Summer 7-10-2017

An Investigation of the Neural Components and Saccade Sequences that Enable Direct Navigation through Virtual Space

Daniel R. Barto
University of New Mexico

Recommended Citation

Barto, Daniel R.. "An Investigation of the Neural Components and Saccade Sequences that Enable Direct Navigation through Virtual Space." (2017). https://digitalrepository.unm.edu/psy_etds/219

Daniel Barto
Candidate

Psychology
Department

This dissertation is approved, and it is acceptable in quality and form for publication:

Approved by the Dissertation Committee:

Dr. Derek Hamilton , Chairperson

Dr. Tom Caudell

Dr. Jim Cavanagh

Dr. Ben Clark

AN INVESTIGATION OF THE NEURAL COMPONENTS AND SACCADE SEQUENCES THAT ENABLE DIRECT NAVIGATION THROUGH VIRTUAL SPACE

by

DANIEL ROBERT THOMAS BARTO

B.A. Psychology, University of Chicago, 2008
M.Ed, Psychology, Harvard Grad School of Education, 2011
M.S. Psychology, University of New Mexico, 2013

DISSERTATION

Submitted in Partial Fulfillment of the
Requirements for the Degree of

Doctor Of Philosophy
Psychology

The University of New Mexico
Albuquerque, New Mexico

July, 2017

DEDICATION

To my family whose support and love enabled me to pursue my most difficult questions.

ACKNOWLEDGMENTS

Special thanks to my research assistants Rodolfo Marin, Catlin Ami, Niharika Ravichandran, and Trevor Claw who helped me perform the experiments and whose curiosity encouraged me through the project. Also special thanks to the undergraduates and graduate students that volunteered to participate in the study. Thanks to the PCNC lab group and Dr. Vince Clark who provided the equipment I used for recording. Thanks to my dissertation committee, Dr. Jim Cavanagh, Dr. Ben Clark, and Dr. Tom Caudell who all helped me to expand my research while staying focused on the core scientific question at hand. Finally, thanks to my mentor Dr. Derek Hamilton who taught me to create my own solutions to previously unexperienced obstacles.

AN INVESTIGATION OF THE NEURAL COMPONENTS AND SACCADE SEQUENCES THAT ENABLE DIRECT NAVIGATION THROUGH VIRTUAL SPACE

By

Daniel Robert Thomas Barto

BA, Psychology, University of Chicago, 2008
M.Ed, Psychology, Harvard Graduate School of Education, 2011
MS, Psychology, University of New Mexico, 2013
Ph.D, Psychology, University of New Mexico 2017

Abstract

Spatial navigation is a critical behavior for nearly all life forms. The ability to navigate to a destination and to remember how to return to that destination involves numerous brain processes such as perception, attention, memory, learning, proprioception, and distance estimation. The study of spatial navigation, in various organisms and on different sorts of maze-apparatuses, has revealed what is required of the brain and what is required of the environment to enable successful navigation. This dissertation adds to this vast literature by examining the physiological and behavioral components involved in human navigation in a virtual environment.

The primary aim of this dissertation is to use the virtual Morris water task (vMWT) to distinguish how eye gaze patterns, frontal- parietal neural oscillations, and navigation path trajectories differ between participants who learn to take direct paths to the hidden escape platform compared to participants that use non-direct strategies to

reach the platform. The vMWT is a virtualization of the Morris water task that is used with rats to find a hidden escape platform within a circular pool of water. While the vMWT has been used extensively and demonstrated sufficient translational value, there is still the specific remaining question of what physiological signals correlate with direct navigation in the virtual domain and how these physiological signals change as a function of learning.

The final two aims of this dissertation build upon this initial investigation by 1) examining if these difference in learning can be generalized to other mazes or explained by other factors such as sex and motivation, 2) if a manipulation of viewing perspective can impact navigation performance and how this sort of manipulation is represented in the brain. Together these three aims demonstrate how the differences in navigation strategy within the virtual domain co-occur with differences in eye-gaze, neural-oscillations and path trajectory. Specifically, evidence will be provided as to how direct navigators in the vMWT 1) exhibit higher ERP amplitude at FCz upon finding the platform, 2) preferentially gaze at the distal cue closest to the hidden platform during last block of training, 3) utilize a saccade sequence pattern between the pool wall and pool water to calculate distance vector information, 4) have higher NT170 amplitude upon right turns to the reinforced alley of the T-maze, and 5) exhibit different theta and alpha/mu power spectra during artificial changes to viewing perspective.

TABLE OF CONTENTS

List of Figures

List of Tables

Chapter 1: Introduction

Before the investigation into the neural correlates of direct navigation within the virtual domain can occur, the first question to address is—why? This dissertation project is a study of basic scientific research to understand how the brain changes as a function of spatial learning in an artificial environment.

Learning to navigate in real or virtual space is a complicated task that through the course of evolution has been rendered trivial. The ease and automaticity of navigation belies the complex problem of moving through a world of changing stimuli. Organisms with small ganglia composed of only a handful of neural connections, such as bees or ants, have optimized navigation for efficient foraging. Birds are able to locate hidden nests, or traverse across entire hemispheres with only a "bird-brain." Mammals such as dolphins and whales can navigate large distances underwater with minimal visual stimuli to reach feeding and spawning areas. Human beings, arguably the most intelligent lifeform, are able to effortlessly and efficiently travel to both new and familiar destinations. Although sometimes they outsource these calculations to computer global positioning systems (GPS).

Only when these complicated systems break down do we realize how difficult navigation is. When the GPS runs out of batteries suddenly we are completely lost. When the mind begins to degrade with Alzheimer's disease, navigation even to familiar destinations such as one's home becomes an impossible ordeal. Thus it is vital to understand how the brain accomplishes successful navigation so that we might be able to understand 1) the early indications of spatial memory degradation (Cushman, Stein, & Duffy, 2008), and 2) how to possibly intervene within the individual or alter the environment to accommodate easy navigation (Moffat, 2009). These interventions are outside the scope of this dissertation project but the investigations provided here could be used to guide an understanding of how to mitigate future societal problems related to spatial memory loss.

Moreover, this project builds upon the work of many prior generations that have attempted to understand how the external world is represented within the internal system of the organism. Navigation, a behavior preserved since lifeforms began freely moving, is ultimately the relationship between the individual organism and the external world at large. The empirical study of navigation, spanning back to 1901, has offered incredible insight into this relationship between the internal world of the individual and the external perceptual environment.

1.1 History of spatial-navigation tasks in real space

The empirical study of spatial navigation first began with Willard Small, the first psychologist to examine the rat's ability to learn how to navigate through a large, sprawling Hampton court hedge maze (Small, 1901). These early animal experiments offered novel advantages over the testing of human participants. Rats readily learn tasks with food motivation, they are small enough to be able to run in a tiny maze, and they do not have confounds of language, culture, or social-economic status that might variably affect learning rates. Moreover rats could be operated upon and subjected to experimental lesions of brain areas. John Watson continued the study of maze learning in rodents by systematically lesioning different parts of the rats' nervous system to determine which parts of the brain and sensory systems were required for direct navigation (Watson, 1913).

Decades of lesion work followed as scientists attempted to identify which neural structures were involved specifically with learning and memory. Deficits in maze learning could mostly clearly be seen by lesioning sensory areas crucial to vision in what would later be identified as visual processing area V1 (Hubel & Wiesel, 1968). While these lesion studies illustrated maze learning deficits related to visual processing, there was no clear indication of a system devoted solely to memory and learning. This lead Lashley to conclude that memory is a process distributed across the brain (Lashley, 1930). The critical question of where spatial memory is stored would be revisited 50 years later with emphasis on the unique functions of the hippocampus. But the inconclusive results of the lesion studies, whether due to imprecise surgical technique or the use of ambiguous spatial tasks, spurred researchers to consider the information content provided by the maze environment itself.

Spatial navigation research thus transitioned from using large sprawling mazes (Watson, 1907) to precise mazes such as the T-maze (Hull, 1932) or radial arm maze (Olton & Samuelson, 1976). These mazes were simplified and focused on the animal’s decision to navigate at a singular junction. This allowed for both faster training and distilled the animal’s behavior into punctate decision points that allowed for more advanced statistical analysis (Shannon, 1953). Additionally, the simplified mazes allowed for researchers to make predictions of animals’ behavior based on rotation, translation or scaling of the maze (Knierim & Hamilton, 2011). As figure 1 illustrates, researchers transitioned from testing an animal’s ability to escape an elaborate maze to consideration of how the location of the maze within a constellation of distal cues influences the strategies the animal uses to navigate.

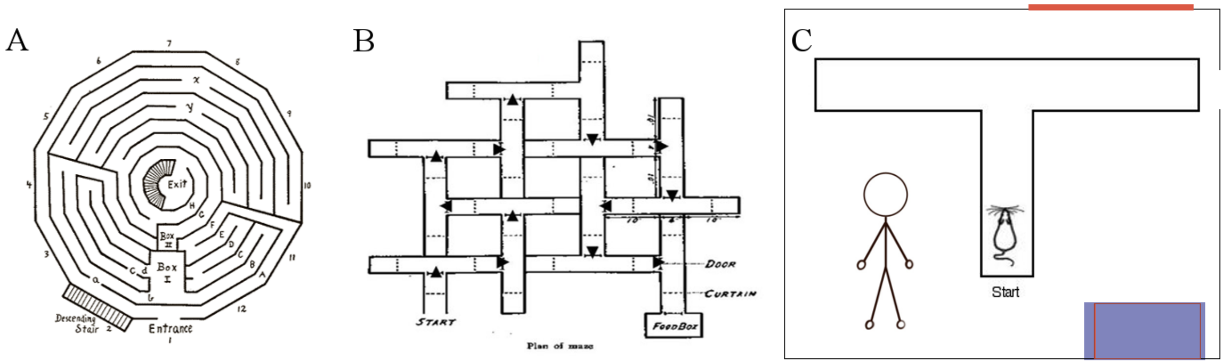

Figure 1.1: Progression of mazes apparatuses from complex to simple. A) Watson's (1913) Hampton court maze featuring layout with multiple path options. B) Tolman's (1930) maze consisting of changeable junctions to test place learning against response learning. C) Blodgett's (1949) use of a single T-maze that can be rotated and translated in a room to investigate contributions of local and distal sources of spatial information.

With these new maze types, there was great debate as to what aspects of the environment the rat was using to successfully navigate through mazes. Advocates were divided between three different navigational strategies: 1) response learning, the learning of egocentric sequence of left/right turns, (Spence, 1936), 2) place navigation, which was learning to navigate to an allocentric place in the absolute coordinates of the room, (Tolman, 1948), and 3) directional responding, or learning to navigate towards an allocentric heading in the room, such as general movement towards a visible landmark (Blodgett, McCutchan, & Mathews, 1949). The arguments became quite acrimonious, with each lab producing results to exclusively support their position. This debate was never formally solved due to the fact that rats most likely utilize any given strategy depending upon the information embedded in the maze environment. Different maze configurations created by each lab would have biased a rat to navigate in a particular way.

For example, Restle demonstrated that animals in a well lit room are able to perform place navigation to an allocentric point within the room. However when the lights are dimmed then rats are still able to navigate through the same maze, except now navigation is primarily based upon an egocentric path integration of memorized motor sequences (Restle, 1957). Thus, there might not necessarily be one dominant way a navigator responds; rather the navigator uses the most efficient strategy based upon the stimuli available to it.

1.1.1 Contemporary Theories of place learning

The fallout out over the debate of the rat's preferred navigation strategy led to a lull of research activity in spatial navigation for twenty years. The next milestone in spatial navigation research would be the conjunction of the discovery of the hippocampal place cell and the development of the Morris water task (MWT) in 1981. Previous mazes tasks, such as the radial arm maze, required extensive training to reach a criterion of performance. The nature of these multiple arm mazes required elements of associative learning and working memory distinct from spatial memory (Morris, 1984). The MWT on the other hand is an open field task that allows for freeform movement. The MWT consists of placing an animal in a circular pool of opaque water. The goal of the task is for the animal to navigate to a hidden platform that is submerged just below the surface of the water. Animals are released from four locations around the circular pool thus requiring path trajectories to the fixed hidden platform from a variety of angles and distances. Rats are natural swimmers and are able to easily move throughout pool but they are highly motivated to find an escape. Initial trials are usually marked by thigmotaxis, the circling of the pool wall as the rat tries to escape. If the animal does not swim to the platform in the allotted time the animal is placed upon the escape platform by the experimenter before being removed from the pool and the trial is concluded. Eventually the initial pool wall circling behavior is extinguished and the animal takes more or less direct trajectories to the escape platform. Performance reaches asymptotic levels quite rapidly, often between the first and second session of training. Parameters such as water temperature, pool radius, and platform size all affect learning performance (Vorhees & Williams, 2006). Navigation of the animal is recorded on an overhead camera. The task itself offers many different dependent measures including, but not limited to, time to escape (s), distance of path (m), time spent in target platform quadrant (s), time spent searching after removal of escape platform, cumulative heading error (radians), and similarity of trajectory path (unitless value) (Vandam, Lenders, & Dedeyn, 2006). The ease of the task, the high motivation to escape the pool, and the freeform movement aspects of the MWT have made the task one of the most popular contemporary neurobiological assays.

Importantly, there are no salient visual cues provided by the platform nor is there any disambiguating information provided by the circular local apparatus cue of the pool wall. The circular pool does not contain any corners or any markings. Thus there must be at least two distal visual cues to enable navigation in the MWT (Prados & Trobalon, 1998). These distal cues are visual landmark that can be seen from the pool, but cannot be reached; usually they are posters mounted on the wall or other stimuli such as a shelf or a doorframe. Initially, Morris concluded that because the local pool wall had no disambiguating information it was not required for spatial localization—distal cues were sufficient on their own (Morris, 1981). However manipulations to the local pool wall cue, such as boundary reduction (Hamilton, et al., 2009) or translation of the pool (Hamilton, Akers, Weisend, & Sutherland, 2007) indicate that the pool wall does provide an important source of spatial information. Most likely the distal cues provide information as to orientation and distance vector calculations, while the pool wall serves as a vector for distance calculation (Knierim & Hamilton, 2011). This hypothesis will be further confirmed in experiment 1 of the dissertation.

1.2 Neurological and Behavioral signatures of navigation in virtual space

1.2.1 Neurological cell types in Rats

The development of the MWT was not only to create a new spatial behavior task. Part of the development of MWT was the need to create a task that could test new theories about cell-specific responses located in the hippocampus (O’Keefe, 1976). The first cell type postulated, the “place cell” is a cell type the fires when the rat is in a particular location. The place cell was originally identified through recording in the CA1 of the hippocampus (O’Keefe & Dostrovsky, 1971). Place cells are predominantly located in the hippocampus, with the highest occurrence in the subregions CA3, CA1 and the dentate gyrus (Burgess & O’Keefe, 1996). As the rat explores and learns about the environment, individual place cells fire to form a pattern or “place field” that designates a coherent organization of the environment. Certain place cells will fire when the rat is at a goal location, whereas others place cells will fire once the rat is positioned in its homebase. By plotting the place cell spikes as a function of movement through the environment, researchers can determine how the place cells of the hippocampus fire as function of navigation within the apparatus and room reference frames.

Place fields are determined by both the boundaries of the apparatus enclosure (Hartley, Burgess, Lever, Cacucci, & O'Keefe, 2000) and also landmarks present in and outside of the apparatus enclosure (Knierim, Kudrimoti, & McNaughton, 1995). Place fields can be generated and maintained in darkness (McNaughton, Leonard, & Chen, 1989). Blind and deaf rats have some place cell firing but only to the local apparatus reference frame (Hill & Best, 1981). Lesions of the entorhinal cortex, the cortical input into the hippocampus, disrupts place fields (Miller & Best, 1980). Altering the scale of the boundaries of the apparatus will also result in a place cell scaling (O'Keefe & Burgess, 1996). Changing the apparatus or altering the distal visual cues completely, for example in the extreme case of replacing all visual cues, will cause the place cells to remap. Thus the interaction between local visual cues, distal visual cues, and internal path integration systems are critical for the generation of place fields.

Place fields can encode both aspects of distal and local cues (Gothard, Hoffman, Battaglia, & McNaughton, 2001). Original manipulations of distal cue rotations led researchers to assume that place cells were solely bound to the room reference frames. Brown and Skaggs demonstrated that a "double rotation" or rotating the distal cues opposite to the local apparatus cues produced both place fields bound to the local apparatus frame and place fields bound to the distal reference frame (Brown & Skaggs, 2002). Yoganarasima & Knierim also used this double rotation paradigm to explore how place cells remapped as a rat moved around a track that was rotated. This manipulation revealed high individual differences; some animals had a majority of place cells that remapped to the local frame of reference, others had a majority of place cells that remapped to the distal cue frame of reference while others showed more split representations (Yoganarasimha & Knierim, 2005).

There is also strong evidence that place cells are able to switch between apparatus and room reference frames even within a trial depending on which cues are attended (Fenton et al., 2010). Two groups of rats were trained to navigate to a goal location on a stationary apparatus; however during place cell recording one group of rats were forced to navigate to the goal location under intermittent rotation. This had the effect of making the local apparatus irrelevant as a cue set for locating the goal location; subsequently the place codes of the animal established a preference for the room reference frame. These series of studies illustrate that decreasing the predictive value of cues within a reference frame can cause conflict between the room and apparatus reference frames.

There are two other major cell types afferent to place cells in the hippocampus that couple the place cell response (Yoganarasimha & Knierim, 2005). These cell types are head direction cells and grid cells. Whereas the place cell fires when the animal is in a given location, the head direction cell-type is a separate class of cells that fire in the preferred direction of the animal's heading. This cell-type fires independently of the animal's behavior or place location within the apparatus (Taube, Muller, & Ranck, 1990). The head direction cells were initially observed in the dorsal presubiculum, and subsequently have been identified in other subcortical areas such as the anterior dorsal thalamic nucleus, the striatum and retrosplenial cortex (Knierim & Hamilton, 2011).The head direction cell firing preference remains stable over the course of many days (Taube et al., 1990).

Most importantly, the head direction cell type fires in a particular direction of the allocentric frame of reference, regardless of the animal's head relative to its body. While there is some evidence that the head direction cells can encode a local apparatus frame of reference if the cues are divided into two options (such as the case of a T-maze with few disambiguating distal cues) (Clark, Harris, & Taube, 2012), in most cases of recording within an open field apparatus, the head direction cells are strongly linked to the distal cue reference frame (Zugaro, Berthoz, & Wiener, 2001). The relation of head direction cell firing with distal cues suggest that the head direction cells are locking onto cues that do not perceptually change that much as an animal moves around an environment thus providing an anchor for direction (Knierim & Hamilton, 2011). This is in contrast to local cues within an apparatus that change dramatically depending on the egocentric movement of the navigator.

Whereas place cells signify the location of the animal, and head direction cells correspond to the animal's allocentric heading, grid cells encode a tessellating hexagonal array (Kropff & Treves, 2008). Grid cells fire once the animal crosses a vertex of this internally generated hexagonal array. The grid cell-type is located in the medial, lateral entorhinal cortex and subiculum. Grid cells are believed to deal largely with path integration computations of speed and direction (Moser, Kropff, & Moser, 2008); with perhaps initial sensory information setting the parameters of the grid (Fyhn, Hafting, Treves, Moser, & Moser, 2007) . Grid cells arrange themselves depending on head direction input, as blockade of the head direction signal arising from the anterior thalamic nuclei cause a disruption in the orderly nature of the grid cell response (Winter, Clark, & Taube, 2015). Grid cells do rotate once distal cues are rotated, similar to place cells, however grid cells are resistant to remapping as compared to place cells. The grid cells retain their spacing and arrangement in novel environments and persist in the absence of the learned environment, suggesting that the grid cell type encodes path integration metrics apart from sensory visual cues (Hafting, Fyhn, Molden, Moser, & Moser, 2005)

The evidence of hippocampal cells that respond specifically to different aspects of the spatial environment has reignited spatial navigation research. It is the strongest evidence to date about how our brain represents the natural world around us and offers data to centuries of philosophical speculation as to how we interpret the space and time of this world (Kant, 1998) . If these cell types are evident in the rat, then presumably there are similar aspects to navigation in humans.

1.3 Translating tasks performed in real space to virtual space

The rich history of spatial navigation has provided compelling evidence as to how specific cells of the hippocampus encode aspects of the environment and also how local and distal cues provide disambiguating information to allow for direct navigation. The question then remains: how does one translate this wealth of knowledge into investigations of human navigation? Spatial navigation historically has relied on studying place learning by using rodents or insects (Gallistel, 1990). It is a difficult proposition to house and maintain a maze large enough to drop humans into. Researchers have created real world analogs of the radial arm maze and Morris water task (Overman, Pate, Moore, & Peuster, 1996). For example, the invisible sensor task, requires a human to find an object situated under a carpet (Bohbot, Allen, & Nadel, 2006), similar to how the rat must find a hidden escape platform submerged under water. While these real world approximations capture the concept of the spatial navigation tasks, they are often impractical to administer and constrain the control the experimenter has in terms of manipulating local and distal cues. Researchers have turned to using virtual tasks to study place learning in humans which offers certain benefits over testing in real space.

Virtual navigation tasks typically involves the participant seated at a computer. The participant uses a keyboard or game controller to navigate in a first person perspective. Optic flow is simulated by the screen changing to reflect the updated positions within the virtual environment. Participants are encouraged to try their best to quickly solve the task. Motivation such as money or course credit can be offered as incentive. These motivational factors are not as salient to humans compared to a starved rat finding a food reward or a rat trying to escape drowning. Despite these differences, the evolution of path trajectories in the virtual domain correspond to rats in real-world tasks (Foreman et al., 2000). Humans appear to be using a combination of distal and local cues in a similar way to rats to navigate to the hidden platform (Hamilton, Johnson, Redhead, & Verney, 2009). Assessments of navigation strategy by use of a pool translation after training also indicates similar preferences for responding in rats and humans in the virtual domain (Hamilton, et al., 2009).

The vMWT also provide a useful translational tool in comparing human performance with artificial agents. Studies involving vMWT completion using a simulated agent (Wilkie & Palfrey, 1987) or a neural network (Brown & Sharp, 1995) provides insight into the salient features of the environment required to solve the maze that might not be evident by examining the behavior of human or rats. Additionally since the perspective of the subject is consistently recorded (effectively a first-person replay of the entire session) neural networks could be directly trained on actual human performance for a direct comparison between biological and computer systems. While navigation in a virtual environment might not be exactly translatable to real-life navigation, the virtualized environment facilities further comparison with artificial agents.

1.3.2 Hippocampal—Parietal circuit activation during Virtual Navigation

The extensive lesion work in rats have indicated hippocampal and parahippocampal structures involvement in encoding spatial information during navigation. There is reason to assume that similar mechanisms and cell types are also involved in human spatial navigation within the virtual domain. These assumptions are based on either experiments with patients having hippocampal lesions or studies of humans navigating while using fMRI neuroimaging.

Detailed evidence implicates the hippocampus as necessary for navigation in humans. Human spatial navigation studies using lesion patients or fMRI imaging have confirmed similar hippocampal structures are necessary for successful spatial navigation (Burgess, Maguire, & O’Keefe, 2002) . Impairments in spatial memory are related to progressive disease pathology of the hippocampus and medial temporal lobe in Alzheimer’s patients (Kolb & Whishaw, 1996). Patients with lesions to the right hippocampus and right parahippocampal cortex are impaired at the invisible sensor task (Bohbor, 1998). Conversely, navigators that are required to learn and recall complex routes, such as London taxi cab drivers, demonstrate significantly larger gray matter volume in the posterior hippocampus as compared to controls (Maguire, Frackowiak, & Frith, 1997). Hippocampal activations in virtual tasks during fMRI have been replicated many times (Burgess et al., 2002), and some researchers have postulated fMRI evidence of place cell and grid cell signal in the hippocampus (Morgan, MacEvoy, Aguirre, & Epstein, 2011) and entorhinal cortex (Doeller, Barry, & Burgess, 2010).

For this dissertation project, the spatial depth limitation of human EEG recording restricts analysis to neocortical structures and cannot reliably detect subcortical regions such as the hippocampus and retrosplenial cortex. However there is compelling evidence that posterior parietal and prefrontal areas exhibit signal fluctuations that are related to changes as a function of learning maze navigation.

In rats it has been demonstrated that posterior parietal lesions impair spatial orientation (Kolb, Sutherland, & Whishaw, 1983; Rogers & Kesner, 2007). Recent animal research has identified a posterior parietal cortex (PPC) cell type that encodes spatial heading as a function of egocentric and allocentric coordinates (Wilber, Clark, Forster, Tatsuno, & McNaughton, 2014). Rats in this task were required to navigate to a random blinking light on a circular apparatus and then turn and head to a blinking light on the opposite side of the apparatus, which effectively required the rat to cover a full range of headings and cue directions at different spatial locations. Recordings in the PPC revealed a cell type that fired neither in response to the egocentric cue reference frame, nor the allocentric head direction but rather in conjunction to these two frames. While there is a possibility that this conjunctive signal originates upstream in the retrosplenial cortex, there is evidence that the posterior parietal cortex has signals related to evaluations of distal and local cue attentional switch. Few parietal and frontal cortex recordings of freely moving animals exist (Ekstrom, Arnold, & Iaria, 2014), but evidence is mounting that the parietal cortex is involved in route selection (Nitz, 2009), and another animal study implicates the prefrontal cortex as being involved with detour management (Spiers & Gilbert, 2015). Thus, while there is significant animal evidence that the hippocampus is involved with navigation, research has begun to examine the interactions between hippocampal structures and neocortical areas during navigation. These neocortical areas can be investigated with high timing precision through EEG time frequency analysis.

