SEX DIFFERENCES IN NAVIGATION IN A TABLETOP OCTAGON NAVIGATION TASK

MASHAL FIDA Bachelor of Science, University of Lethbridge, 2016

A Thesis Submitted to the School of Graduate Studies Of the University of Lethbridge In Partial Fulfillment of the Requirements of the Degree

MASTER OF SCIENCE

Department of Neuroscience University of Lethbridge LETHBRIDGE, ALBERTA, CANADA

© Mashal Fida, 2018

SEX DIFFERENCES IN NAVIGATION IN A TABLETOP OCTAGON NAVIGATION TASK

MASHAL FIDA

Date of defense: February 8th, 2018

Dr. R. Sutherland Supervisor	Professor	PhD
Dr. A. Gruber Thesis Examination Committee Member	Associate Professor	PhD
Dr. J. Doan Thesis Examination Committee Member	Associate Professor	PhD
Dr. A. Iwaniuk Chair, Thesis Examination Committee	Associate Professor	PhD

Abstract

The Morris water task (MWT) is a test of spatial learning and memory commonly used in research on spatial cognition. From this research it is clear that the hippocampus is necessary for accurate navigation and that sex differences exist. Most often, a virtual MWT is used with humans. In our previous study, we found that men use an allocentric spatial frame of reference to guide locomotion, but women use an egocentric spatial frame of reference. Therefore, we designed allocentric and egocentric tabletop versions of the MWT, called the Octagon Navigation Task to study the use of these spatial frameworks. Men outperformed women in the allocentric condition. Women outperformed men in the egocentric condition. No sex differences were found in the neutral condition, which allowed the use of either spatial reference frameworks to navigate. Together, these results suggest that sex differences in spatial navigation result from different prepotent spatial frameworks guiding performance.

Acknowledgments

I would first like to thank my supervisor, Dr. Robert Sutherland for taking a chance on me as an undergraduate student, for giving me opportunities and independence to work on projects that sparked my interest. Finally, for holding our weekly lab meetings, they will forever remain a cherished memory of my undergraduate and graduate school career.

I would also like to thank Dr. Erin Zelinski for being my mentor and teaching me the fundamentals of being a good, honest researcher while also being a good person.

I would like to thank my lab mates Justin Lee, Sean Lacoursiere, Kate Chua and Keiko McCreary for being the best colleagues a girl could ask for. A special thanks to Leonardo Molina for his help on the script and Scott Diebel for ensuring I remained on track through out my thesis.

I would like to thank Dr. Aaron Gruber for his helpful advice on my thesis work and for serving on my thesis examination committee. I would like to thank Dr. Jon Doan for his willingness to be on my committee on short notice, I will forever be grateful of your kindness. A special thanks to Amanda Mauthe-Kaddoura for helping me out with all the technicalities of Graduate school, your pleasantness made my graduate school experience better.

Finally and most importantly, I would like to thank my rock: Kilian, my family and friends whose unconditional love and support motivate me to be the best version of myself.

iv

Table of Contents

Abstract.
Acknowledgement
List of Figures.
List of Tables.
List of Abbreviations
Introduction
Methods
Procedure
Experimental Apparatus
Analysis
Experiment 1. Allocentric Condition
1.1 Participant
1.2 Training
1 3 Retention Test
Results Allocentric Condition
1.5 Trials to Criterion
1.6 Latency
1.7 Path length
1.8 Root Square Mean Error
1.0 Heat Man with Centroid Analysis
1.9 Heat Map with Centrole Analysis
1.10 Taiget Retention (Trobe trial)
Experiment 2 Egocentric Condition
2.1 Derticipants
2.1 Faiticipalits
2.2 Italining
2.5 Retention Test
2.5 Trials to Original
2.5 Irials to Criterion
2.6 Latency
2. / Path length
2.8 Root Square Mean Error
2.9 Heat Map with Centroid Analysis
2.10 Target Retention (Probe trial)
2.11 Trajectory (Probe trial).
Experiment 3. Neutral Condition
3.1 Participants
3.2 Training
Results. Neutral Condition
3.3 Trials to Criterion
3.4 Latency
3.5 Path length
3.6 Root Square Mean Error
3.7 Heat Map with Centroid Analysis
3.8 Target Retention (Probe trial)
3.9 Trajectory (Probe trial)

4. Non-Parametric Test	31
4.1 Education	31
4.2 Video Game Use	31
4.3 Navigational Skill	32
4.4 Task Difficulty	32
4.5 Summary of Non-Parametric Tests	32
Discussion	34
References	44
Appendices	47
1. Script for Octagon Navigation Task	47
2. Exclusion Criteria for Octagon Navigation Task	47
3. Photo of the Experiment Room	48
4. Consent Forms	49
5. Sample Questionnaire	52

List of Figures

Octagon Navigation Task	8
Illustration of the most direct trajectories	10
Accurate trajectories during the probe trial	14
Trials to Criterion-Allocentric Condition	14
Latency-Allocentric Condition	15
Path Length - Allocentric Condition	16
Root mean square error-Allocentric Condition	16
Heat map -Allocentric Condition	17
Target Retention- Allocentric Probe Condition	18
Probe trajectories -Allocentric Condition	19
Trials to Criterion-Egocentric Condition	20
Latency - Egocentric Condition	21
Path Length -Egocentric Condition	21
Root mean square error - Egocentric Condition	22
Heat map - Egocentric Condition	23
Target Retention- Egocentric Probe Condition	24
Probe trajectories -Egocentric Condition	24
Trials to Criterion- Neutral Condition	25
Latency -Neutral Condition	26
Path Length- Neutral Condition	27
Root mean square error - Neutral Condition	28
Heat map - Neutral Condition	29
Target Retention – Neutral Probe Condition	30
Probe trajectories – Neutral Condition	30
Video Game Use	32
	Octagon Navigation Task Illustration of the most direct trajectories Accurate trajectories during the probe trial Trials to Criterion-Allocentric Condition Latency-Allocentric Condition Path Length - Allocentric Condition Root mean square error-Allocentric Condition Heat map -Allocentric Condition Trials to Criterion- Allocentric Condition Target Retention- Allocentric Condition Probe trajectories -Allocentric Condition Trials to Criterion- Egocentric Condition Path Length - Egocentric Condition Root mean square error - Egocentric Condition Root mean square error - Egocentric Condition Trials to Criterion- Neutral Condition Trials to Criterion- Neutral Condition Trials to Criterion- Neutral Condition Probe trajectories -Egocentric Condition Probe trajectories -Lagocentric Condition Trials to Criterion- Neutral Condition Probe trajectories -Lagocentric Condition Probe trajectories -Lagocentric Condition Probe trajectories -Lagocentric Condition Probe trajectories -Lagocentric Co

List of Tables

Table 1	Number of participants in all three experimental conditions	5
I WOIC I	i unice of pullepulle in un ence experimental contantons.	•

List of Abbreviations

- EEG Electroencephalography
- Functional magnetic resonance imaging Magnetic resonance imaging Morris water task fMRI
- MRI
- MWT
- Object location memory Octagon navigation task OLM
- ONT

Introduction

Sex differences in human spatial navigation are well known and have been extensively documented in the research literature (e.g. Jones et al 2003; Maguire et al, 1999). Tests measuring spatial abilities in human and nonhuman animal models have often revealed that males have superior spatial abilities, but the magnitude and direction of the difference depends on the nature of the spatial task and type of spatial ability being measured (Halpern, 1992). Men are reported to have superior Euclidean-based spatial abilities while women excel when tasks depend on landmark-based strategies (Coluccia & Louse, 2004; Maguire et al, 1999; Saucier et al; 2002). Females are also reported to have an advantage relative to males when remembering location of objects in space, commonly referred to as object location memory (OLM) (Saucier et al, 2008). The pattern of differences suggests a sexually dimorphic capacity to use Euclidean vs. OLM or landmark spatial information during navigation (McBurney et al, 1997; Saucier et al, 2008; Silverman and Eals, 1992).

Navigation in humans and other non-human animals is often studied using maze exploration type spatial tasks (Morris, 1981; Sutherland et al, 1982; Astur et al, 1998). The Morris water task (MWT) is a unique task that assesses spatial ability in rodents during which rats or mice are usually required to navigate to a hidden escape platform in a pool of milky water using environmental cues outside the apparatus (Morris, 1981; Sutherland et al, 1982). The MWT has been adapted for use in humans to assess many cognitive functions such as spatial learning, spatial memory, movement control and cognitive mapping (Maguire et al, 1999). These cognitive functions are tested in humans typically by adapting the MWT as a virtual reality (Astur et al., 1998; Moffat et al, 1998). The use of virtual reality has made it easy to evaluate the effect of environmental layout on spatial memory and learning in humans.

