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Gender Differences in Working Memory in Humans Tested on a Virtual Morris Water Maze.

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ABSTRACT

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A computerized virtual version of the Morris water maze (vMWM) was used to assess human gender differences in spatial working memory. In Experiment 1, the release point and platform location was changed on every other trial for 20 trials. Men had significantly reduced acquisition latencies and more accurate heading errors on the first daily trial compared to women. In Experiment 2, the release point and platform location was changed every fourth trial for 20 trials. Men had significantly shorter acquisition latencies and path lengths than women. Experiment 3 was identical to Experiment 2, except that environmental cues were changed throughout testing. Men had significantly shorter acquisition latencies and path lengths than did the women. These studies are the first to demonstrate significant gender differences in a spatial working memory version of the vMWM.

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CHAPTER 1

INTRODUCTION

Spatial ability differences between men and women have long been widely acknowledged, but the generality and the importance of these differences have been debated. For many years, a number of spatial ability tasks have tests have shown that men do better on spatial memory tasks than do women (Linn & Peterson, 1985; Maccoby & Jacklin, 1974; McGee, 1979; Tapley & Bryden, 1977). However, more recent work has shown that men do not have an advantage on all spatial tasks and that women do better or as well on some tasks. For example, Tapley and Bryden have reported that men do better on mental rotation tasks, but McBurney, Gaulin, Devineni, and Adams (1997) have reported that women do better on object memory and location memory tasks.

Spatial ability is an important cognitive process, but there has been some disagreement about what constitutes spatial ability. In general, spatial ability refers to manipulations of nonlinguistic symbolic material (Linn & Peterson, 1985). Several different tasks have been used to study spatial ability: mental rotation, object recognition, object location, rod and frame, water level tests, spatial visualization, and wayfinding. Gender has been obtained with all of these tasks. This study is specifically interested in human gender differences in spatial navigation, using a virtual reality Morris water maze task.

Morris Water Maze

Morris (1981) described a simple, yet efficient means of measuring spatial learning in rats, called the Morris water maze (MWM). Morris designed the task in response to the idea that spatial learning may be different from other associative learning tasks. Morris was interested in the underlying mechanisms involved in spatial orientation, specifically proximal orientation versus distal orientation. Proximal orientation includes tasks with a visible goal, while distal

orientation includes tasks where the goal is invisible with no local cues to guide the subject. The significance of which type of orientation was being used was difficult to determine because few tasks fell cleanly into one category or the other. Morris created an aversive task that forced the subject to use its spatial localization system to guide it to the goal. He demonstrated that the rats could learn a goal that they could not see, hear, or smell from solely using distal cues. Briefly, the MWM uses a circular pool of opaque water with a hidden platform located just below the surface. During a series of trials an animal learns to swim to this hidden platform and escape the water. Often a probe or transfer trial follows training during which the platform is removed and retention of the platform location is measured through analysis of swim patterns of the animal to the former platform location. Presumably, animals that have learned the platform location will spend the majority of their time in the area where the platform was formally located. Many variations of the MWM have been created including manipulations of training regimens, use of different contexts, and change of location of the platform across trials, also known as the matching-to-place or working memory version of the task (for a review, see Brandeis, Brandys, & Yehuda, 1989; Gerlai, 2001). The place version of the MWM is designed to study place learning, which is the ability of the animal to locate a stationary hidden platform in the pool. Tolman described place learning as using knowledge of spatial (or distal) cues to navigate toward a goal.

Another version commonly used is the match-to-place (MTP) version of the MWM. This version has been hypothesized to analyze working memory. Working memory refers to memory of trial specific information, or information needed for the task at hand that later may be discarded (Hodges, 1996). In the MTP version of the water maze, the platform location is moved to a new location each day. Typically animals are given two trials a day over a series of four to five days. Whishaw (1985) has argued that the MTP version of the water maze is a more difficult test of spatial ability due to its demands on both reference memory, or task specific information, and working memory. Reference memory is the long-term retention of information necessary for

future similar tasks. The animals must remember the location of the platform from the previous day (reference memory) but also have to learn and remember the new location of the platform on the second trial each day (working memory). Significant improvement from the first to second trials is indicative of working memory retention.

The Virtual Morris Water Maze (vMWM)

Recently, a virtual version of the Morris water maze has been developed using a virtual environment presented to humans on a computer. Participants find themselves in a three-dimensional room with a pool of water in the center. The room is usually ringed by various visual cues such as doors, windows, and pictures. The participants must navigate through the water, either by a joystick or a keyboard, to a hidden platform just under the surface. Different aspects of the program may be manipulated by the experimenter such as the environment, platform location, starting location, number of trials, duration of trials, hidden or visible platforms, etc. The platform may also be removed for a probe trial. This virtual Morris water task (vMWM) has been used to examine many aspects of human spatial navigation. Past reports have demonstrated significant gender differences (Astur, Ortiz, & Sutherland 1998), differences in hippocampal functioning (Astur, Taylor, Mamelak, Philpott, & Sutherland, 2002; Maguire, et al., 1998), and basic learning trends including place learning, observational learning, and latent learning (Jacobs, Laurance, & Thomas, 1997; Jacobs, Thomas, Laurance, & Nadel, 1998; Thomas, Hsu, Laurance, Nadel, & Jacobs, 2001). Interestingly, there has been very little research on the MTP version of the virtual water maze; most of the work has concentrated on the place version of the task.

This study was designed to answer three questions regarding spatial navigation and working memory. (1) How do humans use the information from their environment to navigate through space on a task that is specialized to test working memory? (2) Are there gender

differences in spatial navigation abilities in terms of working memory? (3) Is the MTP version of the virtual Morris water maze a valid test of spatial working memory?

<center>Theoretical Background</center>

<u>Cognitive Mapping and Hippocampal Function</u>

Tolman (1948) coined the term "cognitive map". He described this map as a picture of the environment including routes, paths, and locations of objects within the environment that an animal uses to navigate toward a goal (Tolman). Once a cognitive map has been created, an animal can reach a goal from any direction within the environment. Tolman also suggested the concept he called vicarious trial and error, which he believed provided additional support for cognitive map building. An organism was not solely acquiring various stimuli presented but also actively compared the stimuli. Moreover, it also was relating them to a cognitive map, and information was incorporated into the cognitive map as necessary. Experiments on place learning were designed to show that the subject was not moving through the maze according to a fixed set of movements, but rather that the subject was capable of varied behavior according to the orientation of itself and the environment. Tolman tested his theories using a variety of mazes that he developed. In one of his more famous studies (Tolman, Ritchie, & Kalish, 1946), he tested place learning directly against response learning with an elevated plus maze. The response learning group was tested in a random alteration sequence of two different starting locations; it always found the reward by turning right. The place learning group also was tested at a random alteration of two starting locations but always went to the same location for the reward, regardless of their point of origin. This meant that some of the time they would turn left for the reward and some of the time they would turn right for the reward. The place learning group was much more successful than the animals in the response learning condition. All of the rats in the place learning group learned within eight trials. None of the response learning group reached

criterion as rapidly, and five of the rats in this group did not reach criterion after 72 trials. There there were many extramaze cues in the testing environment. Thus, it was clear that place learning was simpler than response learning.

Whishaw (1991) asserts that rats use associative processing and not cognitive mapping in the MWM. Associative theory says that performance is related to previous experience with environmental cues by movement through the environment. Morris (1981) argued that rats demonstrate instantaneous transfer in his task, which is consistent with cognitive mapping theory. That is, once rats have learned the location of the platform from one starting position, they are able to swim to the platform location accurately from a novel start position. Whishaw (1991) operationally defined instantaneous transfer as errorless swims with latencies approaching 5 sec. In a MTP task, rats had improved performance, but instantaneous transfer was not occurring. Whishaw suggests that accurate performance depends upon three things: swimming using the room cues for guidance, viewing the room cues from the goal, and practice, all of which support the idea that rats use associative rather than cognitive mapping processes in spatial navigation tasks in a swimming pool. Whishaw admits that proactive interference may have been occurring in the task. The rats had a tendency to swim to the previous day's location before searching for the new location, which could have been interfering with instantaneous transfer.

Although Tolman formed much of the foundation of current ideas about spatial navigation, he did not discuss any neurological or biological basis for the cognitive map. O'Keefe and Nadel (1978) were among the first to claim that the hippocampus is intricately involved in the formation and storage of cognitive maps. The hippocampus is a horseshoe shaped region of the subcortical brain located in the temporal lobe in humans and animals. This structure has been implicated in spatial memory and the construction of mental maps of environmental locations. The hippocampus is also thought to play a role in short term memory. It is thought that memories are first processed and then temporarily stored in the hippocampus before they move to the cerebral cortex for permanent storage (O'Keefe & Nadel). Often people with damage to

the hippocampus retain previous memories of events but have difficulty in remembering new information (Scoville & Milner, 1957). This would seem to imply that the hippocampus is active in working memory (Olton, Becker, & Handelman, 1980).

O'Keefe and Nadel identified neurons within the hippocampus that fired when a rat was visiting a particular place. If objects were moved in the environment, these 'place cells' ceased to fire in locations they had previously been active. By O'Keefe and Nadel's definition, a cognitive map is an area in long-term memory of a representation of different places connected by distance and direction. The strategy of learning maps was called cartographic strategy, and it was proposed that this was an independent, entirely different type of learning. Navigation based on cognitive maps is separate from navigation toward a visible target, also called a taxon. An important aspect of this theory is the exploratory behavior involved in cognitive mapping. When a mismatch occurs between the cognitive map and the perceived environment 'displace cells' in the hippocampus fire, which leads to exploration, during which any changes present in the environment are then incorporated into the map. This would suggest that locomotion plays an important role in the making of cognitive maps. The theta rhythm, a part of the brain that determines storage of sensory inputs into the hippocampus, codes sensory inputs and, at the end of movement, everything in the environment is related into the cognitive map (O'Keefe & Nadel, 1978). O'Keefe and Nadel suggested that the hippocampus both created and stored the cognitive map. This view has been altered more recently to suggest that although the hippocampus is important in forming the cognitive map it may be stored elsewhere in the brain (Eichenbaum, Otto, & Cohen, 1994; Jarrard 1993; Olton, Becker, & Handelman, 1979; Rawlins, 1985).