Theta oscillations have been demonstrated in virtual navigation tasks in the hippocampus and frontal cortices but there are few reports of theta signal in the parietal cortices. The animal literature indicates the parietal cortex as an efferent to the retrosplenial cortex which deals with switches between references frames concerning the allocentric hippocampal network and more egocentric frontal-parietal network. Additional evidence of posterior and superior parietal involvement during navigation comes from studies of patients with lesions to the superior parietal cortex that have egocentric disorientation (Aguirre & D’Esposito, 1997). These patients have difficulty in understanding spatial relationships of an object with respect to their own position and orientation. there are few studies explicitly linking a change in signal oscillation of the parietal cortex during virtual navigation. One recent study investigating misplaced objects in virtual reality have located an N400 component over a mid-parietal region, but the authors concluded this was a result of memory of a misplaced object rather than a shift in reference frame (Plank, Snider, Kaestner, Halgren, & Poizner, 2014). Another series of studies performed by Gramann identify alpha frequency suppression in the posterior parietal cortex during a passive optic flow task of a subject moving through a virtual tunnel that curves (Gramann, 2013). The lack of a parietal theta oscillation in a majority of these studies could perhaps be due to the structure of the task.

1.3.3 Prefrontal theta indexing maze difficulty

The contemporary literature on neuroimaging in human spatial navigation has established theta oscillatory components related to navigation as seen in animal recordings (Buzsáki, 2002). The theta frequency, a range of frequencies centered around 8 hz in rats, and a range of frequencies centered around 3 hz in humans, (Watrous et al., 2013) has been implicated in many behavior activities related to movement (Whishaw & Vanderwolf, 1968) and memory (Green & Arduini, 1954). The nominal “theta” frequency label has been used to describe rhythmic slow activity in a variety of species in various behavioral contexts (Robinson, 1980) . In the rat hippocampus, theta rhythms have been suggested as a mechanism to differentiate between states of encoding and retrieval (Hasselmo, Bodelón, & Wyble, 2002).

The proclivity of theta is also observed in human navigation during virtual tasks. Just as movement related-theta is observed in freely moving rats, theta oscillations are elicited by virtual movement (Ekstrom et al., 2005). MEG studies indicate theta in left anterior hippocampus and parahippocampus during goal-directed navigation relative to a control condition of aimless movement in the virtual Morris water task (Cornwell, Johnson, Holroyd, Carver, & Grillon, 2008). In virtual tasks, hippocampal theta peaks about 1-2 seconds after the onset of both goal directed and aimless movement trials, with goal directed movement eliciting a higher theta power peak relative to aimless movement. Rhythmic theta oscillations also seem to be related to the complexity of a virtual navigation. Intracranial EEG recordings placed in the hippocampus of epileptic patients had greater global theta power activation in T mazes with long junctions as compared to mazes with shorter number of junctions (Kahana, Sekuler, Caplan, Kirschen,

& Madsen, 1999). In virtual T mazes, theta episodes occur when a new hallway comes into view, or after navigational mistakes have been realized and are corrected (Bischof & Boulanger, 2003).

1.3.4 The NT170: An ERP component related to feedback during spatial task

In addition to evidence of spatial-navigation activation from MEG, fMRI and intracranial recordings, Baker and Holroyd postulate evidence of an event related potential component, the NT170 related to feedback upon reaching a reinforced spatial location within a T-maze (Baker & Holroyd, 2009). Through EEG source localization they conclude that this dipole is generated from the right medial temporal lobe (MTL). The MTL is a large region comprised of both the hippocampal formation and the surrounding para-hippocampal structures such as the perirhinal and entorhinal cortices. Figure 2 indicates the layout of the MTL and the parahippocampal cortex involvement in generation of the NT170. The global MTL system has been demonstrated to store information related to environment (O’Reilly & Rudy, 2000; McNaughton & O’Reilly, 1995).

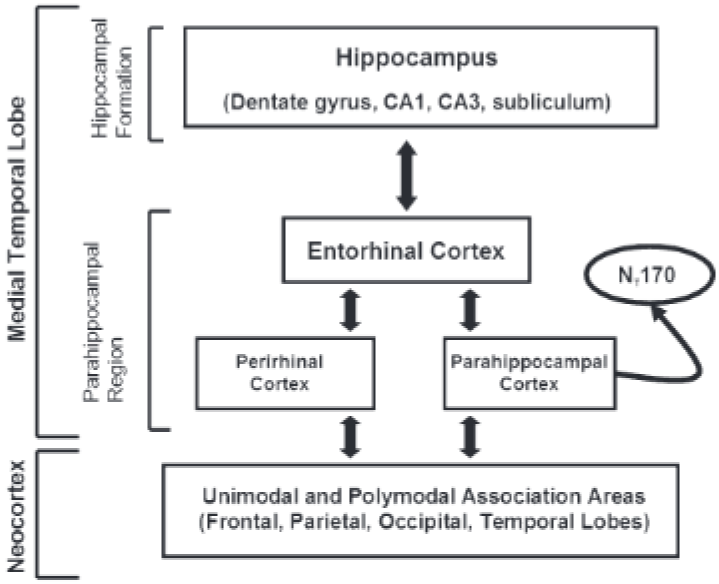

Figure 1.3. A schematic view of the neural connectivity within the MTL system (adapted from Squire (Squire, Stark, & Clark, 2004) and Baker (T. E. Baker & Holroyd, 2009). The NT170 is a component of the event related potential waveform that originates from parahippocampal areas and is associated with spatial location of reinforcement.

The NT170 is a negative polarity event that occurs approximately 170-200 milliseconds after feedback (Baker & Holroyd, 2013). It is maximally generated at electrode site PO8. The component is sensitive to the spatial location of reinforcement, occurring slightly faster for feedback following a rightward turn as opposed to a leftward turn. The component also reflects individual differences in maze proficiency. The consistency and reliability of the NT170 component offers neurological evidence as to how human participants relate feedback to spatial location in virtual space.

1.3.5 Eyetracking during navigation tasks

In addition to time-locked EEG analysis, another under-utilized tool to examine the dynamic, moment to moment, aspect of navigation is eye tracking. Examining gaze location as a function of path trajectory can reveal qualitative shifts in behavior for the initial and terminal segments of a trial. For example, there is evidence to suggest that place cells code an initial and terminal segment of a path trajectory (Gothard et al., 2001). Initial segments of swim trial in rats are marked by head swiping behavior, where the rat rapidly moves its head around presumably to sample visual stimuli (Hamilton, Rosenfelt, & Whishaw, 2004). These specific behavioral and neural changes are unable to be studied in virtual reality (VR). But tracking the movement of the participant's gaze over the course of a virtual navigation trial can differentiate initial and terminal segments of a trial. Hamilton et al demonstrated that human participants who solve the virtual Morris water task display a significant difference in gaze dwell time on certain visual stimuli compared to those who are unable to learn the goal location (Hamilton, Johnson, et al., 2009). The successful navigators initially gaze at the distal room cues to orient their heading and trajectory; then at a certain distance in their path length they switch to gazing at the apparatus cues which convey only distance information. Moment-to-moment knowledge of where the subject was looking during the course of the trial is important to rule out impaired navigation due to poor visual search strategy. Thus, impairments of lesion patients in virtual mazes may not be entirely related to impoverished spatial memory but could be a manifestation of maladaptive visual search strategy. This issue can only be addressed through dynamic moment to moment analysis of virtual tasks.

1.3.6 Caveats to studying spatial navigation in virtual space

Despite the potential for VR experiments in psychology there are some important caveats to the use of VR in spatial navigation research. The most apparent constraint is the lack of vestibular input during movement through virtual space (Taube, Valerio, & Yoder, 2014). This has significant implications considering how essential path integration input is to formulating place and grid cells (Stackman, Clark, & Taube, 2002), (Wallace, Hines, Pellis, & Whishaw, 2002). Navigation in real space involves feedback from many proprioceptive and muscular systems that connect to cerebellar and deep hindbrain structures (Boisgontier & Swinnen, 2014). Navigation through virtual space on the other hand, does not incorporate movement of the legs. fMRI studies even attempt to minimize any movement that would cause artifacts in recording (Logothetis & Wandell, 2004). However in the studies presented here in this dissertation there are still an element of proprioceptive movement in the form of the subject holding down a joystick with their finger. The time and force applied to the joystick offers a physical estimation of distance. Obviously this does not emulate the sensation of walking. Laborites have begun to investigate spatial navigation using a mobile setup of head mounted immersive (Bohil, Alicea, & Biocca, 2011) which effectively captures the advantages of the flexibility of virtual environment presentation with the proprioceptive sensation of moving through real space. Already immersive VR has provided compelling evidence as to how sensory systems in insects change as a function of artificial changes to the environment during free flight (Fry, Rohrseitz, Straw, & Dickinson, 2008).

Another potential confound with translating real-space into the virtual domain is the question of scale and distance estimation. Participants often overestimate heading error during rotation (Klatzky et al., 1998) without proprioceptive input. Participants also tend to underestimate the distance of objects in virtual space. It is unclear if these incorrect estimations are due to the inherent experience of VR, or incongruities in graphic display during experiments. For example, one particular study (Hartley, Maguire, Spiers, & Burgess, 2003), had graphics rendered at an infinite distance, which would cause the cues to be the same regardless of subject movement. Rendering the cues closer in distance to the subject would cause a different visual experience as the subject moved. Co-localizing cues, such as an audio cue played at regularly spaced intervals also improves distance estimation (Witmer & Kline, 1998). Psychological experiments in a virtual environment must incorporate a level of artistic detail to create illusions of depth. Textural cues such as shadowing and changes in detail and lighting based on distance could allow for better accuracy in estimates of distance and heading.

The final caveat to virtual experimentation is the occurrence of simulator sickness. Simulator sickness is similar, though distinct, from motion sickness. Whereas vestibular stimulation alone is sufficient to induce motion sickness (such as being in a cabin on a ship), stimulation sickness can occur strictly with visual stimulation (LaViola, 2000). Simulator sickness can occur with any presentation of a virtual stimulus. Usually the more the virtual presentation occupies the participant’s field of view, the greater the severity of the symptoms. The symptoms of simulator sickness include eyestrain, vertigo, ataxia, nausea, and vomiting. There are significant gender and age related effects to simulator sickness (Kolasinski, 1995). The origin of simulator sickness is believed to be related to 1) a discordance between visual and vestibular cues, 2) lack of control in the visual updating of movement 3) an evolutionary mechanism to vomit once perceptual distortion is experienced (Kolasinski, 1995). The neural mechanisms of stimulator sickness are not well understood, but much research has been conducted in how to avoid causing simulator sickness in virtual environments. Elements such as sudden movement velocity, lag, poor refresh rate, and graphically intense virtual environments have been identified as significant causes of simulator sickness (Yao et al., 2014).

While these caveats are important to acknowledge as detriments to studying navigation in VR, the main advantage of creating stimuli that could not possibly exist in the real world and the ability to manipulate stimuli in real time are significant advantages that warrant further research in VR. This ability to create stimuli in a way that might not be possible in real life allows for extension of animal experiments. For example, Hamilton et al selectively varied the salience of the apparatus cue in the Morris water task by filling the pool up with water (Hamilton et al., 2007). However even with the pool at maximum occupancy, there still was a small part of the apparatus still visible to rats. Hamilton et al was able to replicate this experiment in the virtual domain with the apparatus cue totally eliminated and observed the participant's preference for place navigation (Hamilton, Johnson, et al., 2009). Movement in the virtual domain can also be restricted without visual effects. Sutherland et al studied instantaneous transfer in the Morris water task by restricting access to specific quadrants of the pool by using Plexiglas to block the movement of the rat (Sutherland, Chew, Baker, & Linggard, 1987). The Plexiglas was transparent but was physically removed during the testing phase, which confounded the results and led researchers to question if the results were due to a generalization decrement (Matthews & Best, 1997). Hamilton et al replicated this study in the virtual domain by creating totally invisible barriers restricting movement to certain quadrants of the pool (Hamilton, Driscoll, & Sutherland, 2002). This confirmed the hypothesis that rats transferred knowledge of novel release points only by swimming around the entire pool. Manipulations that can only be approximated in real life can be created absolutely in a virtual environment. Observing how participants react in artificial domains can reveal important aspects of behaviors that cannot be observed in the real world.

1.4 Purpose, scope, and aims of this dissertation

This dissertation project has three broad aims related to the study of navigation in the virtual domain. The first primary aim is to classify navigators that are able to learn how to directly navigate to a hidden platform within the vMWT contrasted with those subject that do not take direct paths. Using these classifications, I will then explore how 1) neural oscillations of the frontal-parietal network, 2) event related potential components related to feedback, and 3) eye-gaze sequence patterns differ between classifications as a function of learning.

Navigation involves many behaviors, strategies, and brain regions. These brain regions are varied, ranging from the hippocampus, entorhinal cortex, parahippocampal cortex, striatum, frontal cortex, and parietal cortex. All of these regions are postulated to support different cognitive or behavioral processes. Previous evidence of neural recordings in animals and fMRI activation in humans clearly indicate a role of hippocampal and retrosplenial cortex activation during both real world and virtual navigation. The following experiments presented in this dissertation project attempt to extend findings in deep brain structures with their cortical outputs as identified through EEG. The electrodes selected in these analyses are based on a priori hypotheses that the parietal cortical activations are related to the hippocampal- retrosplenial network (Nitz, 2009). The parietal cortex is interesting because it is a network downstream and has demonstrated activation related to navigation and orientation (Epstein, 2008). Additionally, the activation of the human parietal cortex during real-time virtual navigation has yet to be observed in EEG, despite reports of its involvement in animal (Chiu et al., 2012) and human fMRI studies (Sack et al., 2002).

The second aim of this dissertation is to extend the findings of the first aim and explore if the classifications of direct and non-direct navigators extend to other maze types. Additionally I will explore alternative hypotheses that could account for the behavioral differences such as sex and motivation. The third and final aim of the dissertation is to explore how changes in viewing perspective effect neural oscillations and path trajectory. This exploratory aim leverages the ability of the virtual environment to create manipulations not possible in real-space.

This dissertation project builds upon many convergent lines of animal, human and computer research spanning over a century of work. The overall goal is to reach an understanding of how the nervous system represents movement through virtual space. Many previous researchers have made progress in understanding this goal. However the dissertation presented is novel in that it 1) simultaneously records EEG and eyetracking during the vMWT, 2) incorporates a viewing perspective manipulation within a trial, 3) offers a new way to evaluate eye-gaze across a 3d environment in realtime.

Chapter 2: Classification of performance in the virtual Morris water task

2.1 Hypothesis

The MWT has been extensively used to demonstrate how the hippocampus is involved in using distal and local cues to reach a hidden platform location (Redish & Touretzky, 1998). The vMWT has also been used to demonstrate similar behavioral results and hippocampal dependence (Cornwell et al., 2008). Despite the utility of the vMWT there remains the question of what are navigators doing *within* a trial? Previous research suggests the sequence of distal and local cue sampling differs between direct and non-direct navigators (Hamilton, Johnson, et al., 2009). This chapter will examine this sampling sequence and other microbehaviors that unfold during a trial and how these differ between direct and non-direct navigators.

2.2 Methods

Participants in all experiments reported here were undergraduate students enrolled in Psychology courses and were awarded 3 hours of credit per completion of the experiment. The same sample participated in all 3 experiments. Individuals with a history of neurological disorder, impaired vision, currently on psychoactive medication use, were left-handed, or individuals who had previously participated in our virtual navigation experiments were not allowed to participate. 24 total participants were recruited for this project. Two of these participants withdrew from the study due to sleepiness and noncompliance in participating in experiment directions. One participant's behavioral data was lost due to an error in file writing permissions. This left 21 participants used for data analysis. 6 earlier participants were recruited as pilot data to adjust trial numbers, movement speed, and restrict backwards movement; their data will not be reported. All participants gave informed consent to participate in accordance with the guidelines for human research at the University of New Mexico. Questionnaires were obtained without subject identifying information and kept in a locked drawer in Logan Room 246.

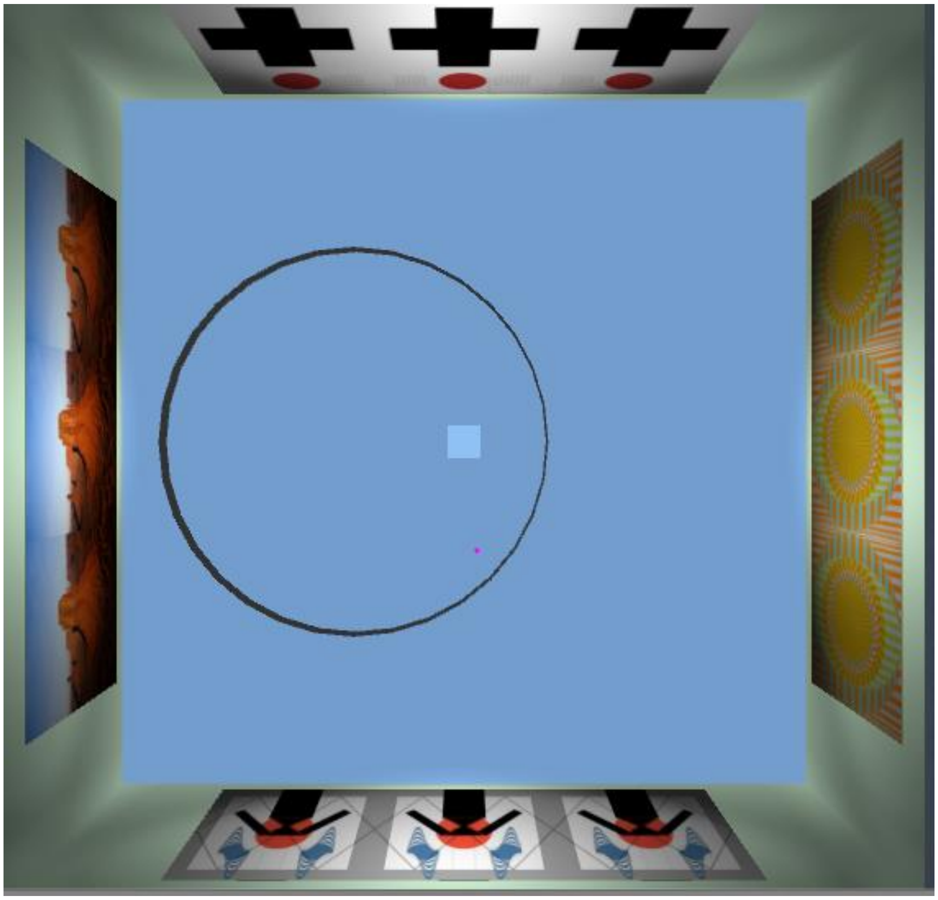

Figure 2.1 Overhead layout of the environment used for Experiment 1. Distal cues are tiled 3 times on each wall and platform is visible. 24 trials of training occurred with the pool enclosure in this position. Once training was completed a probe trial occurred in which the pool enclosure was shifted one radius to the east. Note: this is a schematic view of the environment; the subject navigated this task in first person perspective.

2.2.1 Materials and Apparatus

The virtual environment was constructed in the Unity game engine. Texture geometry such as the room walls, distal cue tiles, and pool enclosure were constructed in Blender and imported into Unity. The distal room geometry was 130 virtual units in diameter with the room centered at 0,0,0. Distal cues were 30x40 virtual units in diameter and placed on the distal room walls. The central cue was located at the midpoint of the wall and tiled on either side of the central cue. The pool enclosure was 80 virtual units in diameter. For experiment 1 the pool center was at room coordinate -25,0,0, to later be shifted 40 virtual units towards the eastern side of the room during the probe trial. The pool floor extended to the perimeter of the room, but the subject could only see the texture within the pool apparatus. The pool floor was colored blue and had no texture or form features. Overhead lighting was provided by a single directional light positioned at (–45,28,-1) with a rotation of (90,352,0). The intensity of the directional light was .64. Each distal cue set was illuminated by an angled spot light. Each spot light was 2 virtual units away from the distal cue and had a range of 100, spot angle of 135.6, and intensity of 5. The hidden escape platform was square and approximately 1.75% of the pool area. After 30 seconds the platform became visible and extended 1 virtual unit above the pool surface. Once the subject entered the platform movement control ceased and the subject was pulled to the center of the platform. The platform border became semi-translucent white around the player. An indication appeared on screen indicating the trial was over and the countdown to the next trial would begin. The subject remained on the platform for 5 seconds while the transparency of the platform border linearly interpolated from .2 to 1. The screen remained totally white for .4 seconds before fading to black with a centrally located fixation screen that remained on screen for a randomly selected range between 1-2 seconds.

Experiment 1 was conducted entirely in first person. Figure 2.2 demonstrates a representative view of the first person environment, however note that this is not a view of the distal cues used in experiment 1. The player avatar was constructed in Unity. It was a rigidbody with a 1,1,1 scale and a height of 2 virtual units. The camera was one virtual unit above the body center and had a frontal perspective projection. The field of view was set at 60 degrees.

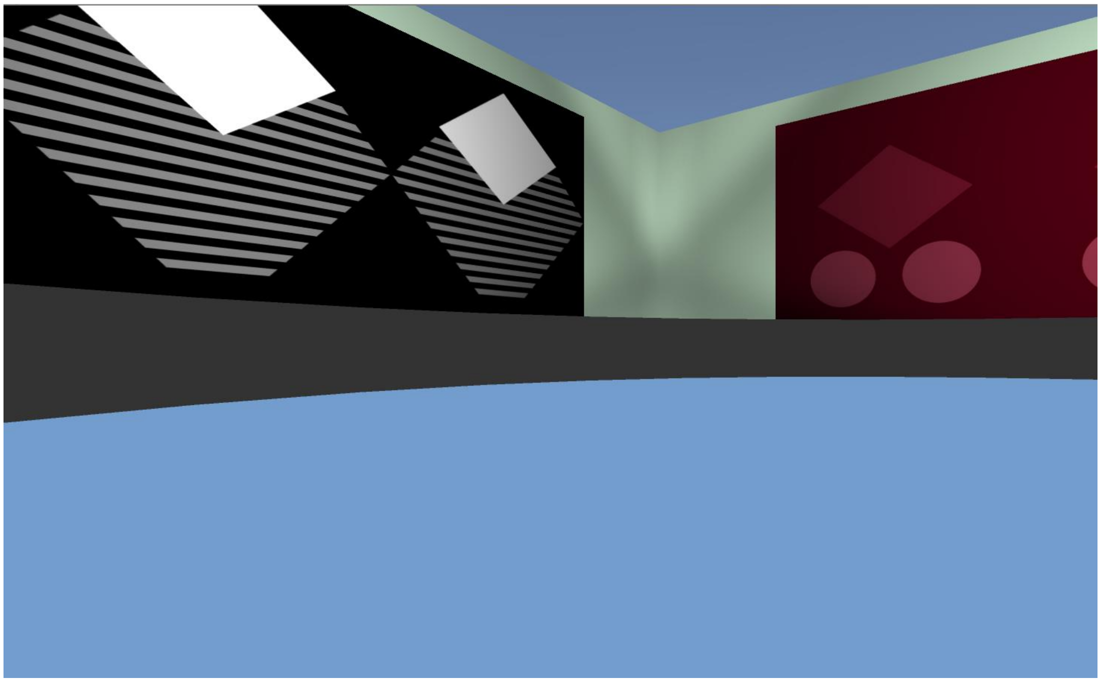

Figure 2.2 Representative view of the virtual environment in a first person perspective. Pictured are two different tiled distal cues, the grey circular pool wall and the blue pool floor.

Max forward speed was 10 with a max ground velocity of 30. It took 8.45 s to navigate the diameter of the pool in a straight line. Navigation was controlled by a Logitech game controller. The d-pad controlled forward movement. Left and right buttons turned the rigidbody at 10 speed, thus completing a complete stationary rotation in 6.61 s. Backward movement and adjustments in pitch and roll of the local view were not permitted during the data collection phase of this dissertation.

All participants were tested individually. Participants began each trial facing the perimeter wall of the circular pool. No information regarding useful strategies, the location of the platform, or any other design features of the experiment were made known to the participants. For each trial the participant’s position in xyz coordinates were recorded (movement was restricted only to the x,y domain) at 60 hz. The latency and path length to navigate to the platform were determined from this record. The entire experiment took approximately 120 minutes. 60 minutes were devoted to consent, setup, and questionnaire. The runtime of the experiment was approximately 60 minutes. All stimuli were presented at 60 frames per second on a 1920x1200 resolution Dell monitor.