The sex differences in spatial navigation have been attributed to multiple factors such as hormones, brain physiology and environmental factors to name a few (Dabbs et al, 1998). Many studies using rodents performing in the MWT task have demonstrated the importance of hippocampal circuitry engagement during spatial performance (Morris et al, 1982; Sutherland et al, 1982). This was first accomplished by hippocampal lesion studies and more recently the use of chemogenic inactivation methods such as designer receptors exclusively activated by designer drugs (DREADDs) (Varela et al, 2016). Similarly, a study conducted by Astur et al (2002) found that patients with hippocampus damage perform worse than age-matched healthy controls in the virtual analogue of the MWT. Both human and nonhuman animal studies have thus demonstrated that hippocampal circuitry is engaged during performance of Morris water type tasks (Ekstrom et al, 2005; Lovden et al, 2007; Sutherland et al, 2005). Recently, the role of hippocampus and associated neural network activation is being studied to better understand the much-debated spatial sex difference (Gron et al, 2000; Maguire et al, 1999).

Many studies have used imaging techniques to study brain activation patterns while human subjects solve virtual navigation tasks. For example, Gron et al (2000) used a functional magnetic resonance imaging (MRI) to observe brain activation in men and women as they learned to solve a virtual-reality maze. Their sex-specific group analysis revealed distinct activation of the left hippocampus in men, while women consistently displayed right parietal and right prefrontal cortex activation (Gron et al, 2000). These studies point towards the existence of sexually dimorphic capacities to solve spatial tasks that are associated with clear differential brain activation patterns. Often sex differences in spatial abilities have been explained by different gonadal hormone levels affecting cerebral and cognitive development, leading to different neural activation patterns during navigation by adult men and women (William et al, 1990). Early in development gonadal hormones are known to permanently influence physiology and anatomy. These are termed organizational effects, as opposed to the dynamic hormonal physiological changes in adulthood, called activational effects (Arnold & Breedlove, 1985). Many studies using rodents have found that gonadal steroids, specifically the testosterone metabolite estradiol, can cause organizational effects during perinatal development that affect spatial abilities (Meck et al., 1991; Roof et al., 1992). Additionally, studies analyzing the impact of testosterone on spatial performance in adult humans have found sex differences in virtual MWT performance, with better performance correlated with higher circulating testosterone levels (Driscoll et al., 2005). However, it should be noted that the role of adult hormones has been inconsistently reported and many studies have found little or no effect of hormones on spatial ability (Puts et al., 2008).

Men and women are reported to attend to different aspects of an environment when exploring (Mueller et al, 2008). Studies analyzing sex-specific exploration in virtual spatial tasks have consistently found that men and women display differential activation patterns when attending to features of an environment. For example, a study conducted by Kober et al (2011) using electroencephalography (EEG) showed that while navigating through a virtual reality game, women showed increased activity in the theta band when processing landmark based information. Men did not show this kind of change in brain activity when landmark information was presented. This observation suggests that men and women may process landmark-based information differently. Similarly, it has been reported that men attend to secondary environmental stimuli (peripheral information), whereas women tended to ignore the peripheral information while navigating through an environment (Kim et al, 2007). These studies provide support for the idea that spatial sex differences could arise from attention to different types of information (e.g. landmark vs. distal Euclidean) present in the environment.

Zelinski et al (2016) investigated how spatial strategies contribute to the observed sex difference in spatial navigation. They found that women's poorer performance in a realworld analogue of the MWT might be due to the default use of a spatial framework referenced to the body axis (egocentric strategy) by women, instead of using a spatial framework referenced to distal cue locations (allocentric strategy). The latter strategy leads to more efficient learning in the standard version of the task. Zelinski et al (2016) then manipulated the task, such that successful goal location required the use of an egocentric strategy. In this case, women consistently outperformed men. These data suggest that sex differences in spatial navigation might be due to the use of different default navigational strategies or different default spatial frameworks for guiding navigation.

If this were true there should be no sex difference in a spatial navigation task that allows the use of either allocentric and/or egocentric spatial frameworks. We designed a tabletop version of the MWT, called the *Octagon Navigation Task*, in which the strategy that would be more efficient could be easily manipulated. The task was automated using a custom MATLAB program to reduce experimenter bias and to develop a quicker and reliable version that can be easily used in laboratory setting. We developed allocentric, egocentric and neutral experimental versions to selectively manipulate the type of spatial framework of reference that could be implemented by the participant in order to

4

efficiently solve the spatial task. The hypothesis that sexually dimorphic navigation depends only on a difference in which spatial frame of reference is selected by default predicts that: 1) Men and women will both be able to equally solve all versions of the navigation task, despite differences initially during testing; 2) Default spatial frameworks for guiding during spatial navigation will be allocentric for men and egocentric for women; 3) Men will initially excel at the allocentric version of the task; women will initially excel at the egocentric version of the Octagon Navigation Task, and; 4) No sex differences will be observed in the neutral condition as any spatial framework of reverence can be used to solve the task successfully.

Methods

To test our hypothesis, three experiments were conducted. Table 1 presents group assignments and number of participants in each experiment. All participants were recruited from the university through the *Sona System*; an anonymous portal where students can voluntarily sign up and participate in research studies in exchange for course credit at the University of Lethbridge. All procedures were approved by institutional research ethics boards and governing bodies.

Table 1. Number of participants in all three experimental conditions.

Experiment	Males	Females
(I) Allocentric	27	28
(II) Egocentric	27	28
(III) Neutral	28	32

Procedure. All participants signed informed consent forms prior to participation. Participants also filled out a two-part questionnaire. The first part of the questionnaire was administered prior to participation in the behavioural task and was used to collect participants' basic demographic information, health history and daily life style. This information was used to screen participants for inclusion criteria. Participants that did not meet the inclusion criteria were excluded from the analysis i.e. participants with multiple concussions, hormone therapy, incorrect age range, left-handedness etc. Only cis-gender participants were included in the final analysis. The participants were then escorted to the task performance location. For a full list of exclusion criteria, consent forms and questionnaire, please refer to the appendix. All the participants listened to an identical script explaining the task, such that Experiment 1 participants received the same verbal instructions on how to solve the task as Experiment 2 participants. A copy of the script read to the participants is included in the appendix.

Participants from each experiment were exposed to one experimental condition assigned randomly prior to their arrival. Following instructions, the experimenter lead participants to the starting location for the first trial and task performance started. Participants also completed a post-test questionnaire. The post-test questionnaire was used to collect some relevant information pertaining to the experiment, such as self-reported task difficulty, GPS use, self-assessed spatial ability etc. that could potentially provide some insights on individual performance.

Octagon Navigation Task



Figure 1. Octagon Navigation Task. The red squares represent the starting position of all training trials. The blue cylinder represents the starting location of the probe trial. The dotted green zone in the computer screen represents the target location, which is visible to the experimenter but invisible to the participant.

Experimental Apparatus. The experimental apparatus consisted of two components. The first component consisted of a 4032.25 cm² green, flat, wooden board in shape of an octagon (Fig 1). The octagon board was placed on top of a table (height of the table: 79.7 cm). A video camera was ceiling-mounted above the center of the apparatus in order to provide a top-down view of the apparatus and the participant. A mini LED light, referred to as the *navigation stick* was used by the participants to move around the surface of the octagon board. Please refer to the appendix for a photo of the experiment room. The second

component of the apparatus was a custom MATLAB tracking program created in our laboratory. The software was designed to define a circular virtual target location 28 mm² in diameter on the octagon board. The target location was invisible to the participant and could only be identified via the sounding of a computer-controlled beeping when the navigation stick entered the target zone. The participants were instructed that the target location was a specific area on the board associated with the beeping. Participants were asked to move to a designated starting position, and to find the target location again (Fig 1). We refer to this behavioural task as the Octagon Navigation Task. The program was designed to mark the initiation of a trial when the "START" button was clicked and conclude the trial when the "STOP" button was clicked. The program automatically generated trial numbers based on how many times the start/stop buttons were clicked in the program and numbered them in ascending order. Additionally, the software traced the trajectory undertaken by participants based on the path length coordinates and saved all the information in one Excel file for each participant. The entire experiment was recorded via the overhead video camera.



