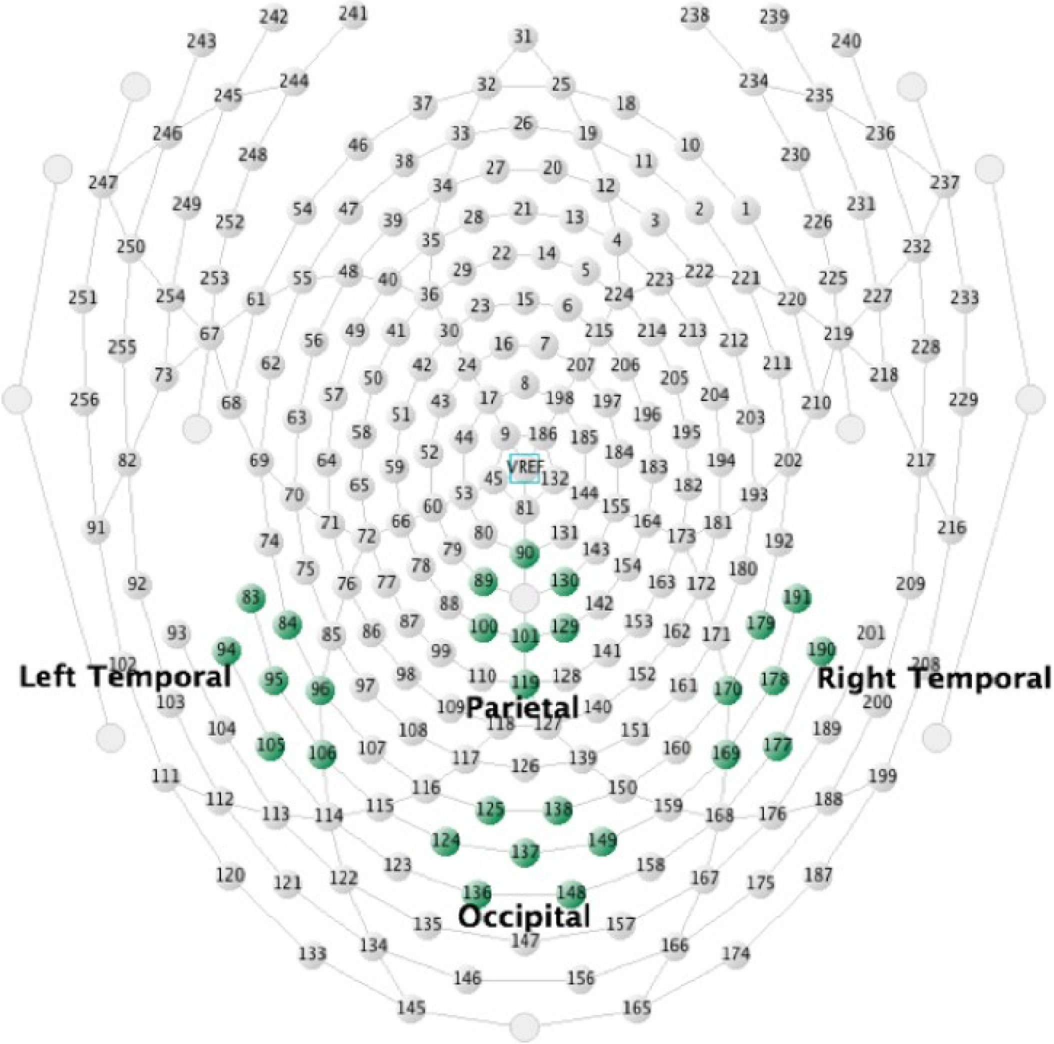


Figure 3-02 Caption:

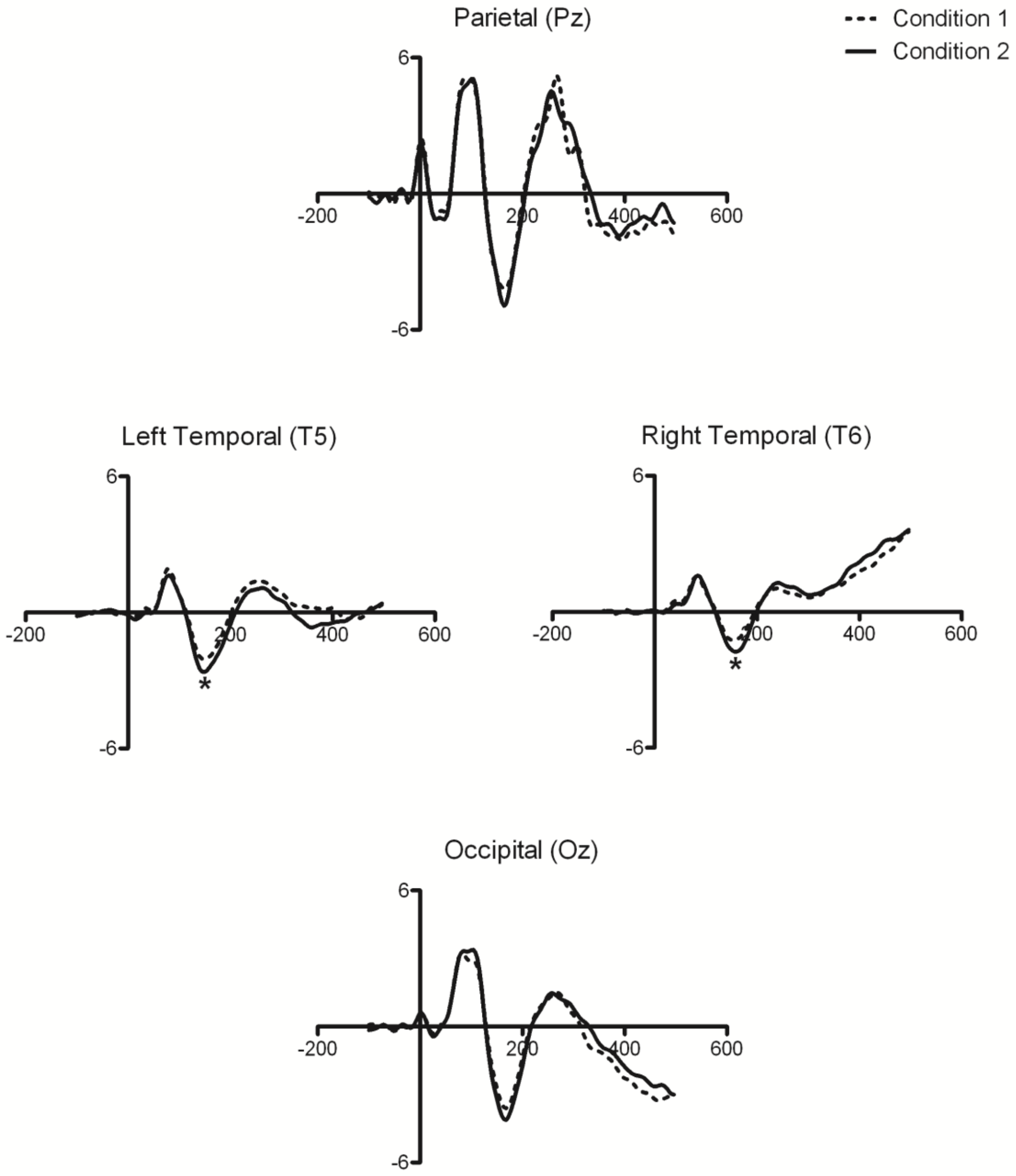
Sensor layout and analysis clusters, which are shown in green. The N170 ERP component for conditions 1 and 2 were compared at the following temporal, parietal, and occipital electrode clusters.

Table 3-01

Mean amplitudes and latencies (with standard deviations) of the N170 ERP component

Region	Condition 1 N170 amplitude [μV]	Condition 2 N170 amplitude [μV]	Marginal Mean	Condition 1 N170 latency [ms]	Condition 2 N170 latency [ms]	Marginal Mean
Left Temporal	-2.7 ± 1.6	-3.3 ± 1.7	-3.0	171.3 ± 47.8	173.5 ± 49.1	172.4
Right Temporal	-2.4 ± 2.0	-2.8 ± 2.1	-2.6	187.3 ± 51.2	182.5 ± 52.8	184.9
Parietal	-4.4 ± 3.6	-4.5 ± 3.3	-4.5	199.4 ± 48.5	190.4 ± 38.6	194.9
Occipital	-4.8 ± 5.1	-5.3 ± 4.2	-5.1	189.4 ± 46.2	185.3 ± 43.1	187.4
Marginal Mean	-3.58	-3.98		186.85	182.93	

Figure 3-03


Parietal (Pz)

Left Temporal (T5)

Right Temporal (T6)

Occipital (Oz)

Figure 3-03 Caption:

ERP plots for the central electrode within each electrode cluster (T5, T6, Pz, Oz). Conditions 1 and 2 are plotted for each electrode, with voltage (µV) plotted on the x-axis and time (ms) on the y-axis.

Table 3-02

Mean amplitudes and latencies (with standard deviations) of the N170 ERP component

Region	Condition 1 N170 amplitude [μV]	Condition 2 N170 amplitude [μV]	Marginal Mean	Condition 1 N170 latency [ms]	Condition 2 N170 latency [ms]	Marginal Mean
Left Temporal	-2.9 ± 2.0	-2.9 ± 1.7	-2.9	189.2 ± 39.1	189.6 ± 41.8	189.4
Right Temporal	-2.0 ± 1.2	-2.2 ± 1.2	-2.1	200.1 ± 32.5	217.2 ± 26.0	208.7
Parietal	-2.1 ± 1.3	-2.0 ± 1.2	-2.1	164.0 ± 39.1	168.0 ± 40.8	166.0
Occipital	-3.3 ± 2.2	-3.2 ± 1.9	-3.3	191.3 ± 44.2	204.8 ± 50.5	198.1
Marginal Mean	-2.58	-2.58		186.15	194.90	

Figure 3-04

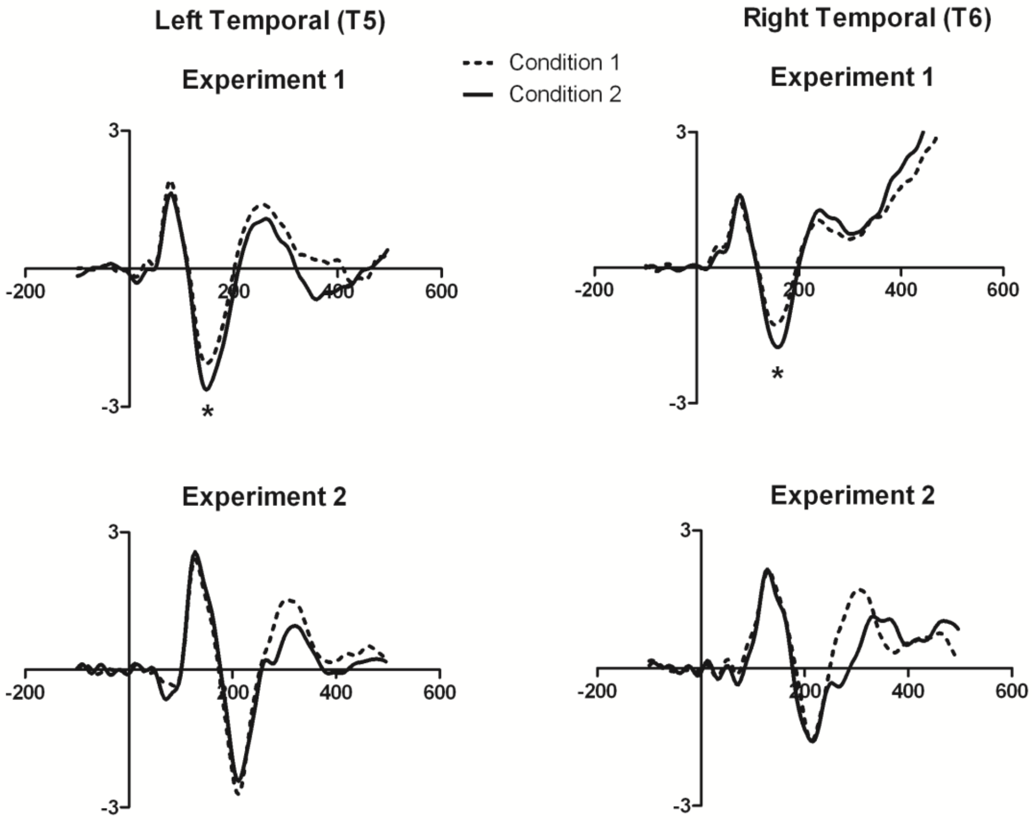

Left Temporal (T5)
Right Temporal (T6)
Condition 1
Condition 2
Experiment 1
3
-3
-200
200
400
600
*
Experiment 1
3
-3
-200
200
400
600
*
Experiment 2
3
-3
-200
200
400
600
Experiment 2
3
-3
-200
200
400
600

Figure 3-04 Caption:

ERP plots for the central electrode within each temporal area cluster (T5 and T6). Conditions 1 and 2 are plotted for each electrode, with voltage (lV) plotted on the x-axis and time (ms) on the y-axis. Experiment 1 results are shown above the control results for comparison.