EEG recording and analysis

EEG was recorded from a 128 channel biosemi EEG system. In addition two separate bipolar channels for recording horizontal and vertical eye movement were collected. Data were acquired continuously at 2048 hz with an active reference in DC mode. Files were outputted in a .bdf format and imported into Matlab via EEGLAB. The bdf files were imported using the last channel D32 as a reference. Data were then interpolated to recover the lost channel, down sampled to 512 hz, and referenced to the average voltage of the 128 scalp electrodes. Raw EEG data were visually inspected to identify bad sections of motor movement and bad channels to be removed. Data were then epoched -1500 ms to 1500 ms around each event of interest. These epochs were cleaned of eye blinks and muscle artifacts through the APPLE software package (Cavanagh & Castellanos, 2016) which is comprised of independent component analysis from the EEGLAB toolbox (Delorme & Makeig, 2004), Gratton Eyeblink removal (Gratton, Coles, & Donchin, 1983) and the ADJUST toolbox (Mognon, Jovicich, Bruzzone, & Buiatti, 2011). After data processing datasets were separated into two identical sets for analysis. The event related potential epochs were baseline corrected to the average of -500 ms prior to event and filtered with a 20 hz low pass filter. These epochs were then averaged over first by condition within subject and then across all participants.

Time frequency data were not filtered or baseline corrected in the processing pipeline. Time-frequency calculations were computed using custom-written Matlab routines (Cavanagh, Cohen, & Allen, 2009), (Cohen, Ridderinkhof, Haupt, Elger, & Fell, 2008). Time-frequency decomposition was conducted via wavelet analysis in which the EEG time series was convolved with a set of complex Morlet wavelets, defined as a Gaussian-windowed complex sine wave of the form

$$\boldsymbol{e}^{i2\pi tf}\boldsymbol{e}^{-t^2/(2*\sigma^2)} \qquad (1)$$

Where t is time, f is frequency, which increased from 1 to 30 hz in 40 logarithmically spaced steps. σ defines the width of each frequency band and was set to 4/(2πf). After convolution of the wavelet with EEG power was defined as the modulus of the resulting complex signal in the form of

$$Power = real\big(z(t)\big)^2 + imag\big(z(t)\big)^2 \qquad (2)$$

For presentation and analysis the power is displayed as decibel conversation from baseline depicted as

$$\text{dB power} = 10 * log10\left(\frac{power}{baseline}\right) \qquad (3)$$

The baseline for time-frequency calculations were presented as the average frequency power from -300 to -200 ms prior to the onset of the event (Luu, Tucker, &

Makeig, 2004). Power spectra were outputted in a (frequency x time x trial) matrices. For group comparisons, power was averaged within subject between trials and then across all participants resulting in a (frequency x time) output matrix of the group totals for each condition. Statistical analyses were conducted by identifying rectangular ROI's on time-frequency matrices corresponding to the delta (1-3hz) and theta frequency band (4-8hz) and within the epoch of the time locked event. Time-frequency decomposition ROI's were then averaged over to a single scalar for each subject for statistical tests. Multiple comparisons were accounted for by using a bonferri correction in the form of α / number of hypotheses.

Eye tracker methods

Eye tracking and pupillometry were recorded from an Eyelink 1000 system (SR Research, Kanata, ON, Canada). The eyelink is a desktop high speed infrared camera that triangulates the location of the gaze based upon the center of the pupil, and the reflection of infrared light upon a point in the cornea of the eye. See Figure 2.3 The eyelink was configured using a 35-mm lens, 13-point gaze location calibration, monocular sampling rate of 500 hz and elliptical fitting for pupil area recordings. Participants were seated 65 cm away from the eye tracker. The eyetracker was recalibrated prior to each subject and a drift check was performed at the end of each break period.

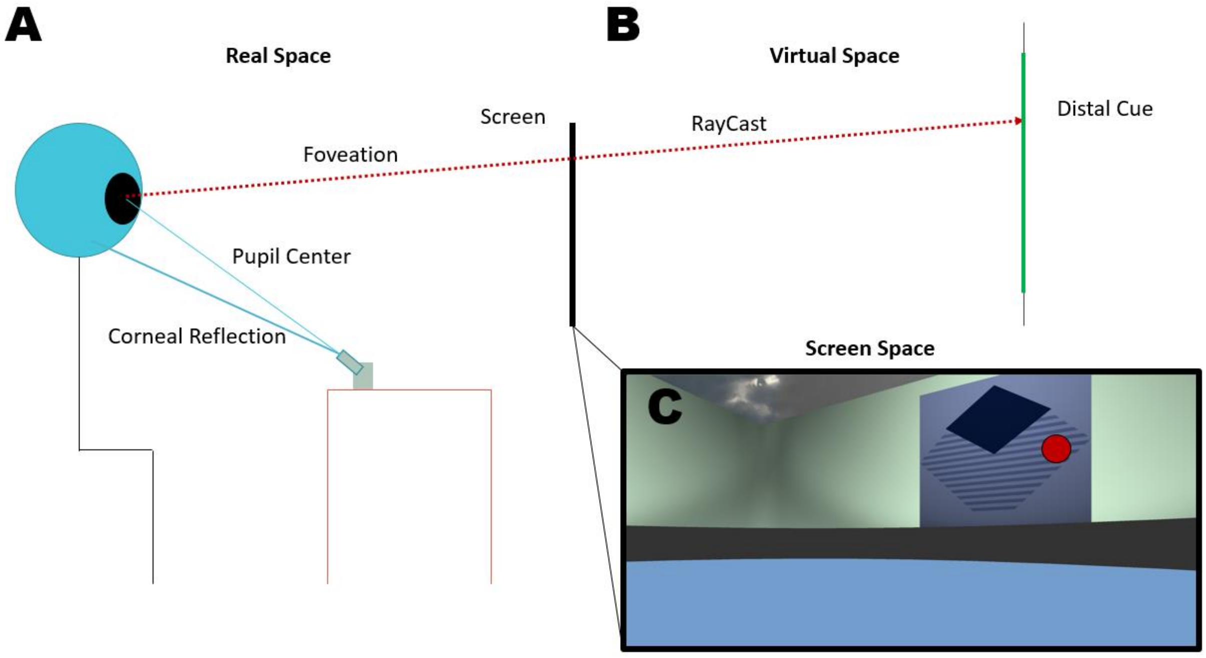

Figure 2.3 Schematic of eyetracker use and saccade raycast. A) The eyetracker sits atop a table and beams an infrared light onto the participant's eye. A high speed infrared camera triangulates the location of gaze based upon the pupil center, the reflection of the infrared beam upon the cornea and the base of the eyetracker. B) Once a saccade is completed the position of the eye is raycast through virtual space until it collides with a mesh object. C) An image of the screen with an eyegaze overlaid upon a distal cue.

The eyetracker interfaced with Unity through a custom made dynamic-link library (.dll) (Jangraw, Johri, Gribetz, & Sajda, 2014). The .dll was extended to allow Unity to access the eye tracker API and saccade detection routines[1]. Eye tracking data was calculated online based on the occurrence of saccade events. A saccade event was defined as an eye movement that exceed a velocity threshold of 30 degrees/sec, an acceleration threshold of 8000 degrees/sec^2 and a motion threshold of 0.15 degrees. Once the saccade was terminated the position of the xy gaze upon the monitor was raycasted out through virtual space until it collided with an object. Saccadic events were discarded if they

---

[1] See http://www.nede-neuro.org/downloads/plugins for download

occurred within 40 ms of blink or if the saccade location was off-screen. Data reported here are the number of collisions of the raycast with one of the distal cues, the pool wall cue or the pool water cue as a proportion to the total number of saccades. The ratio of collisions was reported instead of total number of saccades in order to account for variability of trial length.

Design and Procedure

Experiment 1 was conducted in 4 phases. Prior to phase 1, the subject was read the instructions for the task. During phase 1, the subject performed 4 hidden navigation trials in a neutral environment to become acquainted with the control and concept of the task. After confirmation that they understood the task phase 2 began which consisted of 6 blocks of hidden platform trial with the platform located on the central west side of the pool. Each block consisted of 4 trials that varied by release point. The starting location of each trial was selected pseudorandomly without replacement from the four cardinal compress points around the perimeter of the pool (N, S, E, W). After these 24 trials, the subject had a break and given the instructions for the 3rd phase. In this phase the subject was instructed to navigate to where the thought the platform was and click the right trigger button to end the trial. The center of the pool enclosure was shifted one pool radius length to the east and the platform was removed. This manipulation probes the navigation preference of the subject and requires the subject to make an assessment of the platform location to end the trial. Phase 3 of these first experiment followed the probe trial by transporting the subject to a new vMWT environment with novel distal cues. The subject was instructed to navigate to the hidden platform but that certain visual cues might not be visible at all points of the trial. There were 4 blocks of four trials. Each trial would start with either the distal or local visual cues visible. Once the subject traversed a path length equal to 1/4 of their average length by release point they travelled during phase 2 the visibility of the distal and local cues switched. Phase 3 was designed to test the order in which the participants gazed at stimuli with conditions of distal and local cue visibility counterbalanced. However the random selection of the visibility manipulation was not equally distributed across release points

2.2 Methods

Participants were classified as direct (n=13) or non-direct(n=8) based on a qualitative judgment of their trajectories of their last block of trials during phase 2 of vMWT hidden platform training. Three raters were used and determined for each subject if they travelled directly or non-directly to the platform during the last block of trials. Interrater reliability was calculated as a percent agreement between all three raters and was measured at 85%. For participants the raters disagreed with, the majority classification was used. This qualitative assessment has been used previously (Akers & Hamilton, 2007) and is desirable in discriminating the evolution of path trajectories characteristics as a function of task learning. As Figure 2.4 illustrates the movement patterns between a non-direct and direct navigator differ in their topographies.

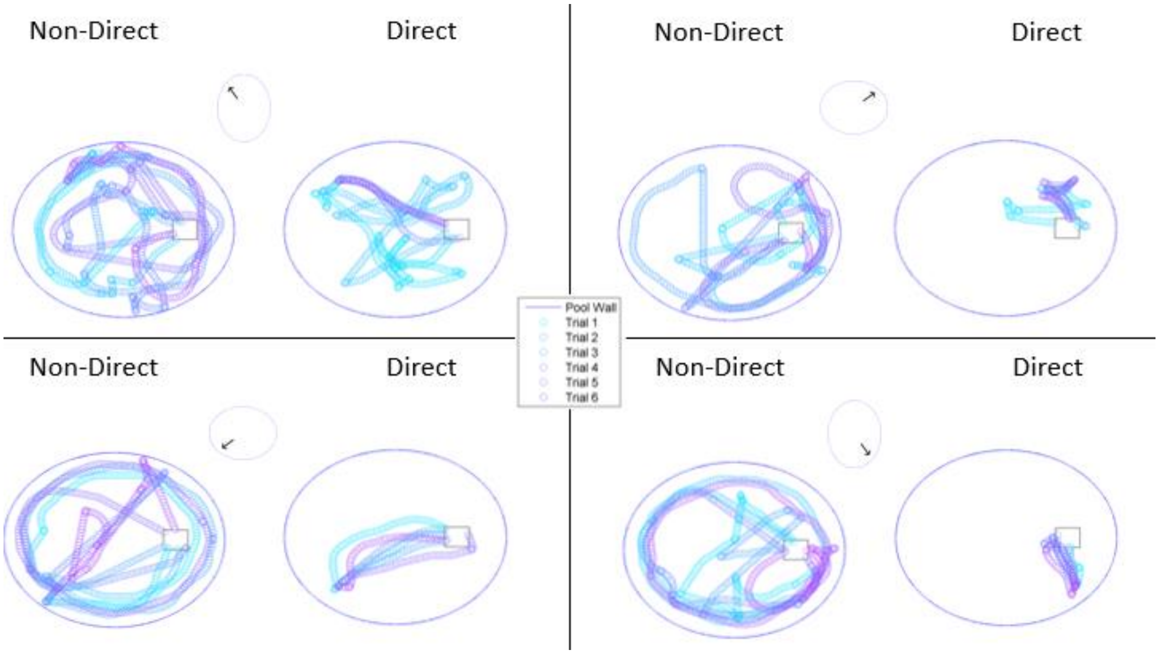

Figure 2.4: Representative path trajectories of one non-direct learner (right side) and one direct learner (left side). Each quadrant is a release point proceeding from top left: northwest release point, top right: northeast release point, bottom right: southeast release point, bottom right: southwest. Trajectories of each path is colored with trial one a blue color and trial 6 a purple colors. Trials are listed within release point but presented in a block format during vMWT hidden platform training.

2.3 Results

For vMWT analyses virtual distance travelled were analyzed using a repeated measures ANOVA with each block as within participants factor and the classification type as the between participants factor. There was a main effect of block on F(5,19) = 3.37, *p*= .008, η_p^2= .151. There was a main effect of classification F(1,19)=13.06, *p*=.002, η_p^2 = .407. Post hoc analyses using Tukey's HSD indicated a block by classification interaction F(5,19)=4.79 *p*=.001, η_p^2 =201. There was also a significant linear trend for block F(1,19)=9.22, p=.007, η_p^2 =.327. There was also significant linear trend for the classification by block F(1,19)=14.34, p =.001, η_p^2=.430.

vMWT analysis on latency had similar results to distance calculations. See figure 2.1 There was a main effect of block on latency F(5,19) = 4.89, p= .001, η_p^2= .224. There was a main effect of classification F(1,19)=17.51, p=.001, η_p^2 =.507. Post hoc analyses using Tukey's HSD indicated a block by classification interaction F(5,19)=3.30 p=.009, η_p^2=.163. There was also a significant linear trend for block F(1,19)=15.55, p=.001, η_p^2 =.478. There was also significant linear trend for the classification by block F(1,19)=9.42 p =.007, η_p^2 =.357.

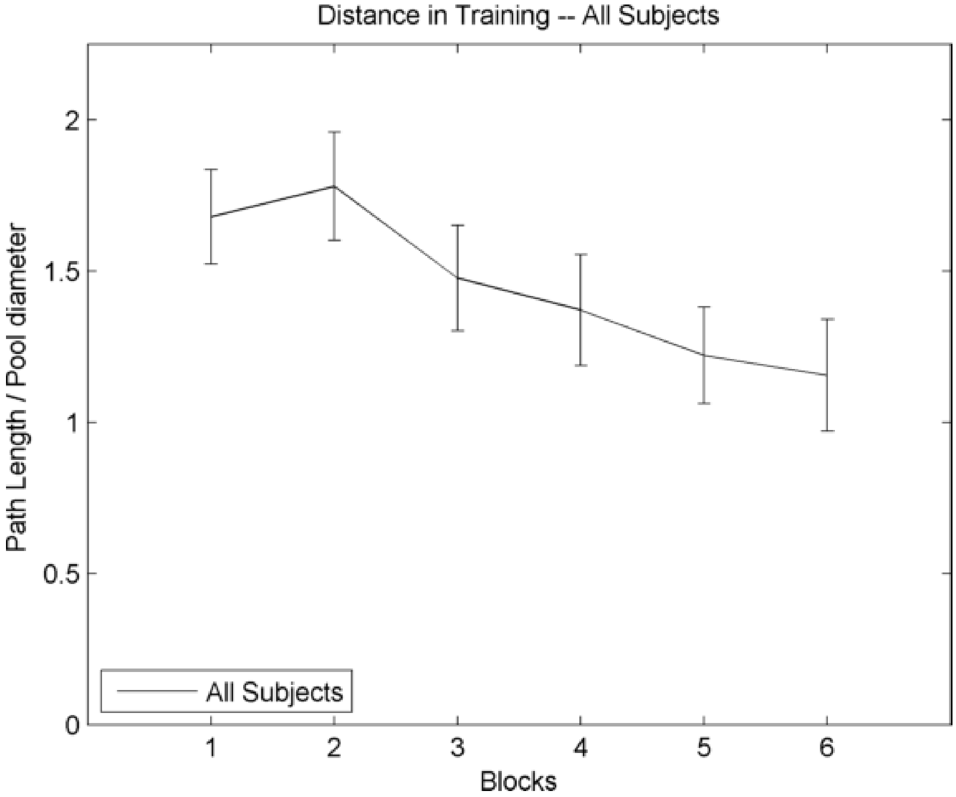

Figure 2.5: Mean Distance for all participants to navigate to the platform in Experiment 1. Each block was composed of four release points randomly selected without replacement. Error bars are +- Standard error of mean.

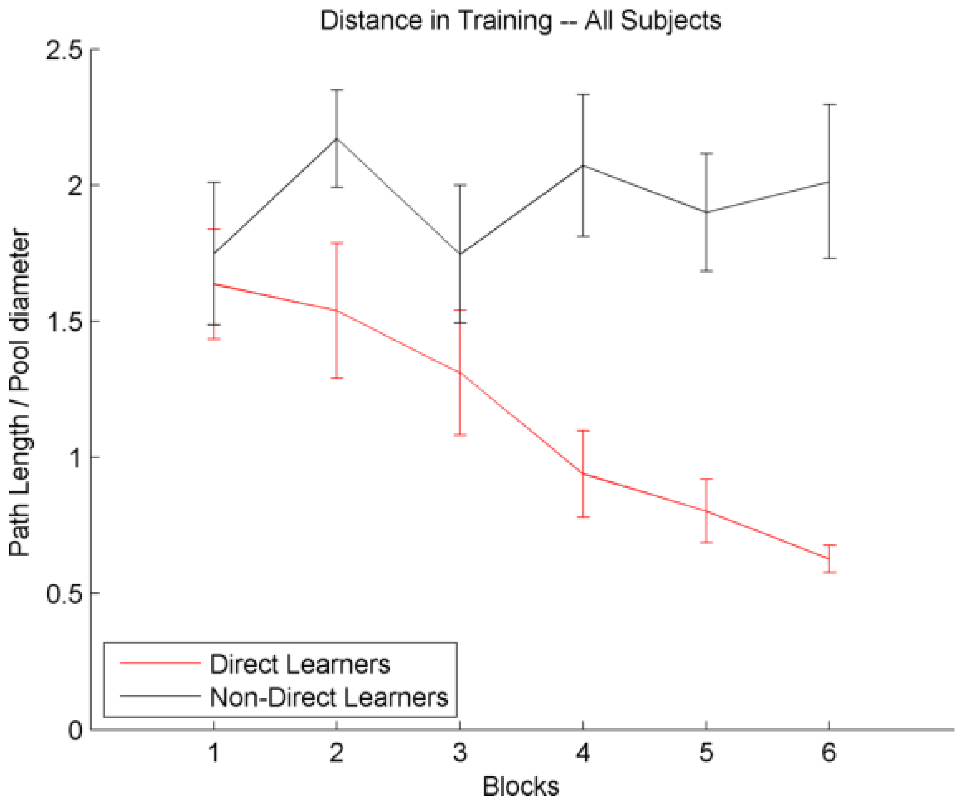

Figure 2.6: Mean Distance for direct learners and non-direct learner to navigate to the platform in Experiment 1. Each block was composed of four release points randomly selected without replacement. Error bars are ± 1 standard error of mean.

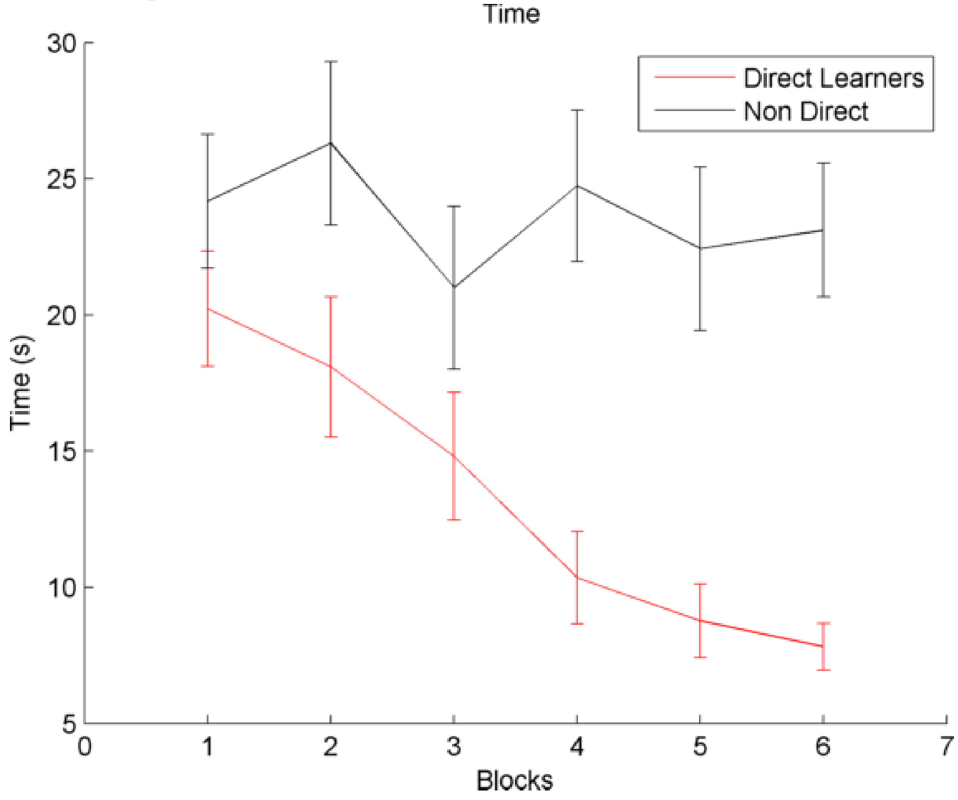

Figure 2.7: Mean Time for direct learners and non-direct learner to navigate to the platform in Experiment 1. Each block was composed of four release points randomly selected without replacement. Error bars are ± 1 standard error of mean.

Gaze measures were collected using the previously described saccade collision method. Participants were excluded from data analysis if the eyetracker could not calibrate on their gaze or if the eye was occluded for more than %40 of the trial. The total number of participants included in analysis was 16 (n direct = 10, n non-direct=6). Gaze analysis was first computed as a function of proportion across all trials for each cue to assess if the navigators target specific cues within the environment. A multivariate analysis of variance (MANOVA) was used with between subject factors as the average proportion of gaze on each cue for the first block of trial, average proportion of gaze on each cue during the last block of trial, and the between participants factor of classification type. All multivariate effects reported as significant met Wilks' criteria at p<.05. For the average first block of trials direct navigators significantly gazed more often at cue 3 F(1,14) F=4.63, *p*=.048 and the pool water cue F(1,14) =8.96, *p*=.010. Non-direct navigators looked more often at the pool wall F(1,14)=59.92, p<.001. During the last block of training direct navigators looked more often at cue 4 F(1,14)=6.52, *p*=.023, the pool water F(1,14)=9.67, *p*=.008. Non-direct navigators looked more often at the pool wall cue during the last block of training F(1,14)=59.92, *p*<.001.

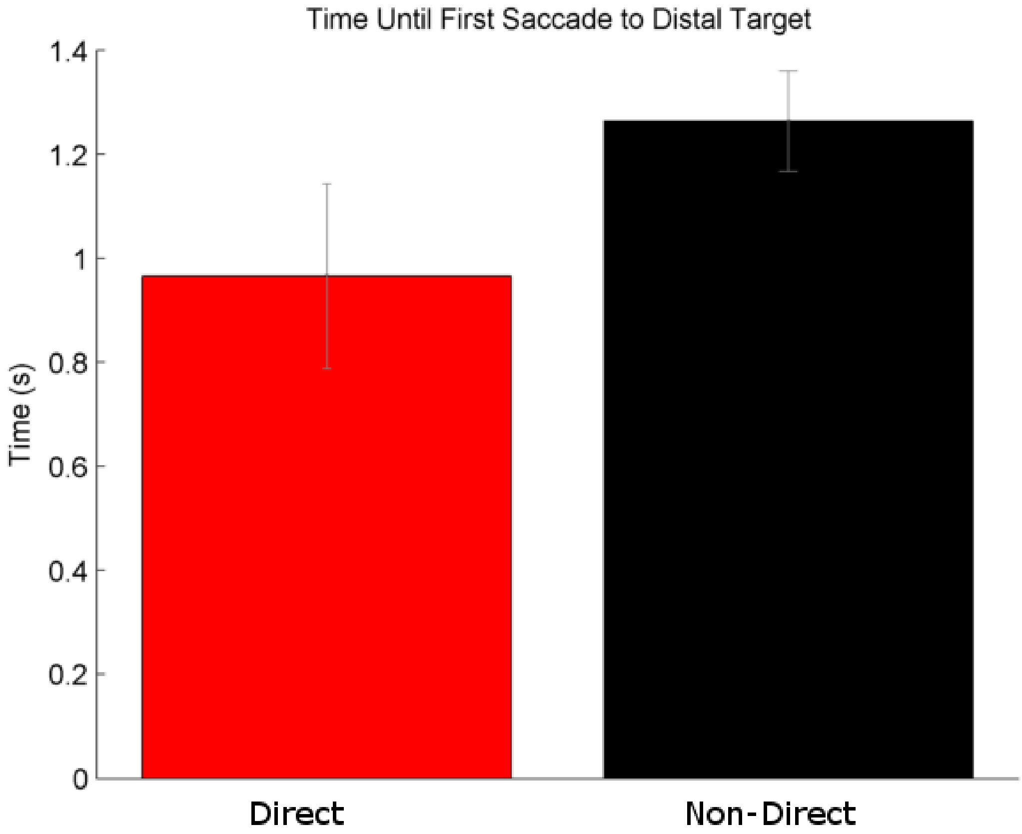

Figure 2.8: Mean time until first saccade to a distal cue at the onset of the trial.