Figure 2. Illustration of the most direct trajectories from the four starting locations to the target location in each experimental condition. The circles represent the four starting locations during training trials. The dotted square represents the invisible target location.

Analysis. Latency to the target location for every experiment was measured by analyzing the recorded videos. The latency measures were then used to analyze total latency per trial, latency to the correct target location in the probe trial and blindfold condition. The program automatically recorded every x-y coordinate traversed during a trial and this information was then used to calculate the path length and root mean square error (RMSE) with a custom MATLAB script (further explained below). The program also recorded the number of trials in each experiment, which was then used to measure trials to criterion for all experiments.

All unpaired independent sample *t*-tests for Experiment 1 - 3 were computed using PRISM-7 statistical software. An unpaired independent sample *t*-test with Welch's correction was used to compare age, trials to criterion, performance on probe trial and blindfold condition between men and women for each experimental condition. A one-way repeated measures ANOVA with sex as the between subject factor and trials as repeated

measures was used to compare the differences in latencies, path length and RMSE during the first five trials between men and women for Experiment 1 - 3. All ANOVA results reported have Bonferroni adjusted alpha levels of .0125 per test (.05/4) for pairwise comparisons. For effect sizes, we report partial eta squared values, as this is the most appropriate measure of effect size for ANOVAs. Effect sizes or partial eta squared range are classified as 0.01 (small), 0.06 (moderate) to 0.14 (large) based on Miles & Shevlin's (2001) guide for reporting effect sizes. The magnitude of the effect size found in our results was compared to the aforementioned standardized ranges.

We calculated the root mean square error for all three experiments identically. The purpose of the measure was to compare each participant's path length data to the shortest path length possible to the target location in each experimental condition. SPSS (version 22) was used to calculate the shortest path, which was measured in pixels, to the correct target location for trials 1 - 5 in each experimental condition. The shortest path will be referred to as ideal path. The ideal paths were then uploaded in MATLAB (version 2016A). The observed paths from all participants including the ideal paths were interpolated using the Interpol function in MATLAB. The Interpol function made all the vectors equal length without changing the information inherent to each vector. All participant path length data for trials 1 - 5 were computed against the ideal path length for each trial. Every experimental condition was analyzed independently. We developed a custom code in MATLAB that calculated the displacement between x-y coordinates of ideal vs. observed paths. Participants who were moving randomly with respect to the ideal path would have high error scores and those moving directly to the target would have low error scores. The resulting error output was uploaded into SPSS and one-way

11

repeated measures ANOVA with Bonferroni correction was performed for Experiments 13. All the graphs presented in this thesis were made using PRISM-7 statistical software.

A heat map for the paths (pixels) taken during the probe trial was computed using MATLAB. Centroid analysis on the heat map was performed using the built-in weighted density centroid function. The heat map shows pixel density of paths; along with peak weighted centroids for men and women during the 15 second probe trial. The heat maps with centroid analysis were calculated identically for Experiments 1 - 3.

Trajectories taken by participants during the first 4 seconds of the probe trial were traced frame-by-frame using iMovie editing software. Traced trajectories were then compiled onto the diagrammatic representation of the Octagon Navigation Task. All images of trajectories were constructed using Adobe Illustrator CC- Graphic designer software. Trajectories for participants were analyzed identically in Experiments 1 - 3. All non-parametric tests were analyzed using SPSS (version 22). Self-reported measures of task difficulty (post), navigational ability (pre), education (pre) and video game use (pre) from pre and post-test questionnaires were used to perform Log-linear analysis to examine the relation between sex and each of the aforementioned self-reported variables for Experiments 1- 3. For variables with a significant main effect of sex, a Chi-squared test was conducted in order to quantify the difference in self-reported variables associated with each sex.

Experiment 1. Allocentric Condition

1.1. Participants

Fifty-five healthy, right-handed participants (27 women) completed the task. Participants were fluent in English and between 18 and 25 years of age (mean \pm SD) = 21.2 \pm 2.5) for men and (mean \pm SD= 19.7 \pm 1.3) for women. There was a significant sex difference in age

between men and women, t (54) = -2.971, p < .004. The mean age difference between men and women was 18 months for Experiment 1.

1.2. Training

Participants explored the 4032.25 cm² octagon board using the navigation stick (Fig 1). There was no information available on the board to indicate the location of the target. The room contained cues that remained consistent for all participants. Four different starting locations were used for all trials (see Fig 1). One at a time each participant was escorted to the starting location of the first trial. A consistent, allocentrically placed virtual target location served as the target for all participants (Fig 2). A trial would begin with a verbal "START" notifying the participant to begin moving the navigation stick to find the target location. When the participant navigated the stick into the target a tone was automatically sounded indicated that the goal had been successfully found and the trial terminated. The participants would then physically walk to the next starting location, the order of which was pseudo randomized. A ten-training trial maximum was implemented for all participants. Training was considered complete when a subject found the hidden platform by taking the most direct path to the target location on three consecutive trials (Fig 2). The most direct trajectory was a straight line from the start location to the goal location.

1.3. Retention Test

A single probe trial was performed immediately after task performance. The start location for the probe trial had not been used during training and participants were not informed that this trial was different in any way from the others (Fig 3). Probe trials lasted for 15 seconds. The virtual target location was disabled during this trial.



Figure 3. Accurate trajectories during the probe trial. The grey circle represents the novel starting position of the probe trial during each experimental condition.

Results. Allocentric Condition

1.5. Trial to Criterion. Men took significantly fewer trials to learn the task compared to

women (Fig 4), *t* (51.8) =5.503, *p* < .0001.





Figure 4. Bar graph representing mean number of trials to criterion (6.74 ± 0.32) for men and (9.04 ± 0.27) for women in Experiment 1. (**** = p < .0001.)

1.6. Latency. Men took significantly less time per trial than women (Fig 5), F (1, 53) = 25.05, p < .0001, $\eta p^2 = 0.321$. Pairwise comparisons of the first five trials revealed that men took significantly less time finding the correct target location from trials 2 - 5 relative to women (p < 0.0001).

1.7. Path length. Men took significantly shorter paths to the target location compared to women (Fig 6), F (1, 53) = 24.34, p < .0001, $\eta p^2 = 0.315$. Pairwise comparisons of the first five trials revealed that men took significantly shorter paths from trials 2 - 5 relative to women (p < 0.0001).



Latency- Allocentric Condition

Figure 5. Mean time \pm S.E.M to find the invisible target location during the first five trials of Experiment 1. Men locate the platform significantly faster than women from trials 2 - 5, (*** = p < .0001).



Figure 6. Mean path length (pixels) \pm S.E.M to find the invisible target location during the first five trials of Experiment 1. Men take significantly shorter paths compared to women from trials 2 - 5, (*** = p < .0001).

1.8. Root Square Mean Error. Men had significantly lower error scores compared to women (Fig 7) in Experiment 1, F (1, 53) = 14.51, p < .0001.



Root Square Mean Error- Allocentric Condition

Figure 7. Mean path error (pixels) \pm S.E.M to find the target location during the first five trials of Experiment 1. Men significantly take a more direct path to the target location compared to women on trials 2 - 5, (*** = p < .0001).

1.9 Heat Map with Centroid Analysis. The heat map shows a denser heat print around the target location for men compared to women (Fig 8.). Weighted centroid analysis of the heat maps revealed higher density peaks around the correct target location for men, while majority of density peaks for women were located further away from the target location as evident in Figure 8.

Allocentric Condition

Men

Women

Figure 8. Heat map of paths during the allocentric probe trial showing weighted centroid peaks (open red circles). The yellow intensity represents high activity levels while the blue represents lower activity levels. Men show a denser heat print and peak activity at the correct target location during Experiment 1 (allocentric condition).

1.10. Target Retention (Probe trial). Men took significantly less time to reach the target

location during probe trial compared to women (Fig 9), t(53) = 3.05, p < .001.

1.11. Trajectory (Probe trial). Plotting of trajectories revealed that men tend to take more direct trajectories to the target location during the probe trial whereas women showed more variance in their performance (Fig 10). Only eleven out of thirty women directly went to the correct target location, whereas twenty-six out of twenty-seven men went directly to the correct target location during the probe trial.



Target Retention - Allocentric Probe Condition

Figure 9. Bar graph representing mean latency to correct target location for men (1.20 ± 0.15) and women (3.61 ± 0.76) during probe trial. Men went to the correct target location quicker compared to females during the probe. (** = p < .001).