Ellen (1980) questioned whether the hippocampus is the actual storage site for cognitive maps, as was suggested by O'Keefe and Nadel. Rats with damage to the hippocampus were tested on the three-table task. In this task, three tables are placed in a triangular formation with runways connecting them, and food is placed on one of the tables. Some animals were allowed to explore the tables prior to surgery while others were not allowed any exploration time. Seven out

of nine animals that were allowed to explore ran directly to the food after complete ablation of the hippocampus. Rats that were not given any exploration time were unable to find the food. This result seems to suggest that once the cognitive map was formed, it remained available for retrieval even after hippocampal damage. Furthermore, this result also suggests that the hippocampus is not the storage site for the cognitive map. Ellen also disagreed with the locomotion aspect of O'Keefe and Nadel's theory. He reasoned that locomotion alone did not ensure the formation of a cognitive map, and furthermore, locomotor behavior between two points is not essential in order for that information to be incorporated into a cognitive map. Maier (1932) used an earlier version of the three-table task to determine if when a rat learns the location of A relative to B did it also learn the location of B relative to A? Rats trained to run in a counterclockwise direction in order to obtain food all chose a longer indirect route to obtain food rather than turning around and reaching the food more quickly by running clockwise. However when the same task had been experienced in both directions, the rats chose the more efficient route for the food, even when not all of the legs of the triangle had been experienced in all directions. This would seem to indicate that mere exposure to spatial cues alone was not sufficient to learn spatial relationships between points in the room. Ellen also referred to the work of McNamara, Long, and Wike (1956) in which animals that were transported in small cars were able to learn location without actually using locomotor movement to explore the environment. Essentially, these results demonstrate that active interaction with the environment is required in order to learn a spatial location.

Recently, Astur, Taylor, Mamelak, Philpott, and Sutherland (2002) used the vMWM to study spatial memory in humans with hippocampal damage. The participants had received unilateral hippocampal removal as treatment for severe epilepsy (five had left-sided removals, five had right-sided removals). Four of the left hemisphere and two of the right hemisphere patients received a selective amygdalohippocampectomy. The other four patients received an anterior temporal lobectomy. All of the participants showed severe impairments on the vMWM

regardless of which hemisphere the hippocampus had been damaged although the amount of damage to the hippocampus in each participant was different in each case. This was unusual of learning/memory performance following hippocampal excision for epilepsy; in the past only damage to the right hippocampal formation resulted in spatial memory impairments. Interestingly, the learning impairment of hippocampus-lesioned rodents seems to be related to the volume of damaged tissue (Moser, Moser, & Andersen, 1993; Moser, Moser, Forrest, Andersen, & Morris, 1995). The participants with hippocampus damage in the vMWM study showed significantly less preference for the platform quadrant during a probe trial than controls. This study clearly shows the involvement of the hippocampus in spatial learning/memory tasks, and it was also important in that it was the first to test humans with damage to the hippocampus on a typically nonhuman spatial memory task.

Working Memory

Working memory has already been defined as containing trial specific information. Olton et al. (1980, p. 240) operationally defined the working memory components of experimental procedures as "those in which information on any single trial is useful only for that trial". Baddeley (1986, p. 34) referred to working memory as "the temporary storage of information that is being processed in any of a range of cognitive tasks". Working memory plays a vital role in many cognitive processes including reasoning, mental calculations, language comprehension, and spatial ability (Baddeley; Olton et al., 1980). All of these tasks require information to be readily accessible while at the same time new information is encoded and stored. The essential difference between working memory and short-term memory is that working memory involves actively manipulating information while short-term memory is passively storing information (Baddeley). Traditionally, working memory was thought to have a limited capacity, restricted only to primary memory (Atkinson & Shiffrin, 1968; Miller, 1956); however, more recent

hypotheses suggest that working memory capacity and duration is much greater if more complex tasks are to be accommodated (Ericsson & Kintsch, 1995).

Damage to the hippocampus has been shown to cause impairments in spatial working memory. Olton et al. (1980) found that rats with fimbria-fornix lesions had impairments on a spatial task with working memory components. The fimbria-fornix is a cholinergic pathway to the hippocampus from the medial septal region areas of the brain, and it is primarily responsible for information flow into the hippocampus proper. Damage to the fimbria-fornix has been shown to produce memory deficits on a variety of tasks including the MWM (Whishaw, Cassel, & Jarrard, 1995), radial arm maze, and other spatial tasks. Other researchers have also found that damage to the hippocampus impaired spatial working memory (Ferbinteanu, Ray, & McDonald, 2003; Pothuizen, Zhang, Jongen-Relo, Feldon, & Yee, 2004).

Other areas of the brain have been shown to be important in spatial working memory tasks. Passingham (1985) showed that monkeys with dorsolateral lesions to the prefrontal cortex were impaired on a spatial working memory task requiring them to test an array of doors for peanuts. The prefrontal cortex has also been implicated in spatial working memory tasks with humans. In a task similar to Passingham's, Owen and colleagues (Owen, Downes, Sahakian, Polkey, & Robbins, 1990) had participants search through a series of boxes to find a hidden token. The token is located in a previously unused location with each subsequent trial. Patients with frontal lobectomies had much greater impairments on this task than controls. Imaging studies also have implicated the prefrontal cortex in spatial working memory. Jonides and colleagues (Jonides, et al., 1993) recorded positron emission topography (PET) during a spatial working memory task. Activation was seen in the right-hemisphere prefrontal cortex. Jonides et al. suggest that the prefrontal cortex is responsible for storing spatial information for short periods of time. Courtney (1998) used functional magnetic resonance (fMRI) to examine participants performing spatial working memory tasks. The fMRI indicated sustained activity in

the superior frontal sulcus, an area in the prefrontal cortex, during spatial working memory tasks. This further implicates the role of the prefrontal cortex in spatial working memory.

Gender Differences and Spatial Ability

Researchers began noting gender differences in spatial ability several years ago. Maccoby and Jacklin (1974) report an advantage in men in spatial ability tasks such as mental rotation, maze performance, spatial orientation tasks, and spatial relationships beginning in adolescence. Indeed, the belief that men are better than women at spatial abilities has been entered into many introductory textbooks. Tapley and Bryden (1977) found that men were more accurate and faster to complete a mental rotation task than women. Briefly, mental rotation involves participants viewing a two-dimensional representation of a three-dimensional object and then matching which of four other objects represent the first in a different orientation (Shepard and Metzler, 1971). Tapley and Bryden suggested that the improved accuracy of men may reflect a general superiority in spatial ability for men.

In a meta-analysis of 172 spatial ability studies, Linn and Peterson (1985) found gender differences on some spatial abilities, but certainly not all spatial abilities. Large gender differences were only found on measures of mental rotation. The mental rotation used pairs of three-dimensional objects rotated to different angles. Participants were asked to determine if the pairs of objects are the same shape or are different shapes. A smaller gender difference was observed on measures of spatial perception. In spatial perception tests, participants must determine spatial relationships with respect to their own bodies despite conflicting information. Men were found to be superior to women on both mental rotation and spatial perception. No gender difference was observed on measures of spatial visualization. Tasks categorized as spatial visualization tests involved complicated, multi-step manipulations of spatial information requiring analytic strategies to solve the tasks. Spatial visualization tasks are may involve processes required for spatial perception and mental rotation but are distinguished by the

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possibility of multiple solution strategies. Multiple theories have been proposed as to why gender-specific differences appear in spatial ability tasks, including both evolutionary theories and theories related to hormonal function.

Evolutionary Theories of Spatial Ability. Two basic hypotheses have been proposed regarding gender and spatial ability. The first contends that spatial navigation skills are related to mating systems among mammals. The second theory points to differences in foraging styles among human hunter-gatherers. Gaulin and colleagues argue that spatial ability evolves in response to environmental demands (Gaulin & Fitzgerald, 1986; Jacobs, Gaulin, Sherry, & Hoffman, 1990). Male polygamous meadow voles have range sizes four to five times larger than female polygamous meadow voles. The sex difference in range size is not evident in immature meadow voles or outside the breeding season, indicating that range expansion is a male meadow vole reproductive tactic. This increased range size gives the male vole an improved advantage in successfully finding breeding mates. This difference in range size is not noted in monogamous prairie voles. Gaulin and collaborators hypothesized that polygamous male voles would have increased spatial ability. Male polygamous voles were found to have superior spatial maze performance than female voles. This difference was not observed in the monogamous vole species (Gaulin, Fitzgerald, & Wartell, 1990). Jacobs et al. (1990) postulates that the laboratory rat is of polygamous ancestry and this explains much about the male dominance of many maze types. Jacobs and colleagues have speculated that if spatial ability was evolutionarily influenced, then differences should arise not only in maze performance but also in physiological differences. They found that only in the polygamous voles did males have significantly larger hippocampi than did polygamous females. No sex difference was noted in the monogamous species. Jerison's principle of proper mass states "The mass of neural tissue controlling a particular function is appropriate to the amount of information processing involved in performing the function" (Jerison, 1973, p. 202).

Silverman and Eals (1992) point out that among hunting-and-gathering peoples, men hunt and women gather. They claim that men should exceed in some types of spatial tasks because they pursue prey and that women should exceed at other types of spatial tasks in which gathering skills are needed. Successful hunting relies on abilities to "orient oneself to objects or places that are either in view or conceptualized across distances, and to perform the mental transformations necessary to maintain accurate orientation during movement" (Silverman & Eals, 1992, p.534). Successful gathering depends on abilities to remember the locations of resources and related stimuli and be able to return to these locations. In a series of studies, Silverman and Eals reported on the exercise of spatial ability tasks; a significant gender difference for mental rotations and space relations favoring men was reported in addition to a significant gender difference for object memory favoring women. In addition, an advantage in location memory has been reported for women (Dabbs, Chang, Strong, & Milun, 1998; Eals & Silverman, 1994; McBurney, et al., 1997; Silverman & Eals, 1992). The results vary depending on a number of variables including type of task, instructions, and type of object presented. McBurney et al. administered the game Memory™, which consists of several small cards with pictures on one side lain face down in front of the participant; the participant then is allowed to turn over two cards at a time and try to match the cards and remove them from the field of play. The researchers deigned the game as an object location task. They also administered a mental rotation task to male and female participants and found that women were significantly better with the recall of object locations and men were significantly better with the object rotation task.