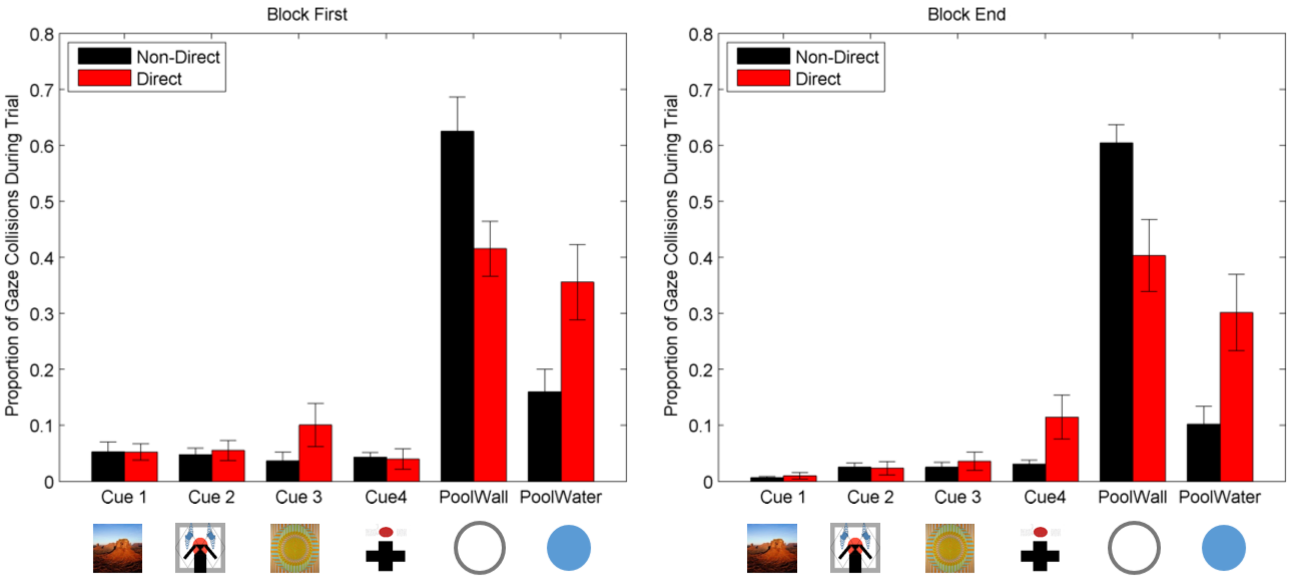

Figure 2.9: Mean gaze proportion for each cue: first and last block. Cue 1 is furthers from platform location. Left graph is average of first block of trials. Right graph is last block of trials. Cue 4 is closest to platform location. Error bars are ±1 SEM.

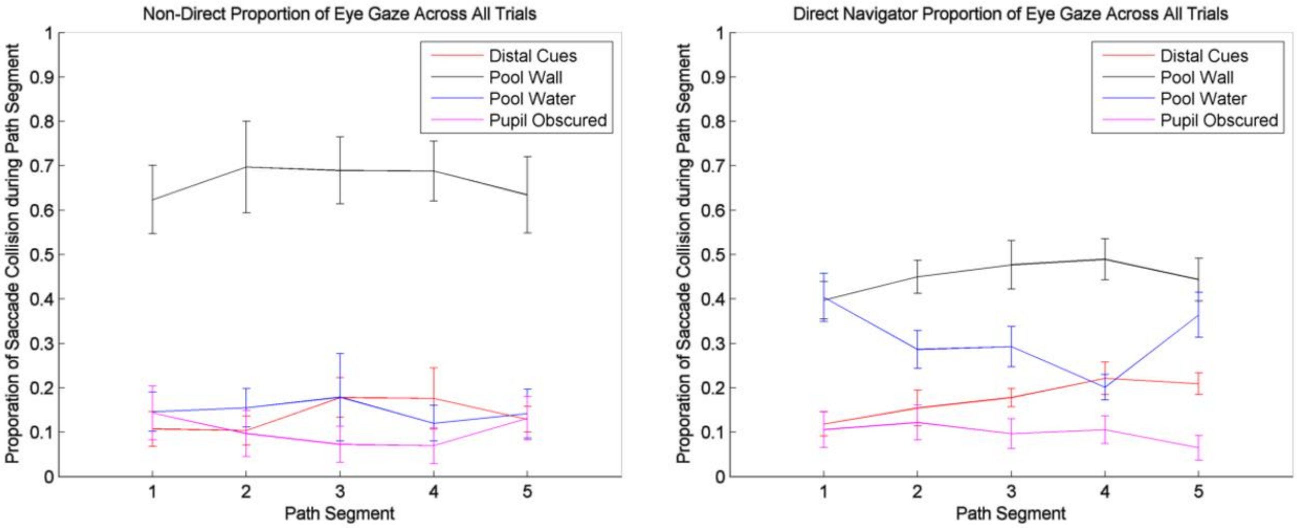

Figure 2.10 Mean gaze proportion for each path segment of the trial. Path segment 1 is the onset of the trial and segment 5 is the last portion of the participant’s trajectory. Error bars are ±1 SEM.

To investigate the cortical-frontal differences in classification, event related potentials were timelocked to the event of reaching the hidden platform. See figure 2.11. A univariate analysis on peak FCz electrode amplitude between the time range of 150 and 300 was run as a function of classification type. There was a main effect of peak amplitude $F(2,19)=7.58$, $p=0.14$ but no significant interaction term. A multivariate ANOVA on theta and delta ROI averages as a function of classification revealed non significant results.

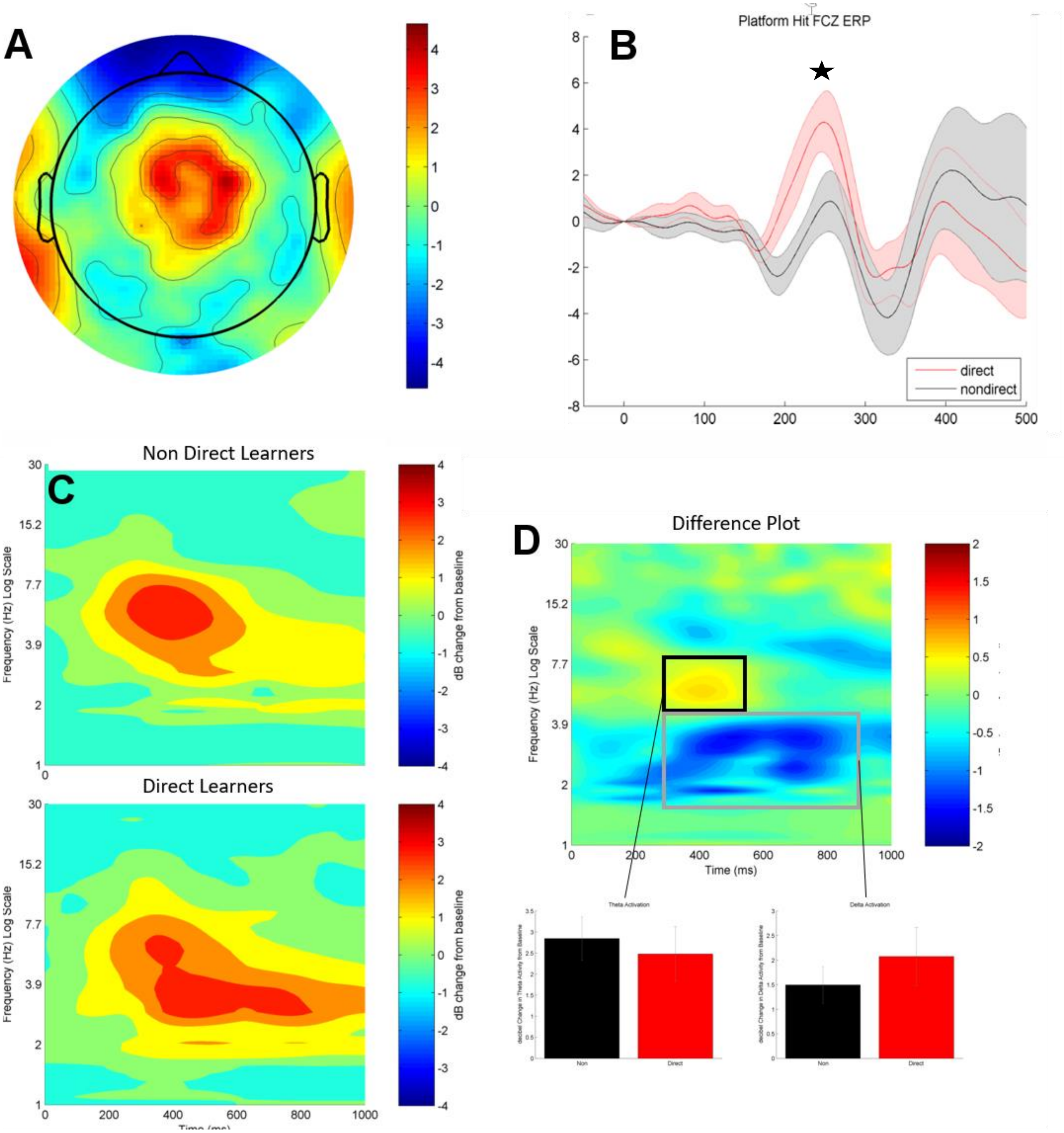

Figure 2.11 EEG results time-locked to arrival at escape platform. A) Topo map of activity averaged from 150 to 300 ms post event. B) ERP of electrode at FCz. C) Group averages of time-frequency decomposition each non-direct learners and direct learners. D) Matrix subtraction of the group averages with Theta ROI and Delta ROI delineated by group. Not significantly different.

Distance and latencies for the probe trial in phase 2 were measured to determine if direct navigators were faster and more direct in placing where they thought the platform would be. See figures 2.11 and 2.12. A two-sample t-test was conducted to detect differences in distance travelled during the probe. There was no significant difference between classification types (*p*=.4671). An additional two-sample t-test was conducted on the time on the probe trial prior to platform placement.   This result was also non-significant (*p*=.1284). Three judges rated the direct navigator's platform placement during the probe trial as closer to the place position relative to the room or the directional position relative to the pool wall. Interrater reliability was 90%. Of the 13 direct navigators 9 exhibited a directional response, 3 exhibited a place response and 1 direct navigator's data was excluded due to a premature click at the onset of the trial.

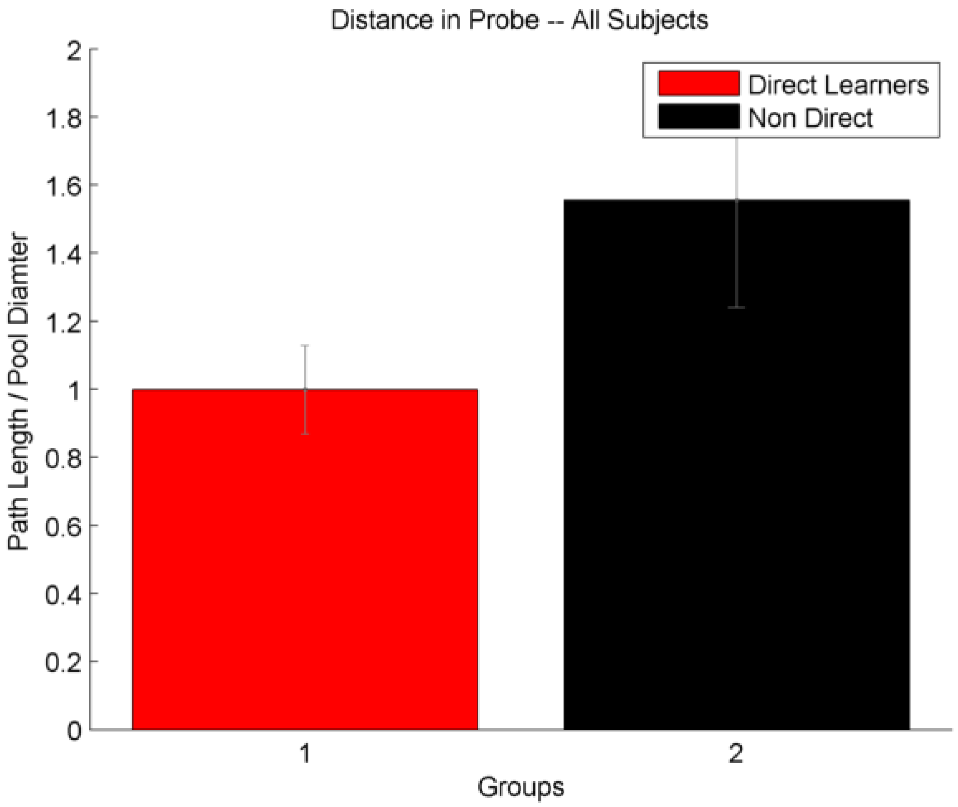

Figure 2.11 Mean distance travelled during probe trial after the pool enclosure was shifted. Trial was concluded once subject pressed button to indicate where they believed the platform to be. Results were non-significant. Error bars are 1 SEM.

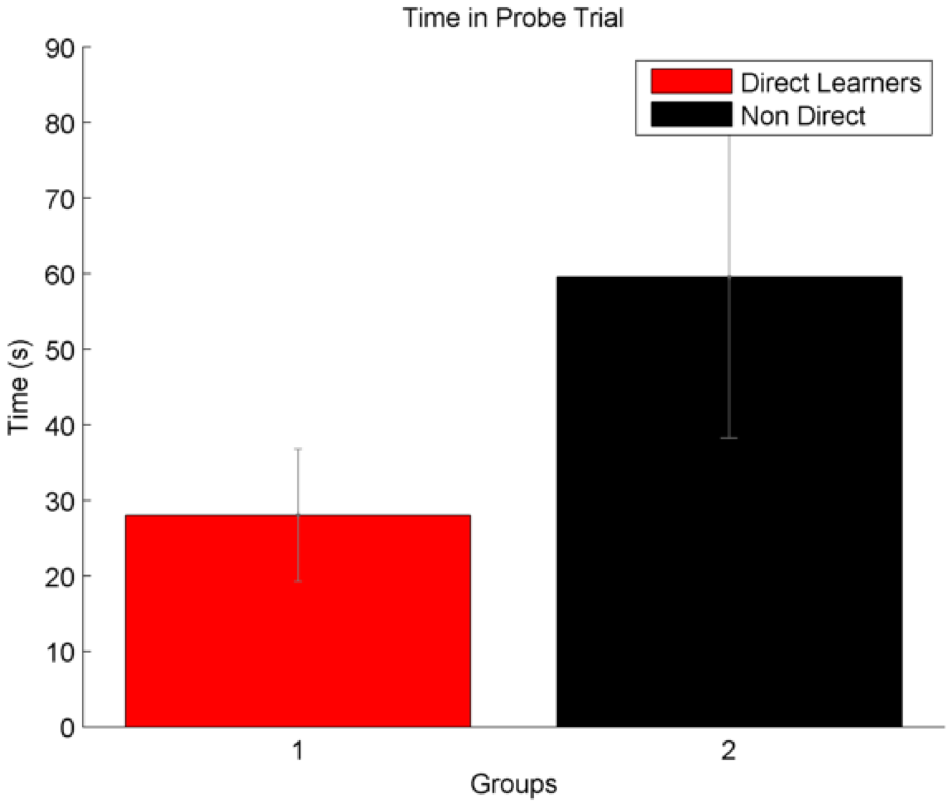

Figure 2.12 Mean time spent during probe trial after the pool enclosure was shifted. Trial was concluded once subject pressed button to indicate where they believed the platform to be. Results were non-significant. Error bars are ±1 SEM.

2.4 Discussion

The results of Experiment 1 demonstrate that navigators that learn direct paths to the hidden platform have shorter latencies and path lengths to reach the platform. This result is not surprising and has been validated in other vMWT paradigms. The purpose of the classifications are to frame the difference in cortical activity and eye-gaze sequence to identify which characteristics enable a navigator to learn a direct trajectory to the platform.

The direct learners are first to gaze at a distal cue, however this was not a significant effect (p=0.10). Both groups first looked at a distal cue about a second after the trial began. Lee, Skelton et al published data reporting that gaze analysis during the first second of a trial identified which strategy the navigator would choose for the trial (Livingstone-Lee et al., 2011), however the present data here suggests that this navigation process takes at the very least one second. This discrepancy could be due to difference in task design and data analysis. Lee et al segmented the screen into a grid and defined the distal and local cues as the points above or below the midpoint line of the screen. This technique restricts analysis to only the onset of the trial before movement occurs and also fails to detect the specific cue that is being foveated upon. The saccade detection paradigm demonstrated here allows much more robust quantification of what navigators are looking at in real-time throughout the course of the trial. The null result of time to first saccade to a distal target argues against the idea that direct navigators utilize a preferential sequence of first scanning distal cues for orientation information (Hamilton et al., 2004). However, this could be an artifact of the task design. In this study navigators began each trial staring at a central fixation screen prior to the trial start. Once the trial began, the navigator began facing the pool wall. The prior fixation screen was overlaid right upon the local cue pool wall and most of the distal cue setting was obscured. The location of the fixation cross and the required small movement before distal cues became visible could obscure a significant effect of direct navigator gazing first at distal cues.

Direct navigators did demonstrate major differences in what types of cues they gazed at. Throughout the vMWT training, both direct and non-direct navigators gazed primarily at local cues over distal cues which replicates prior work (Hamilton, Johnson, et al., 2009). This result is at first counter intuitive considering how the distal cues are much more salient in terms of color and texture than the formless poolwall and poolwater cues. However this result demonstrates how cues contribute to the information content of the environment. The distal cues provide a vector for orientation and global distance information (Knierim & Hamilton, 2011), but when the navigator is correctly oriented and approximately in the area of the platform the local cues are much more useful in locating the platform. The initial block of trials in which all navigators are still learning the task demonstrates equivalent sampling of all distal cues, with cue 3, an adjacent cue to the platform beginning to be preferentially gazed at by direct navigators. Direct navigators significantly gaze longer at cue 4 in the last block of trials, the cue closest to the platform confirming that distal cues were necessarily sampled to disambiguate the location of the platform. Yet much more proportion of saccades were used by both navigator types in sampling local cues.

Despite the similarity of both navigation classifications in sampling local cues, they differed in the rate at which they sampled the pool wall compared to the pool water. The first study examining continuous eyetracking in the vMWT grouped the pool wall and pool water local stimuli together (Hamilton, Johnson, et al., 2009). The results presented here are virtually identical if the local cues are grouped together, however by segmenting the pool wall and pool water cues a major significant difference in gaze proportion between direct and non-direct navigators is observed. Direct navigators preferentially examine the pool water much more than non-direct navigators whom spend most of their time scanning the pool wall. Examining the gaze patterns as function of path segment indicates that the direct navigators are scanning the pool water mostly at the beginning and end of the trial. The pool water itself contains no texture or form to indicate the location of the platform. It is not the case that the direct navigators are staring exclusively at the pool water; rather it seems as though the direct navigators, once oriented to where they believe the platform to be, begin a process of saccading down from the pool wall to the pool water. This scanning behavior sequence provides information as to a distance estimation of the platform location from the pool wall which provides additional support to the idea that the pool wall, while unable to provide orientating information, does in fact provide a key metric for distance estimation particularly during the beginning and end of a trial. Of all the results presented here, it seems as though this saccade pattern best discriminates between direct and non-direct navigators.

Previous studies using the vMWT have identified hippocampal theta rhythm related to a number of components of task navigation ranging from goal-directed navigation (Cornwell et al., 2008), difficulty of task (Kahana et al., 1999), and learning apart from motor movement (Olvera-Cortés, Guevara, & González-Burgos, 2004) among others. The data presented here explored if there were also cortical differences detectable between direct and non-direct navigators. In non-spatial reinforcement tasks there is extensive evidence of frontal-central (FCz) theta reflecting uncertainty and unexpectedness (Cavanagh, Figueroa, Cohen, & Frank, 2012). A topographical analysis of all participants upon reaching the platform demonstrates strong frontal-central activation. There is a significant difference in FCz between direct and non-direct navigators for the ERP waveform with direct navigators having a high positive peak culminating 250 ms post arrival at platform. This effect was followed up with time-frequency decomposition. Both groups had similar theta burst activity for this reward event. The non-direct navigators had largely theta activity while the direct navigators exhibited slightly less theta and more delta activity smeared out to 700 ms post reward stimulus. The difference in the ROI's of theta and delta band activity was not significant. Thus, while there is a significant difference in ERPs, this effect is not captured by time-frequency decomposition. The higher p300 component of the direct navigators could perhaps be related to some sort of goal anticipation that corresponds to the previously described systematic saccade behavior.

Chapter 3: Generalization of navigation strategy to other tasks

3.1 Hypothesis

The proportion of direct navigators compared to non-direct navigators corresponds to previous observations of performance in the vMWT. Experiment 1 highlighted some of the physiological and behavioral differences that could account for these strategy differences. Experiment 2 explores how these classifications of direct and non-direct navigators hold up in a T-maze, a slightly different spatial navigational task.

The junction of the T-maze offers a punctate decision point to time-lock EEG investigation. Previous work has delineated a specific spatial ERP component the topographical NT170. This component is believed to be generated by the right medial temporal lobe (See Figure 3.1). The component occurs during the viewing of the end alley for reinforcement. The NT170 has higher amplitude for rightward turns than leftward and reflects individual differences in spatial learning (Baker & Holroyd, 2013). If the classifications from direct and non-direct navigators hold true for the T-maze then we would expect to see differences in NT170 activation.

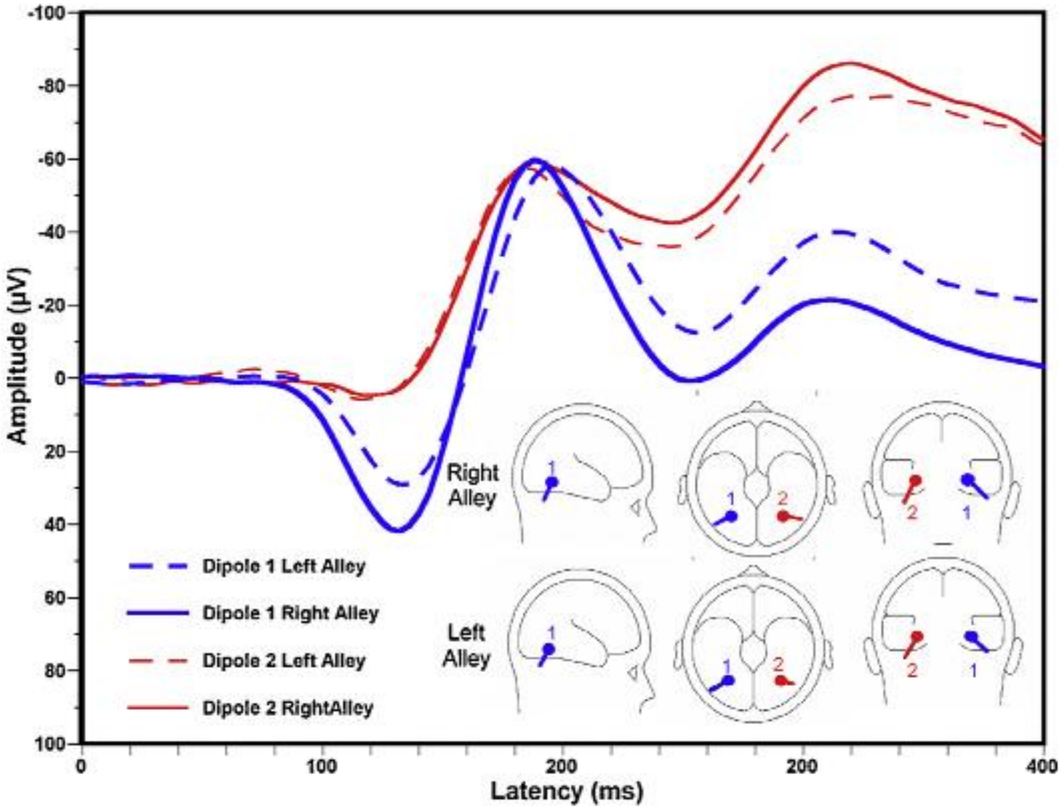

Figure 3.1 Equivalent dipole model solutions for the NT170. Waveform is elicited differential by feedback following left and right turns and peaks in 170 to 200 ms Negative plotted upwards by convention. Adapted from Baker (Travis E. Baker & Holroyd, 2013a).

An additional classification was performed in experiment 1 solely for direct navigators[2]. Depending on their performance during the probe shift trial in the vMWT, direct navigators were either identified as having a place or directional strategy. Here in experiment 2 upon the conclusion of a T-test training, the maze was rotated and/or translated within the room to test the navigational preference of the participant. See Figure 3.2.

---

[2] All subjects performed a shift probe task, but only data from direct navigators was analyzed as non-direct navigators were presumably not using a directional or place strategy of responding

Previous research on spatial navigation differences between direct and non-direct navigators highlight alternative explanations for performance apart from microbehaviors and navigation strategy. In this chapter data concerning experience with first person perspective video games, motivation, and sex effects are reported as control experiments to discount alternative explanations of the variable performance observed in experiment 1.