Chapter 3 References

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Chapter 4:

A Perception-Based ERP Reveals that the Magnitude of Delay Matters for Memory-Guided Reaching

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4.0 Introduction:

The role of vision in goal-directed movement has important implications for how motor behaviors are planned and executed. When continuous visual input is available, dorsal stream mechanisms in the posterior parietal cortex are thought to compute sensorimotor transformations at the time a response is cued (Goodale & Milner 1992; Westwood & Goodale 2003). Thus, visually guided movements are thought to unfold in real-time, and are supported by online control processes (Elliott et al. 2001). Instead, when visual input is unavailable, or vision is occluded at the time a response is cued, a stored perceptual representation must be used instead to inform the motor plan. Under such memory-guided conditions, mechanisms in the ventral stream, particularly those associated with inferior temporal cortex, are engaged (Goodale 1998). Converging neuropsychological, neuroimaging, and kinematic findings support this theory (Goodale et al. 1994; Hu & Goodale 2000; Westwood et al. 2000, 2001; Singhal et al. 2006; Ganel et al. 2008; Cohen et al. 2009). There is ample evidence arguing against a double dissociation between vision-for-action and vision-for-perception however, as many studies have also suggested that the dorsal stream is engaged for actions in which vision of the target is unavailable (Franz et al. 2009; Hesse & Franz 2009). This position is supported by monkey neurophysiology and human fMRI data, which reveal that sustained activity occurs in dorsal-parietal neurons across memory delays (Murata et al. 1996; Buneo et al. 2002; Singhal et al. 2006; Fiehler et al. 2011; Himmelbach et al. 2009). It is likely that while the ventral stream is necessarily engaged for memory-guided action, collaboration between the two streams also occurs and depends on the specific requirements of the task (Schenk & McIntosh 2010).

Recently, we provided the first ERP evidence that action planning in the absence of a visual target engages ventral stream processes, making it possible to investigate the electrophysiological basis of goal-directed reaching. Specifically, the N170 event-related potential (ERP) component, which is an established marker of ventral visual stream processing, was enhanced for actions that relied more heavily on perception-based information (Cruikshank et al. 2012). The N170, which was first described and widely studied in the context of face perception (Eimer & Holmes 2002; Batty & Taylor 2006; Eimer 2011; Wronka & Walentowska 2011), is also elicited in response to visual stimuli (Bentin et al. 1996), reflects the early classification of objects (Rossion et al. 2003; Sreenivasan et al. 2007), is modulated by memory (Morgan et al. 2008; Banko´ et al. 2009), and has a known source in the lateral occipital cortex (LOC) [Rossion et al. 2003]), part of the ventral visual stream. We found that N170 was enhanced for actions that relied more heavily on perception-based information (Cruikshank et al. 2012); it was larger (more negative) when the target disappeared just before reach-initiation (simultaneously with the auditory cue to respond) than when it persisted until movement onset (when the participant initiated a reach). Because participants could not make a 0 ms response, the brief maintenance and recall process in both conditions of our task necessitated perceptual activity in ventral stream brain areas. However, the differential contribution of this activity was reflected in the N170-range amplitude. This ERP may arguably have been a visual N1, as this component is also elicited in response to visual stimuli, arises from the LOC, and it may not be distinct from the N170. Nevertheless, the results of Cruikshank et al. (2012) suggest that the negativity is an index of ventral stream processing during the planning of actions that rely on perception-based information. In that study however, the memory-guided reach initiation occurred only milliseconds after the target stimulus disappeared. In this study, we considered what might happen with longer delays.

We measured EEG during a memory-guided reaching task and the N1/N170-range ERP was computed offline at the time of response cueing following 1, 2, and 3-s delays. In order to retain the same nomenclature used in Cruikshank et al. (2012), we will refer to this component as the N170. While our initial ERP results were consistent with earlier studies assessing ventral stream activity during very short delay periods (Westwood & Goodale 2003; Singhal et al. 2007), other studies have employed much longer delay intervals between stimulus occlusion and response initiation (Hu & Goodale 2000; Milner et al. 2003; Singhal et al. 2006, 2013). Neuroimaging has shown that that the LOC is activated in response to a target stimulus, returns to baseline levels of activity, and is reactivated with the cue to respond. The suggestion is that dorsal stream mechanisms plan and maintain an action; however, at the time a response is cued, motor programming requires reactivation of detailed visual perceptual information in the ventral stream (Singhal et al. 2013). It has also been suggested that as the time interval in delayed action tasks increases, perceptual information about the visual stimulus decays (Glover, 2004). While it is clear that delayed action re-recruits the LOC (Singhal et al. 2013) and that this area is necessarily implicated in delayed, compared to immediate action tasks (Cohen et al. 2009), it is unclear how the integrity of the stored perceptual information is represented. By measuring the N170 at the time of response cueing in our task, we tested whether the negativity reflects reactivation of a stored percept or whether it is simply associated with early planning and residual stimulus processing following very short delays. If the N170 is only associated with early planning and processing of the stimulus that precedes movement programming, there should be no difference in its characteristics across different delay periods of a memory-guided reaching task. That is, we would only expect to notice changes in its morphology depending on whether a target stimulus was either present or absent at the time of response cueing; the length of time a target had been occluded prior to the reach would not have any bearing on whether or not the ventral stream was engaged at movement initiation. If however, the N170 reflects reactivation of a visual percept, then the increased memory demands associated with longer delay periods should affect the stored representation and consequently, the morphology of the N170. As time elapses and visual memory is increasingly taxed, we would expect to see this process reflected in the amplitude and latency of the N170.

In sum, we tested whether the same ventral stream processes were engaged and reflected by the N170 when visual memory was taxed beyond a few hundred milliseconds. We traced the timecourse of the N170 in memory-guided reaching over longer delays in order to determine how perception for action is controlled over time and whether the requirements for perceptual processing are the same for longer, as they are for shorter delays.

4.1 Materials and Methods

4.1.1 Participants.

Thirty (16 female) right-handed undergraduate students, ages 17– 29 (mean 20 yr, SD 2.8 yr) received psychology course credit for participating in this study. Three participants' data were excluded from the analyses due to persistent EMG contamination. All participants had normal or corrected-to-normal vision, and normal hearing. Written informed consent was obtained prior to the experiment in accordance with the University of Alberta's ethical review board, and the Declaration of Helsinki.

4.1.2 Procedure.

The study was conducted in a darkened, electrically shielded, and sound-attenuated chamber. At the start of the experiment, participants were seated in front of a 430.4 mm × 270.3

mm touchscreen. At the beginning of each session, the touchscreen was recalibrated by the participant being tested to ensure that accuracy measures remained reliable across subjects. Based on average distance from the screen (51.4 cm), the horizontal and vertical visual angles of the touchscreen were 45.44° and 29.46°, respectively. The horizontal and vertical visual angles of the stimuli were 1.00° and 1.56°, respectively.

Our task required that participants reach toward and touch 9 mm 14 mm black dots displayed on a touchscreen using E-Prime presentation software version 2.2 (Psychology Software Tools). The participant depressed a button to begin each trial. One second after the button was depressed a target appeared on the screen in a random location, which the participant was told to fixate on. The target remained on the screen for 1500 ms, after which it was extinguished and a blank screen remained for a delay period of either 1, 2, or 3 seconds. Following the delay, an 800 Hz, 64 dB (SPL) tone sounded for 50 ms. The participant was instructed to continue holding down the button until he/she heard the tone, and then to touch the target as quickly and accurately as possible. After participants made contact with the screen, they were to return their finger to the response box and hold down the button, which advanced the next trial after 1 s (Figure 1). Prior to testing, 10 practice trials were administered to ensure that participants understood the task. The 1, 2, and 3 second delay periods were presented randomly, and a total of 360 test trials (120 per condition) were included in a session. Participants were given a self-paced break period every 120 trials.

4.1.3 Behavioral Analyses.

For each trial, reaction time (RT) and movement time (MT) were recorded. RT was defined as the time it took to initiate a movement in response to the beep, and MT was defined as the time it took to fully execute a movement, from release of the response button to contact with the touchscreen. Touch positions were monitored, and absolute error (pixels/mm) was recorded for each trial. Trials were excluded from analyses if RTs were ≤ 150 ms or ≥ 800 ms or MTs were ≤ 200 or ≥ 2000 ms (< 3% of all trials). Statistical analyses were carried out using Matlab 7.1 (The Mathworks) and SPSS (version 18.0).

4.1.4 EEG recording and analysis.

EEG was recorded using a high-density 256-channel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR), amplified at a gain of 1000 and sampled at 250 Hz. Impedances were kept below 50 k and the recording was initially referenced to the vertex electrode (Cz). Signal was preprocessed using EEGlab 7.1.4 (Delorme & Makeig 2004), running under Matlab 7.1 (The Math-Works). Signal was bandpass filtered from 0.5 to 50 Hz and was re-referenced to a common average. Independent component analysis (ICA) was then performed to detect and remove artifacts from the data. Those components accounting for stereotyped artifacts, including eyeblinks, eye movements, and muscle movements, were identified and removed from the data. Artifactual components were determined by visual inspection of the spectral characteristics, time courses, and spatial topographies of all components. Visual inspection of the data revealed eight subjects who had a few continuously bad channels throughout the recording (mean 12 bad channels, SD=8.9). For each subject, these channels were rejected and interpolated using splines. EEG was segmented into 1100-ms epochs, time-locked to the auditory cue to respond (epochs extended from 100 ms prior to the tone to 1000 ms after the tone). Trials were averaged together and baseline-corrected relative to pre-stimulus activity (–100–0 ms). On average, 117 trials of each condition per subject were retained. The maximum negative (N170) peak values between

150–300 ms were extracted and mean voltages were calculated across a window extending one sample in either direction of the peak's maximum. Initially, we extracted the N170 between 100-300 ms in an effort to remain consistent with Cruikshank et al. (2012). However, due to individual subject variability in the peaks, mean values were more consistent with the grand average ERP figure when adopting a slightly narrower, more conservative window. It is important to note that this 150-300 ms window did *not* differentially affect the statistical outcome of our results. Peak latency was also quantified, based on the peak's maximal value. Analysis of the N170 was conducted at left and right temporal electrode clusters, comprised of seven adjacent electrodes, centered around T5 and T6, respectively. Individual electrodes' peak values were averaged together for each cluster. Statistical analysis was conducted using SPSS version 18.0. Bonferroni corrections were also applied where appropriate and Greenhouse-Geisser corrections were made for violations of sphericity.