In a series of three experiments Duff and Hampson (2001) used a spatial working memory task in which participants matched 10 pairs of colored dots. Similar to the Memory™ game, participants lifted flaps and tried to find the match of the colored dot under it. As the colored dots were paired, an experimenter placed a token matching the dot on a Velcro strip next to the array of dots. In this way, participants did not have to keep track of which colors they had already found but instead had to remember the locations of where dots were matched or not

matched. Working memory errors were recorded when a participant chose a pair of locations that had already been searched but did not match or when a participant re-searched an already matched pair. They found that women made fewer working memory errors than men and took less time to complete the task. Concerned that a female advantage in object location memory rather than a working memory component may be the reason for the gender difference, Duff and Hampson tested the same participants on Silverman and Eals' object location memory task. No significant gender difference was seen on this task. Using the object location memory scores as a covariate did not change the findings of the spatial working memory task. Zinser, Freeman, and Jennings (1999) also found female participants to have an advantage over male participants in recalling information about various product advertisements. This further supports a gathering hypothesis of spatial ability.

Men and women have been found to use different navigational strategies (Downs & Stea, 1977). Women tend to use topographic strategies while navigating, while men prefer Euclidian strategies (Choi & Silverman, 1997). Topographic strategies use landmarks, and Euclidian strategies rely more on distance and direction. Researchers also refer to two different types of knowledge used in way-finding: route knowledge and survey, or map, knowledge (O'Keefe & Nadel, 1978). Route knowledge depends on learning a sequence of instructions to get from one place to another, while survey knowledge uses cognitive mapping to integrate relationships of objects. O'Keefe and Nadel maintain that route knowledge is very rigid and more susceptible to loss of guidance or direction. Survey knowledge is much more flexible and allows for new information to be incorporated into the map. Bever (1992) found that women rely more on route knowledge and men rely more on survey knowledge. This correlates well with topographic and Euclidian strategy research. It is easy to see that route knowledge is more topographical, relying on specific directions and landmarks to navigate, and survey knowledge is more Euclidian; with an overall view of an area, it is much easier to guide by distance and direction. In evolutionary terms, hunters would need a "bird's-eye-view" of their location in order to track and hunt game

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through differing terrain, and gatherers likely stayed closer to home, remembering the locations of resources, children, relatives, and other social groups (Dabbs, et al., 1998). This would promote the development of Euclidian strategies in men, and topographic strategies in women.

Hormonal Theory of Spatial Ability. Sex hormones have been hypothesized to be a cause of sex differences in spatial ability. In fact, fluctuations in estrogen have been shown to be important to spatial processing in women (Galea, Ormerod, et al., 2000; Keenan, Ezzat, Ginsburg, & Moore, 2001). Female rats in estrus were more sensitive to spatial changes made within an environment and increased their exploratory behavior in contrast to that of females in proestrus or exploratory behavior in male rats (Tropp & Markus, 2001). Galea et al. (2000) found that pregnant rats were worse on a working memory test on the MWM during the third trimester of pregnancy, when estrogen levels are high, but were better during the first and second trimesters, when estrogen levels are relatively low. Similarly, MWM acquisition was found to be improved in female rats during the estrus phase, a time when estrogen levels are lower, than during proestrus, a time when estrogen levels are higher (Warren & Juraska, 1997). Testosterone injections given during the first week of life (PD 1-7) reversed the typical advantage of male rats over female rats in the MWM (Roof, 1993).

Increases in estrogen may not always be detrimental. Estrogen supplementation has been found to improve performance on aged males and ovariectomized females on the radial arm maze (RAM) (Bimonte & Denenberg, 1999; Daniel, Fader, Spencer, & Dohanich, 1997; Luine & Rodriguez, 1994; Luine, Richards, Wu, & Beck, 1998; Williams, 1996). Intrahippocampal estradiol injections improved MWM acquisition in ovariectomized female and male rats (Packard, Kohlmaier, & Alexander, 1996; Packard & Teather, 1997). Rissanen and colleagues (Rissanen, Puolivali, van Groen, & Rikkenen, 1999) found that ovariectomized mice given low, estrus-like, levels of estrogen were improved on the MWM, but not mice given high, proestrus-like, levels of estrogen. This seems to suggest that the effects of estrogen on spatial learning and

memory may be dose dependent as well as dependent upon the stage of the estrous cycle the female is in when behaviorally tested.

Contradictory results have been found regarding estrogen and working memory. Stackman, Blasberg, Langan, and Clark (1997) found no differences in spatial working memory across the estrus cycle in female rats. However, Daniel and colleagues (Daniel, Roberts, & Dohanich, 1999) found that ovarian associated hormones facilitated working memory, but impaired reference memory. In addition, Bimonte and associates (Bimonte, Hyde, Hoplight, & Denenberg, 2000) found that intact female rats performed better than males on working memory but not on reference memory in a water version of the radial arm maze. Finally, estrogen insensitive female mice made more working memory and reference memory errors on the RAM (LaBuda, Mellgren, & Hale, 2002), suggesting that circulating estrogen may have been impairing RAM performance.

One possible mechanism for hormonal influence on spatial performance is estrogen interactions with the acetylcholine (ACh) system. Estrogen is known to affect hippocampal anatomy and physiology in rats (Foy, Chiaia, & Teyler, 1984; Klintsova, Levy, & Desmond, 1995; Woolley & McEwen, 1992). Dendritic spine density in the CA1 area of the hippocampus proper has shown a 30% increase during proestrus (Klintsova et al.). Furthermore, female mice have been shown to be more sensitive to scopolamine, an ACh antagonist (Berger-Sweeney, Arnold, Gabeau, & Mills, 1995). Coinciding with this, estrodial injections improved MWM acquisition in males, but the effects were blocked by scopolamine (Packard et al.). Another possible mechanism that has been suggested is a stress/estrogen interaction in females. Increased estrogen impairs hippocampal function on aversive tasks, the MWM for example, but not on appetitively motivated tasks, like the radial arm maze (Markus & Zecevic, 1997). Female rats in proestrus have higher levels of stress hormones like corticosterone and adrenocorticotrophin (ACTH) (Viau & Meaney, 1991). Tropp and Markus (2001) suggest that impaired performance on aversive tasks may be due to a stress response during proestrus.

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Empirical Findings

Morris Water Maze Animal Studies

A number of studies have examined sex differences in rodents on the MWM. A large majority of these studies have found male rodents to be more proficient on spatial learning tasks (Einon, 1980; Galea, Kavaliers, & Ossenkopp, 1996; Roof, 1993; Williams & Meck, 1991). However, contradictory results have been found; for example Bucci, Chiba, and Gallagher (1995) did not demonstrate gender differences on the place version of the MWM. They gave the rats two days of pre-training in the water maze. During pre-training, rats received three trials per day with a hidden platform placed at a randomly determined location. Rats were given a probe trial every sixth trial, and no significant differences were found between males and females on acquisition or on the probe trial. Pre-training may account for the lack of differences found and has been suggested elsewhere (Perrot-Sinal, Kostenuik, Ossenkopp, & Kavaliers, 1996). Perrot-Sinal et al. (p. 1309) contend that thigmotaxis, "a behavioral response best described as wall hugging often observed when an animal is introduced to a novel, potentially risky, and thus stressful environment", may account for sex differences on the MWM, as females have been shown to display more thigmotoxic behavior than males (Kvist & Selander, 1994). To account for this, Perrot-Sinal, gave rats a pre-training phase, during which the rats received three trials per day for four days. The platform location changed during each trial. Additionally, a black curtain was placed around the water maze to eliminate all extramaze cues. During all phases of the experiment, pre-training, acquisition, and probe trial, the water temperature was maintained at 28°C, which is considerably warmer than most studies using the MWM employ (21°C). Sex differences were found during pre-training, with females exhibiting greater levels of thigmotoxic behavior. A sex difference favoring males was found in acquisition and the probe trials only in those animals that had not received pre-training. A sex difference favoring females was found on

the probe trial in animals that had been pre-trained. The pre-trained females spent significantly more time in the former platform quadrant. Perrot-Sinal suggested that past differences seen on the MWM may be due to nonspatial aspects of the task, such as stress.

Working Memory Animal Studies

Many of the studies assessing working memory in rodents used the radial arm maze. The RAM has 8-17 equally spaced arms radiating from a round central area. Most often a sub-set of the arms are baited in order to test both working memory and reference memory errors. The baited arms remain constant throughout testing. Re-entering a baited arm that an animal has already retrieved the food from is a working memory error. Entering an arm that has never been baited is a reference memory error. Several studies have found males make fewer working memory and reference memory errors than females (LaBuda et al., 2002; Mishima, Higashitani, Kazuhiko, & Yoshioka, 1986; Williams & Meck, 1991).

Bimonte and collaborators (Bimonte et al., 2000) used a water version of the radial arm maze. In this version four of the eight arms had platforms in them. When a subject found the platform it was returned to its cage and the platform was removed. The subject was then placed back into the maze and allowed to find another platform. This sequence was repeated until all four platforms were found. Working memory and reference memory errors can be recorded in the same way as a dry-land version of the RAM. However, a distinction was made between working memory correct errors (first and repeat entries into any arm from which a platform had been removed) and working memory incorrect errors (repeat entries into an arm that never contained a platform). Reference memory errors were considered to be when an animal made its first entry into an arm that had never contained a platform. Bimonte found that males made fewer reference memory errors during the last half of testing than females and females made fewer working memory errors of both types during the first half of testing than males in both rats and mice.

Gresack and Frick (2003) used Bimonte's water RAM protocol but used slightly different working memory and reference memory definitions. It was considered a working memory error if a subject entered an arm in which the platform had already been removed. It was considered an initial reference memory error the first time a subject entered an arm that had never contained a platform. It was considered a repeated reference memory error if an animal re-entered an arm that had never had a platform (Bimonte defined this as working memory incorrect.) Despite differences in definition, Gresack and Frick's study disagreed with Bimonte's. They found that males made fewer errors of all types during the first half of testing (trials 2-8), but no sex differences were found on the second half (trials 9-15). A possible explanation for the contradictory results could be a difference in training methodology. Bimonte tested her subjects for 12 days, while Gresack and Frick tested their subjects for 15 days.