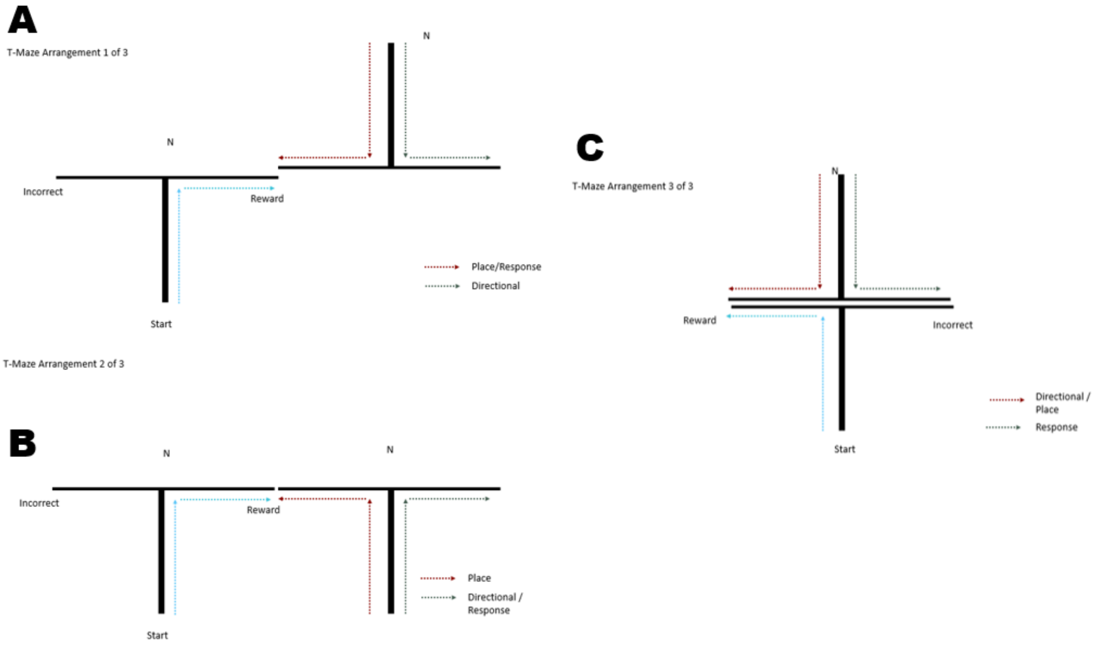

Figure 3.2 Overview of the T-maze rotations used during probe trials. Each configuration had participants trained for reinforcement. Upon completion of training the probe trial began with the maze in a new position. The arm selection made during these probe trials scored the subject with 1 of 3 strategies. The selections were added up and designated as the participant’s preferred strategy. Blue arrows indicate reinforcement during training. Red and green arrows indicate strategy selection during probe trial.

3.2 Methods

Experiment 2 was conducted in a new virtual environment with novel distal cues. A T-maze was used instead of circular pool apparatus. Each trial began with the subject placed in the neutral arm of the T-maze. All trials were conducted in first person perspective. The player's height was 2 virtual units, and the walls of the T-maze had a height of 1 virtual unit. Thus the subject could see distal cues located on the walls of the room. The subject controlled forward movement to the T-maze junction and was required to turn either left or right and travel to an orb located at the end of either arm. Once the subject reached the orb it changed colors to indicate if the trial was correct or incorrect. Turns were different than in experiment 1; one press on the left or right button rotated the subject 90° over the course .3 seconds. This automatic turning behavior was used to control for variability in turn speed. Baker et al's publication assessed the T-maze in a sequential presentation of images. The subject viewed the T-maze junction, indicated direction and then instantly saw the screen depicting the result of the turn. To replicate their findings in a full 3d environment turns were handled automatically to quickly rotate the subject without creating simulator sickness.

T-maze training consisted of 30 trials in the initial position of the maze. Once the 30 training trials were over, the onset of the next probe trial occurred with the maze transported to a new position in the room. The rotation and translations of the maze were situated within the room as to create a conflict between navigation strategies. The participant's cumulative selection during probe trials was used to classify their preferred navigational strategy.

The first T-maze configuration placed the maze in the southern part of the room and reinforced a rightward turn. See figure 3.2. The probe position for this first configuration consisted of a transposition of the maze such that the left arm of the probe maze was in the same place location as the right arm of the training maze position. In this first configuration travel to the right during the probe trial would suggest a directional response. Travel to the left during this probe maze would suggest a place/response strategy. The 2nd training maze configuration positioned the T-maze in the southern part of the room. The probe maze position for this 2nd configuration involved a translation such that the left arm of the probe maze overlapped with the right arm of the original training maze. A left response during this probe trial would suggest a place navigation strategy in that the subject was navigating to the specific place of reinforcement relative to the room. A right response would suggest a direction/response strategy. The 3rd training maze configuration placed the training maze in the southern part of the room with a left response reinforcement. The probe trial for this maze configuration flipped the maze such that the starting arm was diametrical opposite of the starting location for the original training maze. For this 3rd maze configuration a right turn would suggest a place/directional strategy and a left turn would imply a response strategy.

3.3 Results

NT170 component amplitude was calculated base to peak by taking the most positive value of the ERP within a 50-150 ms window following the turn event. Next the maximum negative peak extending from NT170 onset to 200 ms following the event was calculated. The amplitude difference between this local min and max was used in the following reports of the NT170 (Baker & Holroyd, 2013). Electrode A21 (POz) was identified as the electrode with maximum NT170 amplitude for both direct and non-direct navigators. See figure 3.4. An independent-samples t-test was conducted to compare peak amplitude of NT170 on turns for direct and non-direct navigators. For rightward turns there was a significant difference in scores for NT170 amplitude for direct navigators (M=-5.7, SD=1.9) compared to non-direct navigators (M=-2.99, SD=1.2) t=11.3, *p*=0.001. There was no significant difference for leftward turns between groups.

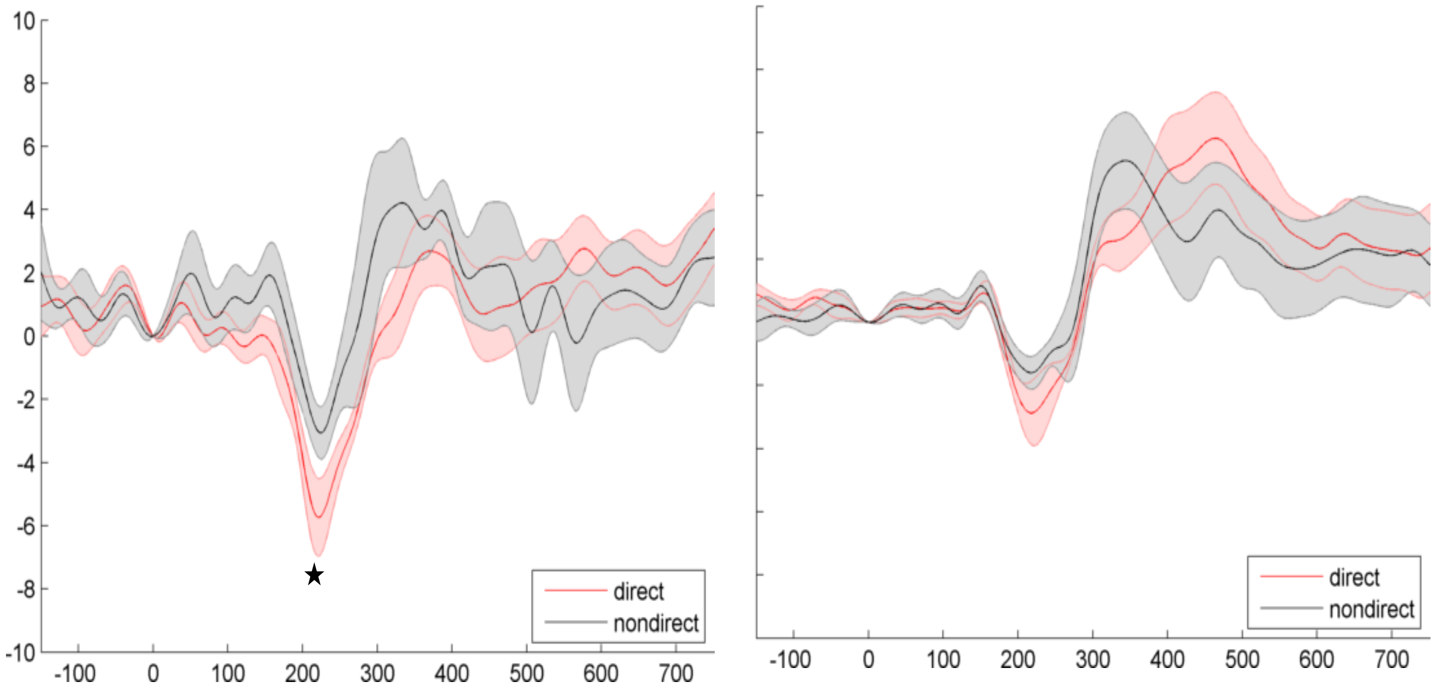

Figure 3.3 ERP wave forms time locked to turn prior to reinforcement. Electrode at POz. Right turn to reward is right graph and left turn is leftmost graph.

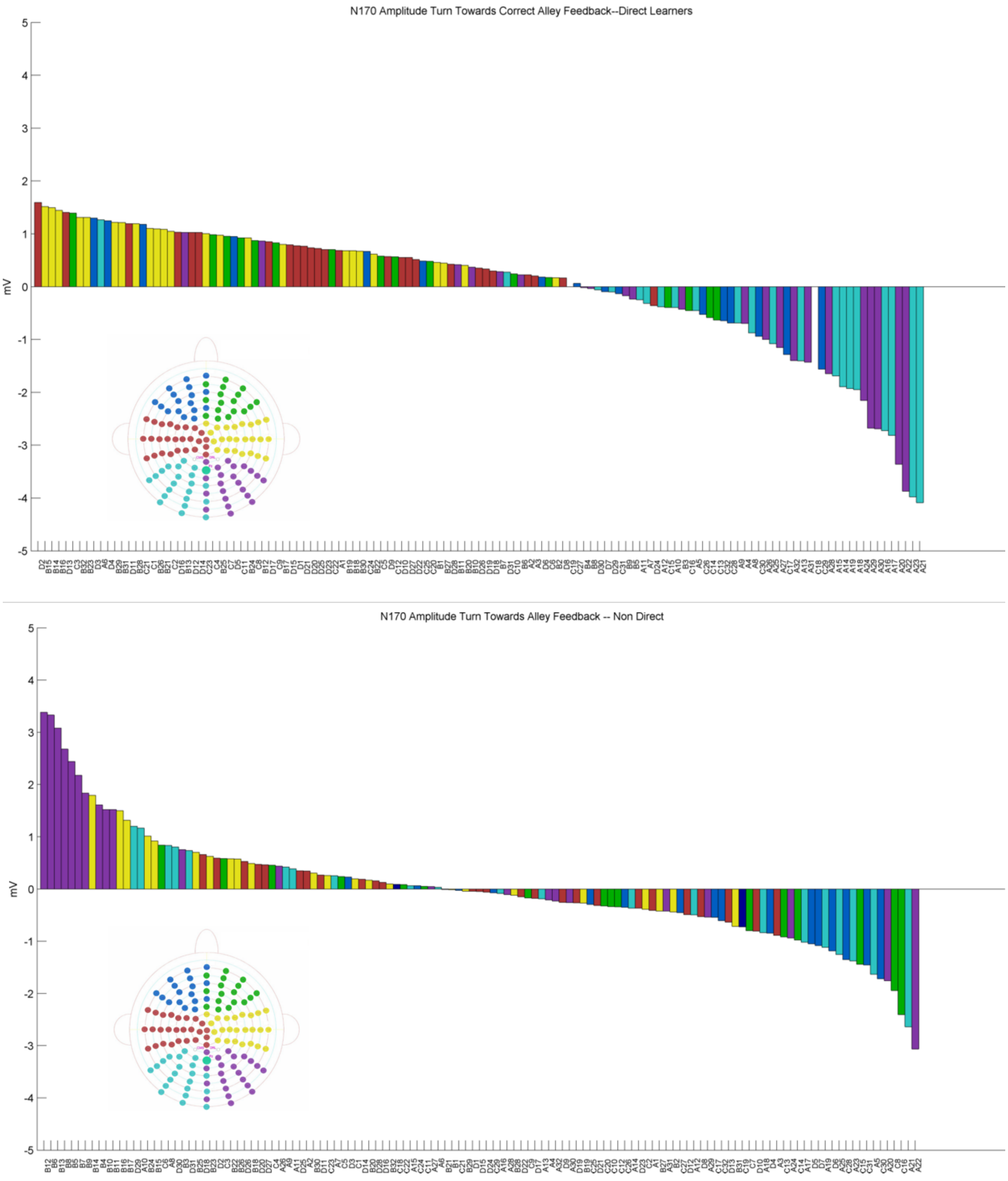

Figure 3.4 Amplitude of NT170 component across all electrodes. X axis contains each of the 128 channels. Inset: Schematic of cap and electrode grouping. Colors correspond to amplitude bars. Top: Direct navigators. Bottom: Non-direct navigators.

Of the 12 direct navigators from experiment one, 9 choose a directional strategy and 3 choose a place strategy in the shift probe test of experiment 1. In the T-maze probe tests of the 9 directional strategy navigators, 6 scored as directional navigators in the T-maze and 3 scored as place navigators in the T-maze. Of the 3 place navigators in the vMWT, all 3 choose a place strategy in the T-maze.

Since previous research groups have identified sex as a source of variance in spatial navigation tasks, the virtual distance travelled during the vMWT was analyzed using a repeated measures ANOVA with each block as a within participants factor and sex as the between participants factor. There was a main effect of block on F(5,19) = 4.102, p= .002, η_p^2= .178. There was no main effect of sex. Since there was not a significant main effect of sex an interaction comparison was not performed. There was also a significant linear trend for block F(1,19)=8.88, p=.008 η_p^2= .319. There was no significant linear trend for the sex by block interaction. A repeated measures ANOVA run on latency as a function of sex did not reveal a significant main effect of sex.

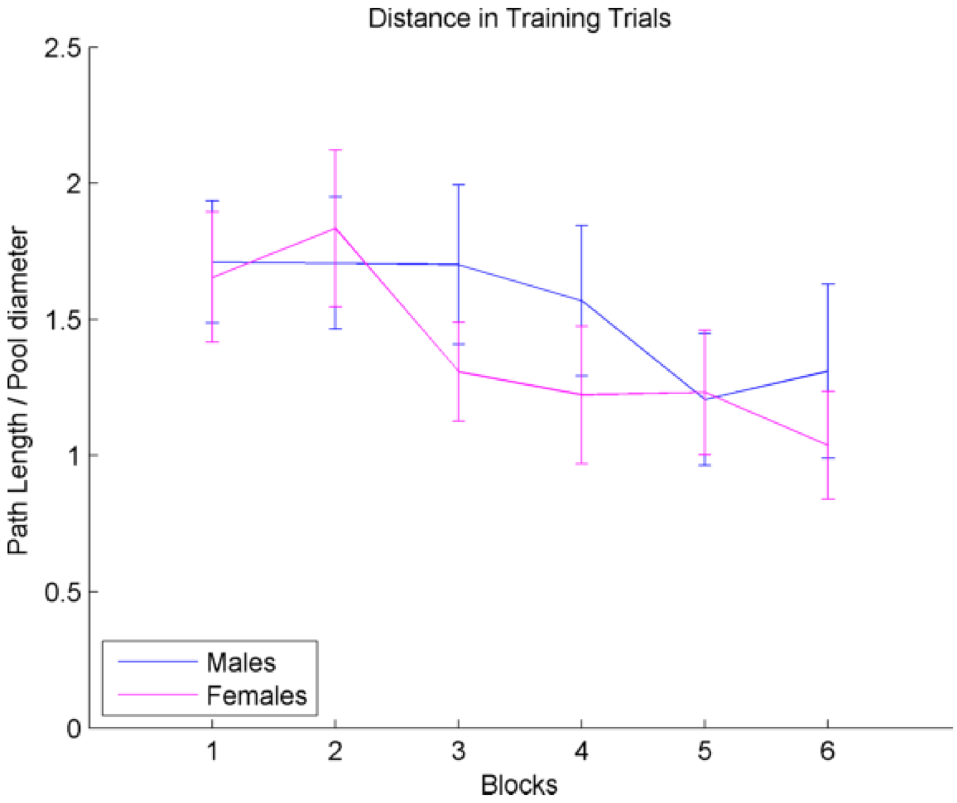

Figure 3.5: Mean Distance for males and females to navigate to the platform in Experiment 1. Each block was composed of four release points randomly selected without replacement. Error bars are ± 1 standard error of mean.

An ongoing question for the vMWT is how motivated are the participants to find the hidden platform. To explore the attentiveness of the subject, a repeated measures ANOVA was run on latency until first movement post fixation screen as a function of classification type. There was a main effect of block on $F(5,19) = 7.07$, $p= .006$, $\eta_p^2 = .183$. There was no main effect of classification on latency to first movement. Since there was not a significant main effect of classification an interaction comparison was not performed. There was also a significant cubic trend for block $F(1,19)=8.21$, $p=.011$, $\eta_p^2= .339$.

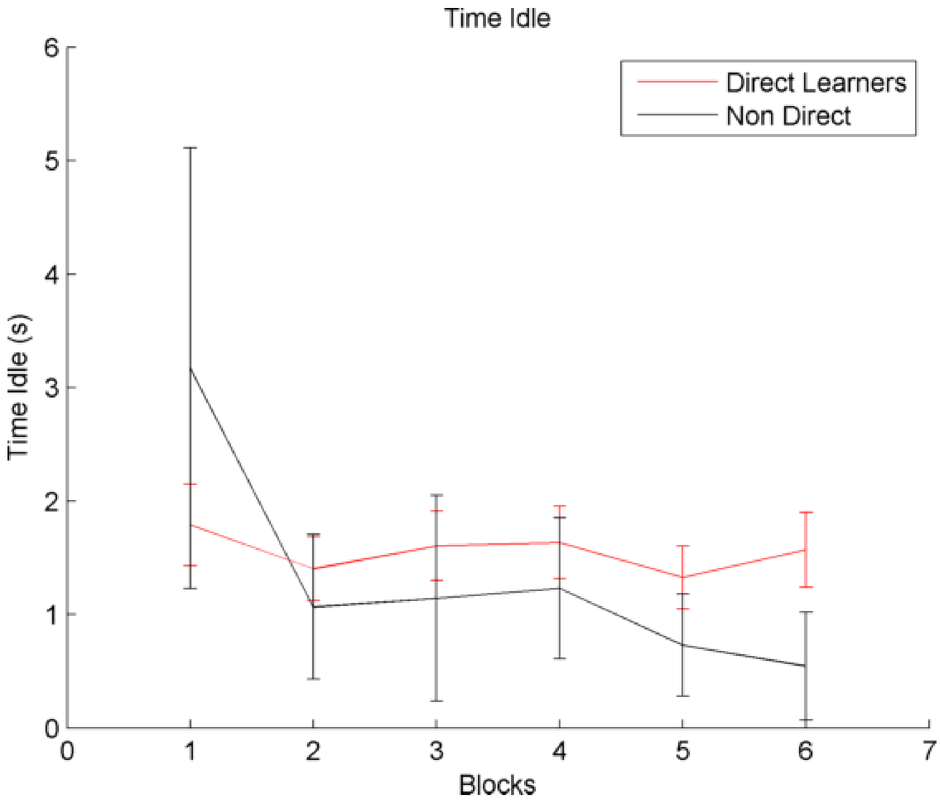

Figure 3.6: Mean time prior to first forward movement for direct and non-direct learners. Each block was composed of four release points randomly selected without replacement. Error bars are ± 1 standard error of mean.

As a control for alternative explanations that could account for the difference between direct and non-direct navigators, or variables that could be a consequence of the difference between direct and non-direct navigators, questionnaire data were collected. See Table 1.

Table 1

Classification Demographics

Factor	Direct	NonDirect	t	p
N	13	8		
Gender	6 M 7 F	3 M 5 F		
Age	23.8 (5.12)	21.2(2.91)	1.29	0.21
GPA	3.32 (0.48)	2.86 (0.65)	1.86	0.07
Videogame Experience with FPS games (Y/N)	92%	43%		
Thought Platform in same place (Y/N)	91 %	75 %		
Caffeine Prior (Y/N)	54%	37.5%		
Perceived Difficulty (10=diff)	3.69 (2.09)	6.83 (2.31)	3.21	0.0046*
Presence Scale--Realism	5.15 (0.81)	5.75 (0.97)	1.53	0.14
Presence Scale—Interface Usability	2.36 (0.99)	3.0 (1.21)	1.32	0.20
Presence Scale—Self Evaluation of performance	5.87 (1.08)	5.0 (1.58)	1.50	0.15

3.4. Discussion

The second experiment was conducted to determine if the classifications produced during the first experiment would still be useful in discriminating between navigators in a new maze type environment. Previous research has demonstrated navigation strategy preference is preserved during turning tasks if the stimuli are ambiguous (Gramann, 2013). Experiment 2 provided data as to if the strategy preference exhibited in the vMWT would translate to the virtual T-maze. Despite the difference in latency and distance travelled during hidden platform vMWT for the direct and non-direct navigators, performance accuracy in the T-maze was not significantly different between groups. Thus accuracy in the T-maze could not discriminate between the classifications created in the vMWT. This result most likely speaks to the nature of the spatial task themselves instead of individual variability. The freeform navigation of the vMWT offers a more qualitative assessment of navigation trajectories than the binary output of the T-maze.

There was a small correspondence between vMWT and the T-maze in terms of the navigation preference exhibited during probe trials when distal and local cues were shifted or repositioned. All 3 place navigators of the vMWT scored as place navigators over the course of the 3 T-maze configurations. Of the 9 directional responders during the vMWT, 6 exhibited a preference for directional responding during the T-maze. The remaining 3 directional responders exhibited a place preference in the T-maze. Although this was only a small subset of participants (i.e. navigators classified as direct during vMWT training) that retained their navigational preference responding between tasks types, it offers preliminary evidence that participants are utilizing similar navigational strategies across maze apparatuses when distal and local cues are placed in conflict.

The NT170 component was identified as the subject turned towards the reinforcement alley for both direct and non-direct participants. Similar to Baker et al, the NT170 amplitude was greater for rightward turns to the reinforcement as compared to leftward turns. However while Baker et al. identified the maximal responding to be localized to electrode PO8, in our study both direct and non-direct groups had maximum amplitude at a more medial electrode, POz. This result argues against the localization of the component to the right medial temporal lobe. The conflicting result could presumably be accounted for by differences in electrode cap montage and referencing. Baker et al used a 32 channel cap and a mastoid reference while the data presented here consisted of a 128 electrode and an average reference montage. The average reference was used to leverage the increased surface area coverage of the 128 electrode cap system. Despite the difference in which specific electrode had maximum NT170 amplitude, our results do confirm that the right posterior parietal cortex (teal and purple electrode groupings) had the most negative NT170 amplitude overall.

There was a significant difference between NT170 amplitude for rightward turns in the T-maze for direct learners as compared to non-direct learners. The difference in NT170 amplitude between learners is similar to previous observations of NT170 amplitude variation as a function of variation in individual spatial traits (Baker & Holroyd, 2009). After the experimental virtual T-maze session, Baker et al had participants draw a reproduction of the T-maze layout and classified participants based upon their accuracy of their drawing. Drawers that most accurately depicted the maze had significantly different NT170 amplitude as compared to the participants that had poor performance in drawing the maze layout. The authors concluded that this was further evidence of the NT170 sensitivity to the localization of reinforcement in a spatial task. For our data, overall T-maze accuracy failed to discriminate between direct and non-direct navigators, however the NT170 amplitude for rightward turns did significantly differ between groups. The difference in right vs leftward turns could be related to the handedness of the subjects; in this study all subjects were right-hand dominant. All together, the results reported here suggests that even with comparable behavioral performance in the T-maze, there was still a distinct difference in neural representation of spatial encoding between direct navigators and non-direct navigators.

Early virtual spatial navigation experiments reported large differences in sex with male participants performing much better than female participants (Astur, Ortiz, & Sutherland, 1998; Driscoll, Hamilton, Yeo, Brooks, & Sutherland, 2005; Moffat, 2009) over a variety of virtual spatial navigation tasks. In the present study there were no significant sex differences for latency or path length in any block during vMWT training. Theses result presented conflict with previous reports. One possible explanation for this conflict is that early sex differences in virtual tasks were mediated by video game experience. Earlier virtual tasks might have not taken into account pre-existing video game experience differences between groups. Experience with video games was one significant predictor of direct navigation in our study and has also been demonstrated as significant predictor of performance in other virtual tasks (Richardson, Powers, & Bousquet, 2011). See Table 1. The contemporary popularity of 3d video games in which first person perspective is utilized may have reduced the sex effects observed in current iterations of virtual navigation experiments.

Motivation is also an alternative explanation to describe the discrepancy between direct and non-direct navigators. Perhaps the non-direct navigators simply were not trying as hard to escape the pool. Motivation to succeed in videogames is difficult to assess (Przybylski, Rigby, & Ryan, 2010), here we approximated motivation in terms of how focused the subject was in moving at the onset of the trial. A subject unmotivated to find the escape to the platform might be slow to react at the trial onset; they may simply idle in place until the platform appeared. We calculated the time until first movement to determine if there was a significant difference in onset movement time between groups. There was only a significant difference during the final block in which non-direct navigators actually moved faster than direct responders. Non-direct navigators had much variability during the first block of trials but their average idle time decreased as function of trial block. This suggests that they were more attentive as the experiment progressed. While this result only approximates motivation and does not correspond to the sensation of swimming to escape an actual pool of water, it does offer insight into the attentional mechanisms occurring at the start of the trial.