4.2 Results

4.2.1 Behavioral Measures.

Mean RT, absolute error, and MT are reported in Table 1. Average RT, absolute error, and MT were compared between the three delays using one-way repeated measures ANOVAs. There was a main effect of delay length on RT, which indicated a decrease in RT as delay length increased, F(1.15, 29.96) = 95.89, $p < 0.01$. Pairwise comparisons revealed that all delay conditions were significantly different from one another and results are consistent with our initial study (Cruikshank et al. 2012). There was also a main effect of delay length on absolute error, F(1.68, 43.57) = 35.27, $p < 0.01$. As delay length increased, absolute error increased. All delay conditions significantly differed from one another. This result is consistent with our initial study

(Cruikshank et al. 2012) and previous findings that actions requiring more perception-based information are less accurate because they rely on the recall of target features (Goodale et al. 1994). Finally, there was a main effect of delay length on MT, $F(1.61, 41.78) = 18.57$, $p < 0.01$. Pairwise comparisons revealed that MT for the 1 s delay was significantly shorter than the 2 and 3 s delay conditions. However, MT between the 2 and 3 s delays was not significantly different.

4.2.2 ERP Measures.

The mean amplitudes and latencies of the N170 component measured at left and right temporal regions are reported in Table 2. Grand average ERPs are shown in Figure 2. We compared the amplitude of the ERP in the latency range of the N170 component across delay conditions at left and right temporal regions.

A region [2] (left temporal/right temporal) □ delay [3](1second/2second/3second) repeated measures ANOVA revealed a main effect of delay length on N170 amplitude, $F(1.49, 38.79) = 14.77$, $p < 0.01$. Posthoc pairwise t tests revealed that N170 amplitude for the 1 s delay was significantly more negative than the 2 and 3 s delay conditions but the N170 amplitude between the 2 and 3 s delays were not significantly different. Taken together with the behavioral results, the N170 amplitude appeared to parallel MT but not RT or absolute error. We wanted to determine whether any of the behavioral measures did in fact correlate with the N170 amplitude across participants, which we assessed with Spearman correlation coefficients (two-tailed) of N170 amplitude with MT, RT and absolute error. If the N170 is relevant to planning of the reach, then a greater N170 might be associated with better reaching performance. The correlations between the averaged T5 and T6 cluster amplitude and MT and RT were not significant at any delay. However, N170 amplitude was correlated significantly with absolute error at the longest delay (3 s); when the N170 was smaller (closer to baseline) and less negative, absolute error was greater (r(26)=0.46, p=0.02). The correlation was not significant at the other two delays, but in the 2-s delay condition, a trend was found (r(26)=0.34, p=0.08). These results suggest that if a participant is able to maintain the N170 amplitude in the more demanding condition, their accuracy benefits.

A region [2] (left temporal/right temporal) X delay length [3](1second/2second/3second) repeated measures ANOVA revealed a main effect of delay length on N170 latency, F(1.65, 42.82) = 7.18, p<0.01. Pairwise comparisons revealed that the N170 peaked later in the 1 s delay condition than the 2 and 3 s delays, which did not differ significantly. These ERP results suggest that there is a transition in the mechanisms subserving memory-guided action planning for shorter (<1 s) compared to longer delay periods.

4.3 Discussion

The aim of this study was to determine whether the same ventral stream processes are engaged and reflected by the N170 when perceptual memory is taxed beyond a few hundred milliseconds. Here, we report the presence of an N170 component during memory-guided reach initiation when 1, 2, or 3 s delays occurred between stimulus offset and the cue to respond. There were clear differences in both the amplitude and latency of the N170 when the delay lasted only 1 s, compared to the 2 and 3-s conditions. The N170 was more negative in amplitude and peaked later for the shorter delay period. Our results suggest that ventral mechanisms involved in movement planning differ according to the length of time a target object has been occluded.

Because the behavioral results of this study follow expected patterns, we are confident that the ERP results also reflect reliable and meaningful differences across condition. Reaction time decreased with increasing delay period, a finding that is consistent with our earlier study, which reported a decrease in RT with target occlusion (Cruikshank et al. 2012). Also, decreasing RT as a function of increasing delay length may reflect additional levels of arousal and anticipation in the longer delay conditions (Carpenter et al. 2004), or a lack of preparedness to respond so shortly after visual occlusion in the 1 s delay condition (Gottsdanker, 1979). We also found that absolute error increased systematically with delay length. This result is consistent with earlier studies that have shown that for tasks in which the reliance on the ventral stream increases, so too does error increase (Klatzky et al. 1993; Westwood & Goodale 2003; Singhal et al. 2007; Armstrong & Singhal, 2011). While these previous studies have compared visually guided (closed loop) actions to those that are memory-guided, other investigations have examined accuracy measures across closed loop, open loop, and memory-guided conditions of various delay lengths. Accuracy has been reported as being higher for closed loop compared to open loop and memory-guided tasks (Westwood et al. 2001), and many studies have revealed a reduction in reach accuracy with increasing delay period (Elliott et al. 1990; Westwood et al. 2001; Heath et al. 2004). Others have reported no diminishing of accuracy over increasing delay periods (Westwood et al. 2001; Heath & Westwood 2003; Heath et al. 2004 Heath 2005; Heath & Binsted 2007), but rather, an increase in spatial endpoint variability. This suggests that stored target information is able to provide the motor system with some substitute (albeit an unstable one) for direct target vision (Westwood et al. 2003). Our results are consistent with this notion and support the idea that actions that engage the ventral stream rely on stored perceptual information that is less accurate than immediate visual information, inducing greater variability in arm and hand actions (Goodale & Milner 1992). In a related vein, movement times towards visually precluded objects also tend to be longer (Goodale et al. 1994; Cruikshank et al. 2012), and increase with increasing task difficulty (Heath et al. 2008). We found as predicted, movement times increased systematically with delay period in our task; however, they did not significantly differ between the 2 and 3-s delays. This suggests that while actions requiring more perception-based information are slower because they rely on the recall of target features (Goodale et al. 1994), there is something fundamentally different about delays extending two seconds and beyond. These behavioral effects are specific to our paradigm, as others have reported continuous decreases in movement time for delays of 0 to 5 seconds (Heath & Westwood, 2003). However, in that study, aiming was completed using a mouse and cursor in which the gain between the two was varied and movements towards near and far targets were compared. Therefore, differences in MT results may be attributable to differences in experimental paradigms

The N170 ERP results follow the same pattern as the movement time data, in that the 1-s delay displays significant differences compared to the 2 and 3-s delays. The N170 was less negative in amplitude and peaked earlier for the 2 and 3-s delay intervals, suggesting that the processes governing these longer memory-guided conditions, or the nature of the information supporting them, is somehow different. In this task, the properties of the target were consistent across condition; therefore, the difference in amplitude cannot be attributed to differences in the stimulus. Furthermore, the physical characteristics of the tone were also identical; thus, a difference in amplitude between conditions cannot be attributed to processes associated with the auditory tone alone. Rather, the maintenance and recall process in all conditions of our task necessitated perceptual activity in the ventral stream. However, the differential contribution of these processes according to delay length is arguably reflected by the N170 overlapping with the auditory response cue, to which the ERPs were time-locked. Our results indicate that there are differences in the neural processes underlying action planning when a delay length of 2 s or more is imposed between target disappearance and response initiation. We suggest that the N170 reflects reactivation of a stored perceptual representation in the ventral stream that is used to inform the motor plan, and that this representation is susceptible to decay.

This interpretation is consistent with others' who have used behavioral and kinematic measures to investigate the time course of visual perceptual memory, and the temporal durability of stored target representations supporting action (Elliott & Khan 2010). For example, Elliott and Madalena (1987) reported that a brief (< 2 s) visual representation is available to the motor system for online control. Similarly, Glover drew a distinction between planning and control, contending that the visual representation guiding control is transient, and that it decays gradually for up to 2 seconds. Beyond this time, movements are executed presumably without the benefit of on-line control, and are performed "entirely as planned", under offline control (Glover, 2004). While we cannot comment on whether the ventral stream mechanisms engaged in our task are used specifically for online control in the 1- s delay condition, we do argue that the N170 reflects reactivation of stored target information. Detailed memory representations of visual objects are known to activate areas within the LOC (Xu & Chun 2006), which are likely reactivated during recall (Nyberg et al. 2000; Wheeler et al. 2000). Because the N170 amplitude diminishes in our task, our results provide support for this theory; as delay length increases beyond 2 s, the stability of the target representation has degraded and is reflected in the smaller amplitude N170. If the stored visual representation were to be stably maintained and persisted throughout the delay, we would expect that the N170 would be comparable in amplitude across delays at the time of movement initiation. If however, the N170 was simply a marker of increased ventral stream activity but did not index the reactivation of a previously held percept (if it only marked the demands of the memory task), we should have seen a systematic increase in amplitude with increasing delay. Finally, if there had been a sustained decay of the target representation, the N170 should have also reflected this, and there should have been a systematic decrease in amplitude with increasing delay. Our results did reflect a decrease in amplitude, suggesting that decay does indeed occur. Because the difference was non-significant in the 2 and 3-s conditions, this further supports the idea that decay has already occurred by this time and that a threshold for perceptual decay exists. While we did not include delay periods beyond 3 seconds, we predict that increasing time intervals would elicit N170 peaks comparable to the two and three second conditions. An alternative, but compatible interpretation of our results is also plausible. While we have focused on perceptual memory decay in the ventral stream, others have shown that motor memory in the dorsal stream exists and may decay beyond 2 seconds (Jax & Rosenbaum, 2007; 2009). It is possible then, that we are actually measuring the ventral input to a dorsal-mediated process. It is very likely that the two streams are interacting in this task, and the fact that both share a similar timecourse for holding information supports a theory of their coordination.

Absolute error correlated with N170 amplitude in the 3-s delay condition. Thus, a larger N170 was associated with the least amount of error, but only in the condition that was most demanding of the ventral stream. This is what we would expect to find if the stored visual representation was not stably maintained or did not persist throughout the delay period. As the N170 becomes more positive, absolute error increases. Therefore, as time unfolds and the perceptual representation in the ventral stream begins to decay, the N170 amplitude decreases. We suggest that a smaller amplitude N170 reflects less reactivation, negatively affecting performance. With a more perceptually demanding task in which different, more abstract, target characteristics require maintenance, perhaps the correlations with the other two delay intervals would emerge as significant. We did report a trend for the 2-s delay interval, and the value of the correlation increased systematically from 1 to 3 s conditions.

We must consider however, an alternative interpretation of our findings. The mode of control and the nature of a reach may also be affected by things like visuomotor uncertainty (Heath et al. 2006). When a participant knows in advance, before the response cue, that visual information about a target will remain available, movements can be supported by online feedback mechanisms (Elliott & Allard 1985; Jakobson & Goodale 1991). However, when the predictability of visual information is unavailable (for example, a participant does not know whether he/she will be required to perform a closed loop, open loop, or memory guided action), there is a greater reliance on ventral stream, offline control mechanisms. In these situations, in which the participant cannot predict whether target information will disappear, movements need to be precomputed, before the response cue. In our task, participants know that every movement will be memory-guided, and the only thing that remains uncertain is the length of the delay. Due of the nature of our task however, participants may quickly come to recognize that as time passes, the probability of an expected response increases. Consequently, an immediate anticipated response is the least predictable in the 1-s delay and the most predictable in the 3-s delay condition. After 2 seconds have elapsed, participants will come to learn that an imminent response will be required of them. Therefore, one could argue that unpredictable *perceptual* feedback could also influence the timecourse of the sensorimotor transformation and the mode of reaching. Just as visuomotor uncertainty results in offline planning, perceptual uncertainty may also result in precomputing movement parameters by the ventral stream. We reported that the N170 amplitude decreased with increasing delay (although the 2 and 3–s conditions did not significantly differ from one another). While we suggest that this reflects the decay of a stored target representation, we cannot rule out the possibility that it reflects the predictability of a required response over time. The N170 could in fact be mitigated by the certainty of an upcoming response in the longer delay conditions. However, if this were the case, we might also expect to see a relationship between N170 amplitude and reaction time. If participants were better able to anticipate the impending response cue for the later delays, they may have been able to prepare the response slightly in advance, which would have been reflected by the N170 amplitude. Rather, we reported a correlation between N170 amplitude and absolute error, which better supports the theory of a decaying visual perceptual representation.