Lukoyanov, Andrade, Madeira, and Paula-Barbosa (1999) examined both young (7 months), adult (16 months), and old (23months) rats on the place version and the match-to-place version of the MWM. In the standard or place version of the MWM they found young rats scored shorter swim distances than adult or old rats and also scored more platform crossings in the probe trial. No differences were seen between the sexes at any age. However, in the match-to-place version, old rats were impaired compared to adults and young rats. Furthermore, older male rats were more impaired than older female rats. No sex differences were observed in young or adult rats.

Virtual Morris Water Maze Human Studies

The development of a virtual version of the MWM, presented an opportunity to test spatial abilities in humans that can be directly related to findings with rodents. Some of the early work done with humans on the vMWM has merely replicated some of the work that had been done with rodents. For example, Jacobs et al. (1997) found that humans could learn the location of the platform based on distal cues alone, and that place learning based on distal cues does not

disappear when proximal cues are present, that place learning occurs when humans begin in novel start positions. This is similar to findings in rats. In a series of follow-up studies, Jacobs et al. (1998) found removing or altering the distal cues in the computer generated environment disrupted place learning, verifying cognitive mapping theory, which means that in the absence of proximal cues, place performance depends on distal cues. Participants were also able to locate the platform after observing it from a fixed location (placement learning) and after observing an experimenter locate the platform (observational learning). Participants allowed access to the experimental environment immediately before acquisition and probe trials (latent learning) did not learn the location of the platform more efficiently than those who were not allowed access. When all three training regimens were compared, it was found that observational learning was most efficient (Thomas et al., 2001).

Astur et al. (1998) were the first to study gender differences in spatial ability on the vMWM. In a series of three different place learning experiments, men had significantly shorter times to find the platform during acquisition, and spent significantly more of their swim distance in the platform quadrant. These differences were observed using a hidden platform, visible platform, and mixed hidden and visible platform versions of the vMWM. Some of the participants in the hidden platform experiment indicated that they thought the platform was moving, although the platform remained in the same position throughout all of the trials. In an attempt to make it apparent that the platform was not moving a variation of the virtual Morris water task was used in which the platform was visible during the first trial and hidden during the second trial, alternating throughout all trials. Men still found the platform faster during acquisition and spent more of their swim distance in the former platform quadrant than women on a probe trial. Additionally, men had significantly more platform crossings during the probe trial than women. This appears to suggest that behavioral mechanisms underlying place and cue learning may be similar, as suggested in a recent paper by Brown and Whishaw (2000b). Because a non-verbal attempt at changing participants' strategies did not work, Astur et al.

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(1998) used a more direct approach. They changed the instructions to indicate that the platform was always in the same location and that participants should use the landmarks and scenery in the room to remember the platform location. Despite this, men continued to show an advantage in all of the previously mentioned areas. No differences in swim speed were noted during any of the experiments.

Spatial working memory has been tested in humans as well as rats. In addition to the virtual Morris water maze, virtual versions of the RAM have also been created in order to test humans. Astur, Tropp, Sava, Constable, and Markus (2004) replicated their previous work with the vMWM. They also administered a mental rotation task and tested participants on the vRAM. Expectedly, men performed significantly better on the mental rotation task than did women. However, no gender differences were found in working memory or reference memory errors on the vRAM. Furthermore, when the response measures of the three tasks were correlated, it was found that only the mental rotation task and the vMWM were significantly correlated, suggesting that the vMWM and the vRAM do not reflect spatial memory in the same way.

Gender Differences and Strategy

A difference in navigational strategy is one explanation for the disparity seen in spatial navigation between men and women. Lawton (1994) administered a way-finding strategy scale and a spatial anxiety scale to introductory psychology students. The way-finding strategy scale measured the participants' use of route strategy versus orientation strategy when driving. Orientation strategy relies on monitoring oneself relative to reference points in the environment. Route-learning strategy relies on learning a sequence of directions or landmarks in an environment. The spatial anxiety scale measured the level of anxiety in situations where navigational skills are used. Lawton found that men were more likely than women to use orientation strategy and women were more likely than men to use route strategy. Furthermore,

women were more likely to report anxiety about navigation. Spatial anxiety was negatively correlated with the orientation way-finding strategy.

Other researchers have also examined gender differences and navigational strategies. Dabbs et al. (1998) administered a local navigation strategy test. Participants were given a map containing streets, intersections, traffic lights, other landmarks, and a legend showing a north arrow and a distance scale. The participants had two minutes to study the map and learn a route from one marked location to another they then turned it over and wrote directions as if they were explaining it to a friend. It was found that men were more likely to use miles and NSEW directions in their instructions, indicating a more Euclidian type of strategy. Women were more likely to use landmarks and left/right directions in their instructions. This research supports Lawton's work as well as Silverman and Eals' hunter/gatherer evolutionary theory of spatial ability.

The virtual water maze has also been used to study spatial navigational strategy. Sandstrom and colleagues (Sandstrom, Kaufman, & Huettel, 1998) administered three versions of the vMWM to participants. In the geometric condition the room was trapezoidal and contained no other landmarks. In the stable landmark condition, the room was octagonal and the landmarks were in the same location throughout all trials. In the random landmark condition the room was trapezoidal and the landmarks moved from trial to trial. No gender differences were observed in the stable landmark condition. Men were not as affected as women were in the geometric and random landmark conditions. Women were unable to learn an adequate strategy in the geometric condition. Both genders seemed to rely on landmarks, but the men were better able to adapt to geometric only conditions in locating the platform.

Astur et al. (2004) did a post hoc examination of swim strategy in their vMWM research. They categorized all the participants as one of four different types of strategy: Direct swim strategy participants swam directly to the platform. Circle strategists swam in circles from a fixed distance from the wall until the platform was located. Participants categorized as using

landmark strategy swam to a certain location, oriented toward a landmark, and then swam to the platform. Finally, participants exhibiting a zigzag strategy swam back and forth in a crisscross manner until the platform was located. Men tended to use a direct strategy, whereas women tended to use nonspatial or unclassified strategies to locate the platform. These classifications indicated that men are more likely to employ a spatial strategy to solve the vMWM compared to women.

Statement of the Problem

The current study was designed to test gender differences and spatial working memory using a match-to-place version of the virtual Morris water maze. The match-to-place task is commonly used to assess working memory in rodents on the MWM. Although gender differences and other aspects of spatial memory have been examined using the vMWM, working memory has not been studied on this particular task. This study is designed to analyze different parameters of gender differences on a working memory version of the virtual water maze. Participants will be tested on a MTP version of the vMWM. In the first experiment, the release point and platform locations changed ever two trials. This methodology was based on the MTP rodent literature. In a second experiment, the release point and platform locations changed every four trials. This methodology was developed in order to reveal a more robust gender difference. In the third experiment, participants received a random cues condition in which the distal cues in the virtual environment change throughout testing. Acquisition latency, path length, heading error, and first movement will be scored as dependent measures.

CHAPTER 2

EXPERIMENT 1

Methods

Participants

Seventy-one undergraduates (22 men; 49 women) from East Tennessee State University were recruited from an upper division psychology class. Students participated in the study as part of a class project.

Apparatus

A Dell personal computer with a 15" SVGA color monitor was used for testing. Participants navigated through the mazes using the arrow keys on a standard keyboard. The virtual water maze program was purchased from NeuroInvestigations (Lethbridge, AB, Canada) with funding from a Ronald McNair fellowship. Briefly, the virtual Morris water maze consists of a three-dimensional environment of a square room with a large circular pool in the center. Various landmarks including a door, window, pictures, and bookshelves surround the pool. Participants were allowed to move freely within the virtual environment by using the arrows in the computer keyboard. At all times, their viewpoints were slightly above the water level. The platform was hidden under the surface of the water. An aerial view of the maze area can be seen in Figure 1, as well as a participant's viewpoint during testing in Figure 2.

Procedure

Participants were given oral instructions on how the task would proceed. All participants were told to use the arrow keys on the keyboard to navigate through the maze. The view on the screen was a first-person view, so that if they pressed the right arrow key, the view on the screen panned to the right, the up arrow key moved them forward, and so on. The virtual room was

square and had one extramaze cue on each wall including a window, door, shelves, and a picture that remained the same throughout testing.

Participants were instructed that they would find themselves in a virtual pool of water, and that their goal was to find the hidden platform in the pool as quickly as possible. Participants started from one of eight different locations in the pool environment. They were released from the north, south, east, west, northeast, northwest, southeast, or southwest release points. Note that these starting points are not compass points; rather, they are directional relative to the pool environment. Starting locations were determined at random, and all starting locations were used by all participants. The platform was located in one of 10 different locations in the virtual pool. The platform and starting locations changed every two trials for a total of 10 pairs of trials. The rationale for this procedure is based on the rodent literature, and studies typically use a training methodology of two training trials/day to a new daily platform location (Brandeis, et al., 1989; Morris, 1981; Whishaw, 1985). However, in this case, a daily training regimen was not possible as all training was completed in one session. Once a participant navigated to the platform location, the viewpoint on the screen would rise slightly above the water and a message stating "Platform found!" was displayed, along with a number of points awarded for that trial.. If the participant did not find the platform within 60 s, the platform was indicated by a visible cue appearing on top of the platform. Additionally, a message was displayed on the screen stating "The platform is visible, swim to it." The amount of time for the experiment to be completed averaged between 15 to 25 minutes.

Experimental Design

Acquisition latency, path length, first movement, and heading error were recorded and analyzed as dependent measures for each trial. Acquisition latency was the length of time measured in seconds the participant spent searching for the platform. Path length was the distance the participants moved from the release point to the platform relative to pool diameter.

First movement was the amount of time elapsed before the participant began to move from the release point. Heading error was measured as the angular deviation from a straight trajectory to the center of the platform from the starting position and was measured at the first instance when the subject's distance is greater than 25% of the pool diameter from the start position. If the subject found the platform before this criterion was met, the last point prior to climbing onto the platform was used to compute heading error.

Separate repeated measures analyses of variance (ANOVAs) were conducted on each dependent measure with trial block as the repeated measure. For analysis of Experiment 1, the average of each group of four trials were averaged to form five total trial blocks of two trials each. Thus, a 2 x 10 mixed factor ANOVA was used on each dependent measure. Additionally, the first and second trials were measured separately using a 2×5 repeated measures ANOVAs. All reported effects were significant at $p \leq 0.05$.