Chapter 4: Optimizing performance in the Virtual Morris Water Task with additional perspective information

4.1 Hypothesis

Experiment 3 extends the traditional format of navigation in the vMWT with a new manipulation in which the viewing perspective is manipulated once during the course of the trial. A previous study has examined fMRI activation in which a subject viewed a survey-level view of an environment for 10 seconds before navigating though the environment in either first person, third person, or overhead survey perspective (Sherrill et al., 2013). The environment itself had no identifying landmarks so the subject needed to encode the orientation and implantation of a planned route to the exit. Successful navigation in which the perspective had been switched significantly recruited hippocampal and posterior parietal cortical areas.

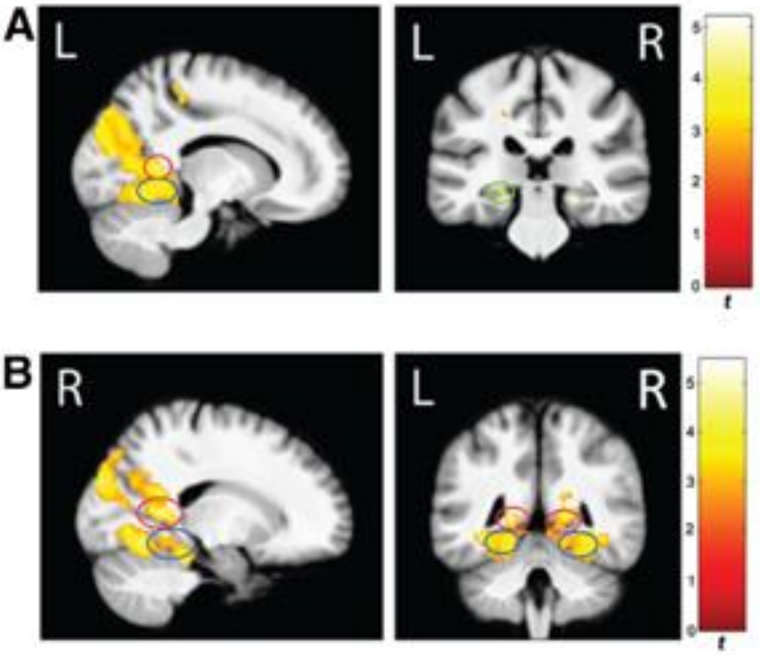

Figure 4.1: fMRI Hippocampal-Parietal activity related to shifts in viewing perspective. Activity originates in hippocampal areas and connects through to retrosplenial cortex to cortical posterior parietal area. Adapted from Sherrill et al. (Sherrill et al., 2013). A) Left medial view. B) Right medial view.

The demonstration of cortical-parietal activity related to perspective switching offers insight into how the brain reconciles virtual manipulations that could not be possible in the real world. Since Sherrill et al detected cortical activity, this phenomenon could be further tested in the vMWT with EEG. While EEG is poor in detecting the activity of deep hippocampal sources, it is sufficient to examine cortical activity. The advantage EEG has over fMRI is an increase in temporal precision that could be used to identify moment-to-moment changes in frequency dynamics that occur in the partial cortex during a shift in perspective.

Based upon the results of Sherrill et al, our a priori hypothesis was that switching perspectives would produce activity in the parietal cortex. This activity would likely be a burst of theta activity in the 4-8 hz range representing a resetting of phase involved in memory recall (Buzsáki, 2002).

4.2 Methods

Experiment 3 consisted of testing the participants previously reported in a new vMWT environment consisting of new distal cues and pool enclosure centered in the middle of the room. The goal of the task was similar to experiment 1 in which participants were instructed to escape from the pool as quickly as possible. After confirmation that they understood, experiment 3 began which consisted of 12 blocks of hidden platform trial with the platform located on the central west side of the pool. Each block consisted of 4 trials that varied by release point. The starting location of each trial was selected pseudorandomly without replacement from the four cardinal compress points around the perimeter of the pool (N, S, E, W). After these 48 trials, the subject had a break and given the instructions for the probe phase. In this phase the subject was instructed to navigate to where they thought the platform was and to click the right trigger button to end the trial. There were two probe tests for experiment 3, one probe for each perspective.

The key difference between experiment 1 and experiment 3 is that in experiment 3, each trial started in either a first person perspective or an overhead survey perspective. See Figure 4.2. The survey perspective was a stationary camera looking straight down. The player avatar in the survey view was represented as a magenta triangle which gave directional heading information. All movement parameters were the same as experiment 1. After a random amount of time selected in range of 1 to 1.5 seconds the experimental manipulation began. Movement was locked and a transparent Gaussian blur was overlaid on the screen. The blur began at .3 transparency and was linearly interpolated to maximum blur over the course of 1.5 seconds which completely obstructed the view. The blur was removed over the course of .5 seconds at which the screen returned to either the same view perspective as the onset of the trial ('same' condition) or the alternative viewing perspective ('switch' condition'). Events were time-locked to the point in which the blur was completely removed.

Experiment 3 was a 2x2 factorial design to test the contribution of retaining the memory of the initial perspective compared to the visual experience of ending in one perspective or the other. This allows for collapsing over condition types to examine which factor contributed most to the difference between groups.

Table 2

Experiment 3 Cross Design

	End In First Person View	End in Survey View
Stay Perspectives	Condition A1	Condition A2
Switch Perspectives	Condition B1	Condition B2

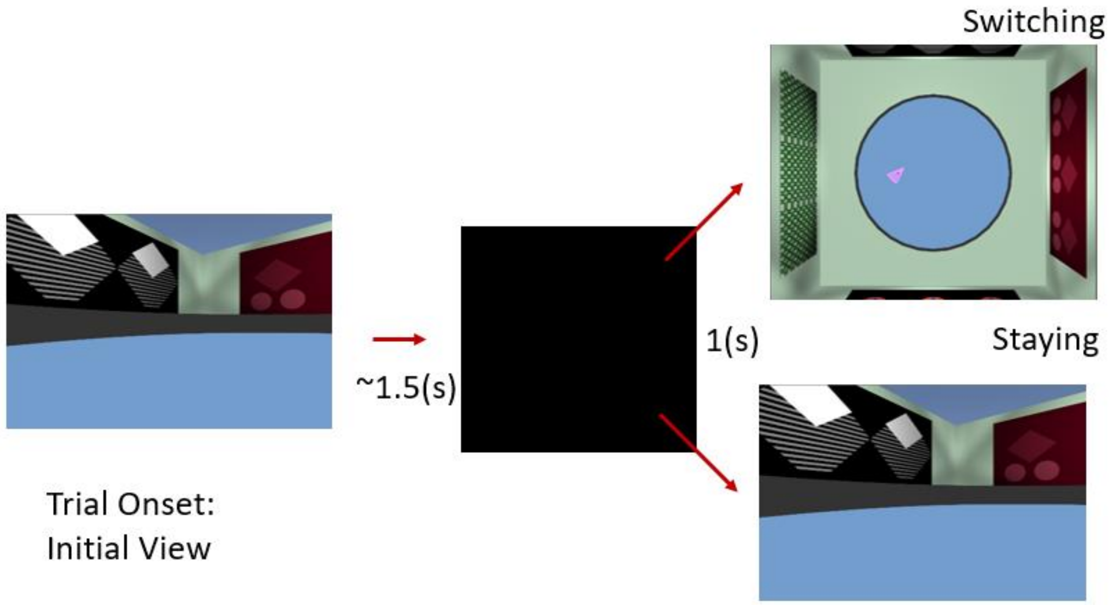

Figure 4.2: Schematic overview of Experiment 3. Left) The trial begins with vMWT in either a first person or overhead perspective. After a randomly selected period of time ranging from 1 to 1.5 seconds the screen fades to black before fading back into either the same perspective as the onset of the trial (staying) or the opposite perspective (switching).

Based upon previous work describing the recruitment of the posterior parietal cortex via the hippocampus (Sherrill et al., 2013) and the mechanism of hippocampal memory encoding/retrieval via theta frequency bursts (Hasselmo et al., 2002) we hypothesized that theta activity would be present in conditions in which the perspective switched. We defined an ROI from 4-8 hz post blur event. Post hoc analysis included an additional ROI in the mu frequency range (8-12 hz) related to differences in viewing perspective.

4.3 Results

For the perspective switch vMWT virtual distance travelled was analyzed using a repeated measures ANOVA with each block as within participants factor and the classification type as the between participants factor. There was a main effect of block on distance F(11,19) = 9.408, $p<.001$, $\eta_p^2 = .331$. There was not a significant main effect of classification F1(,19)=3.71, p=.069, η_p^2= .164. There was also a significant linear trend for block F(1,19)=18.22, p<.001, η_p^2 = .490. There was no significant linear trend for the classification by block F(1,19)=2.71, p =.116, η_p^2= .125.

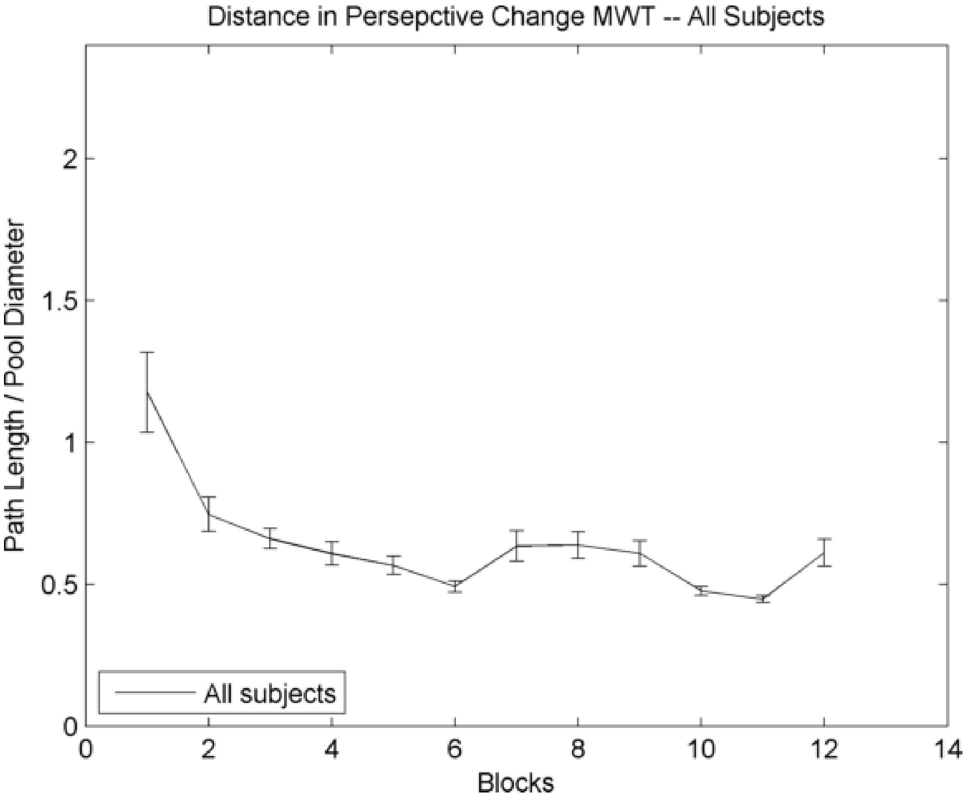

Figure 4.3 Mean Distance for all participants to navigate to the platform in Experiment 3. Each block was composed of four release points randomly selected without replacement. Error bars are ± 1 standard error of mean.

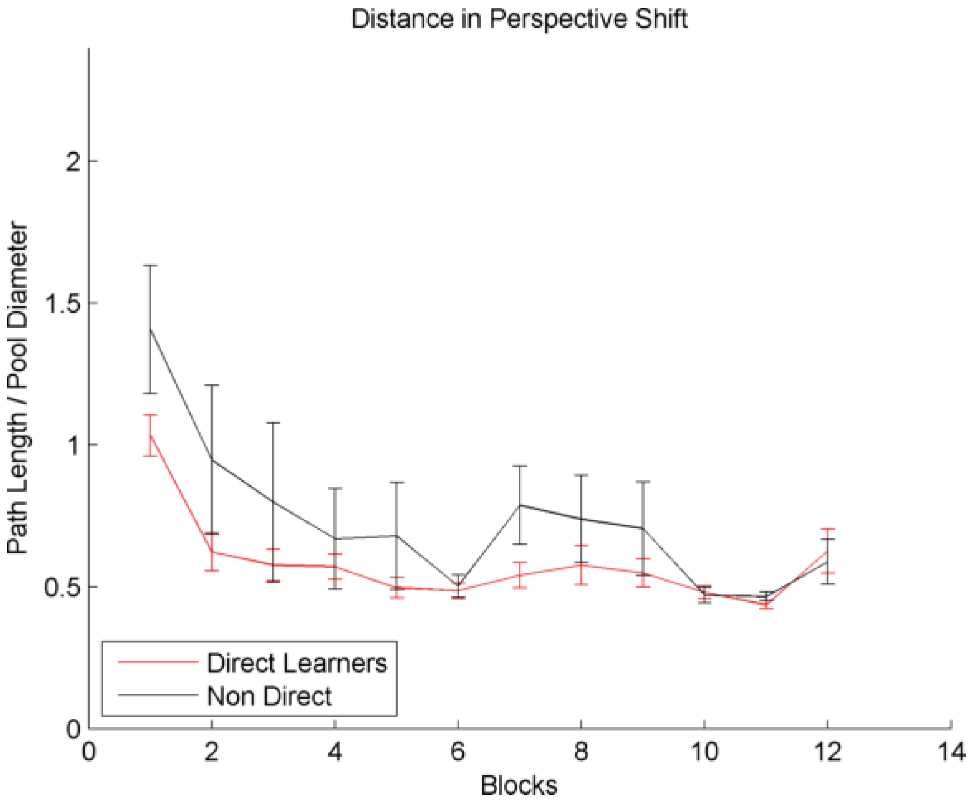

Figure 4.4 Mean Distance for direct and non-direct learners to navigate to the platform in Experiment 3. Each block was composed of four release points randomly selected without replacement. Error bars are ± 1 standard error of mean.

A 2x2 factorial repeated measures ANOVA was performed to examine the contribution of either switching or staying in a perspective and navigating the remainder of the trial in first person or survey perspective upon power spectra of the mu band activity. See figure 4.5. Since this ANOVA was run separately for each classification group, a Bonferroni correction was applied where α/2 corrected for the two multiple comparisons performed. For the non-direct navigators no significant main effect survived the multiple comparisons adjustment for either main effect of switching/staying (*p*=.43) or ending in first person / survey perspective (*p*=0.669). For the direct navigator group, there was a significant effect on first person viewing perspective (*p*=.014). There was no significant effect on switching or staying, so the interaction term was evaluated.

A 2x2 factorial repeated measures ANOVA was performed to examine the contribution of either switching or staying in a perspective and navigating the remainder of the trial in first person or survey perspective upon power spectra of the theta band activity. See figure 4.5 and 4.6. Since this ANOVA was run separately for each classification group, a Bonferroni correction was applied where $\alpha/2$ corrected for the two multiple comparisons performed. For the non-direct navigators there was a significant main effect for switching/staying (p=.43). There was significant main effect for ending in first person / survey perspective (p=0.01). For the direct navigator group, there was a significant effect on switching viewing perspective (p=.019). There was no significant effect on final viewing perspective, so the interaction term was not evaluated.

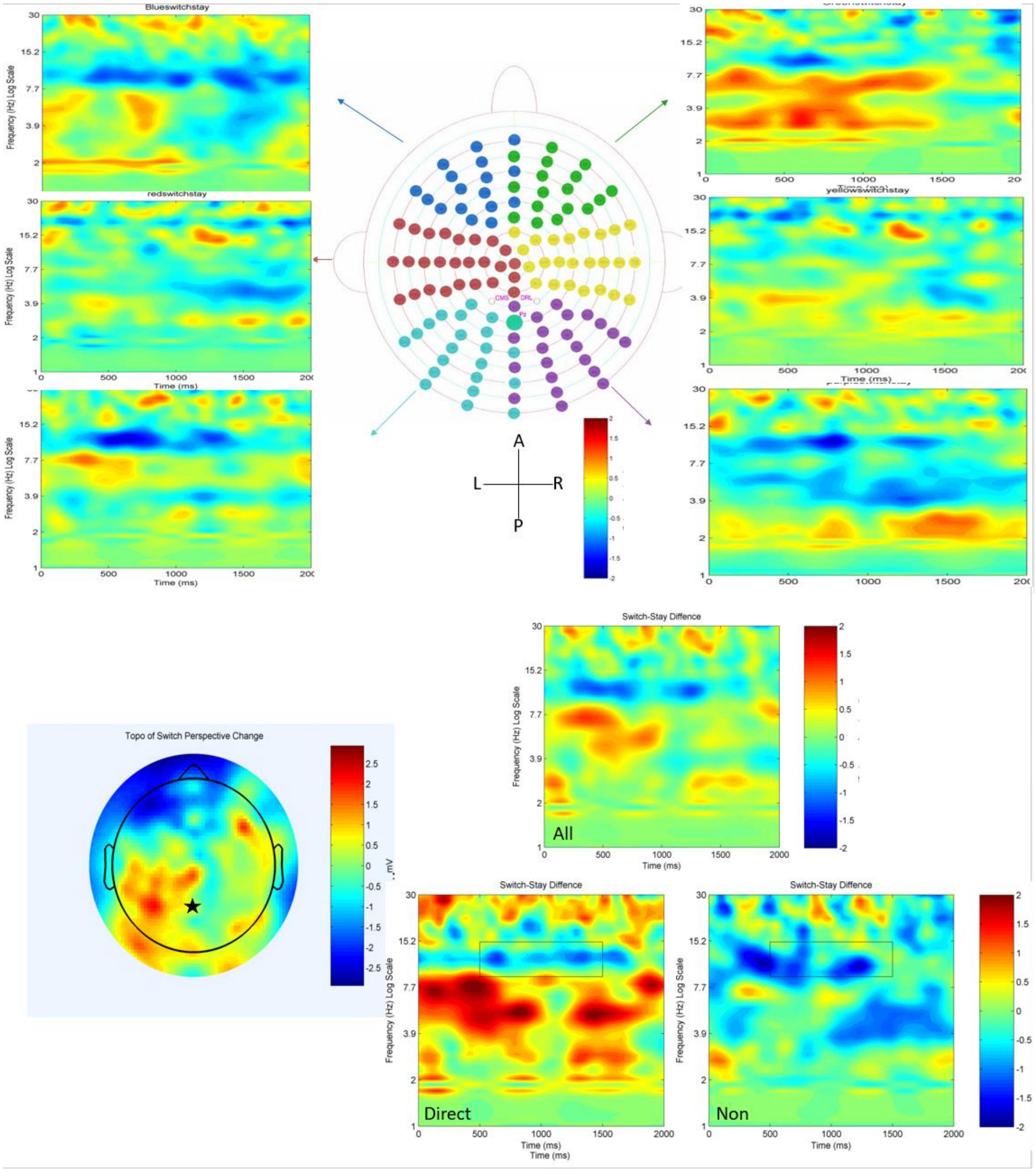

Figure 4.5 Time frequency decomposition for switch-stay difference comparison. Top: All participants data were averaged into six groups of electrodes (left/right for each anterior, middle, anterior as shown on colored 2d plot in middle. Bottom: Voltage topography of switch-stay difference for all participants. Right: All subject switch-stay difference for electrode P0z. Bottom Right: switch-stay difference for direct participants with mu activity ROI. Bottom Left: switch-stay difference for nondirect subject with mu activity ROI.

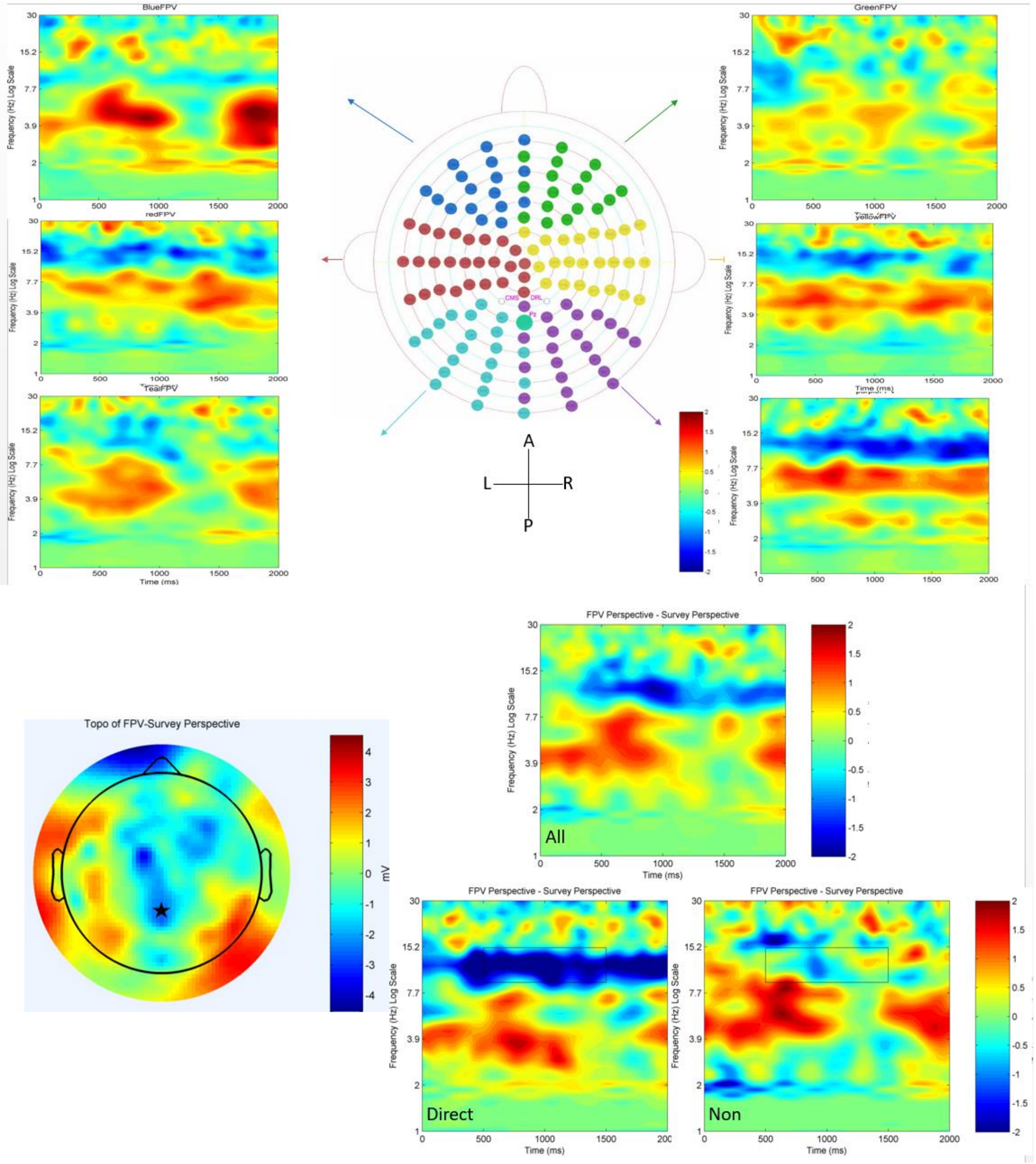

Figure 4.6: Time frequency decomposition for FPV-survey difference comparison. Top) All participants' data were averaged into six groups of electrodes (left/right for each anterior, middle, anterior as shown on colored 2d plot in middle. Bottom) Voltage topography of FPV-survey difference for all participants. Right: All subject FPV-survey difference for electrode P0z. Bottom Right: FPV-survey difference for direct participants with mu activity ROI. Bottom Left: FPV-survey difference for non-direct subject with mu activity ROI.

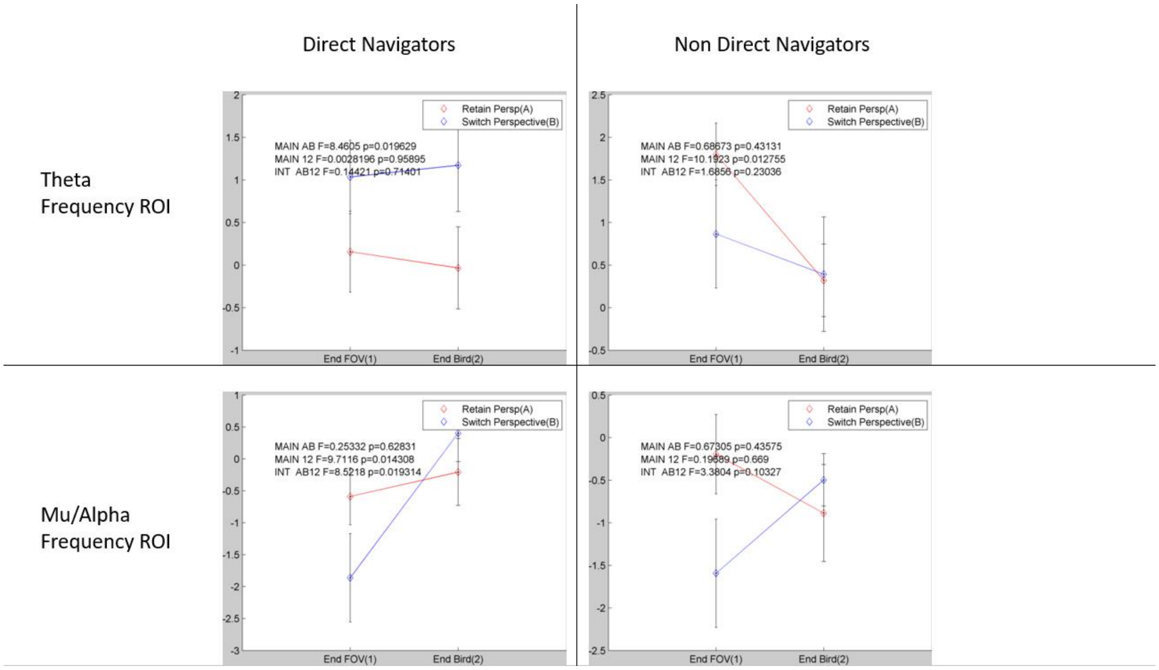

Figure 4.7: 2 x 2 ANOVA results time frequency decomposition of perspective range. Top Row: Theta frequency ROI results. Bottom Row: Mu/Alpha Frequency Results. Left Column: Direct Navigators. Right Column: Non direct navigators. Data is extracted from time frequency power ROIs as pictured in Figures 4.4 and 4.5.