As reaches are planned and executed, different neural processes are engaged. To our knowledge, this is the first study to examine a known electrophysiological marker of ventral stream activity during a memory-guided task in which delay interval varies. Previous findings have revealed that the N170, overlapping with the auditory cue ERP is a reliable marker of increased activity within the ventral stream during the planning of actions that rely more heavily on perception-based information. The current results extend this finding and suggest that the N170, while reflective of action planning, may also reflect aspects of action execution, particularly those involved in the precision of a movement. Our electrophysiological results corroborate earlier findings, which suggest that the visual representation guiding control and movement programming decays. The N170, which was previously shown to reflect the activation level of the ventral stream, appears to also reflect the accuracy of the stored visual representation when information must be held over longer periods.

Figure 4-01

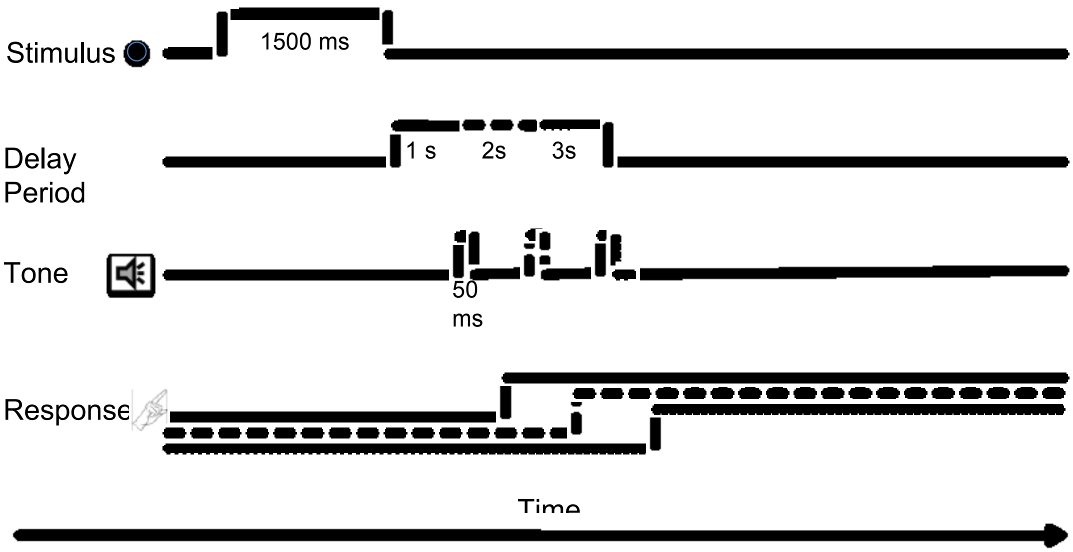
Stimulus
1500 ms
Delay
Period
1 s
2s
3s
Tone
50
ms
Response
Time

Figure 4-01 Caption:

Behavioral procedure. One hundred and twenty trials of each delay condition were presented to participants within a session. Delay conditions 1, 2, and 3 determined whether the target disappeared 1, 2, or 3 s before the auditory cue to respond, respectively.

Table 4-01

Mean behavioural measures with standard errors of the mean (SEM)

	1 s Delay	**2 s Delay**	**3 s Delay**
Reaction Time	352.0 (11.1)	311.3 (10.0)	303.8 (10.1)
Absolute Error	6.5 (0.4)	7.1 (0.4)	7.6 (0.5)
Movement Time	561.6 (23.5)	610.2 (24.6)	639.7 (25.1)

Table 4-02

Mean amplitudes and latencies (with SEMs) of the N170 ERP component

	Left Temporal	**Right Temporal**
N170 amplitude [µV]		
1 s delay	-1.28 (0.3)	-2.15 (0.4)
2 s delay	-0.77 (0.2)	-1.48 (0.3)
3 s delay	-0.85 (0.2)	-1.57 (0.4)
N170 latency [ms]		

Figure 4-02

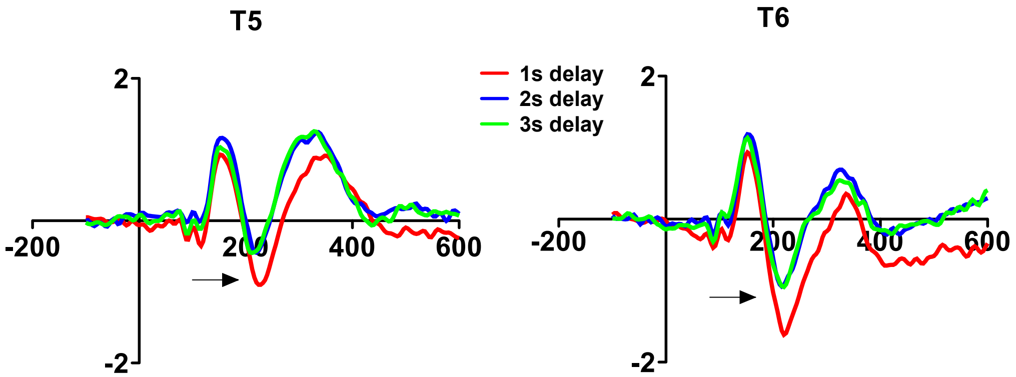
T5
T6
1s delay
2s delay
3s delay
2
-2
-200
200
400
600
2
-2
-200
200
400
600

Figure 4-02 Caption:

ERP plots for T5 and T6, the central electrodes within each temporal cluster. Delay conditions 1, 2, and 3 are plotted for each electrode, with voltage (µV) plotted on the x-axis and time (ms) on the y-axis. Arrows indicate the presence of an N170 component, peaking between 150 and 300 ms.

Chapter 4 References

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Chapter 5:

The N170 Reveals That The Right Hemisphere May Be Functionally Specialized for Ventral Stream Processing During Delayed Action

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5.0 Introduction

Rather than distributing our movements equally between the left and right hand, the majority of people use a dominant, or preferred hand for every day tasks like brushing teeth, combing hair, writing, throwing, pointing etc. The vast majority of the population is right-hand dominant (90%), while only 10% of the population is left-hand dominant, and even fewer people are ambidextrous (Hardyck & Petrinovich, 1977; van Mier, 2006). Thus, right-handed movements have been well studied, and it is perhaps unsurprising that right-handers are better at aiming, tapping, and finger sequencing tasks when using their right, as opposed to their left hand (Adam, Muskens, Hoonhorst, Pratt, & Fischer, 2010). The preferred right hand is faster and more accurate, exerts more force, and is more consistent than the non-preferred left hand (Woodworth, 1989, Annett, Annett, Hudson, & Turner, 1979; Armstrong & Oldham, 1999; Peters & Durding, 1979; Todor & Kyprie, 1980).

It has been suggested that the strong bias towards right-hand dominance may have arisen from a functional specialization of the two hemispheres. The left hemisphere, which controls the right hand, is proposed to be better suited for the coordination of motor behavior (Goble & Brown, 2008). Evidence for this theory comes from studies of neuropsychological patients as well as healthy controls. For example, optic ataxia patients display greater deficits in goal-directed movements when there is damage to the left, but not the right hemisphere (Perenin & Vighetto, 1988). Similarly, patients with unilateral lesions or tumors in the left hemisphere demonstrate bilateral impairments, whereas those with right hemisphere lesions or tumors demonstrate only contralateral impairments (Haaland, Cleeland, & Carr, 1977; Hanna-Pladdy, Mendoza, Apostolos, &

Heilman, 2002). Furthermore, functional imaging of the motor cortex in healthy adults has demonstrated similar hemispheric asymmetries during finger movements. In both left- and right-handed participants, the right hemisphere primarily increases in activity during contralateral finger movements, whereas the left hemisphere increases in activity during both contralateral and ipsilateral movements (Kim et al., 1993). Transcranial magnetic stimulation TMS studies have reported consistent findings, in that motor evoked potentials (MEPs) are enhanced in the contralateral arm during right hemisphere stimulation and in both arms when stimulation is delivered to the left hemisphere (Ghacibeh et al., 2007). Taken together, these studies suggest that networks mediating sensorimotor behavior may be functionally specialized in the left hemisphere.

The concept of hemispheric specialization has also been applied to what we know about visuomotor processing pathways in the brain. The perception-action model of Goodale & Milner (1992) suggests that vision-for-action relies on the dorsal stream whereas vision-for-perception relies on the ventral stream. While both pathways are represented in the left and right hemispheres, a recent study has shown that the left hemisphere may be more functionally specialized for the visual control of action (Gonzalez, Ganel, & Goodale, 2006). In their study, both left- and right-handed subjects were required to grasp, with either hand, objects that were embedded in visual illusions. As has been previously reported, pictorial illusions have an effect on perception but not on grasping (Aglioti, DeSouza, & Goodale, 1995; Dewar & Carey, 2006). However, previous studies have only looked at the dominant-hand actions of right-handed participants. This study found that precision grasping with the left hand (in both left and right-handed individuals) was sensitive to the illusions, whereas the right hand was immune. Because the right hand of both groups was able to accurately scale its grip suggests that the left-hemisphere may be specialized for the visual control of action, independent of handedness (Gonzalez, Ganel, & Goodale, 2006). One interpretation of the Gonzalez et al. (2006) study is that the left hand displayed sensitivity to the illusions, not because it was simply the less effective hand, but because of a right hemispheric *advantage* for the perceptual control of action. This does not stand in contradiction to their own interpretations, but rather, fits well with an overarching view that the perception (ventral) and action (dorsal) systems are functionally segregated within the two hemispheres (Adam, Muskens, Hoonhorst, Pratt, & Fischer, 2010) or interact differently within each hemisphere. One neuropsychological study reported that the visuomotor and visuoperceptual streams are more dissociated in the left than the right hemisphere, an interpretation that also fits with Gonzalez et al. (2006). If the two streams interact less within the left hemisphere, one stream (dorsal) is likely functionally dominant. Adam et al. (2010) also determined that the left-hemisphere advantage extends to other visually guided actions. Their study investigated whether reaching movements of the left and right hand were differentially sensitive to visual information (Adam, Muskens, Hoonhorst, Pratt, & Fischer, 2010). Participants were instructed to reach towards targets that were presented either independently or alongside placeholders. They reported that the presence of placeholders significantly slowed the left-handed movements, but not the right, irrespective of handedness. Together, the results of Gonzalez et al. (2006) and Adam et al. (2010) suggest that the left hemisphere is more sensitive to visual information (Gonzalez, Ganel, & Goodale, 2006); however, they also raise inquiries as to whether the right hemisphere may be more sensitive to perceptual information.