<u>Hypotheses</u>

<u>Hypothesis 1</u>:

Based on previous vMWM research, men will have shorter acquisition latencies than women.

<u>Hypothesis 2</u>:

Based on previous vMWM research, men will have shorter path lengths than women.

<u>Hypothesis 3</u>:

Based on previous vMWM research, men will have more accurate heading errors than women.
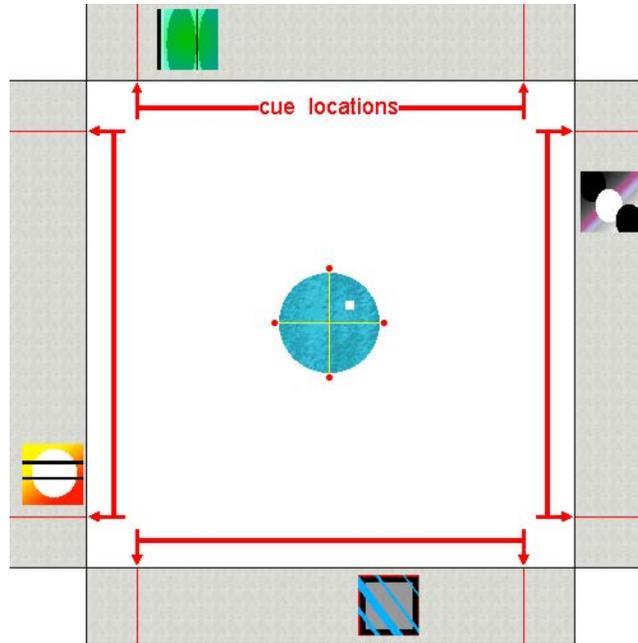
Figure 1. Aerial View of Maze. Note that surrounding cues are closer than they appear here.
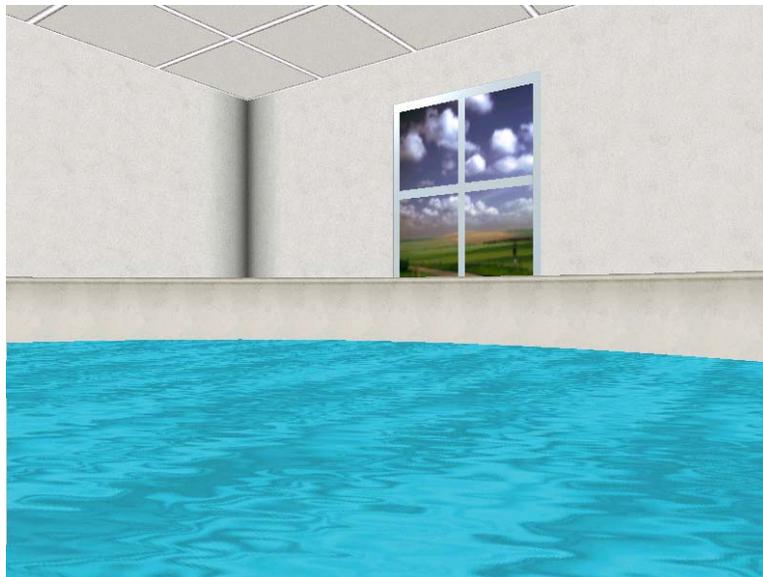

Figure 2. Screen Shot of Pool as Seen by Participant

Acquisition latency to locate the hidden platform was analyzed using a two-way repeated measures ANOVA which revealed a significant main effect of gender $F(1, 69) = 6.094$, $p = .016$ and trial block $F(9, 621) = 27.32$, $p < .0001$, but the Gender × Trial Block interaction was not significant ($p = .80$). As seen in Figure 3, men demonstrated significantly shorter latencies to find the platform compared to women. No significant differences between men and women were observed in path length $F(1, 69) = .07$, $p = .9341$, first movement $F(1, 69) = .397$, $p = .5308$, or heading error $F(1, 69) = 3.328$, $p = .0724$. However, a significant difference in heading error between men and women was found when analyzing the first trial of the trial blocks only $F(1, 69) = 4.339$, $p = .041$. The results (presented in Figure 4) appear to suggest that men were able to adjust to the changing platform location more rapidly than the women.
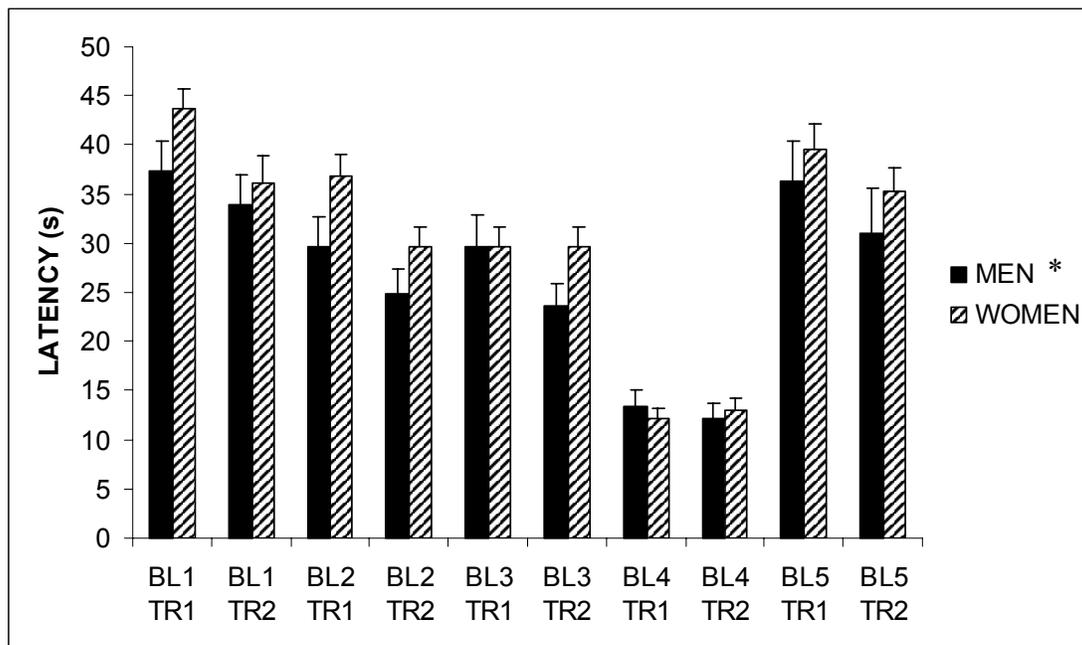

Figure 3. Experiment 1 Mean Acquisition Latency. As indicated by *, men had significantly shorter acquisition latencies than women.
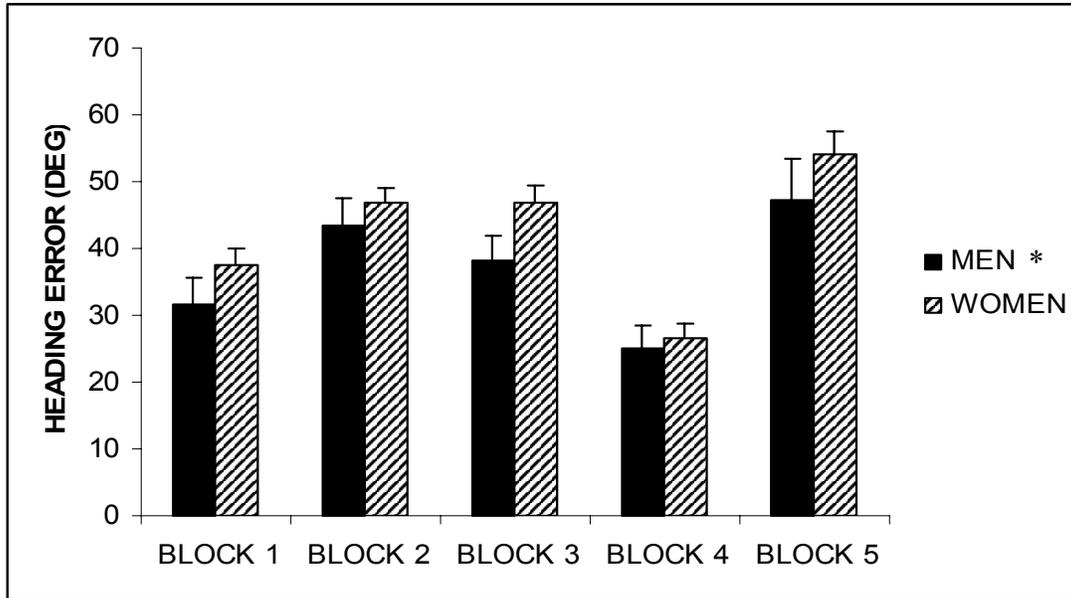
Figure 4. Experiment 1 Mean Trial 1 Heading Error. As indicated by *, men had significantly more accurate heading errors than women.

Discussion

As expected, the results of this experiment revealed that men were able to locate the platform location more rapidly than women and were able to adjust to the changing location of the platform more quickly than women. However, men did not have significantly shorter path lengths than women, as was hypothesized, although it approached significance ($p = .07$). As can be seen in Figure 3, the participants were demonstrating learning of the task until trial block 4. In this trial block, the platform and release points were located very near to one another. It appears that all participants were able to locate the platform extremely quickly during this trial block; however, in the last trial block all of the participants took longer to find the platform, similar to the first trial block. It is probable that finding the platform so quickly in one trial block actually hindered participants' performance on the subsequent trials. The methodology of this experiment was based on the rat literature. Although we were unable to have participants come back over a

series of days, as in the rat literature, they were given two trials before moving the platform. However, because they received all 20 trials in one day, it may have been more likely for proactive interference to occur. Many of the participants verbally indicated after completion of the task that they believed that the platform location was moved on every trial.

Based on the results from this experiment, a second experiment was designed that employed a new training methodology. The platform was to remain in the same location for four trials rather than two. We hypothesized that the participants should demonstrate better performance to locate the platform. However, this may also hinder flexibility. As stated in the introduction, past studies have shown that men demonstrate more flexibility in spatial ability than women (Lawton, 1994; O'Keefe & Nadel, 1978; Roof & Stein, 1999; Sandstrom, et al., 1998). If this is true, then using a four-trial procedure to each new platform location may reveal more robust gender differences than that shown in Experiment 1.