The overlap of the Mu and Alpha frequency bands prohibits speculation as to the cognitive generator of the dominant 9-15 hz frequency band observed for direct navigators after a transition in perspective. The alpha frequency typically indicates a bored or idle state and is maximally generated at parietal sites (Chiu et al., 2012). The Mu frequency meanwhile, is strongest at horizontal motor cortex sites (Pfurtscheller, Brunner, Schlögl, & Da Silva, 2006). As seen in Figure 4.8, additional channels were examined to determine where the 9-15 hz oscillation was most dominant. This signal appears to be most dominant in parietal sites, implying an alpha oscillation cognitive mechanism.

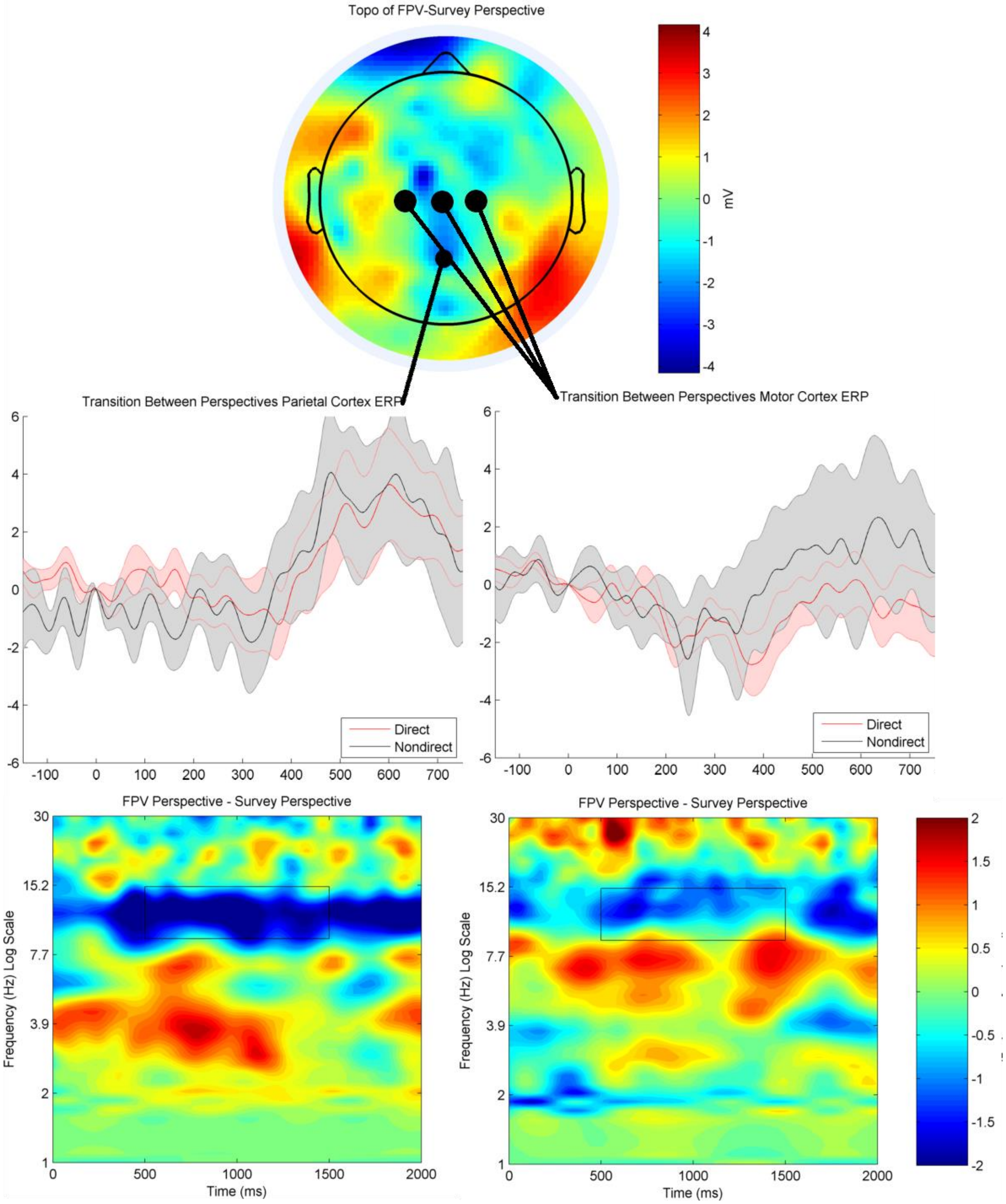

Figure 4.8: Comparison of parietal and motor cortex contribution to 9-15 hz activity. Top: topographical map of electrical activity occurring after a transition. Middle: event related potentials of event time locked to transition. Left column is parietal electrode, right column is the motor cortex electrodes. Bottom: Time frequency decomposition of activity with rectangle ROI centered on 9-15 hz activity occurring 500 ms. after transition.

To further confirm the implication that 9-15 hz alpha activity as the cognitive source for the observed oscillations, path length was correlated with neural frequency activity. Under the assumption that alpha depicts boredom, one would expect to see a positive relationship between alpha frequency representation and path length. A shorter path length suggests the navigator finds the task easy and would be accompanied by a linear increase in alpha frequency. As see in Figure 4.9, a correlation between alpha levels and path length reveals no association (r= -0.17, p=0.14).

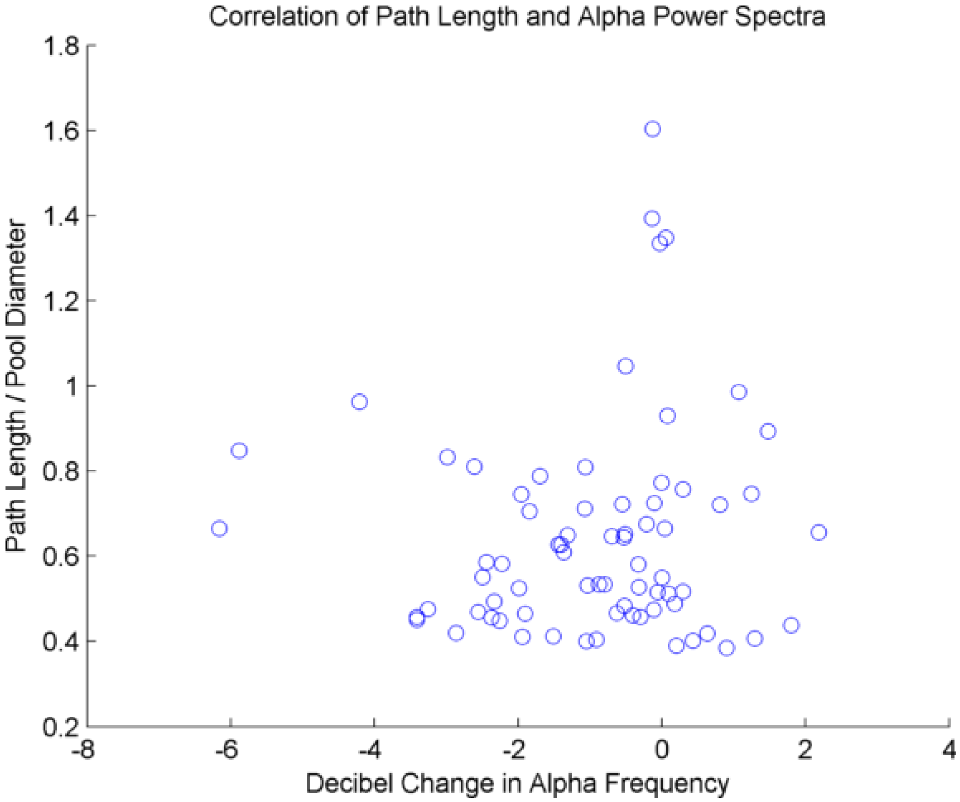

Figure 4.9: Correlation between path length and power spectra. Each subject’s path length for each condition plotted against change in alpha oscillation from baseline.

The difference in eye gaze between Direct and Non-Direct navigators observed during hidden vMWT in experiment 1 was followed up in experiment 3. Since experiment 3 involved multiple perspective shifts, eye gaze analysis was conducted separately for trials performed in first person perspective and overhead view.

For trials conducted in first person view, percentage of gaze targets during a trial was conducted between Direct and Non-Direct navigators. This analysis was similar to experiment 1 in which Direct navigators preferentially gazed at the target distal cues and proximal pool water cue. For experiment 3 in first person perspective there were no significant differences of cue gaze targets. As seen in Figure 4.10, the Non-Direct navigators have changed to using the pool water as gaze target as frequently as the Direct navigators.

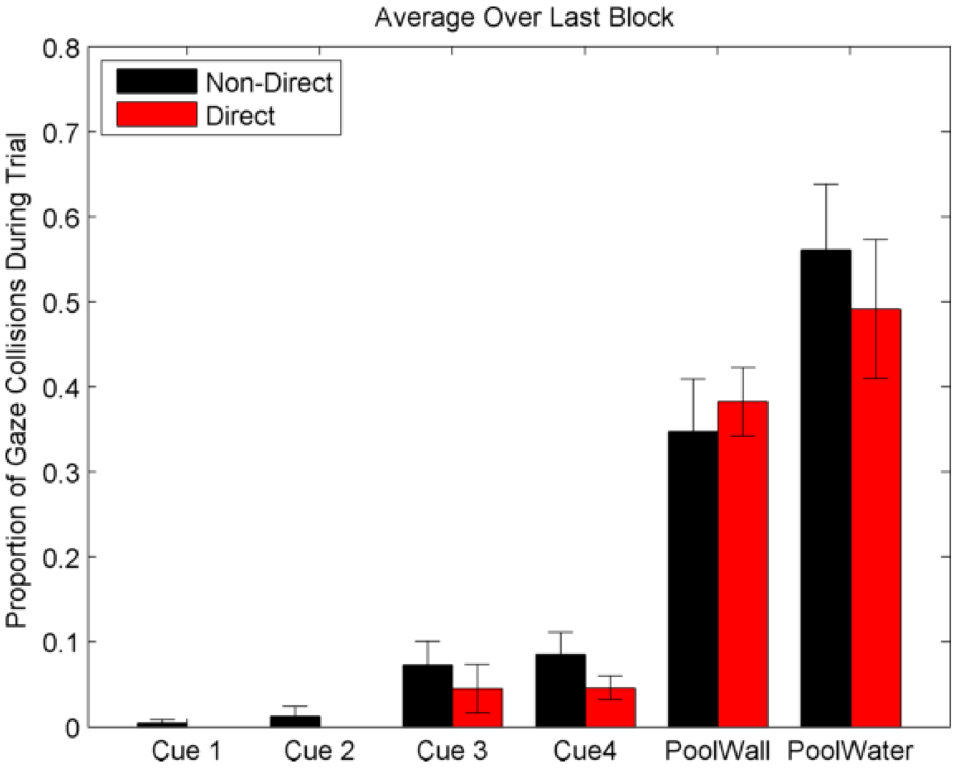

Figure 4.10: Mean gaze proportion for each cue during last block of experiment 3. Error bars are ±1 SEM.

The difference in gaze and path length observed in experiment 1, but not observed in experiment 3 suggests that the Non-Direct navigators have adapted their spatial strategy. However a question remains—perhaps the initial results observed in experiment 1 was due not to differences in spatial strategy but rather the results could be due to intrinsic differences in attentional mechanisms. To explore this question, an analysis was done to determine what the navigator was gazing at in overhead view during experiment 3. If the gaze was focused on the hidden platform location during the overhead survey mode this would suggest that there was a predictive action in which the navigator has an idea of where the platform is before they begin their trajectory.

To explore this question, the percentage of gaze during the course of a trial that fell within a region of interest expanding 100 pixels circularly from the platform center during trials in which there was an overhead perspective was calculated. As seen in figure 4.11, there was no difference between direct and Non-direct navigators. Both groups preferentially gazed at the platform location.

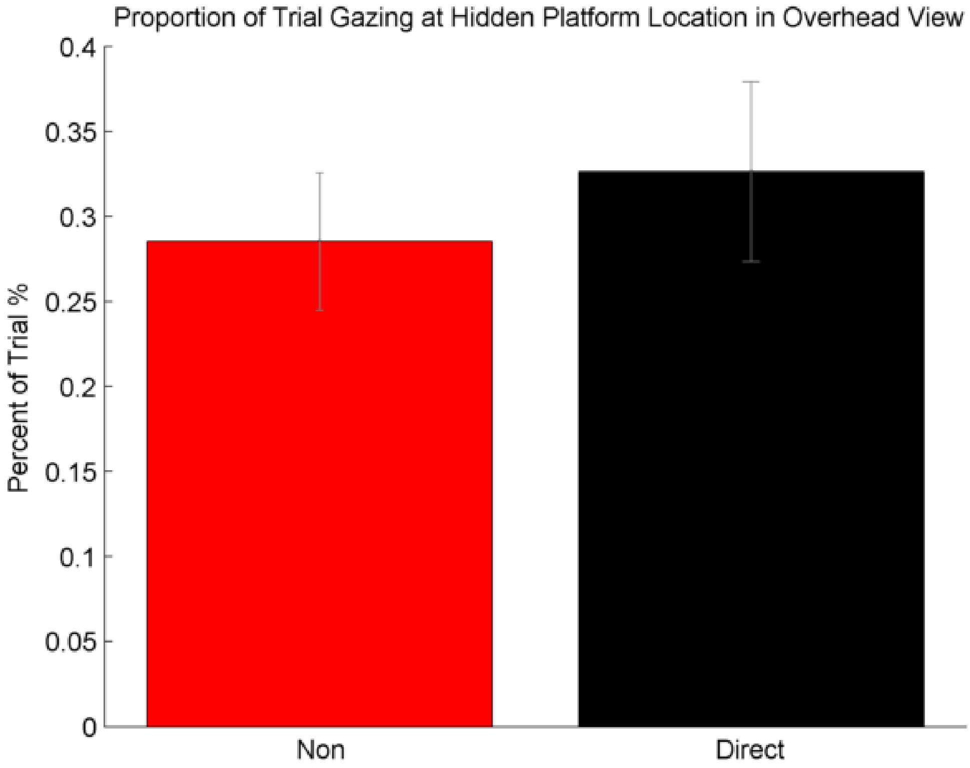

Figure 4.11. Mean proportion of subject’s gaze over hidden platform during over-head survey viewing perspective.

4.4 Discussion

Experiment 3 examined how a manipulation to the viewing perspective during a trial impacted navigation in the vMWT. Performance for both direct and non-direct groups both improved and were not significantly different over the course of the majority of trial blocks. The overhead perspective aided direct navigation by providing a source of information in which the subject could triangulate the location of the platform relative to the cues in the environment.

Since this was the last experiment for the participants and it consisted of 6 more trial blocks than the first experiment, the null effects of performance could possibly be ascribed to overtraining or order effects. That is, perhaps non-direct navigators in the first experiment simply needed more trials to develop a direct trajectory. This hypothesis cannot be ruled out based on the current dataset. However overtraining experiments in the MWT suggest that rats maintain their initial strategy until they are forced to change due to manipulations to the platform (Kealy et al., 2008). The rationale to include more blocks during this experiment was to provide more perspective switching occurrences to aid time-frequency decomposition analysis.

The eye gaze results observed in experiment 1 between Direct and Non-direct navigators was not observed in experiment 3. Both groups equally looked at the relevant distal cues to disambiguate the location of the hidden platform in first person perspective. Additionally in trials conducted in overhead view, both groups equally gazed at the location of the hidden platform. Thus the non-direct navigators adapted their behavior to match the performance of direct navigators for experiment 3.

Despite the similarities in behavioral performance, there were group differences in theta and mu frequency band power spectra during a perspective change. The direct navigators had higher theta power as function of switching perspectives. The presence of theta suggests that the direct navigator were retaining the initial viewing perspective in memory and experienced a reset once a novel perspective was displayed. Theta activity has been observed in humans when they experience a novel hallway, or after navigational mistakes have been realized and are being corrected (Bischof & Boulanger, 2003). This might be a similar phenomenon in which theta activity occurs when the perspective is switched.

An unanticipated result was the presence of 9-15 hz activity for the direct group as a function of the final viewing perspective type. Activity in this frequency range has been observed in many different EEG studies; there are two competing explanations as to what this neural oscillation could be depicting. The 9-15 hz could be described as Alpha wave activity, a frequency band that is associated with boredom and sleepiness, most strongly localized to occipital-visual areas (Romei, Gross, & Thut, 2010). The alpha hypothesis would suggest that direct navigators found this experiment boring and were fatigued by the end of the experiment. The alternative hypothesis is that this frequency band activity is related to the mu rhythm. Mu rhythm is maximally localized over the motor cortex and is associated with movement agency (Pfurtscheller et al., 2006). The mu wave is suppressed when movement occurs; this is true even when movement is imagined or when watching someone else perform a movement (Oberman, Ramachandran, & Pineda, 2008). Movement agency does not cause an increase in mu rhythm—rather the motor cortex is constantly idling at the mu frequency and this power band frequency is suppressed once movement is engaged. The results observed here—specifically the suppressive aspects of the mu rhythm observed in the contrast of first person perspective – survey perspective imply that this is phenomenon is mu related. The follow-up analysis identifies the parietal cortex as the dominant generator for this 9-15 hz activity. This suggests that the observed neural oscillation was an alpha-related boredom effect for direct navigators. Yet there was no correlation between alpha and path length.

The direct navigators experienced the most mu suppression when the perspective was switched from survey to first person perspective during a trial. It seems that the transition from movement in the overhead perspective to movement in the first person movement caused a change in the direct navigator. This transition suddenly evoked movement agency to be ascribed to the self. The motor input and speed was identical for each perspective; the only difference was the optic flow provided to the subject. Additionally the participant’s position was represented by a triangle which could have induced the subject to depersonalize movement while in an overhead perspective. Other studies have explored differences in ascribed movement to various avatar objects (Oberman et al., 2008). Further research is needed to understand the nature of this frequency band in regards to navigation through the virtual domain.

Chapter 5: Conclusion

General Discussion

This dissertation thesis has provided specific evidence as to group differences between direct and non-direct navigators. Through a series of three experiments, evidence has been provided as to how direct navigators in the vMWT 1) exhibit higher ERP amplitude upon finding the platform, 2) preferentially gaze at the distal cue closest to the hidden platform during last block of training, 3) utilize a saccade sequence pattern between the pool wall and pool water to calculate distance vector information, 4) have higher NT170 amplitude upon right turns to the reinforced alley of the T-maze, and 5) exhibit different theta and alpha/mu power spectra during artificial changes to viewing perspective. Additional information was provided to control for alternative explanations. Sex and idle time were not significant contributors to group differences. Other factors such as video game experience and perceived difficulty of the task were significantly correlated with direct navigation.

One of the main distinctions between direct and non-direct navigators in the vMWT suggests that the groups were differing in their sampling of the virtual visual environment. The direct navigators utilized many more gazes to the closest distal cue and then to the poolwall despite the poolwall's ambiguity in terms of providing orientation information. This sampling sequence implies that the direct navigators learned to systematically view stimuli in an ordered fashion within the artificial environment. It is important to consider this finding in light of future virtual navigation studies. Variance in navigational tasks designed to test spatial memory might in fact be discriminating participants based upon their perception within the presentation interface. In other words it could be the case that the difference between groups is not a function of memory capacities per se; rather difference in performance could be affected by the participant's ability to sample the relevant distal and local cues. This dissertation project provides evidence in that participants differing on initial performance in the vMWT could have similar performance on other spatial memory measures such as the T-maze. Future work will need to assess other spatial tasks to disassociate memory impairments with variance in perceptual sampling as a function of learning to navigate within the vMWT.

Direct and non-direct navigators did differ on a number of EEG measures in other tasks such as ERP potential on platform hit during the vMWT, righthand turn to reinforcement in the vMWT and differential time frequency activations on the perspective shift vMWT. These results could approximate the differences in participants' reward expectations (Cohen, Elger, & Ranganath, 2007), goal-direction (Bischof & Boulanger, 2003), boredom (Katayama & Natsume, 2012), and/or movement-agency during virtual tasks (Oberman et al., 2008). Previous studies have elucidated the role of hippocampal-generated signals involved in virtual navigation tasks. These cortical activations offer a novel development in examining how neural oscillations vary in the dynamic navigation task of the vMWT. Future work will need to examine if these cortical activations are unique to the spatial context, or if they can be replicated in subjects in a non-spatial paradigm (Baker & Holroyd, 2009) or demonstrate similar characteristics in associative learning tasks such as the transverse patterning discrimination task (Driscoll, et al., 2003)

The equalization of performance during the perspective switch vMWT suggest that the best way to optimize navigation in the real world is to offer individuals multiple real-time perspectives. Each perspective offers a unique source of information; for example first person perspective offers detailed information of the distal and local cues and distance estimates based upon shadows and occlusion. Overhead perspective offers information as to the participant’s movement in relation to the constellation of distal cues. Additional perspectives, such as third-person overhead could also provide contextual information for the individual. All these information streams could be provided through a technological device such as a smartphone or overlaid upon a visual display such as a vehicle dashboard or augmented reality glass overlay. The results of experiment 3 demonstrate that participants readily utilize these transitions and the ordering of transition switching could be used as a means to invoke an attentional set switch.

Limitations

The project described here had some drawbacks that will need to be addressed in future studies. The first is a lack of whole body proprioceptive input. While virtual tasks do provide valuable transitional value and demonstrate similar navigational behaviors across species, seated navigation is not the same as whole body movement. To understand the complexities of navigation and leverage the possibilities of a virtual environment, a totally immersive experience is required.

Another limitation of the study is the reduction of multidimensional data to scalar values for statistical analysis. Complex data that fluctuates across space and time is difficult to represent as single digits, for example time-frequency power spectra could be washed out as a function of averaging across electrodes. Other possibilities such as nonparametric testing, similarity analysis, and feature selection could be used to identify the unique neural signatures that change due to experimental manipulations.

The data structure I used for outputting variables also delayed analysis. The Unity engine is a great tool for creating the virtual environment, but the functions I created to output data could be greatly improved upon. The approach of opening, writing and closing a unique text file for each trial proved to be very unwieldly for preprocessing data analysis. Holding the data online to be dumped into an SQL database would make data analysis much easier for myself and future collaborations.

Future Directions

This project serves as a link between a century of spatial navigation research and future explorations of navigation in virtual reality. Extensive work has been done in elucidating how the neural architecture of an organism utilizes the information content embedded in real space. Future projects will continue to assess how these navigational processes are translated into immersive virtual space.

One application of this project is to use the saccade raycasting technique to make more realistic graphical displays in immersive virtual reality. Human vision in real space consists of a central point of clear foveatation with vision slightly blurring into the periphery. However current graphical displays of immersive VR render the entire scene in equal clarity. By raycasting the gaze point through the virtual environment, graphical blur filters could be rendered extending radially from the point of foveatation. This replication of vision could reduce eye strain and possibly reduce visual discrepancy that produces simulator sickness.

Virtual reality experimentation offers many new directions and new opportunities to examine how brain and behavior combine to make sense of the external world. The existing literature of spatial navigation tasks in animals provides a background in how organisms organize the world around them. The ability to simulate novel worlds through virtual reality then allows for scientists to explore how changing the sensory information content of the environment affects the organism.

Works Citied

Aguirre, G. K., & D'Esposito, M. (1997). Environmental Knowledge Is Subserved by Separable Dorsal/Ventral Neural Areas. *The Journal of Neuroscience*, *17*(7), 2512–2518.

Akers, K. G., & Hamilton, D. A. (2007). Comparison of developmental trajectories for place and cued navigation in the morris water task. *Developmental Psychobiology*, *49*(6), 553–564. https://doi.org/10.1002/dev.20227

Astur, R. S., Ortiz, M. L., & Sutherland, R. J. (1998). A characterization of performance by men and women in a virtual Morris water task:: A large and reliable sex difference. *Behavioural Brain Research*, *93*(1), 185–190.