Allocentric Condition



Figure 10. Trajectories taken by men and women during the first four seconds of the probe trial. The black circle represents that starting position for the probe trial. The red dotted square represents the target location. The majority of the men go directly to the correct target location compared to women, who show more variation in their performance

Experiment 2. Egocentric Condition

2.1. Participants.

Fifty-five healthy, right-handed participants (28 women) completed the task. Participants were native English speakers and between 18 and 25 years of age (M \pm Std.= 20.88 \pm 2.3) for men and (M \pm Std.=20.06 \pm 2.7) for women. There was no significant difference in age between men and women in Experiment 2, *t* (54) = -1.210, *p* = 0.231.

2.2. Training.

The experimental apparatus and conditions were identical to Experiment 1. Four starting locations were used (Fig 1). The participant was escorted to the starting location of the first trial. A virtual, invisible target location was placed with respect to the body axis and starting position of the participant (Fig 2). The participant had to learn that the target location was

consistent with respect to their body axis and starting position. This condition tested the participants' ability to use egocentric navigation.

2.3. Retention Test.

The probe condition was identical in all three experiments.

Results. Egocentric Condition

2.5. Trial to Criterion. Women took significantly fewer trials to learn the task compared to men (Fig 12), t(51) = 3.39, p < .001.

2.6. Latency. Women took significantly less time to find the correct target location compared to men (Fig 13), F (1, 53) = 11.12, p < .001, $\eta p^2 = 0.176$. Pairwise comparisons of the first five trials revealed that women took significantly shorter time locating the correct target location from trials 2-5 relative to men (p < 0.001).



Trials To Criterion- Egocentric Condition

Figure 11. Mean number of trials to criterion (8.94 \pm 0.32) for men and (7.31 \pm 0.36) for women in Experiment 1. (** = p < .001).

2.7 Path length. Women took a significantly shorter path to the target location than men (Fig 14), F (1, 53) = 13.36, p < .001, $\eta p^2 = 0.201$. Pairwise comparisons of the first five trials revealed that women took significantly shorter paths from trials 2 - 5 relative to men (p < 0.001).



Figure 12. Mean time \pm S.E.M to find the invisible target location during the first five trials of Experiment 2. Women locate the platform significantly faster than men from trials 2 - 5, (*** = p < .0001).

Path Length-Egocentric Condition



Figure 13. Mean path length (pixels) \pm S.E.M to find the invisible target location during the first five trials of Experiment 2. Women take significantly shorter path to the target location compared to men from trials 2 - 5, (** = p < .001).

2.8. Root Square Mean Error. Women had significantly lower error scores compared to men in Experiment 2 (Fig 15), F (1, 53) = 20.99, p < .0001.

Root Square Mean Error- Egocentric Condition





2.9 Heat Map with Centroid Analysis. The heat map shows a slightly concentrated heat print around the target location for women compared to men (Fig 16). Weighted centroid analysis of the heat maps revealed higher density peaks around the correct target location for women, while majority of density peaks for men were located further away from the correct target location.



Egocentric Condition

Men

Women

Figure 15. Heat map showing weighted centroid peaks (red open circles) during the probe trial. Women show a slightly denser heat print and peak activity at the correct target location. Men show a weaker heat print and lower peak activity at the target location during Experiment 2 (egocentric condition).

2.10. Target Retention (Probe trial). Women took significantly less time to reach the

correct target location during probe trial compared to men as seen (Fig 17), t (38.14) =

2.439, *p* < .01.

2.11. Trajectory (Probe trial). Majority of women go directly to the correct target location compared to men (Fig 18). Trajectories taken by men varied between random and direct trajectory to the correct allocentric target location. Twenty-four out of the twenty-seven women directly go to the correct target location, whereas trajectories taken by men were split between random and allocentric target location (Fig 18). Only four out of twenty-eight men went to the correct egocentric probe target location, whereas eight out twenty-eight men went to the allocentric target location during probe trial.



Target Retention-Egocentric Probe Condition

Figure 16. Bar graph representing mean latency to correct target location for men (4.40 ± 0.75) and women (2.34 ± 0.38) during probe trial. Women went to the correct target location quicker compared to men during the probe (* = p < .01).

Egocentric Condition



Figure 17. Trajectories taken by men and women during the first 4 seconds of the probe trial. The black circle represents that starting position for the probe trial. The red dotted square represents the target location and the yellow dotted square represents the allocentric target location. The majority of the women go directly to the correct target location compared to men. Trajectories taken by men varied between random and direct trajectory to the correct allocentric target location.

Experiment 3. Neutral Condition

3.1. Participants.

Sixty healthy, right-handed participants (30 women) completed the task. Participants were fluent in English and between 18 and 25 years of age (M \pm Std.= 20.4 \pm 1.7) for men and (M \pm Std.= 19.8 \pm 2.2) for women. There were no significant differences in age between men and women in Experiment 3, *t* (57) = 5.797, *p* = 0.170.

3.2. Training.

The experimental apparatus and conditions were identical to Experiment 1 and Experiment

2. Four distinct starting locations were used for all trials (Fig 1). An invisible, virtual target

location was placed in the center of the octagon board (Fig 2). The participant could use an allocentric and/or egocentric strategy to solve the task. This experimental condition tested the participant's ability to use either strategy and served as an experimental control. Remaining procedures and data analyses as in previous experiments.

Results. Neutral Condition

3.3. Trial to Criterion. No significant sex differences between men and women were found with respect to trials to criterion (Fig 20), t (52) = 0.525, p = 0.605.





Figure 18. Bar graph representing mean number of trials to criterion (6.46 ± 0.34) for men and (6.23 ± 0.26) for women in Experiment 3. No significant differences (p = 0.601) were revealed between men and women with respect to trials to criterion.

3.4. Latency. No significant sex differences in latency to correct target location were found between men and women (Fig 21), F (1, 58) = 2.67, p = .108, $\eta p^2 = 0.046$. Pairwise comparisons of the first five trials further revealed no sex differences for (p = 0.108).

3.5 Path length. No significant sex difference in path length to the target location was found between men and women (Fig 22), F (1, 58) = < .001, p = 0.982, $\eta p^2 = < .0001$.

Pair-wise comparison of trials 1- 5 path lengths further reveled no sex differences (p = 0.982).



Figure 19. Mean time \pm S.E.M to find the invisible target location during the first five trials of Experiment 3. No significant sex differences were found in mean latency from trial 1 - 5, (p = 0.108).



Path Length- Neutral Condition

Figure 20. Mean path length (pixels) \pm S.E.M to find the invisible target location during the first five trials of Experiment 3. No significant sex differences were found for path length from trials 1 - 5 (p = 0.982).
3.6. Root Square Mean Error. No significant difference in error scores was found between men and women (Fig 23), F (1, 58) = 0.045, p = 0.885.



Root Square Mean Error- Neutral Condition

Figure 21. Mean delta path length (pixels) \pm S.E.M to find the invisible target location during the first five trials of Experiment 3. No significant sex difference in error score between men and women (p = 0.885).

3.7 Heat Map with Centroid Analysis. The heat map shows a slightly concentrated heat print around the target location for men compared to women (Fig 24). Weighted centroid analysis of the heat maps revealed similar density peaks around the correct target location for men and women (Fig 2)

Neutral Condition



Figure 22. Heat map showing weighted centroid peaks (red open circles) during the probe trial. Men and women show very similar concentrations in the heat print and similar peak centroids.

3.8. Target Retention (Probe trial). No significant sex differences in latency to correct target location during probe trial were found between men and women (Fig 25), t (47.9) =

1.527, *p* = 0.133.

3.9. Trajectory (Probe trial). Men and women go directly to the correct target location during the probe trial (Fig 26). However, women show more exploration around the correct target location compared to men during the probe trial.

Target Retention-Neutral Condition



Figure 23. Bar graph representing mean latency to correct target location for men (0.539 ± 0.04) and women (0.657 ± 0.065) during probe trial. Women went to the correct target location quicker compared to men during the probe trial (p = 0.133).

Neutral Condition



Figure 24. Trajectories taken by men and women during the first four seconds of the probe trial in Experiment 3. The black circle represents that starting position for the probe trial. The red dotted square represents the correct target location. Majority of men and women go directly to the correct target location. Women show more exploration around the target location relative to men.