CHAPTER 3

EXPERIMENT 2

Methods

Participants

Sixty-six undergraduates (30 men; 36 women) from East Tennessee State University were recruited either by the ETSU research participant pool or directly from the classroom and received extra credit for their participation.

Apparatus

The apparatus used in Experiment 1 was also used in this experiment.

Procedure

The procedure for this experiment was identical to Experiment 1 except as stated below. The participants were released from the north, south, east, west, or southeast release points. Starting locations were determined at random and all starting locations were used by all participants. The platform was located in one of five different locations in the virtual pool environment. The participants were asked to perform 20 trials with the platform and starting locations moving every four trials for a total of five trial blocks. The same environmental cues from Experiment 1 were used and remained stationary throughout testing.

Experimental Design

The same dependent measures were employed in this experiment as in were in Experiment 1. Separate 2×10 repeated measures analyses of variance (ANOVAs) were conducted on each dependent measure with trial block as the repeated measure. For analysis of Experiment 2, every two trials were averaged to form two trials for each trial block. All reported

effects are significant at $P \le 0.05$ and Fisher's LSD post hoc tests were used to analyze any significant interactions.

<div align="center">Hypotheses</div>

Hypothesis 1:

Based on the results from Experiment 1 as well as previous vMWM research on gender differences, men will have shorter acquisition latencies than women.

Hypothesis 2:

Based on the results from Experiment 1 as well as previous vMWM research on gender differences, men will have shorter path lengths than women.

Hypothesis 3:

Based on the results from Experiment 1 as well as previous vMWM research on gender differences, men will have more accurate heading errors than women.

<div align="center">Results</div>

Acquisition latency to locate the hidden platform is presented in Figure 5. A two-way repeated measures ANOVA revealed a significant main effect of gender $F(1, 64) = 6.182$, $p = .015$, trial block $F(9, 576) = 10.874$, $p < .001$, as well as a significant gender × trial block interaction $F(9,576) = 2.843$, $p < .002$. As presented in Figure 5, Fisher's LSD post hoc tests revealed that men had significantly shorter latencies to find the platform than women at trial 1 of the first trial block and trials 1 and 2 of the second trial block.

Path length is presented in Figure 6. No significant main effect of gender was seen in path length ($p = .62$); however, a significant Gender × Trial Block interaction was observed for path length $F(9,576) = 2.049$, $p = .032$. Fisher's LSD post hoc tests revealed that men had significantly shorter path lengths than did women on trial 1 of the first trial block and both trials of trial block 2. No significant differences between men and women were observed in heading error $F(1,62) = 2.333$, $p = .13$ or first movement $F(1,63) = 2.442$, $p = .12$.

Because of the similar effects across both acquisition latency and path length, we ran an additional analysis. A Pearson's r correlation coefficient was used to correlate these two dependent measures, and acquisition latencies were found to be highly positively correlated with path lengths ($r = .933$, $p < .0001$). Therefore, it appears that the time to locate the platform and length of the search path may be highly related.
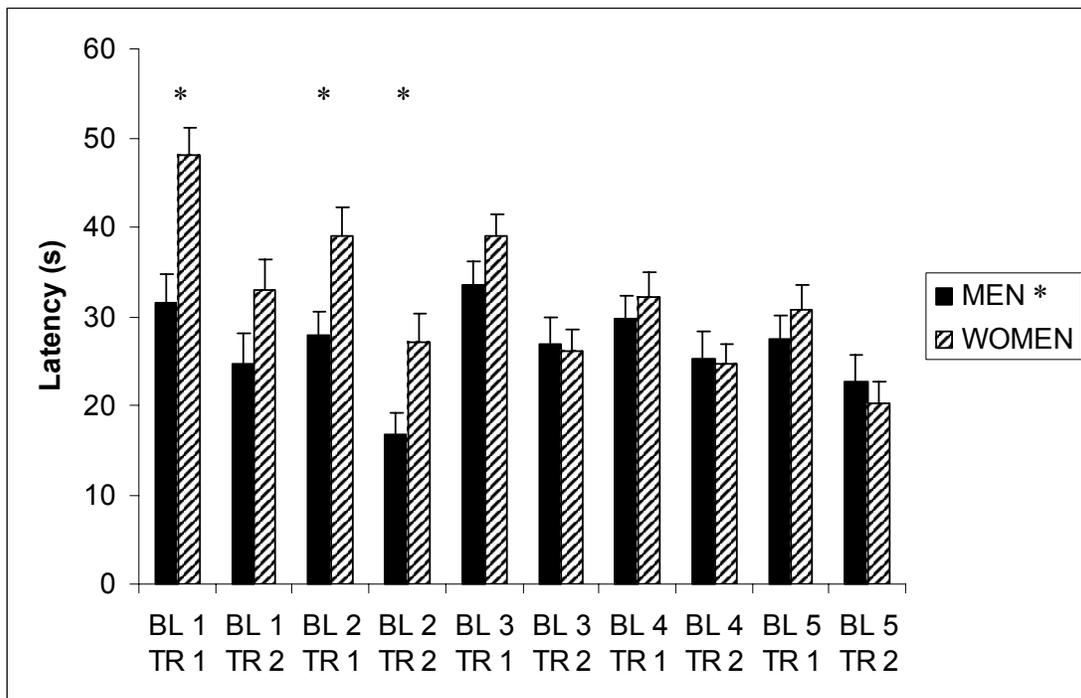

Figure 5. Experiment 2 Mean Acquisition Latency. As indicated by *, men had significantly shorter acquisition latencies than women at block 1 trial 1 and both trials of block 2.
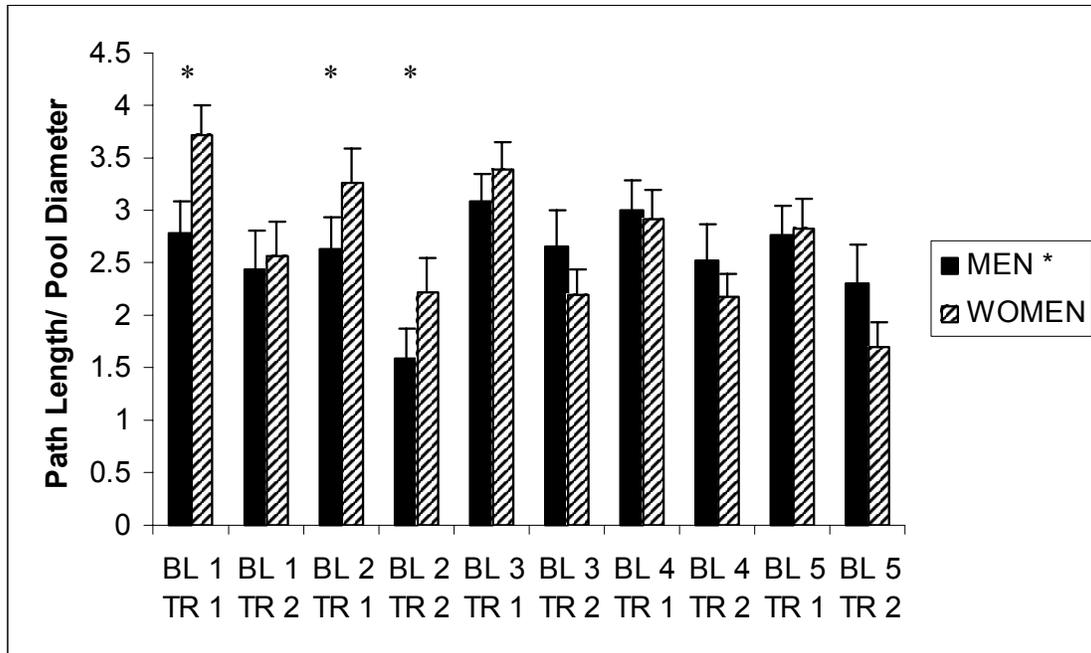
Figure 6. Experiment 2 Mean Path Lengths. As indicated by *, men had significantly shorter path lengths than women at block trial 1 and both trials of block 2.

<div align="center">Discussion</div>

As hypothesized, the results of Experiment 2 revealed that men navigated to the platform locations at a faster rate compared to the women, especially in the first two trial blocks. Men also had shorter path lengths to the platform in the first two trial blocks. However, there were no significant differences between men and women in heading error accuracy. This may be due to the additional trials the participants received with the platform located in the same location. The longer trial blocks may have allowed the women participants to learn that the platform was moving and to expect when the location changed. As can be seen in Figures 5 and 6, women were performing nearly equal to men by the end of testing. It appears that women were learning the task; however, men were learning it faster, indicating a rate of learning difference between men and women on this task. Additionally, women seemed to be more disrupted by the changing

platform location than men. As can be observed in Figure 7, women had more of a tendency than men to return to the previous trial's platform location before searching for the new location, especially in the first half of testing.

In order to determine how men and women use the information in their environment to navigate through space, a third experiment was conducted based on the results of the first two. In Experiment 3, participants were placed in a random cues condition in which the distal cues in the virtual environment changed throughout testing. Presumably, with no proximal cues present, and unpredictable distal cues, both men and women should be impaired in a spatial task. However, we hypothesize that men have an improved ability as compared to women to adjust the changing extramaze cues.