While hemispheric specialization has been studied in the context of visually guided actions, it has yet to be systematically investigated in the context of delayed actions, or those that rely on perceptual memory. When direct vision is unavailable, or vision is occluded at the time a response is cued, a stored perceptual representation must be used instead to inform the motor plan. Under such memory-guided conditions, mechanisms in the ventral stream, particularly those associated with the lateral occipital cortex (LOC), are engaged (Goodale, 1998). Converging neuropsychological, neuroimaging, and kinematic findings support this theory (Goodale et al. 1994; Hu and Goodale 2000; Westwood et al. 2000, 2001; Singhal et al. 2006; Ganelet al. 2008; Cohen et al. 2009). One particular fMRI study found that the LOC is activated in response to a target stimulus, returns to baseline levels of activity, and is activated again with the cue to respond (Singhal et al. 2013). Thus, it appears that during delayed action, mechanisms in the ventral stream become reactivated at movement initiation. This reactivation may access the stored percept and is also thought to determine the accuracy of the target location (Cruikshank et al., 2014). In addition to neuroimaging and behavioural studies, Cruikshank et al. (2012) provided the first ERP evidence that action planning in the absence of a visual target engages ventral stream processes. Specifically, the N170 event-related potential (ERP) component, which is an established marker of ventral visual stream processing, was enhanced for actions that relied on perceptual memory during movement planning (Cruikshank et al. 2012). In a goal-directed reaching task, the N170 was more negative in amplitude when the target disappeared during the reach-initiation phase of trials (with the auditory cue to respond), than when it remained visible until movement onset. These results suggest that the N170 reflects activity within the ventral stream during delayed action. That study examined only right-handed actions of right-handed participants. A more stringent test of Cruikshank et al.'s (2012) hypothesis that the N170 as a reliable marker of ventral stream processing, one would like to test whether the N170 is greater for ventral-stream-dependent movement initiation for movements made by the left hand, as well as by left-handed participants. Regarding hemispheric specialization, left-handed participants are an important group to include, as the majority of them have similar lateralization of function to right-handed individuals (Kolb & Whishaw, 2008) but, by definition, have different dominant hands. Left-handed participants, in this way, can help untangle effects due to hemispheric specialization versus simple hand-dominance. If 'vision-for-action' and 'vision-for-perception' are differentially represented within the left and right hemispheres, the N170 should reveal this as well. Stored perceptual information needs to be reactivated in the ventral stream during a memory task (Cruikshank et al., 2014), and this perceptual contribution to planning is intimately linked to the motor act itself. Visual information, even if it arrives symmetrically at the two hemispheres, needs to be sent to the relevant motor cortex for programming a movement. Because right-sided visual areas are more directly connected to right-sided motor areas, and vice versa for the left (no crossing of the callosum is needed), one might assume that the left ventral stream is more relevant for right-handed movements and the right for left-handed movements. If however, the ventral stream is functionally specialized in the right hemisphere, then that hemisphere should be more relevant for all delayed actions (e.g., as a main effect), regardless of the hand being used.

In short, we compared the N170 during the response initiation phase of two different reach-to-point trials. The target was either present (condition 1) or absent (condition 2) during initiation, thereby altering the contribution of perceptual memory, and thus, the ventral stream, during the motor planning phase. The goals of this study were two-fold. First, we wanted to determine whether the enhancement of the N170 in the delayed condition that we previously observed also extends to non-dominant hand actions in both right and left-handers. If the N170 is a marker of ventral stream processing during delayed action, it should be larger in amplitude for condition 2 (which recruits ventral stream resources more than condition 1) regardless of hand used or handedness. The N170 should thus be greater in condition 2 than condition 1 in left-handed movements as well as in left-handed participants, using both hands. If instead, the N170 reflects aspects of motor programming that also involve selection of the dominant hand, there should be no difference in N170 amplitude between condition 1 and condition 2 when the non-dominant hand is used. Secondly, just as the left hemisphere is thought to specialize in the visual control of action, we tested whether the right hemisphere may be functionally specialized for the perceptual control of action. Both behavioural and ERP measures were examined. Behaviourally, if the dominant hand is simply better at everything, right-handers should be better at delayed action using their right hands and left-handers, their left. Absolute error should be lower when participants utilize their dominant hand. If instead, the right hemisphere is specialized for vision-for-perception, we might predict that both groups are better using their left hands in condition 2 (controlled by the right hemisphere). The left-handed participants would then also enjoy the added benefit of using their dominant hand *and* the putative specialized hemisphere. Right-handers, though they would engage the specialized hemisphere to control the limb, would be at a disadvantage using their non-dominant hand. In terms of electrophysiology, if the right hemisphere is specialized for ventral stream processing, it should contribute more to the processes associated with delayed action planning, which would appear as a main effect of hemisphere (electrode) on the difference between the N170 during condition 2 and condition 1.

It is important to consider that although we manipulated handedness and hand-used in this experiment, we did not manipulate laterality of the visual routes. Participants were told to fixate on the target; thus, we can assume that visual information arrived symmetrically and that both hemispheres had equal access to the target-location. If ventral reactivation is lateralized to the right hemisphere, there should be a greater difference in the N170 amplitude between conditions over the right hemisphere, regardless of the hand being used. If however, the right ventral stream is not specialized for delayed action, then we should expect the difference in N170 amplitude between conditions 1 and 2 to be largest over the hemisphere contralateral to the movement.

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5.1 Materials and Methods

5.1.1 Participants.

Thirty (19 female) right-handed and twenty-six (11 female) left-handed undergraduate students, ages 17-27 (mean 20 yr, SD 2.3 yr) received psychology course credit for participating in this study. Handedness was assessed by the Edinburgh Handedness Inventory (Oldfield, 1971) where the criterion for inclusion was scores > +40 for right-handers and < – 40 for left-handers. All participants had normal or corrected-to-normal vision, and normal hearing. Written informed consent was obtained prior to the experiment in accordance with the University of Alberta's ethical review board, and the Declaration of Helsinki.

5.1.2 Procedure.

The study was conducted in a darkened, electrically shielded, and sound-attenuated chamber. At the start of the experiment, participants were seated in front of a 430.4 mm □ 270.3 mm touchscreen. At the beginning of each session, the touchscreen was recalibrated by the participant being tested to ensure that accuracy measures remained reliable across subjects. Based on average distance from the screen (52.3 cm), the horizontal and vertical visual angles of the touchscreen were 44.73° and 28.98°, respectively. The horizontal and vertical visual angles of the stimuli were 0.99° and 1.53°, respectively.

The task was the same as that used by Cruikshank et al. (2012), but with the modification that participants switched hands during different blocks of the experiment. Participants were required to reach towards and touch 9 mm x 14 mm black dots displayed on a touchscreen using E-Prime presentation software version 1.2 (Psychology Software Tools). The participant depressed a button to begin a trial. One second after the button was depressed, a target appeared on the screen in a random location, which the participant was told to fixate on. An 800 Hz, 64 dB (SPL) tone sounded 1–3 s after the target appeared. The participant was instructed to continue holding down the button until he/she heard the tone, and then to touch the target as quickly and accurately as possible. In condition 1, the target disappeared as soon as the button was released (i.e., with movement onset). After 1 s, if the participant had not yet initiated a movement, the target disappeared. In condition 2, the target disappeared simultaneously with the onset of the tone (Figure 1). After participants made contact with the screen, they were to return their finger to the response box and hold down the button, which advanced the next trial after 1 s. Condition 1 and condition 2 trials were presented in random order with the restriction that a particular condition did not occur more than 5 times consecutively. A total of 360 test trials (180 per condition) were included in 4 blocks per session. Each block contained either 90 left- or 90 right-handed trials, in which participants were instructed to reach with only that hand for the duration of the block. Blocks were counterbalanced and participants were given a break period for a self-determined length of time after every block. If reaching with the right hand, participants were instructed to keep their left hand in their lap and vice versa.

5.1.3 Behavioral Analyses.

For each trial, reaction time (RT) and movement time (MT) were recorded. RT was defined as the time it took to initiate a movement in response to the beep, and MT was defined as the time it took to fully execute a movement, from release of the response button to contact with the touchscreen. Touch positions were monitored, and absolute error (pixels/mm) was recorded for each trial. Trials were excluded from analyses if RTs were ≤ 150 ms or ≥ 800 ms or MTs were ≤ 200 or ≥ 2000 ms (< 5% of all trials). Statistical analyses were carried out using Matlab 7.1 (The Mathworks) and SPSS (version 18.0).

5.1.4 EEG recording and analysis.

EEG was recorded using a high-density 256-channel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR), amplified at a gain of 1000 and sampled at 250 Hz. Impedances were kept below 50 kΩ and the recording was initially referenced to the vertex electrode (Cz). Signal was preprocessed using EEGlab 7.1.4 (Delorme and Makeig 2004), running under Matlab 7.1 (The Math-Works). Signal was bandpass-filtered from 0.5 to 50 Hz and was re-referenced to a common average. Independent component analysis (ICA) was then performed to detect and remove artifacts from the data. Those components accounting for stereotyped artifacts, including eyeblinks, eye movements, and muscle movements, were identified and removed from the data. Artifactual components were determined by visual inspection of the spectral characteristics, time courses, and spatial topographies of all components. EEG was segmented into 1100-ms epochs, time-locked to the auditory cue to respond (epochs extended from 100 ms prior to the tone to 1000 ms after the tone). Trials were averaged together and baseline-corrected relative to pre-stimulus activity (–100–0 ms). On average, 97% of trials for each of the 4 conditions (condition 1_right hand, condition 1_left hand, condition 2_right hand, condition 2_left hand) per subject were retained. The maximum negative (N170) peak values between 100–300 ms were extracted and mean voltages were calculated across a window extending one sample in either direction of the peak's maximum. Peak latency was also quantified, based on the peak's maximally negative value. Analysis of the N170 was conducted at T5 and T6 electrodes. Statistical analysis was conducted using SPSS version 18.0.

5.2 Results

5.2.1 Behavioral Measures

Mean absolute error and MT are reported in Table 1. Average absolute error (Figure 2) was compared using a 2 X 2 X 2 repeated-measures ANOVA. Within-subjects' factors were condition (1/2) and hand used (dominant/non-dominant). Handedness was a between-subjects' factor. A main effect of condition, F(1, 53) = 12.93, p <0.01, revealed that absolute error was greater for condition 2 than condition 1, consistent with previous findings (Cruikshank et al. 2012; Cruikshank et al., 2014) and a theory that actions requiring more perception-based information are less accurate because they rely on the recall of target features (Goodale et al. 1994). There was also a two-way, condition X hand-used interaction, F(1 53) = 7.22, p <0.05. Simple effects revealed that condition 1 dominant-hand actions were more accurate than condition 1 non-dominant hand actions, p<0.05. However, for condition 2, dominant-hand actions were no different in terms of accuracy than non-dominant hand actions. These results are consistent with previous studies, which have demonstrated that visually initiated actions are performed better when individuals use their dominant hands. However, our novel finding was that actions initiated in the absence of a visual target appear to be performed equally well with either hand, regardless of handedness.

Movement time was analyzed using a 2 X 2 X 2 repeated measures ANOVA with the same design. Handedness was a between-subjects' factor. Only the main effect of hand used was significant, F(1, 54) = 4.91, p<0.05, revealing that actions were performed faster with the dominant than non-dominant hand.

5.2.2 N170

To test our first hypothesis, that the N170 reflects ventral-stream activity quite generally, we conducted ANOVAs collapsing the N170 ERP values across left and right-handed participants and T5 and T6 electrodes, where the N170 is typically reported, and coded hand-used as dominant vs. non-dominant. The grand-average ERP is shown in Figure 2. A condition[2] (1/2) × hand used[2](dominant/non-dominant) repeated measures ANOVA revealed a main effect of condition on N170 amplitude, F(1.00, 54) =32.00, p <0.01. Condition 2 trials were more negative in amplitude than condition 1, replicating our previous result (Cruikshank et al., 2012) and extending it to left-handers and left-handed actions. The main effect of hand-used and interaction were not significant.