4. Non-Parametric Tests. The following results are analysis of participants' self-reported data from experiments 1 - 3.

4.1. Education. No significant interaction between sex and education level were found in all three experiments [$X^2(4) = 5.592$, p = 0.232]. Partial Chi-square associations further revealed no main effect of sex*education, [$X^2(2) = 0.504$, p = 0.777] or main effect of education*experiment [$X^2(4) = 4.37$, p = 0.359].

4.2 Video Game Use. No significant 3-way interaction between

sex*videogame*experiment, were found [$X^2(2) = 2.351$, p = 0.309]. Partial Chi-square associations further revealed a significant main effect of sex*videogames, [$X^2(1) = 66.8$, p < 0.0001] but no main effect of videogames*experiment [$X^2(2) = .510$, p = 0.775]. A Chi-square revealed men significantly played more video games than women (Fig 28), [$X^2(1, N = 168) = 62.20$, p < .0001].

4.3 Navigational Skill. A significant 3-way interaction between sex* navigation skill*experimental condition, $[X^2(8)=15.87, p=0.044]$ was found for Experiments 1 - 3. Partial Chi-square associations further revealed a significant main effect of sex*navigation skill, $[X^2(4)=38.61, p<0.0001]$ but no main effect of navigation skill*experimental condition $[X^2(8)=2.54, p=0.960]$. The Chi-square test revealed men significantly reported themselves as having "Above Average" spatial navigation abilities compared to women who mainly reported having average to below average navigational ability, $[X^2(3, N = 168) = 32.94, p < .0001]$. **4.4. Task Difficulty.** No significant interaction between sex, task difficulty and experimental condition, [$X^2(8) = 8.04$, p = 0.430] was found for Experiments 1 – 3. Partial Chi-square associations further revealed no main effect of sex*task difficulty, [$X^2(4) = 3.963$, p = 0.449] or main effect of experiment*task difficulty [$X^2(8) = 9.281$, p < 0.319].



Figure 25. Bar graphs representing the frequency of video game use between men and women across three experimental conditions. Men play more video games then women in all three experiments, $X^2 (1, N = 168) = 62.20, p < .0001$.

4.5. Summary of Non-parametric results. Log linear analysis found significant differences between men and women for self-reported navigation skill and video game use. Men reported mainly having "Above Average" navigational ability while women reported having average to below average navigational abilities. Men played more video games then women across all three experimental

onditions (Fig 28). No significant differences were found in self-reported task difficulty or education level in any experiment.

Discussion

The aim of this study was to measure if sex differences in spatial navigation are due to differing spatial ability or default strategy preference. We created a tabletop analogue of the Morris water task called the Octagon Navigation Task (ONT) in order to assess performance of participants on this commonly used test of human spatial cognition (Jones et al., 2003; Astur et al, 1998; Astur et al, 2004). The results from the first two experiments supports our second and third prediction that men would outperform women in the allocentric condition (Experiment 1) and women would outperform men in the egocentric condition (Experiment 2) of the ONT. Similarly, probe trajectory analysis revealed that default frame of reference during navigation was allocentric for men and egocentric for women. In addition, no sex differences were found during the neutral condition (Experiment 3), which provides support for our fourth prediction that when men and women are provided with a condition in which the use of allocentric and egocentric spatial frameworks were equally effective, they are equally capable of successful performance on spatial tasks.

However, our results disproved our first prediction, which stated that both men and women will be equally able to solve all versions of the ONT despite initial differences. The results from Experiment 1 and Experiment 2 clearly show a double dissociation in performance even by the tenth training trial suggesting an inability to equally solve all versions of the ONT task. In Experiment 1, only one out twenty-seven men didn't reach criterion by the end of training, whereas eighteen out of twenty-eight women were unable to reach criterion by the end of training. In Experiment 2, twenty out of twenty-seven males did not reach criterion by the end of training whereas only six out of twenty-eight women

were unable to reach criterion by the end of training (Please refer to the appendix for graphs showing all training trials). These data clearly suggest that men and women did not have equal ability to solve all versions of the ONT and each sex had a selective advantage depending on the type of spatial frame of reference being enforced during the spatial task. Our results therefore indicate that when competition between two spatial frameworks of reference is created during navigation, men have an inherent ability to use allocentric spatial reference while women have an inherent ability to use egocentric spatial reference during navigation. The emerging sex differences in spatial navigation could therefore result from different prepotent spatial frameworks guiding performance as oppose to a simple difference in strategy preference.

The first experiment tested for the participant's ability to solve the spatial task using an allocentric spatial frame of reference. Men learned and retained the spatial location better than females. Furthermore, on average, men solved the allocentric spatial task by the second trial, whereas women struggled to effectively use allocentric spatial frame of reference to find the target location throughout the first five trials. Trajectory analyses of the probe data further revealed that majority of women were unable to find the correct allocentric target location. The results suggest that, in contrast to men, women had difficulty using an allocentric spatial frame of reference even after five training trials, whereas men quickly adapted to the use of an allocentric spatial frame of reference to find the target location by the second trial.

In the second experiment, successful performance depended on the implementation of egocentric spatial frameworks during navigation. Women outperformed men on all measures of acquisition and retention. The majority of women by the third trial had learned to implement egocentric spatial frameworks to find the correct target location, but most men were unable to solve the task using an egocentric spatial frame of reference even by the end of training. Trajectory analysis of the probe trial revealed that most women had adopted the use of egocentric spatial framework when locating the target location. Interestingly, the analysis further revealed that not only were most men not using egocentric spatial information to find the target location but also, some men continued to employ an ineffective allocentric spatial frame of reference to the find the target location, suggesting that men find it relatively more difficult to adapt to egocentric spatial frameworks.

Men and women performed equally well on all measures of acquisition and retention in the third experiment, when the task could be solved using distal cues/geometric information (allocentric) or self-centered navigation (egocentric). The results from Experiment 1 and 2 show a large double dissociation in performance between men and women, but these differences disappear when participants can use either allo- or egocentric frames of reference during navigation. These initial dissociations in task performance during selective reinforcement of either allocentric or egocentric spatial reference frameworks suggests that superior performance on a spatial task depends on the type of spatial information being tested. Women may have a superior ability to use an egocentric frame of reference during navigation, whereas men have a superior ability to use allocentric frame of reference during navigation. Our research therefore provides support to the idea that both men and women have equal navigational ability at the most general level, but each sex has an inherent advantage depending on the required spatial

reference frame (reliance on self-centered navigation vs. geometric information) that must be used for successful navigation.

Our findings generally support the conclusions of previous studies assessing sex differences in spatial strategy during spatial navigation tasks (Mueller et al, 2008; Sandstrom et al, 1998; Saucier et al, 2002; Saucier et al, 2003). Some human and nonhuman animal studies have shown female advantage during object location memory, whereas male advantage has been consistently reported in Euclidean based spatial navigation tasks (Astur et al. 1998; Saucier et al, 2008). However, it should be noted that meta-analyses analyzing effect size of spatial studies investigating sex differences report cumulative small to moderate effect sizes (see for review, Linn & Petersen, 1985; Voyer et al, 1995), whereas we had very large effect sizes for the sex differences in the allocentric and egocentric conditions. The large effect size of our results further strengthens the reliable and robust sex difference found in our experiments and underlines the potential importance of difference spatial reference frame usage as a key to understanding differences more generally.

The results obtained from Experiment 1 show a more robust sex difference in the allocentric condition compared to Zelinski et al's (2016) real-world navigation task data. Zelinski et al's study showed that, on average, women were able to employ an allocentric navigational strategy by the third trial, albeit slower than men. This differential performance on an allocentric spatial task in real world vs. laboratory setting may shed some light on the reliance on real-world vestibular input during navigation in women. Our study was able to replicate Zelinski et al's (2016) findings of male difficulty in using an egocentric frame of reference to solve spatial tasks. Our tabletop study lacked spatially

useful real-world proprioceptive input, which may have affected women more than men during allocentric navigation performance. The fact that men performed poorly during real-world navigation and laboratory setting in the egocentric version and excelled in the allocentric condition could mean that men are not as reliant on real-world proprioceptive input as women are during ecologically relevant spatial navigation

A meta-analysis conducted by Coluccia & Louse (2004) found that sex differences in spatial tasks emerged favoring men when the tasks required high cognitive demands and the differences disappeared when the task was reported to be less cognitively demanding. However, our study found no sex differences in self-reported task difficulty across all three experimental conditions and thus variation in task difficulty is not likely to account for the observed sex differences. It could also be argued that explicit verbal instructions on how to use each strategy was not provided, however studies using virtual versions of the MWT found no diminution in the sex differences even when participants were provided with explicit verbal instruction on how to solve the spatial task (Astur et al, 1998).