Woman
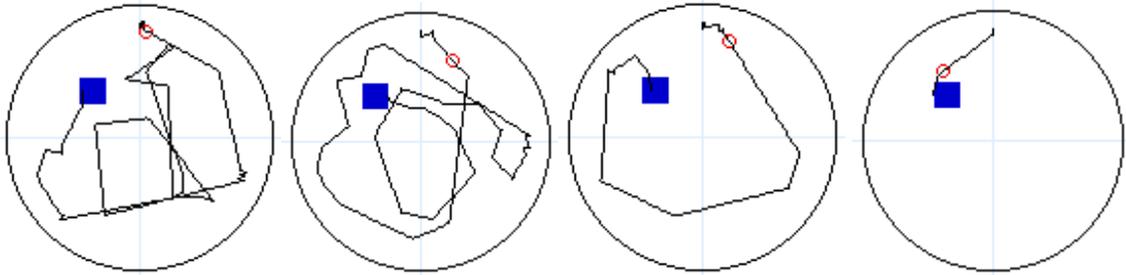
Block 1
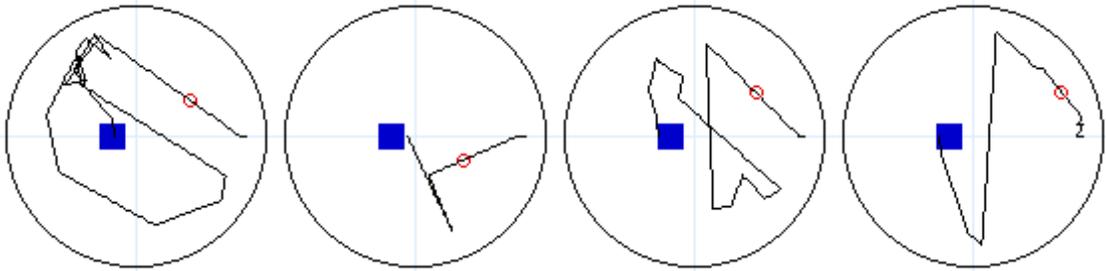
Block 2

Men

Block 1

Block 2

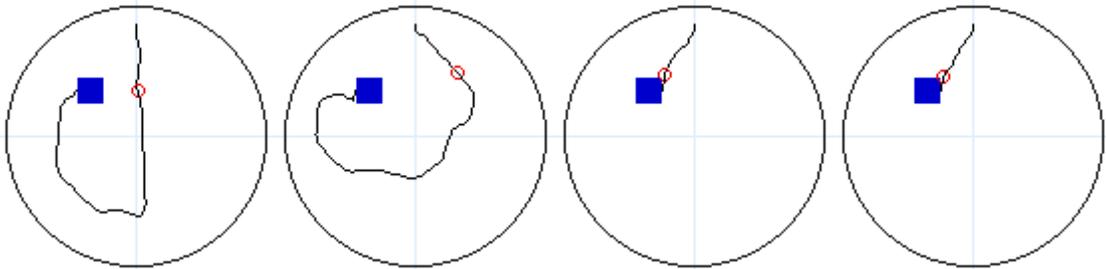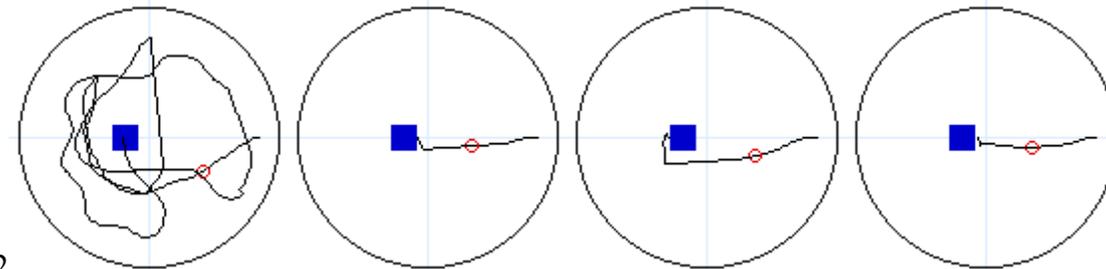*Figure 7*. Experiment 2 Representative Swim Paths. Note that the woman returned to the block 1 platform location more often than did the man during block 2.

CHAPTER 4

EXPERIMENT 3

Methods

Participants

Fifty-seven undergraduates (20 men; 37 women) from East Tennessee State University were recruited either by the ETSU research participant pool or directly from the classroom and received extra credit for their participation.

Apparatus

The same apparatus from Experiments 1 and 2 was used for this experiment.

Procedure

The procedure for this experiment was identical to Experiment 2 with a few exceptions. First, the environmental cues alternated randomly throughout testing between two different configurations. Environment A was identical to the one used in Experiments 1 and 2. Each wall displayed one of four cues: a window, door, bookshelves, or a picture. Environment B contained four new abstract art pictures on the wall; one picture represented on each wall. Additionally, the cues in environment B were not centered on the walls as the cues were in environment A. The pattern of environmental cue presentation was randomly assigned for each trial block as follows: trial block 1: ABAB; trial block 2: AABB; trial block 3: AABA; trial block 4: ABBA; trial block 5: BBBA. In trial blocks 1, 2, and 5, environment A and B were both presented twice. Note that in trial block 3 environment A was presented three times and environment B was presented once; In trial block 5, environment B was presented three times with environment A presented once. As in Experiment 2, the platform remained in the same location for each trial block and then

moved to a new location. To allow for comparisons across participants, all participants received the same pattern of environments during testing.

<u>Experimental Design</u>

The same dependent measures were used in this experiment as in were in Experiments 1 and 2. Separate 2 × 10 repeated measures analyses of variance (ANOVAs) were conducted on each dependent measure with trial block as the repeated measure. For analysis of Experiment 3, every two trials were combined to form two trials for each trial block. Additionally, the first and second trials were measured separately using repeated measures ANOVAs. All reported effects are significant at $p \leq 0.05$.

<div align="center">Hypotheses</div>

Hypothesis 1:

Based on the results from Experiments 1 and 2 as well as previous vMWM research on gender differences, men will have shorter acquisition latencies than women.

Hypothesis 2:

Based on the results from Experiment 1 and 2 as well as previous vMWM research on gender differences, men will have shorter path lengths than women.

Hypothesis 3:

Based on the results from Experiment 1 as well as previous vMWM research on gender differences, men will have more accurate heading errors than women.

<div align="center">Results</div>

Acquisition latency is presented in Figure 8 and was analyzed using a two-way repeated measures ANOVA which revealed a significant main effect of gender $F(1,55) = 10.831$, $p = .0017$, trial block $F(9,495) = 5.232$, $p < .0001$. However, the Gender × Trial Block interaction

was not significant F(9,495) = 1.628, *p* = .10. As can be observed in Figure 8, men had significantly shorter acquisition latencies than did women.

Path length is presented in Figure 9. A significant main effect of gender was revealed in path length F(1,55) = 4.520, *p* = .0380 and trial block F(9,495) = 5.232, *p* < .0001, but the Gender × Trial Block interaction was not significant F(9,495) = 1.759, *p* = .07. As observed in Figure 9 men had significantly shorter path lengths than did women. No significant differences between men and women were observed in heading error F(1,55) = 2.250, *p* = .1394 or first movement F(1,55) = .547, *p* = .4626. Additionally, acquisition latencies were found to be positively correlated with path lengths (*r* = .919, *p* < .0001).
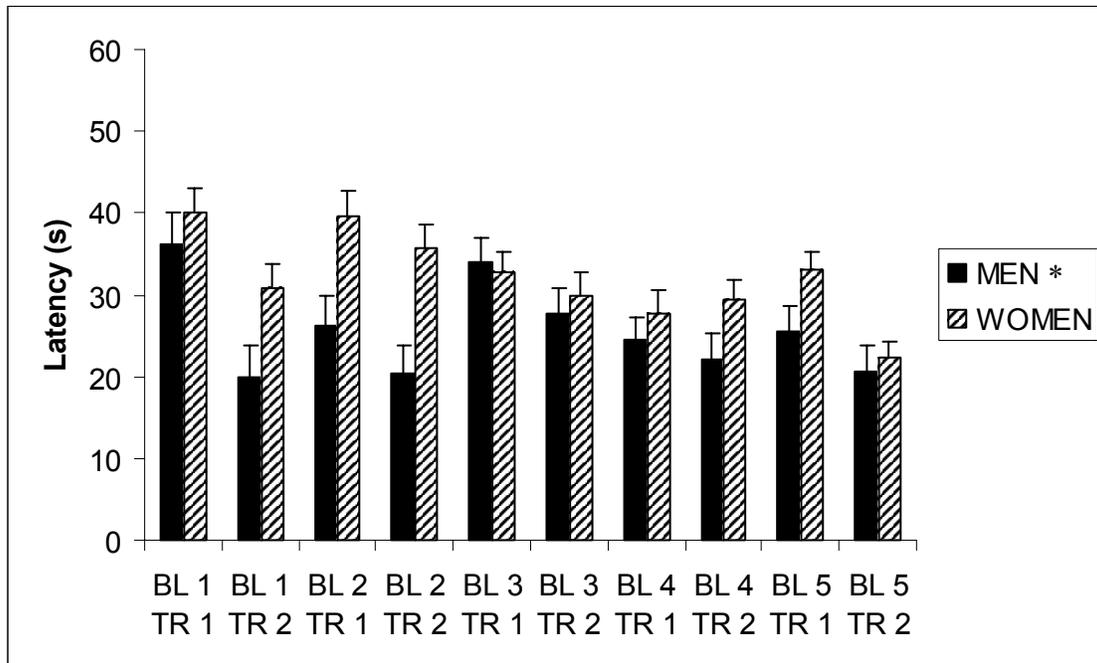
Figure 8. Experiment 3 Mean Acquisition Latency. As indicated by *, men had significantly shorter acquisition latencies than women.
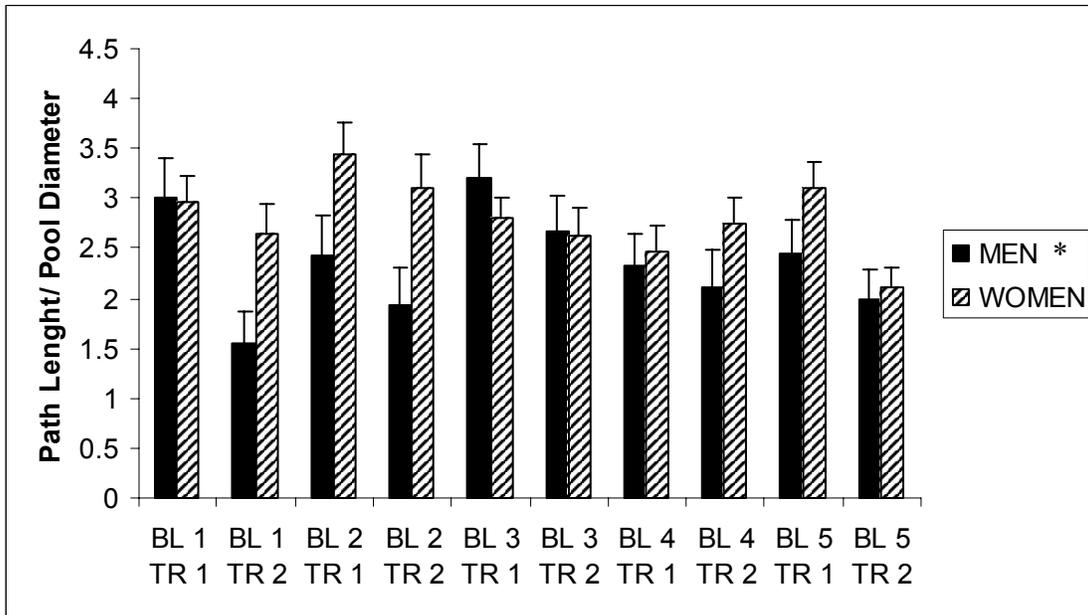
Figure 9. Experiment 3 Mean Path Lengths. As indicated by *, men had significantly shorter path lengths than women.