To test the hypothesis that the right hemisphere is specialized for ventral-stream processing, we asked whether there was a greater difference in N170 amplitude between condition 1 and condition 2 over the right hemisphere during the planning phase of actions. We did not examine the absolute amplitude of the N170 over T5 and T6 electrodes, but rather, the difference in amplitude between conditions. The N170 is likely the sum of several generators; thus, to test our hemispheric specialization hypothesis, the difference in N170 amplitude between conditions was the measure, with the aim of isolating the portion of the N170 peak that is related to ventral-stream activity. Figure 3 presents the grand average ERP figures for each electrode and handedness group. Figure 4 plots the difference in N170 amplitude between conditions 1 and 2 as a function of electrode (T5 and T6), hand-used and handedness. A mixed, repeated-measures 2 × 2 × 2 ANOVA (within-subjects factors were condition and hand used; the between-subjects factor was handedness) revealed a main effect of electrode, F(1 53) = 7.30, p <0.01; there was a greater difference in N170 amplitude between condition 1 and 2 at the right (T6) electrode. There was also an electrode X handedness interaction, $F(1, 53) = 5.17$, $p < 0.05$. Simple effects revealed that the amplitude difference (condition 2 – condition1) was still significant when the left-handed participants were analyzed on their own, but not for right-handed participants.

5.3 Discussion

The first aim of this study was to determine whether the same ventral-stream processes are engaged and reflected by the N170 during memory-guided actions, regardless of hand-dominance or the hand being used. Here, we examined both right and left-handed actions, and included both right and left-handed individuals. Results revealed that regardless of handedness or hand used, the N170 was more negative in amplitude for condition 2 than condition 1. Because the target is occluded during the initiation phase of condition 2 trials, this result lends further support to the N170 as a marker of ventral stream activity. During a memory task, stored representations of perceptual information must be recruited during recall (Goodale & Milner, 1992; Klatzky et al., 1993). Furthermore, the process of remembering often reactivates sensory cortices that were initially activated during stimulus encoding (Johnson, Mitchell, Raye, D'Esposito & Johnson, 2007; Geng, Ruff, & Driver, 2009). If the N170 amplitude had remained the same between visually and memory-initiated trials when participants utilized their non-dominant hand, we might conclude that the component did not in fact reflect general ventral stream processes required for action. Rather, the N170 would in that case have reflected hand dominance effects, or the brief maintenance and recall process involved in selecting the dominant hand when performing delayed action. Similarly, if the N170 amplitude did not differ between conditions for left-handed participants, our initial interpretations (Cruikshank et al., 2012) would not generalize to the broader population. Rather, because there was a difference in amplitude after collapsing across handedness, these results corroborate earlier findings and suggest that the N170 may be a reliable marker of increased activity within the LOC during delayed action. Ventral-stream regions reactivate during a memory-initiated task (Singhal et al., 2013; Cruikshank et al., 2014), and the N170 appears to reflect this reactivation in both left and right-handed individuals.

Our second aim was to test the hypothesis that the right hemisphere is specialized for vision-for-perception. For visually initiated trials (condition 1), participants were more accurate using their dominant hand. This is not surprising and fits with a large body of literature indicating that the dominant hand is more accurate and consistent when performing aiming tasks. However, those actions that were initiated using a perceptual memory (condition 2) were found to be equally accurate using either hand. This novel result is surprising for a number of reasons. First, one could argue that it does not support a theory of hand dominance. Even though the task still involves reaching and pointing, it suggests that actions requiring perceptual memory somehow mitigate the deficits one suffers when using their non-dominant hand. Though this was an unexpected result, the fact that the interaction was significant in condition 1 demonstrates that we had sufficient power to detect a similarly sized effect in condition 2. Additionally, condition 2 actions were faster with the dominant hand, which suggests there is at least some influence of hand-dominance on the behaviour. Perhaps the task of remembering the target location requires such an increase in processing that it offsets the difficulty of coordinating the non-preferred hand. Because the target was always changing from trial to trial and participants were not given immediate accuracy feedback, the cognitive demand may have interfered with motor execution. Studies should be conducted to examine the left-handed actions of visual agnosics to determine whether or not their deficits extend to the non-dominant hand. Recently, a study found that patient D.F., who has bilateral damage to her LOC, had large and consistent impairments pointing with her left and right hand towards targets (Hesse et al., 2014). She appears to be a patient who suffers from combined ventral *and* dorsal damage (Hesse et al., 2014) and it's been suggested that she uses haptics, rather than intact vision-for-action, to reach for objects (Schenk, 2012). Patients with less diffuse damage that is localized to one hemisphere should be examined; however, focal lesions rarely occur naturally.

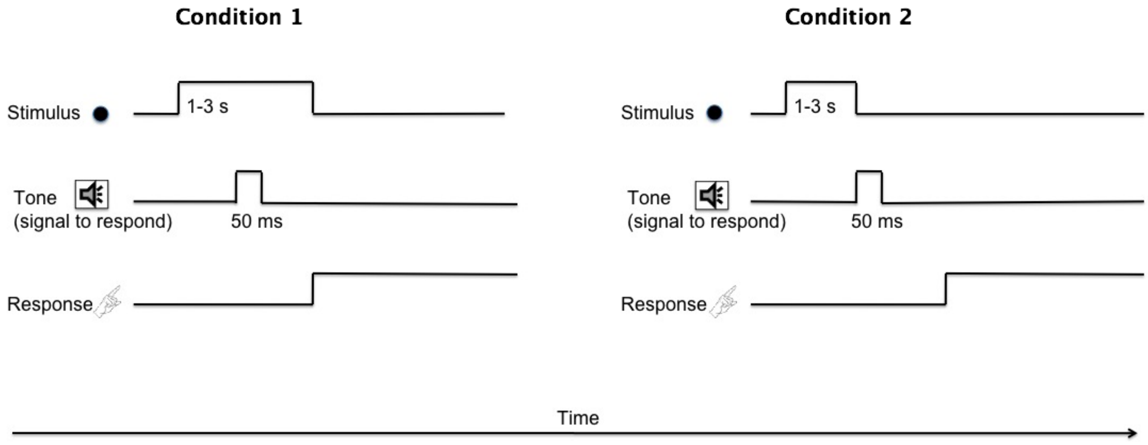
Secondly, the absolute error results do not corroborate Gonzalez et al.'s (2006) study. They reported that the left hand was sensitive to visual illusions, regardless of handedness. In accordance with their results, we would have expected the left hand to be sensitive to perceptual information as well and thereby display an advantage for delayed action. However, the Gonzalez et al. study had participants grasping objects that were embedded in two separate visual illusions. Precision grasping involves a different functional anatomy than basic pointing, and pictorial illusions are much more complex stimuli. Therefore, it is difficult to directly compare our task to theirs. The fact that left- and right-handers were equally as good using either hand in our study suggests that hand dominance does not affect perceptually driven actions and this does not support a right hemispheric functional specialization for the ventral stream. However, if we consider alternative interpretations, they are not supported by the results either. The left hemisphere cannot be dominant for memory-initiated action because there was no accuracy advantage when performing right-handed condition-2 actions. Furthermore, such an interpretation would contradict a whole body of previous work. The fact that there is a cross-over interaction for condition 1 actions (error rate decreases when participants use their dominant hands), suggests that our accuracy measures are reliable and further supports this argument. Our movement time results also confirm that our task is sound; our initial findings were replicated (Cruikshank et al., 2010; 2012; 2014) and demonstrate that actions requiring more perception-based information are slower. Taken together, our behavioral results do not argue strongly in support of a right hemispheric ventral stream advantage, but they do not rule it out either.

The ERP results, on the other hand, revealed that the N170 difference between conditions was greatest over the right hemisphere. This result was still significant when the left-handed participants were analyzed separately, but was not significant for the right-handed participants alone. These results support a theory of right-hemispheric specialization for ventral-stream function. Because left-handers were engaging both their dominant hand and the putative specialized hemisphere for condition 2, it makes sense that the N170 difference was larger over T6 compared to the right-handers. For the right-handed group, hand-dominance effects appear to have acted against the right-hemispheric dominance for memory-guided action.

5.4 Conclusion

At face value, the results of this study are complicated, but when one unravels effects of hand-dominance from hemispheric specialization, the results may lend some support to the hemispheric specialization theory. Absolute error in this task indicates that hand dominance is important for visually initiated tasks; however, the preferred hand does not display an advantage for tasks that are more perceptually driven. The electrophysiological results of this study extend boundary conditions implicating the N170 as a marker of ventral-stream activity. They also support a theory of right hemispheric specialization for perception-for-action. Our findings suggest that whereas visually guided action is left-dominant, memory-guided action may be right-dominant.

Figure 5-01



Condition 1
Condition 2
Stimulus
1-3 s
Tone
(signal to respond)
50 ms
Response
Stimulus
1-3 s
Tone
(signal to respond)
50 ms
Response
Time

Figure 5-01 Caption:

Schematic of the behavioral paradigm. 180 trials of each condition were presented to participants within a session. In condition 1, the tone sounds and the stimulus disappears when the participant lifts his/her finger from the response box. In condition 2, the tone sounds simultaneously with the disappearance of the target. 4 blocks (2 in which participants moved with their right hands, 2 with their left) were counterbalanced across subjects.

Table 5-01

Mean behavioural measures (with standard deviations)

	Right-Handed Participants				**Left-Handed Participants**			
	Dominant Hand		**Nondominant Hand**		**Dominant Hand**		**Nondominant Hand**	
Condition	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
Absolute Error [#pixels]	5.69 ± 1.4	5.98 ± 1.4	6.00 ± 1.1	6.17 ± 1.4	5.56 ± 1.4	6.36 ± 1.8	6.11 ± 1.6	6.27 ± 1.5
Movement Time [ms]	528. 1 ± 113.9	525.7 ± 114.6	547.9 ± 112.7	547.8 ± 126.0	612.3 ± 242.6	616.1 ± 258.7	626.6 ± 208.5	630.4 ± 209.3

Figure 5-02

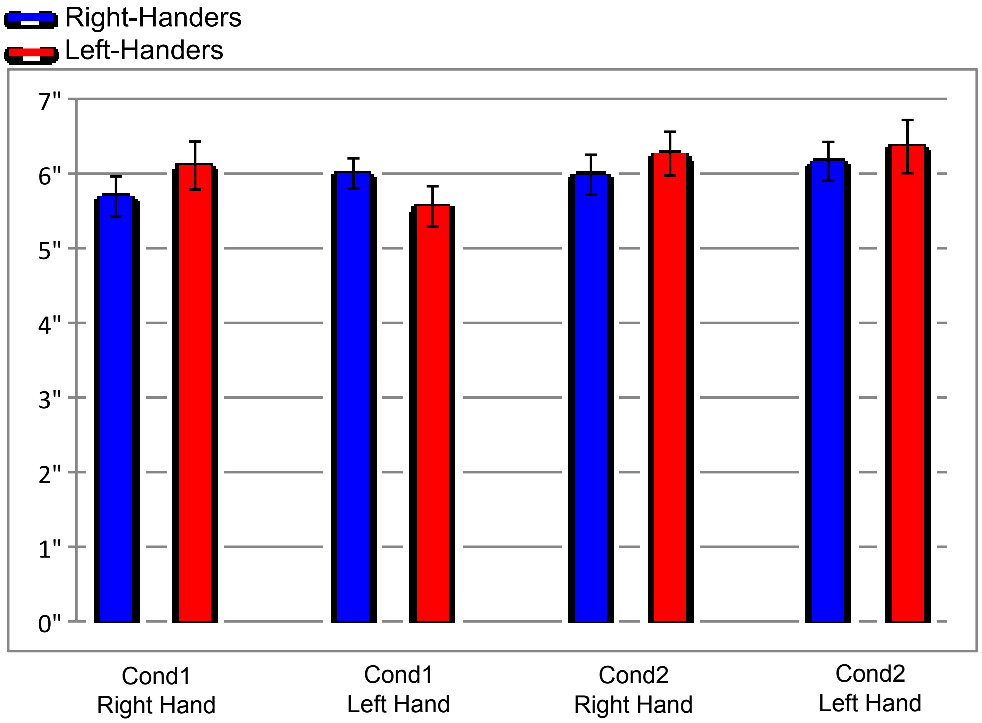

Right-Handers
Left-Handers
7"
6"
5"
4"
3"
2"
1"
0"
Cond1
Right Hand
Cond1
Left Hand
Cond2
Right Hand
Cond2
Left Hand

Figure 5-02 Caption:

Absolute error for both handedness groups, across conditions and hand used. Error bars represent standard error.