All of the experiments presented in this thesis were conducted by a woman experimenter, which could potentially be a confounding factor as men in the experiment could assume the experimenter was wrong during trials they didn't perform well in. However, if that were the case, men should have performed similarly in all experimental conditions but that is clearly not the case. Hence, experiments conducted solely by a woman should have little to no effect on the results obtained. Another confound in our data was the non-adjustable height of the table. The height of the table could have been a disadvantage to very tall participants as it could affect their kinesthetic-proprioceptive

input during navigation. As our results were so robust, this minor confound probably did not effect our results. However, in future experiments, height of the table can be adjusted to the participant's height in order to eliminate the height confound from the analysis.

Our results suggest that the robust sex differences found on the ONT cannot simply be explained by the idea that initial strategies are different between men and women. If that were the case, women in the allocentric condition would have switched their navigation strategy when their initial navigation strategy proved to be ineffective. Similarly, men in the egocentric condition would have switched to using egocentric frame of reference to find the target location when their initial search strategy was failing. Women's ability to quickly adapt to an egocentric spatial navigation task could mean women having a pre-existing ability to use egocentric spatial frame of reference during navigation. Similarly, men easily use an allocentric strategy during allocentric navigation and continue to ineffectively employ allocentric search strategy even during the egocentric condition points towards pre-existing ability to use allocentric spatial frame of reference during navigation. One could argue that men and women are unable to switch strategies based on their inability to adapt to their non-preferred navigation strategies. However, Zelinski et al's study (2016) shows that at least in the real world, women adapted to an allocentric search strategy by the third trial during the allocentric condition. Men in the ONT and the real world navigation task were unable to switch to using an egocentric spatial frame of reference, which suggests that men may be less flexible in their ability to adapt their spatial frame of reference during navigation compared to women. More research is needed to further study the switching ability between allocentric and egocentric spatial frame of references in men and women.

Our decision to not provide explicit verbal instructions on how to use each strategy and automate the acquisition and retention phases of the task were intended to reduce experimenter's bias/involvement and encourage participants to employ navigational strategy that would naturally come to them, similar to when navigating in the real world. Similarly, to account for the reliance on rote-memorized movements towards the target location from the four starting positions of the training trials, the probe trial was started from a novel starting position. Performance on the probe trial further revealed robust sex differences during differential strategy reinforcement and therefore the observed sex differences cannot be due to reliance on rote memorization, at least during the allocentric condition (Experiment 1). It could be argued that participants could rely on rote-memorized movements during the egocentric condition (Experiment 2). If that were the case, men would have performed equally well as women in Experiment 2. Therefore, the reliance on rote-memorized movements towards the target locations seems unlikely to account for the robust sex differences observed in Experiment 2.

Our findings have clear clinical significance. We created a very simple, straightforward spatial memory task that is extremely sensitive to sex differences in navigation while being completely automated, quick and user friendly. Most memory tests screening for memory deficits are pen and pencil tasks such as the Mini-Mental State Exam (MMSE), and Montreal Cognitive Assessment (MoCA) that are not as sensitive to spatial memory deficits (Wouters et al, 2011). As dementia related illness show spatial memory deficits, it is important to screen for spatial memory deficits (Kesner et al, 1989). Our unique apparatus contains a simple tabletop spatial game and virtual software automation that can accurately measure performance and accounts for sex difference in

spatial navigation. The results obtained will ensure that the deficits we see are due to underlying cognitive spatial deficits and not because the patient has an inherent disadvantage at solving the spatial task.

An average experiment takes 5 - 7 minutes making it a quick and reliable tool that can be used in both research and clinical setting. Our research along with others highlights the existence of sex difference in how men and women differ in encoding spatial information (Mueller et al, 2008). This information can help us redesign our school curriculum to give both sexes an equal opportunity to perform well in the STEM fields. Our current system relies heavily on pre-existing ability for mental rotation/ Euclidean based spatial ability to excel in the physical sciences. If we teach our generation the physical sciences in a way that is equally understandable to both sexes, we can hope to see increased interest of women in the STEM fields.

The ONT is a sensitive spatial task that shows a very clear double dissociation in spatial abilities between the two sexes. The simplicity of the task with complex testing ability confers an advantage of being easily implemented in an fMRI study in order to analyze brain activity while participants solve allocentric and egocentric versions of the ONT. It can be used to measure if different neural activation pattern are observed between men and women while solving different versions of the task.

Studies using nonhuman animals and human spatial cognition studies have reported on the role estradiol plays in enhancing spatial cognition (Driscoll et al., 2005, Galea et al., 2006; Luine, 2014; William & Meck, 1991), thus, in addition to brain imaging, an indepth analysis of other physiological factors such as the influence of hormones on spatial abilities should be assessed to get a more accurate representation for the bases of these sex differences.

Majority of studies analyzing sex differences in spatial navigation show male superiority in various navigational tasks. In humans, predominantly the use of virtual analogues of the MWT has been used to measure the reported male advantage. As a traditional MWT strictly tests for allocentric navigation, based upon our findings, the reported results are biased towards finding male superiority. Our results have shown that when a spatial task is manipulated such that successful performance required the use of egocentric spatial frame of reference, superior female navigational performance emerges. Our study therefore shows that there is no sex difference in overall spatial navigational ability at the most general level, but the difference lies in complementary superiority in the use of different types of spatial frame of reference. Furthermore, not only were we able to show robust sex differences in every single measure of performance by reinforcing two differential spatial frameworks using a quick, automated spatial task, but also we were also able to eliminate those sex differences with our neutral condition. That observation, together with the clear double dissociation between the two experimental conditions, rules out simple differences in motivation, movement or task complexity as being the cause of the sex differences.

In conclusion, our findings show that when a spatial task requires competition between two sources of spatial reference frameworks, an egocentric strategy is more salient in women whereas an allocentric strategy is more salient in men. This difference persists after several training trials, indicating poor ability to switch to the non-dominant

strategy by both sexes. Finally, if either spatial reference frame can be used, the sex difference disappears.

References

Arnold, A. P., & Breedlove, S. M. (1985). Organizational and activational effects of sex steroids on brain and behavior: A reanalysis. *Hormones and Behaviour*, *19*(4), 469-498.

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*(1-2), 185-190.

Astur, R. A., Tropp, J. A., Sava, S., Constable, R. T., & Markus, E. J. (2004). Sex differences and correlations in a virtual Morris water task, a virtual radial arm maze, and mental rotation. *Behaviour Brain Research*, *151*(1-2), 103-115

Coluccia, E., & Louse, G. (2004). Gender Differences in Spatial orientation: A review. *Journal of Environmental Psychology*, 24(3), 329-340.

Dabbs Jr., J. M., Chang, E., Strong, R. A., & Milun, R. (1998). Spatial Ability, Navigation Strategy, and Geographic Knowledge Among Men and Women. *Evolution and Human Behaviour*, *19*(2), 89-98.

Driscol, I., Hamilton, D., Yeo, R. A., & Brooks, W. A. Sutherland, R. J., (2005). Virtual navigation in humans: the impact of age, sex, and hormones on place learning. *Hormones and Behaviour*, *47*(3), 326-335.

Ekstrom, A. D., Caplan, J. B., Ho, E., Fried, i., Shattuck, K., & Kahana, M. J. (2005). Human hippocampal theta activity during virtual navigation. *Hippocampus*, *15*(7), 881-889.

Galea, L. A., Spritzer, M. D., Barker, J. M., & Pawluski, J. L. (2006). Gonadal hormone modulation of hippocampal neurogenesis in the adult. *Hippocampus*, *16*(3), 225-232.

Gron, G., Wunderlich, P. A., Spitzer, M., Tomczak, R., & Riepe, M. W. (2000). Brain activation during human navigation: gender-different neural networks as substrate of performance. *Nature Neuroscience*, *3*(4), 404-408.

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*, 154-169.

Jones, C. M., Braithwaite, V. A., Healy, S. D. (2003). The evolution of sex differnces in spatial ability. *Behavioral Neuroscience*, (117)3, 403-411.

Kesner, R. P., Adelstein, T. B., & Crutcher, K. A. (1989). Equivalent spatial location memory deficits in rats with medial septum or hippocampal formation lesions and patients with dementia of the Alzheimer's type. *Brain and Cognition*, *9*(2), 289-300.