Baker, T. E., & Holroyd, C. B. (2009). Which Way Do I Go? Neural Activation in Response to Feedback and Spatial Processing in a Virtual T-Maze. *Cerebral Cortex*, *19*(8), 1708–1722. https://doi.org/10.1093/cercor/bhn223

Baker, T. E., & Holroyd, C. B. (2013a). The topographical N170: Electrophysiological evidence of a neural mechanism for human spatial navigation. *Biological Psychology*, *94*(1), 90–105. https://doi.org/10.1016/j.biopsycho.2013.05.004

Baker, T. E., & Holroyd, C. B. (2013b). The topographical N170: Electrophysiological evidence of a neural mechanism for human spatial navigation. *Biological Psychology*, *94*(1), 90–105. https://doi.org/10.1016/j.biopsycho.2013.05.004

Bischof, W. F., & Boulanger, P. (2003). Spatial Navigation in Virtual Reality Environments: An EEG Analysis. *CyberPsychology & Behavior*, *6*(5), 487–495. https://doi.org/10.1089/109493103769710514

Bohbot, V. D., Allen, J. J. B., & Nadel, L. (2006). Memory Deficits Characterized by Patterns of Lesions to the Hippocampus and Parahippocampal Cortex. *Annals of* *the New York Academy of Sciences, 911*(1), 355–368. https://doi.org/10.1111/j.1749-6632.2000.tb06737.x

Bohil, C. J., Alicea, B., & Biocca, F. A. (2011). Virtual reality in neuroscience research and therapy. *Nature Reviews Neuroscience*, *12*(12), 752–762. https://doi.org/10.1038/nrn3122

Boisgontier, M. P., & Swinnen, S. P. (2014). Proprioception in the cerebellum. *Frontiers in Human Neuroscience, 8*. https://doi.org/10.3389/fnhum.2014.00212

Brown, J. E., & Skaggs, W. E. (2002). Concordant and Discordant Coding of Spatial Location in Populations of Hippocampal CA1 Pyramidal Cells. *Journal of Neurophysiology*, *88*(4), 1605–1613.

Brown, M. A., & Sharp, P. E. (1995). Simulation of spatial learning in the Morris water maze by a neural network model of the hippocampal formation and nucleus accumbens. *Hippocampus*, *5*(3), 171–188. https://doi.org/10.1002/hipo.450050304

Burgess, N., Maguire, E. A., & O’Keefe, J. (2002). The human hippocampus and spatial and episodic memory. *Neuron*, *35*(4), 625–641.

Burgess, N., & O’Keefe, J. (1996). Neuronal computations underlying the firing of place cells and their role in navigation. *Hippocampus*, *6*(6), 749–762.

Buzsáki, G. (2002). Theta oscillations in the hippocampus. *Neuron*, *33*(3), 325–340.

Cavanagh, J. F., & Castellanos, J. (2016). Identification of canonical neural events during continuous gameplay of an 8-bit style video game. *NeuroImage*, *133*, 1–13. https://doi.org/10.1016/j.neuroimage.2016.02.075

Cavanagh, J. F., Cohen, M. X., & Allen, J. J. B. (2009). Prelude to and Resolution of an Error: EEG Phase Synchrony Reveals Cognitive Control Dynamics during Action Monitoring. *The Journal of Neuroscience*, *29*(1), 98–105. https://doi.org/10.1523/JNEUROSCI.4137-08.2009

Cavanagh, J. F., Figueroa, C. M., Cohen, M. X., & Frank, M. J. (2012). Frontal Theta Reflects Uncertainty and Unexpectedness during Exploration and Exploitation. *Cerebral Cortex*, *22*(11), 2575–2586. https://doi.org/10.1093/cercor/bhr332

Chiu, T.-C., Gramann, K., Ko, L.-W., Duann, J.-R., Jung, T.-P., & Lin, C.-T. (2012). Alpha modulation in parietal and retrosplenial cortex correlates with navigation performance: Performance-related EEG dynamics in navigation. *Psychophysiology*, *49*(1), 43–55. https://doi.org/10.1111/j.1469-8986.2011.01270.x

Cohen, M. X., Elger, C. E., & Ranganath, C. (2007). Reward expectation modulates feedback-related negativity and EEG spectra. *Neuroimage*, *35*(2), 968–978.

Cohen, M. X., Ridderinkhof, K. R., Haupt, S., Elger, C. E., & Fell, J. (2008). Medial frontal cortex and response conflict: Evidence from human intracranial EEG and medial frontal cortex lesion. *Brain Research, 1238,* 127–142. https://doi.org/10.1016/j.brainres.2008.07.114

Cornwell, B. R., Johnson, L. L., Holroyd, T., Carver, F. W., & Grillon, C. (2008). Human Hippocampal and Parahippocampal Theta during Goal-Directed Spatial Navigation Predicts Performance on a Virtual Morris Water Maze. *Journal of Neuroscience*, *28*(23), 5983–5990. https://doi.org/10.1523/JNEUROSCI.5001-07.2008

Cushman, L. A., Stein, K., & Duffy, C. J. (2008). Detecting navigational deficits in cognitive aging and Alzheimer disease using virtual reality. *Neurology*, *71*(12), 888–895.

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21.

Doeller, C. F., Barry, C., & Burgess, N. (2010). Evidence for grid cells in a human memory network. *Nature*, *463*(7281), 657–661. https://doi.org/10.1038/nature08704

Driscoll, I. (2003). The Aging Hippocampus: Cognitive, Biochemical and Structural Findings. *Cerebral Cortex*, *13*(12), 1344–1351. https://doi.org/10.1093/cercor/bhg081

Driscoll, I., Hamilton, D. A., Yeo, R. A., Brooks, W. M., & Sutherland, R. J. (2005). Virtual navigation in humans: the impact of age, sex, and hormones on place learning. *Hormones and Behavior*, *47*(3), 326–335. https://doi.org/10.1016/j.yhbeh.2004.11.013

Ekstrom, A. D., Arnold, A. E. G. F., & Iaria, G. (2014). A critical review of the allocentric spatial representation and its neural underpinnings: toward a network-based perspective. *Frontiers in Human Neuroscience, 8*, 803. https://doi.org/10.3389/fnhum.2014.00803

Epstein, R. A. (2008). Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends in Cognitive Sciences*, *12*(10), 388–396. https://doi.org/10.1016/j.tics.2008.07.004

Fenton, A. A., Lytton, W. W., Barry, J. M., Lenck-Santini, P.-P., Zinyuk, L. E., Kubík, Š., … Olypher, A. V. (2010). Attention-Like Modulation of Hippocampus Place Cell Discharge. *The Journal of Neuroscience*, *30*(13), 4613–4625. https://doi.org/10.1523/JNEUROSCI.5576-09.2010

Foreman, N., Stirk, J., Pohl, J., Mandelkow, L., Lehnung, M., Herzog, A., & Leplow, B. (2000). Spatial information transfer from virtual to real versions of the Kiel locomotor maze. *Behavioural Brain Research*, *112*(1–2), 53–61. https://doi.org/10.1016/S0166-4328(00)00159-5

Fry, S. N., Rohrseitz, N., Straw, A. D., & Dickinson, M. H. (2008). TrackFly: Virtual reality for a behavioral system analysis in free-flying fruit flies. *Journal of Neuroscience Methods*, *171*(1), 110–117. https://doi.org/10.1016/j.jneumeth.2008.02.016

Gallistel, C. R. (1990). *The organization of learning.* The MIT Press.

Gothard, K. M., Hoffman, K. L., Battaglia, F. P., & McNaughton, B. L. (2001). Dentate Gyrus and CA1 Ensemble Activity during Spatial Reference Frame Shifts in the Presence and Absence of Visual Input. *The Journal of Neuroscience*, *21*(18), 7284–7292.

Gramann, K. (2013). Embodiment of Spatial Reference Frames and Individual Differences in Reference Frame Proclivity. *Spatial Cognition & Computation*, *13*(1), 1–25. https://doi.org/10.1080/13875868.2011.589038

Gratton, G., Coles, M. G., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, *55*(4), 468–484.

Green, J. D., & Arduini, A. A. (1954). Hippocampal electrical activity in arousal. *Journal of Neurophysiology*, *17,* 531–557.

Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., & Moser, E. I. (2005). Microstructure of a spatial map in the entorhinal cortex. *Nature*, *436*(7052), 801–806. https://doi.org/10.1038/nature03721

Hamilton, D. A., Akers, K. G., Johnson, T. E., Rice, J. P., Candelaria, F. T., & Redhead, E. S. (2009). Evidence for a shift from place navigation to directional responding in one variant of the Morris water task. *Journal of Experimental Psychology: Animal Behavior Processes*, *35*(2), 271–278. https://doi.org/10.1037/a0013260

Hamilton, D. A., Akers, K. G., Weisend, M. P., & Sutherland, R. J. (2007). How do room and apparatus cues control navigation in the Morris water task? Evidence for distinct contributions to a movement vector. *Journal of Experimental Psychology: Animal Behavior Processes*, *33*(2), 100–114. https://doi.org/10.1037/0097-7403.33.2.100

Hamilton, D. A., Johnson, T. E., Redhead, E. S., & Verney, S. P. (2009). Control of rodent and human spatial navigation by room and apparatus cues. *Behavioural Processes*, *81*(2), 154–169.

Hamilton, D. A., Rosenfelt, C. S., & Whishaw, I. Q. (2004). Sequential control of navigation by locale and taxon cues in the Morris water task. *Behavioural Brain Research*, *154*(2), 385–397. https://doi.org/10.1016/j.bbr.2004.03.005

Hamilton, D., Driscoll, I., & Sutherland, R. (2002). Human place learning in a virtual Morris water task: some important constraints on the flexibility of place navigation. *Behavioural Brain Research*, *129*, 159–170.

Hartley, T., Burgess, N., Lever, C., Cacucci, F., & O'keefe, J. (2000). Modeling place fields in terms of the cortical inputs to the hippocampus. *Hippocampus*, *10*(4), 369–379.

Hartley, T., Maguire, E. A., Spiers, H. J., & Burgess, N. (2003). The well-worn route and the path less traveled: distinct neural bases of route following and wayfinding in humans. *Neuron*, *37*(5), 877–888.

Hasselmo, M., Bodelón, C., & Wyble, B. (2002). A proposed function for hippocampal theta rhythm: separate phases of encoding and retrieval enhance reversal of prior learning. *Neural Computation*, *14*(4), 793–817.

Hill, A. J., & Best, P. J. (1981). Effects of deafness and blindness on the spatial correlates of hippocampal unit activity in the rat. *Experimental Neurology*, *74*(1), 204–217. https://doi.org/10.1016/0014-4886(81)90159-X

Hubel, D. H., & Wiesel, T. N. (1968). Receptive fields and functional architecture of monkey striate cortex. *The Journal of Physiology*, *195*(1), 215–243.

Hull, C. L. (1932). The goal-gradient hypothesis and maze learning. *Psychological Review*, *39*(1), 25.

Jangraw, D. C., Johri, A., Gribetz, M., & Sajda, P. (2014). NEDE: An open-source scripting suite for developing experiments in 3D virtual environments. *Journal of Neuroscience Methods*, *235*, 245–251. https://doi.org/10.1016/j.jneumeth.2014.06.033

Kahana, M. J., Sekuler, R., Caplan, J. B., Kirschen, M., & Madsen, J. R. (1999). Human theta oscillations exhibit task dependence during virtual maze navigation. *Nature*, *399*(6738), 781–784. https://doi.org/10.1038/21645

Kant, I. (1998). Critique of Pure Reason (translated and edited by Paul Guyer & Allen W. Wood).

Katayama, T., & Natsume, K. (2012). The Change in EEG When We Are Bored. *Journal of Signal Processing*, *16*(6), 637–641.

Kealy, J., Diviney, M., Kehoe, E., McGonagle, V., O'Shea, A., Harvey, D., & Commins, S. (2008). The effects of overtraining in the Morris water maze on allocentric and egocentric learning strategies in rats. *Behavioural Brain Research*, *192*(2), 259–263. https://doi.org/10.1016/j.bbr.2008.04.009

Knierim, J. J., & Hamilton, D. A. (2011). Framing Spatial Cognition: Neural Representations of Proximal and Distal Frames of Reference and Their Roles in Navigation. *Physiological Reviews*, *91*(4), 1245–1279. https://doi.org/10.1152/physrev.00021.2010

Knierim, J. J., Kudrimoti, H. S., & McNaughton, B. L. (1995). Place cells, head direction cells, and the learning of landmark stability. *The Journal of Neuroscience*, *15*(3), 1648–1659.

Kolasinski, Eugenia. (1995). Simulator Sickness in Virtual Environments. *U.S. Army Research Institute: Technical Report 1027*.

Kolb, B., Sutherland, R. J., & Whishaw, I. Q. (1983). A Comparison of the Contributions of thee Frontal and Parietal Association Cortex to Spatial Localization in Rats, *97*(1), 13–27.

Kolb, B., & Whishaw, I. Q. (1996). *Fundamentals of human neurophysiology*. Freeman, New York.

Kropff, E., & Treves, A. (2008). The emergence of grid cells: Intelligent design or just adaptation? *Hippocampus*, *18*(12), 1256–1269. https://doi.org/10.1002/hipo.20520

Lashley, K. S. (1930). Basic neural mechanisms in behavior. *Psychological Review*, *37*(1), 1–24.

LaViola, J. J., Jr. (2000). A Discussion of Cybersickness in Virtual Environments. *SIGCHI Bull.*, *32*(1), 47–56. https://doi.org/10.1145/333329.333344

Livingstone-Lee, S. A., Murchison, S., Zeman, P. M., Gandhi, M., van Gerven, D., Stewart, L., … Skelton, R. W. (2011). Simple gaze analysis and special design of a virtual Morris water maze provides a new method for differentiating egocentric and allocentric navigational strategy choice. *Behavioural Brain Research*, *225*(1), 117–125. https://doi.org/10.1016/j.bbr.2011.07.005

Logothetis, N. K., & Wandell, B. A. (2004). Interpreting the BOLD Signal. *Annual Review of Physiology*, *66*(1), 735–769. https://doi.org/10.1146/annurev.physiol.66.082602.092845

Luu, P., Tucker, D. M., & Makeig, S. (2004). Frontal midline theta and the error-related negativity: neurophysiological mechanisms of action regulation. *Clinical Neurophysiology*, *115*(8), 1821–1835. https://doi.org/10.1016/j.clinph.2004.03.031

Maguire, E. A., Frackowiak, R. S. J., & Frith, C. D. (1997). Recalling Routes around London: Activation of the Right Hippocampus in Taxi Drivers. *The Journal of Neuroscience*, *17*(18), 7103–7110.

Matthews, D. B., & Best, P. J. (1997). Evidence for the flexible use of spatial knowledge in the rat. *Psychobiology*, *25*(4), 294–302.

McNaughton, B. L., & O'Reilly, R. C. (1995). Why There Are Complementary Learning Systems in the Hippocampus and Neocortex: Insights From the Successes and Failures of. *Psychological Review*, *102*(3), 419–457.

Miller, V. M., & Best, P. J. (1980). Spatial correlates of hippocampal unit activity are altered by lesions of the fornix and entorhinal cortex. *Brain Research*, *194*(2), 311–323. https://doi.org/10.1016/0006-8993(80)91214-7

Moffat, S. D. (2009). Aging and Spatial Navigation: What Do We Know and Where Do We Go? *Neuropsychology Review*, *19*(4), 478–489. https://doi.org/10.1007/s11065-009-9120-3

Mognon, A., Jovicich, J., Bruzzone, L., & Buiatti, M. (2011). ADJUST: An automatic EEG artifact detector based on the joint use of spatial and temporal features: Automatic spatio-temporal EEG artifact detection. *Psychophysiology*, *48*(2), 229–240. https://doi.org/10.1111/j.1469-8986.2010.01061.x

Morgan, L. K., MacEvoy, S. P., Aguirre, G. K., & Epstein, R. A. (2011). Distances between Real-World Locations Are Represented in the Human Hippocampus. *The Journal of Neuroscience*, *31*(4), 1238–1245. https://doi.org/10.1523/JNEUROSCI.4667-10.2011

Morris, R. (1984). Developments of a water-maze procedure for studying spatial learning in the rat. *J Neurosci Methods*, *11*(1), 47–60.

Morris, R. G. M. (1981). Spatial localization does not require the presence of local cues. *Learning and Motivation*, *12*(2), 239–260. https://doi.org/10.1016/0023-9690(81)90020-5

Nitz, D. (2009). Parietal cortex, navigation, and the construction of arbitrary reference frames for spatial information. *Neurobiology of Learning and Memory*, *91*(2), 179–185. https://doi.org/10.1016/j.nlm.2008.08.007

Oberman, L. M., Ramachandran, V. S., & Pineda, J. A. (2008). Modulation of mu suppression in children with autism spectrum disorders in response to familiar or unfamiliar stimuli: the mirror neuron hypothesis. *Neuropsychologia*, *46*(5), 1558–1565.

O'Keefe, J. (1976). Place units in the hippocampus of the freely moving rat. *Experimental Neurology*, *51*(1), 78–109.

O'Keefe, J., & Burgess, N. (1996). Geometric determinants of the place fields of hippocampal neurons. *Nature*, *381*(6581), 425–428. https://doi.org/10.1038/381425a0

O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, *34*(1), 171–175.

Olton, D. S., & Samuelson, R. J. (1976). Remembrance of places passed: Spatial memory in rats. *Journal of Experimental Psychology: Animal Behavior Processes*, *2*(2), 97–116.

Olvera-Cortés, E., Guevara, M. A., & González-Burgos, I. (2004). Increase of the hippocampal theta activity in the Morris water maze reflects learning rather than motor activity. *Brain Research Bulletin*, *62*(5), 379–384. https://doi.org/10.1016/j.brainresbull.2003.10.003

O’Reilly, R. C., & Rudy, J. W. (2000). Computational principles of learning in the neocortex and hippocampus. *Hippocampus*, *10*(4), 389–397.

Overman, W. H., Pate, B. J., Moore, K., & Peuster, A. (1996). Ontogeny of place learning in children as measured in the radial arm maze, Morris search task, and open field task. *Behavioral Neuroscience*, *110*(6), 1205.

Pfurtscheller, G., Brunner, C., Schlögl, A., & Da Silva, F. L. (2006). Mu rhythm (de) synchronization and EEG single-trial classification of different motor imagery tasks. *NeuroImage*, *31*(1), 153–159.

Plank, M., Snider, J., Kaestner, E., Halgren, E., & Poizner, H. (2014). Neurocognitive stages of spatial cognitive mapping measured during free exploration of a large-scale virtual environment. *Journal of Neurophysiology*, jn.00114.2014. https://doi.org/10.1152/jn.00114.2014

Prados, J., & Trobalon, J. B. (1998). Locating an invisible goal in a water maze requires at least two landmarks. *Psychobiology*, *26*(1), 42–48.

Przybylski, A. K., Rigby, C. S., & Ryan, R. M. (2010). A motivational model of video game engagement. *Review of General Psychology*, *14*(2), 154–166. https://doi.org/10.1037/a0019440

Redish, A. D., & Touretzky, D. S. (1998). The role of the hippocampus in solving the Morris water maze. *Neural Computation*, *10*(1), 73–111.

Restle, F. (1957). Discrimination of Cues in Mazes: A Resolution of the “place vs. response” Question. *Psychological Review*, *64*, 217–228.

Richardson, A. E., Powers, M. E., & Bousquet, L. G. (2011). Video game experience predicts virtual, but not real navigation performance. *Computers in Human Behavior*, *27*(1), 552–560. https://doi.org/10.1016/j.chb.2010.10.003

Robinson, T. E. (1980). Hippocampal rhythmic slow activity (RSA, theta): A critical analysis of selected studies and discussion of possible species-differences. *Brain Research Reviews*, *2*(1), 69–101.

Rogers, J. L., & Kesner, R. P. (2007). Hippocampal–parietal cortex interactions: Evidence from a disconnection study in the rat. *Behavioural Brain Research*, *179*(1), 19–27. https://doi.org/10.1016/j.bbr.2007.01.019

Romei, V., Gross, J., & Thut, G. (2010). On the Role of Prestimulus Alpha Rhythms over Occipito-Parietal Areas in Visual Input Regulation: Correlation or Causation? *Journal of Neuroscience*, *30*(25), 8692–8697. https://doi.org/10.1523/JNEUROSCI.0160-10.2010

Sack, A. ., Hubl, D., Prvulovic, D., Formisano, E., Jandl, M., Zanella, F. ., … Linden, D. E. . (2002). The experimental combination of rTMS and fMRI reveals the functional relevance of parietal cortex for visuospatial functions. *Cognitive Brain Research*, *13*(1), 85–93. https://doi.org/10.1016/S0926-6410(01)00087-8

Shannon, C. E. (1953). A mind-reading machine. *Bell Laboratories Memorandum*.

Sherrill, K. R., Erdem, U. M., Ross, R. S., Brown, T. I., Hasselmo, M. E., & Stern, C. E. (2013). Hippocampus and Retrosplenial Cortex Combine Path Integration Signals for Successful Navigation. *Journal of Neuroscience*, *33*(49), 19304–19313. https://doi.org/10.1523/JNEUROSCI.1825-13.2013

Small, W. S. (1901). Experimental Study of the Mental Processes of the Rat. II. *The American Journal of Psychology*, *12*(2), 206. https://doi.org/10.2307/1412534

Spence, K. W. (1936). The nature of discrimination learning in animals. *Psychological Review*, *43*(5), 427–449. https://doi.org/10.1037/h0056975

Spiers, H. J., & Gilbert, S. J. (2015). Solving the detour problem in navigation: A model of prefrontal and hippocampal interactions. *Frontiers in Human Neuroscience*, *9*, 125. https://doi.org/10.3389/fnhum.2015.00125

Squire, L. R., Stark, C. E. L., & Clark, R. E. (2004). THE MEDIAL TEMPORAL LOBE. *Annual Review of Neuroscience*, *27*(1), 279–306. https://doi.org/10.1146/annurev.neuro.27.070203.144130

Sutherland, R., Chew, G., Baker, J., & Linggard, R. (1987). Some Limitations on the Use of Distal Cues in Place Navigation by Rats. *Psychobiology*, *15*, 48–57.

Taube, J. S., Muller, R. U., & Ranck, J. B. (1990). Head-direction cells recorded from the postsubiculum in freely moving rats. I. Description and quantitative analysis. *The Journal of Neuroscience*, *10*(2), 420–435.

Taube, J., Valerio, S., & Yoder, R. (2014). Is Navigation in Virtual Reality with fMRI Really Navigation? *Journal of Cognitive Neuroscience*, *25*(7), 1008–1019.

Tolman, E. C. (1948). Cognitive maps in rats and men. *Psychological Review*, *55*(4), 189.

Vandam, D., Lenders, G., & Dedeyn, P. (2006). Effect of Morris water maze diameter on visual-spatial learning in different mouse strains. *Neurobiology of Learning and Memory*, *85*(2), 164–172. https://doi.org/10.1016/j.nlm.2005.09.006

Vorhees, C. V., & Williams, M. T. (2006). Morris water maze: procedures for assessing spatial and related forms of learning and memory. *Nature Protocols*, *1*(2), 848–858. https://doi.org/10.1038/nprot.2006.116

Wallace, D. G., Hines, D. J., Pellis, S. M., & Whishaw, I. Q. (2002). Vestibular information is required for dead reckoning in the rat. *The Journal of Neuroscience*, *22*(22), 10009–10017.

Watrous, A. J., Lee, D. J., Izadi, A., Gurkoff, G. G., Shahlaie, K., & Ekstrom, A. D. (2013). A comparative study of human and rat hippocampal low-frequency oscillations during spatial navigation: Comparison of Human and Rodent Theta. *Hippocampus*, *23*(8), 656–661. https://doi.org/10.1002/hipo.22124

Watson, J. B. (1907). *Kinaesthetic and organic sensations: Their role in the reactions of the white rat to the maze* (Vol. 8). Review Publishing Company.

Watson, J. B. (1913). Psychology as the behaviorist views it. *Psychological Review*, *20*(2), 158.

Whishaw, I., & Vanderwolf, C. (n.d.). Hippocampal EEG and Behavior: Changes in Amplitude and Frequency of RSA (Theta Rhythm) Associated With Spontaneous and Movement Patterns in Rats and Cats.

Wilber, A. A., Clark, B. J., Forster, T. C., Tatsuno, M., & McNaughton, B. L. (2014). Interaction of Egocentric and World-Centered Reference Frames in the Rat Posterior Parietal Cortex. *The Journal of Neuroscience*, *34*(16), 5431–5446. https://doi.org/10.1523/JNEUROSCI.0511-14.2014

Wilkie, D. M., & Palfrey, R. (1987). A computer simulation model of rats' place navigation in the Morris water maze. *Behavior Research Methods, Instruments, & Computers*, *19*(4), 400–403.

Witmer, B., & Kline, P. (1998). Judging Perceived and Traversed Distance in Virtual Environments. *Presence*, *7*(2), 144–167. https://doi.org/10.1162/105474698565640

Yao, R., Heath, T., Davies, A., Forsyth, T., Mitchell, N., & Hoberman, P. (2014). Oculus VR Best Practices Guide. *Oculus VR*. Retrieved from http://treyte.ch/oculus/tools/0.4.2/documentation/OculusBestPractices.pdf

Yoganarasimha, D., & Knierim, J. J. (2005). Coupling between place cells and head direction cells during relative translations and rotations of distal landmarks. *Experimental Brain Research*, *160*(3), 344–359. https://doi.org/10.1007/s00221-004-2016-9

Zugaro, M. B., Berthoz, A., & Wiener, S. I. (2001). Background, but not foreground, spatial cues are taken as references for head direction responses by rat anterodorsal thalamus neurons. *The Journal of Neuroscience*, *21*(14), RC154.