Figure 5-03

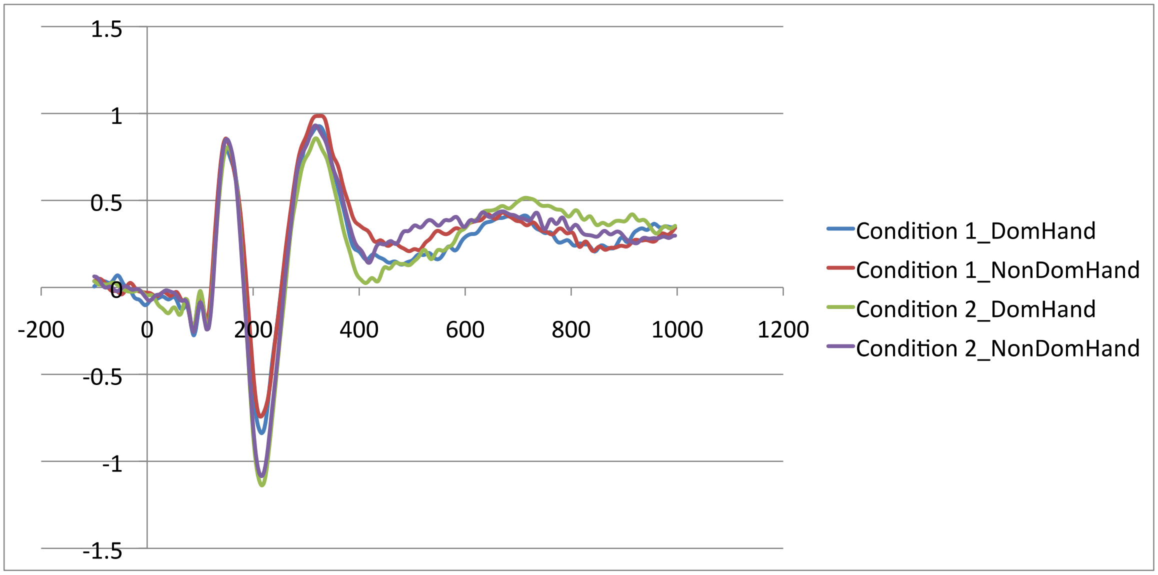

1.5
1
0.5
0
-0.5
-1
-1.5
-200
0
200
400
600
800
1000
1200
Condition 1_DomHand
Condition 1_NonDomHand
Condition 2_DomHand
Condition 2_NonDomHand

Figure 5-03 Caption:

Grand average ERP, averaged across T5 and T6 electrodes. Voltage (μV) is plotted on the y-axis and time (ms) on the x-axis.

Figure 5-04

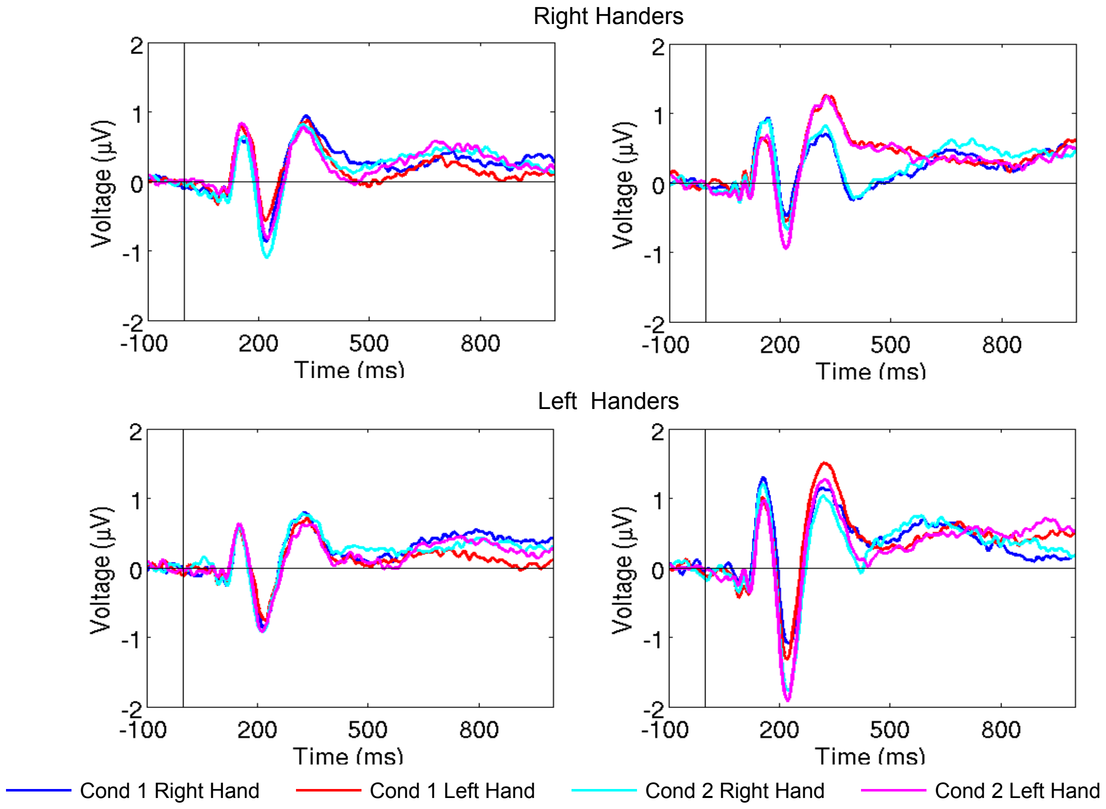

Right Handers
2
1
0
-1
-2
Voltage (µV)
-100
200
500
800
Time (ms)
Left Handers
Cond 1 Right Hand
Cond 1 Left Hand
Cond 2 Right Hand
Cond 2 Left Hand

Figure 5-04 Caption:

Grand average ERPs for right and left-handed participants. The T5 electrode is depicted in the two left panels, and T6 on the right.

Figure 5-05

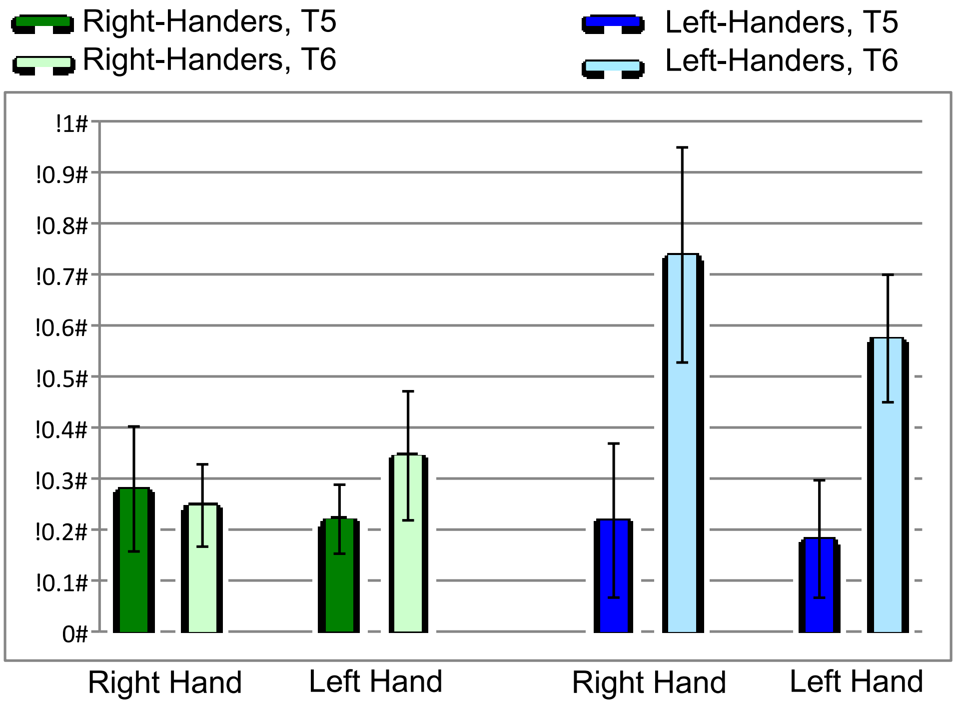

Right-Handers, T5
Right-Handers, T6
Left-Handers, T5
Left-Handers, T6
!1#
!0.9#
!0.8#
!0.7#
!0.6#
!0.5#
!0.4#
!0.3#
!0.2#
!0.1#
0#
Right Hand
Left Hand
Right Hand
Left Hand

Figure 5-05 Caption:

The difference in N170 amplitude between conditions 1 and 2. Voltage is plotted on the y-axis. Error bars represent standard error.

Chapter 5 References

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Chapter 6:

General Conclusion

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6.1 Chapter Review

The purpose of the preceding experiments was to investigate the electrophysiological basis of human sensorimotor integration. EEG has the strong advantage of providing excellent temporal resolution (millisecond time-range), and while the technique has certainly been used before to investigate sensorimotor behaviour, the particular measures that I used and the hypotheses that I tested were novel. I was interested in the visuomotor processes that contribute to delayed action and how the brain coordinates both immediately available visual information and visual memory to execute a movement. In order to address this, I examined patterns of brain activity for which there was a precedent for reflecting communication between the sensory and motor networks. By implementing a unique goal-directed reaching paradigm, I was able to include slight procedural differences that had profound implications for which brain regions support the reach behaviour. In the basic paradigm, participants were auditorily cued to touch target dots on a touchscreen. Two viewing conditions varied with respect to the contribution of the ventral visuomotor stream during response initiation. In condition 1, the target disappeared with movement initiation whereas in condition 2, it disappeared with the cue to respond. Because participants cannot make a 0 ms response, the ventral stream was presumably engaged to a greater extent for condition 2. Chapters 2, 3, and 5 all compare these two conditions. In chapter 4, the ventral stream is necessary for response initiation in all conditions, but I extended the delay interval to possibly increase its demand.

In chapter 2, I examined theta (4-8 Hz) oscillations, a putative rhythmic mechanism for sensorimotor integration in rats. Electroencephalographic recordings from the hippocampus of many animals reliably display a robust, large amplitude oscillation occurring at a frequency of 3-12 Hz. These theta oscillations have been implicated in various animal behaviors, including locomotion (Vanderwolf, 1969, Yoshi et al., 1966, Buno & Velluti, 1977, Komisaruk, 1970, Black et al., 1972), exploratory behavior (Buzsaki, 2005, Grastyan et al., 1966, Routtenberg & Kramis, 1968, Macrides et al., 1982, Kahana et al., 2001), neural coding of place (Yamaguchi et al., 2007, O'Keefe & Recce, 1993, Jensen & Lisman, 2000, O'Keefe & Conway, 1980, Sutherland & Rodriguez, 1989), memory (Berry & Thompson, 1978, Griffin et al., 2004, Berry & Thompson, 1979, Winson, 1978), and LTP (Larson et al., 1986, Orr et al., 2001, Pavlides, 1988, Holscher et al., 1997, Huerta & Lisman, 1996). However, Bland (1986) proposed an alternative function of theta oscillations: to integrate sensory and motor information during sensorimotor behavior. Thus, the Theta Model of Sensorimotor Integration posits that theta oscillations serve as a type of carrier wave, which the sensory and motor systems use to inform and update one another, and coordinate activity (Bland, 2007). However, it was unknown whether cortical theta activity underlies sensorimotor integration in humans. Rather, the mu rhythm (8-12 Hz) is typically reported during motor behavior and desynchronizes with movement. Because of the robustness of mu activity, researchers may have been distracted from following up on possible theta synchronization during movement. I measured oscillatory EEG activity for the two conditions of my reaching paradigm and tested the hypothesis that theta activity would reflect changes in the relevant sensorimotor network. I found that condition 2 engaged ventral stream mechanisms to a greater extent than condition 1. Theta oscillations were indeed more prevalent during movement initiation and execution than during periods of stillness, consistent with a sensorimotor relevance for theta activity. Most importantly, theta activity was more prevalent at temporal sites, which overlie the ventral stream, in condition 2 than condition 1 during response initiation. This suggests that theta activity is present within the necessary sensorimotor network. Mu activity also desynchronized more during condition 2 than condition 1, suggesting mu desynchronization is specific to the sensorimotor network as well. In summary, I found that cortical theta synchronization and mu desynchronization may represent broadly applicable rhythmic mechanisms for sensorimotor integration in the human brain.