Koppen, J. R., Winter, S. S., Loda, E. L., Hamilton, D. A., & Wallace, D. G. (2012). Analysis of Movement Kinematics on Analogous Spatial Learning Tasks Demonstrates Conservation of Direction and Distance Estimation Across Humans (Homo sapiens) and Rats (Rattus norvegicus). *Journal of Comparative Pyschology*. doi:10.1037/a0030162

Linn, M. C., & Petersen, A. C. (1985). Emergence and Characterization of Sex Differences in Spatial Ability: A Meta-Analysis. *Child Development*, *56*(6), 1479-1498.

Lovden, M., Herlitz, A., G-Hutter, B., Kruger, A., & Lindenberger, U. (2007). Quantitative and qualitative sex differences in spatial navigation. *Scandenevian journal of psycology*, *48*(5), 353-358.

Luine, V. N. (2014). Estradiol and cognitive function: Past, present and future. *Hormones and Behaviour*, *66*(4), 602-618

Maguire, E. A., Burgess, N., & Keefe, J. O. (1999). Human spatial navigation: cognitive maps, sexual dimorphism, and neural substrates. *Current Opinion in Neurobiology*, *9*(2), 171-177.

Miles, J and Shevlin, M (2001) Applying Regression and Correlation: A Guide for Students and Researchers. Sage:London.

Moffat, S. D., Hampson, E., & Hatzipantelis, M. (1998). Navigation in a "Virtual" Maze: Sex Differences and Correlation With Psychometric Measures of Spatial Ability in Humans. *Evolution and Human Behaviour*, *19*(2), 73-87.

Moffat, S. D., Zonderman, A. B., & Resnick, S. M. (2001). Age differences in spatial memory in a virtual environment navigation task? *Neurobiology of Aging*, 22(5), 787-796

Morris, R. J. (1981). Spatial localization does not require the presence of local cues. *Learning and Motivation*, *12*(2), 239-260.

Morris, R.j, P. Garrud, JNP Rawlins, J. O'Keefe; Place-navigation impaired in rats with hippocampal lesions. Nature, 297 (1982), pp. 681–682.

Mueller, S. C., Jackson, C. P., & Skelton, R. W. (2008). Sex differences in a virtual water maze: An eye tracking and pupillometry study. *Behaviour Brain Research*, *193*(2), 209-215.

Puts, D.A., McDaniel, M.A., Jordan, C.L. et al. Arch Sex Behav (2008) 37: 100. https://doi.org/10.1007/s10508-007-9271-3

Roof, R. L., & Havens, M. D. (1992). Testosterone improves maze performance and induces development of a male hippocampus in females. *Brain Research*, *572*(1-2), 310-313.

Sandstorm, N. J., Kaufman, J., & Huettel, S. A. (1998). Males and females use different distal cues in a virtual environment navigation task. *Brain research. Cognitive Brain Research*, *6*(4), 351-360.

Saucier, D. M., Green, S. M., Leason, J., Bell, S., & Elias, L. J. (2002). Are sex differences in navigation caused by sexually dimorphic strategies or by differences in the ability to use the strategies? *Behavioural Neuroscience*, *16*(3), 403-410.

Saucier, D., Bowman, M., & Elias, L. (2003). Sex differences in the effect of articulatory or spatial dual-task interference during navigation. *Brain and Cognition*, *53*(2), 346-35

Sutherland, R. J., Kolb, B., & Whishaw, I. Q. (1982). Spatial mapping: definitive disruption by hippocampal or medial frontal cortical damage in the rat. *Neuroscience letters*, *12*(2), 271-276.

Varela, M., Weiss, S., Meyer, R., Halessa, M., Wilson, M., Goosens, K. A., & Bendor, D. (2016, May 4). Tracking the Time-Dependent Role of the Hippocampus in Memory Recall Using DREADDs. *PLOS ONE*. doi:https://doi.org/10.1371/journal.pone.0154374

Voyer, D., Voyer, S., & Philip, B. (1995). Magnitude of sex differences in spatial abilities: A meta-analysis and consideration of critical variables. *Psychological Bulletin*, *117*(2), 250-270.

Williams, C. L., & Meck, W. H. (1991). The organizational effects of gonadal steroids on sexually dimorphic spatial ability. *Physconeuroendrocrinology*, *16*(1-3), 155-176.

Wouters, H., Van Campen, J., Appels, B., Buiter, M., de Haan, R. J., Zwindermann, A H., & Schmand, B. (2011). Does adaptive cognitive testing combine efficiency with precision? Prospective findings. *Journal of Alzhimer's Disease*, 25(4), 595-603.

Zelinski, E. L. (2016). *The influence of context and strategy on spatial task performance* Doctoral dissertation, ProQuest, Lethbridge.

Appendices:

1. Script for Octagon Navigation Task

For the letter of consent and questionnaire

"Before we start the experiment, I'm going to need you to read over and fill out a letter of consent and a questionnaire. The consent form is a legal document that is stating that you are participating in this experiment willingly. It will ask for your initials for your consent to use footage of you in the experiment. The footage will mainly be focused on your arm, so it will be completely anonymous and confidential. Your initials will give me consent to use your footage in presentations. The questionnaire will also be entirely anonymous, so please be completely honest. As you go through the questionnaire, there will be a section that says to **be completed after**, so you will fill that out after the experiment. Please let me know when you are finished".

Explanation

"We are going to start the task now. This is the board and this flashlight will be your navigation piece. Once you start, I'm not going to be able to help you, so you are going to have to figure it out on your own. There is a location somewhere on this board that I can see on my computer, but you cannot. It doesn't look different than any other place on the board, so you won't be able to tell by looking at the spot. When I verbally say "START" you can begin the trial. When you get to the target spot, an automated beep will continuously sound, notifying you that you have found the target location. The first time you find it will be random. After you find it, we'll get you to come back to this start spot, and then I will move to a new start spot, and get you to try to find that target spot again. Make sure you are not going too fast for the first trial as it will be hard for you to locate where the beep came from. Once you know where the target location is, you can go as fast as you like. Does that make sense?"

Probe Trial

Ignore the last trial, there were some tracking issues **.

** Every time a probe trial was conducted, the participant was told after that the trial didn't count due to tracking issues.

2. Exclusion Criteria for the Octagon Navigation Task

- Participants over 25 years of age were not included in the analysis
- Left handed participants were excluded from the analysis
- Participants with arthritis or any mobility issues were excluded from the analysis
- Participants with chronic illnesses were excluded from the analysis
- Participants with multiple concussions were excluded from the analysis

- Participants with history of addictions (alcohol, drug, etc) were excluded from the analysis
- Participants with diagnosed mental illness were excluded from the analysis
- Participants on hormone therapies were excluded from the analysis
- Transgender participants were excluded from the analysis

3. Photo of the Experiment Room



4. . Allocentric- All Trials



5. Egocentric- All Trials



6. Consent Form:

LETTER OF CONSENT

Human Tabletop Navigation Task (Student)

Participant ID:

Date:

Dear:

You are being invited to participate in a research study about human navigation. In particular, we are interested in whether humans and animals solve the task in a similar fashion.

This research will take a maximum of 30 minutes. Experimenter will meet you at the west entrance to the Canadian Centre for Behavioural Neuroscience where you will be asked to complete a questionnaire about your health history and any medications you are currently taking. This experiment poses no risk to the participants as it takes place indoors in a secured research lab. As a precautionary measure, the experimenter has taken first aid courses and can provide basic first aid as needed. A saliva sample for hormone analysis will be collected via you spitting into a new, sterile specimen vial. Following this interview, you can complete the task. You will also be asked a few questions after you have finished participating.

The anticipated risks related to this research are very low. You will be seated in our research lab and ask to play a board game like navigation task. The experimenters will check ahead of time to ensure that everything related to the experiment is in order to ensure efficient use of your time. Several steps will be taken to ensure your safety during saliva collection. We will follow UofL procedures for handling of biohazardous materials (e.g., the experimenter will wear new, sterile gloves for each specimen collection). Even so, if you feel uncomfortable with any part of this study at any time, you have the right to terminate participation without consequence. You will be monitored for signs of fatigue throughout the study, but due to the quick nature of this task, this concern is unlikely. In the event that you do become fatigued, the experiment will be stopped.

We hope you find participation in this study enjoyable. In addition, by participating in this research you may benefit others by helping scientists to better understand how humans process information about the environment. This information is critically important, as this ability and the neural regions associated with it, are often the first to exhibit impairment during unhealthy aging.

Several steps will be taken to protect your anonymity and identity. All identifying information will be kept confidential in a locked filing cabinet in a secure office. Your name will be translated to a random ID number and all data collected will be labeled with the ID number rather than your name. The only place your name will appear is in

this letter and on the informed consent form. Upon completion of the study, your name will be removed from this document so only the ID number and pertinent demographic information is retained. This information will be kept in the researcher's locked office at the University of Lethbridge. Only the primary researchers involved in this project (Mashal Fida and Robert Sutherland) will have access to your personal information. All staff accessing your data are required to sign research assistant confidentiality agreements. Your participation will be recorded via a video camera, but only your subject ID number will be attached to any images. The camera is recording video from a distance, so it should be difficult to identify you from the footage. Unless otherwise stated, only research assistants will be able to view the footage of your performance. Your participation in this research is completely voluntary. We hope that you will decide to participate in this study. If you choose to participate and then change your mind, you may withdraw from the study at any time, for any reason. We will have two research assistants around you at all times during the experiment, if you decide to withdraw please notify the research assistant closest to you and we will withdraw you immediately without any penaltyIf you do this, you will have the choice of having the information contributed removed from the study and destroyed, or allowing the information contributed until the time of withdrawal to be included in the study, and that no more information or data will be collected from you from that point on. Saliva samples will be destroyed if you choose not to complete the study.

The results from this study will be presented in manuscripts submitted for publication in scientific journals, or oral and/or poster presentations at scientific meetings, seminars, and/or conferences. With your permission, it is possible that your performance could be used to illustrate general patterns in the data. Your personal information including your name will be kept confidential and not be distributed in any way. At no time, will your name be used. If you wish to receive a copy of the results from this study, you may contact one of the researchers at the telephone number listed below.

If you are willing to allow us to use your video footage for illustrative purposes (e.g., during presentations), please initial on this line: ______.

If you require any information about this study, or would like to speak to one of the researchers, please contact Mashal Fida by phone at (902) 324-1668 or email at <u>fidam@uleth.ca</u> at the University of Lethbridge. If you have any other questions regarding your rights as a participant in this research, you may also contact the Office of Research Services at the University of Lethbridge at (403) 329-2747 or <u>research.services@uleth.ca</u>. A copy of this letter will be given to you for your records.

I have read the above information regarding this research study on the patterns of neural activation associated with virtual navigation, and consent to participate in this study.

 (Printed Name of Participant)
 (Signature)
(Date)
(Printed Name of Researcher)
(Signature)
(Date)

5.Sample Questionnaire

Tabletop Navigation Task

Please answer the following questions to the best of your ability. Where you are given several choices, please fill the circle of the option that best describes you. Please ask the experimenter for clarification if there are any questions that are unclear. Likewise, you can ask the experimenter why particular questions have been included. You may skip questions you are not comfortable answering, but you cannot be identified by this questionnaire and it will be stored in a locked cabinet in a secure office. If you answer yes to any of the questions please inform the experimenter immediately as it may be grounds for exclusion from the study.

Date of Birth (dd/mm/year): / /

Age: _____

Are you right or left handed?

Have you ever had a medical emergency that required hospitalization?

oYes

oNo

If yes, please describe the event(s):

Have you ever lost consciousness?						
	oYes	oNo				
If yes, j	If yes, please describe the event(s):					
Do you have a history of seizures or epilepsy?						
	oYes	oNo				
If yes, please describe:						

Subject ID: _____

Have you been diagnosed with a chronic illness (e.g., Diabetes)?				
oYes	oNo			
If yes, please describe:				
	·			
Have you ever had a concussion?				
oYes	oNo			
If yes, please describe:				
. Dia you lose consciousness?				

oYes

oNo

If yes, how long were you unconscious?	minutes or	hours.			
Did you seek medical attention following the injury?					
oYes	oNo				
What treatment or recommendations were made?					
Have you been diagnosed with a mental illness?					
oYes	oNo				
If yes, please describe:					
Please list any medications (including birth control pill	s) you are currently ta	king that have			
been prescribed by a medical professional:					

Please list any over the counter medications or supplements you are currently taking:

Do you use drugs recreationally?

oYes

oNo

If yes, please list the substance(s) and the regularity with which you consume them

(*x* times per day, daily, weekly, monthly):

Alcohol:

_ Cigarettes: _____

Caffeinated beverages (e.g., coffee, tea):

Marijuana:

_ Other (please list other substances below and usage frequency):

Please identify your sex/gender:

oMale-to-female transgender* oFemale-

to-male transgender* oNatal female

oNatal male

oOther (please describe):

*If you are currently on hormone therapy, please provide information on

dosage/medication:

Do you have a history of tripping, falling, or losing your balance?

oYes

oNo

.

If yes, please describe the nature of your difficulties:

. How would you rate your navigational skill?

oFar above average oAbove average oAverage oBelow average oFar below average

If you are going to a new place that you've never been before, what is the likelihood that

you will get lost?

oExtremely likely

oLikely

oNeither likely or unlikely

oUnlikely

oExtremely unlikely

Please describe how you reorient yourself if you become lost?

How often do you use GPS technologies (whether it be with a GPS receiver,

Google maps or a smartphone)?

oVery often oOften oOccasionally oRarely oAlmost never

How often do you use traditional methods of navigation (e.g., paper maps) to get

around?

oVery often oOften oOccasionally oRarely oAlmost never Do you participate in such activities that require extensive navigational skills (e.g., orienteering, travel)?

oYes

oNo

Please list activities you enjoy and engage in on a regular basis:

Do you play video games?

oYes

oNo

Please list video games you've played in the last 12 months:

Which of the following best describes your current mood?

oI am very happy. oI am somewhat happy. oI am relaxed. oI am nervous. o I am angry. oI am frustrated. oI am sad. o I am very sad.

Have you ever been diagnosed with a chronic digestive disease (i.e Crohn's disease)?

o Yes

o No

If yes, what type and when were you diagnosed:

Do you take any medication for it?

o Yes

o No

If yes, list the name(s) of medication(s):

Have you ever been diagnosed with Arthritis?

o Yes

o No

If yes, what type and when were you diagnosed?

Do you take medication for it?

o Yes

o No

If yes, please list the name(s) of all medication(s):

For Females only:

When was the last time you got your period? Please list (dd/mm/yy). If not sure, roughly estimate:

How long is your menstrual cycle (if it varies, roughly estimate):

o 19-21 days

o 21-25 days

o 30+

When are you expected to get your next period? Please list (dd/mm/yy). If you are not sure, roughly estimate:

<<To be completed after task performance>>

Which of the following best describes your current mood?

oI am very happy. oI am somewhat happy. oI am relaxed. oI am nervous. o I am angry. oI am frustrated. oI am sad.

oI am very sad.

How would you rate the difficulty of the task overall?

oExtremely difficult

oDifficult

oNeither easy or hard

How would you rate your ability to remember the positions of the objects?

oVery hard to remember oSomewhat hard to remember oNeutral oSomewhat easy to remember oVery easy to remember

How would you rate your ability to find your way around the tabletop environment?

oVery difficult oSomewhat difficult oNeutral oSomewhat easy oVery easy
Please choose the option that best describes your experience.

oThis task would be much easier if performed on a computer. oThis task would be slightly easier if performed on a computer. oIt does not matter if this task was performed on a computer/tabletop or in the real world. o This task would be much easier if performed on the tabletop version o This task would be slightly easier if performed on the tabletop version oThis task would be slightly easier if performed in the real world.

Please choose the option that best describes your strategy for navigating in unfamiliar spaces.

oI exclusively use my internal compass to navigate.

oI mostly use my internal compass to navigate.

oI use a combination of my internal compass and cues from the environment.

oI mostly use cues from the environment to navigate.

oI exclusively use cues from the environment to navigate.

Please choose the highest level of education completed?

- o Professional degree (MD,ENG)
- o Graduate (Master/ PhD)
- o Undergraduate
- o College diploma
- o High school
- o Grade 1-9
- o None

Please describe the types of characteristics you pay attention to in the environment.

Please list aspects of the environment that stood out to you.

Plrease use this page to write down any other thoughts you have about our study:

Thank you very much for participating in our study!

If you would like to receive a copy of any publications or proceedings related to your

participation, please initial here:

Please leave this page blank