In chapters 3–5, I examined a time-limited neural mechanism of sensorimotor integration: the N170 ERP component. This component was known to reflect visual perceptual processes and to have a source in the lateral occipital cortex (LOC) and temporal-lobe regions. Convergent evidence from neuropsychological and neuroimaging studies suggested that the LOC is recruited for action tasks in which visibility of a target is unavailable and a perceptual memory of the target's characteristics must be used instead. Therefore, I tested the hypothesis that the N170 reflects the contribution of additional ventral-stream processes required for performing actions in which vision of a target is occluded. I predicted that the amplitude of the ERP in the latency range of the N170 would be larger when perceptual mechanisms were engaged to a greater extent. The task was identical to that used in chapter 2 and I found that during the response-initiation phase of reaches, the N170 was larger in amplitude for condition 2. This effect was observed over temporal electrode sites bilaterally, likely reflecting an overlap between auditory cue-related processes and additional perceptual processes within regions in the inferior-temporal cortex. Results of this study suggest that the N170 may be a marker of neural activity within the ventral stream. Thus, they are consistent with the influential perception-action model of Goodale & Milner (1992), which suggests that actions initiated in the absence of a visual target engage the ventral stream. The ventral visual stream is argued to be fundamental for conscious perception and thus, delayed action may be a conscious process that we engage in. Results also help to further explain why visual agnosia patient D.F., who suffers bilateral ventral stream damage, is unable to perform actions to disappearing objects. I would predict that D.F. displays a much smaller, or nonexistent N170 during delayed action. In addition, they support fMRI work that has shown that the LOC is re-activated when actions are performed without vision of a target (Singhal, Kaufman, Valyear, & Culham, 2006). An electrophysiological measure of ventral stream activity has never before been identified, and my results have spawned a brand new direction of research, making it possible, for myself and others, to continue to ask questions about the functions of the ventral visual stream with a new measure (an ERP peak).

In chapter 4, I followed up on the results of chapter 3 and examined longer delay intervals between target occlusion and response initiation. Delayed action research has suggested that perceptual information about a visual stimulus decays over several seconds. Furthermore, behavioral and neuroimaging studies have suggested that when longer delays are employed, reactivation of ventral areas is necessary in order to access a stored representation of a target's characteristics. Therefore, I sought to track the time course of the electrophysiological processes associated with this decay. I predicted that the N170 reflects not only the perception-for- action processes, but also the accuracy of a stored representation. In order to test this, I measured the N170 during memory-guided reaching when 1-, 2-, and 3-s delays separated target occlusion and response initiation.

During reach initiation, the N170 was more negative and peaked earlier for the 1 s than the 2- and 3-s delays and correlated significantly with performance at the longest delay. These results suggest that the neural mechanisms involved in movement planning change for delays beyond 1 s. I concluded that the smaller N170 might reflect an impoverished visual perceptual representation in the ventral stream.

Finally, in chapter 5, extrapolating from the suggestion that the left hemisphere is functionally specialized for visually guided action, I came up with the novel hypothesis that the right hemisphere is in turn, specialized for vision-for-perception. I assessed this by examining left- and right-handed goal-directed reaching, performed by left- and right-handed participants. The basic paradigm was the same as that used previously, in that condition 1 could be initiated by the dorsal visuomotor pathway but condition 2 would have to be initiated with the ventral visuomotor pathway. The N170 during response-initiation was larger in condition 2 than condition 1, regardless of handedness or hand used, extending boundary conditions implicating the N170 as a marker of ventral-stream activity. Thus, these findings showed that my initial result (Cruikshank et al., 2012) is far more general than we knew. In line with the right hemisphere specializing in memory-guided action, the difference between conditions was greatest over the right hemisphere. This result was still significant when the left-handed participants were analyzed on their own, but not for right-handed participants, for whom hand-dominance effects appear to have acted against the right-hemispheric dominance for memory-guided action. These findings further support the N170 as an electrophysiological marker of ventral-stream processing and suggest that whereas visually guided action is left-dominant, memory-guided action may be right-dominant.

6.2 Contributions to the Field

This programme of research has moved the field of memory and action forward in a number of different ways. First, results from my experiments have corroborated various neuroimaging, behavioural, neuropsychological, and animal studies, lending additional support to already established theories of sensorimotor behaviour. To my knowledge, these are the first electrophysiological results to verify the notions that a) actions initiated in the absence of a visual target rely more on perceptual representations than those directed towards visually available targets, and b) there is a decay of visual perceptual information that occurs with increasing time. Secondly, they replicate other electrophysiological studies that have examined sensorimotor behaviour. For example, I found that the mu rhythm desynchronizes in humans during my basic reach-to-point task. Thirdly, these results have provided new insight into how sensorimotor networks coordinate on exceedingly fast timescales to produce a multitude of complex actions. By utilizing EEG/ERP methodology, I was able to broaden our understanding of how rhythmic and non- rhythmic brain-activity produces effective sensorimotor behavior. Novel contributions to this field include a) theta activity is a likely mechanism for sensorimotor integration in the human brain, b) mu suppression is a sensorimotor, and not just a motor phenomenon, c) the N170 reflects ventral reactivation necessary for performing delayed action, d) not all delays are created equal for ventral processes, and e) the right hemisphere may be specialized for vision-for-perception. Lastly, results of this research programme may be able to contribute to other closely related areas of study. They may inform our understanding of the mechanisms involved in certain movement disorders, such as Parkinson's, MS, ALS, and the ataxias. Based on our findings, new means of diagnosing and tracking rehabilitation techniques may be developed. Furthermore, the tasks used in these experiments involve hand and limb actions in conditions that use delayed information. The results of this research may be able to inform neuroprosthetic research that has thus far focused only on immediate, visually guided actions. Lastly, results may also inform research beyond the sensorimotor domain as well, to help us understand how brain regions integrate even in higher-cognitive tasks that have little or no motor component.

6.3 Future Directions

6.3.1 Oscillations

Oscillations may propogate information through the relevant sensorimotor network. When two brain regions simultaneously exhibit synchronized oscillations, their membrane potentials will tend to depolarize together. Thus, a pair of regions will tend to reach threshold and produce action potentials synchronously as well. This process could be what facilitates information transfer between sensorimotor areas.

In chapter 2, I found support for the hypothesis that theta is a mechanism for sensorimotor integration in humans. These results are consistent with a model of (hippocampal) theta in rats during sensorimotor integration, which posits that theta oscillations function like a carrier wave, which the sensory and motor systems use to coordinate their activity. Fast rhythms can involve only small, localized groups of neurons because of axon conduction delays and synaptic delays, whereas slower oscillations can span and recruit a larger population of neurons. Thus far, the theta model of sensorimotor integration extends from animal to human in that theta is present during sensorimotor behavior. We demonstrated that the topography, and proportion of theta activity changes as the cortical circuitry that is required for executing a particular sensorimotor behavior changes. Because theta is a relatively slow oscillation, it may be working to facilitate inter-regional coordination between the dorsal and ventral streams and other areas that are functionally involved in delayed actions. However, it remains unclear whether characteristics of theta in humans co-vary with aspects of behavior. This is important in order to draw firm conclusions about theta's involvement in sensorimotor function. In order to test this, features of sensorimotor behavior need to be directly manipulated to determine whether theta varies systematically with different manipulations. For example, in rats, theta frequency and amplitude have been reported to co-vary with the speed and magnitude of movements, respectively (Vanderwolf, 1969). Smaller movements in rats, such as postural adjustments, are accompanied by smaller amplitude and lower mean frequency theta (Vanderwolf, 1969). Similarly, wheel-running experiments have shown that theta frequency is systematically related to the speed of movement initiation (Oddie et al., 1996, Shin & Talnov, 2001). A jump avoidance study also determined that the amplitude of theta increases with the magnitude of a movement (Bland et al., 2006), or the effort that is required to execute the movement. These findings suggest that theta activity is likely more than just a simple marker of state in animals. In humans, if theta activity is directly involved in sensorimotor function, we should expect to find correlations between characteristics of theta and behavior. In our initial reaching study, participants were required to make goal-directed movements to target dots appearing on a touchscreen. Movement times (speed) only ranged between 200–2000 ms, while the vertical dimension of the touchscreen restricted the height (magnitude) of each reach. Thus, such small differences may not have been enough to elicit any change in the frequency or amplitude of theta. Furthermore, the function of theta oscillations may be to optimize performance during sensorimotor behavior, and characteristics of theta may vary with the precision of a movement, in addition to its speed or magnitude. In our initial study, all targets were the same size. Thus, each response was accurate according to the same criteria. Future studies may directly manipulate the speed of movements, as well as the effort and precision that is required in order to test the hypothesis that characteristics of theta co-vary with these aspects of sensorimotor behavior.

Another future direction involves re-analyzing the data from the experiments presented in chapters 4 and 5 for oscillations. In chapter 4, the time between target occlusion and response was manipulated in order to determine how ventral stream activity varies with delay interval. Because participants know that a response is eventually required in this task, the preparatory phase should require continual updating and integration of perceptual information. Therefore, I would predict that theta oscillations would span the entire time period from visual presentation to response initiation, regardless of the length of the delay. Furthermore, differences in mu activity between visually initiated and delayed reaching may indicate different levels of cortical activation required to perform particular sensorimotor tasks. This may extend to longer delay periods, whereby we see increased mu suppression over longer delays. In chapter 5, I manipulated the hand used to perform delayed action and the handedness of participants. If the right hemisphere is functionally specialized for delayed action, I would predict that theta activity is more robust over the right than the left hemisphere. However, because mu suppression is known to occur most strongly over the hemisphere contralateral to the limb, I would predict to see this pattern of activity instead.

6.3.2 ERPs

In three of the aforementioned experiments, visually initiated and memory-initiated actions were compared. Results revealed that the N170 is a marker of ventral stream processing during delayed action (chapters 2, 3, and 5). However, delayed actions are also known to involve dorsal-parietal regions. Hence, a natural direction for future research is determining whether a neural marker of dorsal stream processing also exists. Experiments that involve truly visually guided conditions, in which the target remains visible throughout the entire reach, should be included as a manipulation. Similarly, tasks in which the target reappears throughout different times of the reach trajectory might reveal how visual information is incorporated with a motor program at different stages of a reach. By reintroducing the target at various stages throughout the reach, we may be able to parametrically manipulate the demands on dorsal-stream activity and isolate a putative neural marker of dorsal processing.

The research outlined in this thesis has opened up many avenues for future exploration, and by continuing to use electrophysiological techniques we may continue to bolster our understanding of the processes involved in sensorimotor integration.

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