Discussion

The results of Experiment 3 revealed that men were able to find the platform locations more quickly and took shorter routes to the platform locations than women. Men and women did not have significantly different heading errors. As in Experiment 2, this may be due to the four-trial trial block. Based on this result, it appears that women were not able to adjust to the changing environment as compared to men, although both men and women demonstrated learning of the task. Although not significantly different, men had slightly lower mean latencies in Experiment 3 than in Experiment 2, while women had slightly higher mean latencies in Experiment 3 compared to Experiment 2. These results suggest that men were able to adapt to changing environmental conditions more quickly than women.

CHAPTER 5

GENERAL DISCUSSION

In this study we demonstrated that men navigate more efficiently than women in a working memory version of the vMWM either when given two trials or four trials before moving the platform location as evidenced by shorter acquisition latencies. These results are consistent with past research on the place version of the vMWM (Astur et al., 1998, 2004) that has shown gender differences exist on this version of the task; however, it extends these findings to a working memory version of the VMWM. Additionally, there has been one study to demonstrate gender differences on the working memory version of the VMWM in the rodent literature (Brown et al., 2005). Surprisingly, we also found that men navigate more efficiently than women in an unreliable landmark condition of the same task as evidenced by shorter acquisition latencies and shorter path lengths to the platform location suggesting that men have a more flexible cognitive map than women. It was also found that men were more accurate than women in the direction they navigated toward the platform in the first trial of the trial block when given two trials before the platform location changed. However, in the subsequent studies this gender difference was not seen, which may be due to the four-trial procedure in these experiments. The longer trial blocks may have allowed for more accurate navigation by the women.

Experiment 1 and 2 Evolutionary Differences

Taken together, the results from Experiments 1 and 2 suggest that men were able to adapt more quickly than women to the changing platform location. Silverman and Eals (1992) hunter/gatherer theory of spatial navigation agrees with these findings. Men would have had to pursue a moving target in order to hunt and would demonstrate an evolutionary advantage in foraging and locating a moving target as compared to women. Women's gathering targets would remain relatively stationary, so it was more important to be able to recognize valuable resources

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and return to the same stable stationary source. Our results show that women were able to learn the location of the platform but were more disrupted when its location changed. According to Silverman and Eals, one of the ways in which men and women are evolutionarily equipped differently is the type of knowledge that they employ to spatially navigate. Men use more flexible survey knowledge allowing them to adapt to new information in their environments, while women use route knowledge which is more rigid and does not adapt as easily to changing information (Bever, 1992; O'Keefe & Nadel, 1978).

<u>Experiment 1 and 2 Anxiety Differences</u>

Women and female rats have been found to have more spatial anxiety than men or male rats, as measured by self-report or thigmotaxis, respectively (Lawton, 1994; Perrot-Sinal et al., 1996), which may help to explain these results. However, Perrot-Sinal only found more anxiety in female rats in aversive tasks such as the MWM. In the virtual MWM, participants do not actually feel any personal discomfort as they would in a real swimming environment. They do not feel fatigued or are under the duress of the possibility of no escape, thus there are limits to these conclusions. Participants were specifically informed that there was a time limit to the experiment and the platform would be revealed to them eventually. Also, human participants are in an environmentally controlled room during testing, unlike the cooler water of the MWM. Women may have felt stress or anxiety during testing but it is more likely that it was due to other sources than aversive task conditions.

Anxiety about the task may have been related to the awareness in the women participants of the stereotype that spatial skills are primarily masculine. If women have been told that they do not perform as well in spatial tasks as men, as has been suggested elsewhere (Harris, 1981; Maccoby & Jacklin, 1974), this may negatively affect their results. Newcombe, Bandura, and Taylor (1983) have argued that activities likely to enhance spatial skills are perceived to be masculine rather than feminine. Maccoby and Jacklin suggest that men may have more

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experience with spatial tasks because of social pressures. Evans (1980) reported that girls in a small New England town had smaller range sizes than boys and had smaller less accurate sketched maps of the area than did boys, coinciding with Gaulin and Fitzgerald's (1986) and Gaulin et al.'s (1990) meadow vole findings. In a review of several evolutionary theories, Jones, Braithwaite, and Healy (2003) found that range size was most consistent with available spatial data. Lawton (1994) found spatial anxiety to be negatively correlated with orientation way-finding strategy and suggested that anxiety may have a negative impact on self-esteem as well as the motivation to explore unfamiliar environments. Interestingly, in a study by Schmitz (1997) of way-finding ability in boys and girls aged 10-17 years in a real environment, girls were found to be more anxious and fearful than boys and moved slower through the maze than boys. Participants who were more anxious and traveled the maze more slowly remembered more landmarks but fewer directions than less anxious participants, correlating with gathering theory of spatial navigation. When the platform location moved during the experiments in the current study it may have increased women participants' confusion levels, and thus anxiety and decreased their ability to focus on the cues necessary to successfully navigate throughout the maze.

Experiment 3 Evolutionary Differences

The results from Experiment 3 agree with hunter/gatherer theory of Silverman and Eals (1992). Not only would men have to pursue a moving prey in order to hunt but they would also have to pursue it through different or possibly even changing environments. In Experiment 3, the environmental cues were changing although the platform remained in the same location for four trials before moving to a new location. Hunters would have dealt with a changing environment on a daily basis; some cues would remain the same but may differ during changing weather patterns and seasonal changes, so the hunters would not have always relied on landmarks but would have attended to many different types of cues such as distance and direction, developing

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Euclidian strategies to solve spatial tasks. Evolutionarily speaking, men should be better suited to the Experiment 3 conditions than women. The gender effect may have been a joint product of both the changing platform location and the changing environmental cues.

<center>Strategy Differences</center>

As discussed previously, stress or anxiety may also have contributed to women's decreased performance in this experiment but may have been compounded by the changing environment. The unstable landmarks in combination with the moving platform locations may have increased confusion levels in women, thus increasing spatial anxiety. Men were not as disrupted by the environment change as women were, raising the question: how were men locating the platform? A possible explanation to this question is that the room geometry did not change throughout testing. Although the room was square, the men may have been able to use the angles of the room to aid them in navigating to the goal. Sandstrom et al. (1998) found that men were better in a random-landmark and geometric-only conditions of the place version of the vMWM but found no gender difference in a stable landmark condition, where the room geometry was of little use. In this experiment, the landmarks were of little use to the participants but the shape of the room remained the same. Williams, Barnett, and Meck (1990) found that male rats attend primarily to the global shape of the environment while female rats give approximately equal weight to landmarks and environmental geometry. Dallal and Meck (1990) suggested a male rat hierarchy of spatial strategy: (1) the metric relationship of each goal's location within the entire environmental framework (e.g. its latitude and longitude), (2) the geometry of the global environment, and (3) the features of the environment, such as landmarks. If men and women attend to different types of environmental cues to solve a spatial working memory task, then Experiment 3 may have been unintentionally biased towards men's spatial abilities due to the changing landmarks but stable room geometry. However, in Experiments 1 and 2, the environmental cues remained stationary and a gender difference was still observed.

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Future research should address this issue by completely eliminating room geometry, possibly by testing in a round room during a random landmark condition.

Another explanation for men's improved vMWM performance involves use of the landmarks. Gwinn, Fernando, James, and Wilson (2002) found that men learned a route on a map faster when landmarks were present than did women but found no gender differences when no landmarks were present. As previously stated, women have more of a tendency than men to rely on landmarks to navigate and recall more landmarks than men (Galea & Kimura, 1993; Williams, Barnett, & Meck, 1990); however Gwinn et al. suggested that men used the position of the landmarks to make distance and direction judgments without paying attention to the nature of the landmarks. Women labeled landmarks and memorized the labels which may have interfered with learning the route. With no landmarks present both genders were hindered. Williams and Meck (1991) agreed that men are predisposed to use a single aspect of the environment, such as landmarks or geometry, to navigate; while women use multiple cues to navigate. Simplifying the environment, as men do according to Williams and Meck, would put less demand on memory. Women attend to more cues, thus putting more demands on memory and possibly interfering with navigation. Women in the current study may have been relying heavily on the landmarks, thus increasing memory demands when the environment changed, while men dismissed the landmarks or used them only cursorily, lessening memory demands.

Path integration may also play a role in the gender differences seen in Experiment 3. During path integration, an organism continuously estimates its position with respect to a reference point by relying on signals derived from locomotion (Etienne & Jeffrey, 2004). These signals may be visual, vestibular, or proprioceptive (feedback from muscles, tendons, and joints). Humans use a combination of path integration and external cues to navigate. When path integration and external cues are in conflict in a minor conflict situation such as one environmental cue moving after a goal has been located, priority is given to landmarks. In a major conflict of path integration and external cues, landmarks are ignored and priority is given

to path integration (Etienne, Maurer, & Seguinot, 1996). Men may be better at path integrating than women. In Experiment 3, women may have been relying on the landmarks to navigate, while men relied on path integration due to the major conflict.

Also male rats have been found to have greater response biases than female rats (Williams & Meck, 1991). A response bias may take the form of a directional bias such as turn left and circle the pool in progressively smaller concentric circles until the platform is located, or possibly crossing the pool or zigzagging until the platform is found. If men were not relying on environmental cues to locate the platform, they may have found the platform more quickly due to some sort of response bias. Upon examination of swim paths, some evidence of a response bias in men can be seen in a few individual cases; however, women seemed more likely to use a directional bias such as circling than did the men, as can be seen in the swim paths in Figure 10. Many women upon completing testing indicated that they did not believe there was any sort of pattern to platform locations. In this case, the women may have relied more heavily upon response biases such as circling than the men did in order to find the platform.

Woman
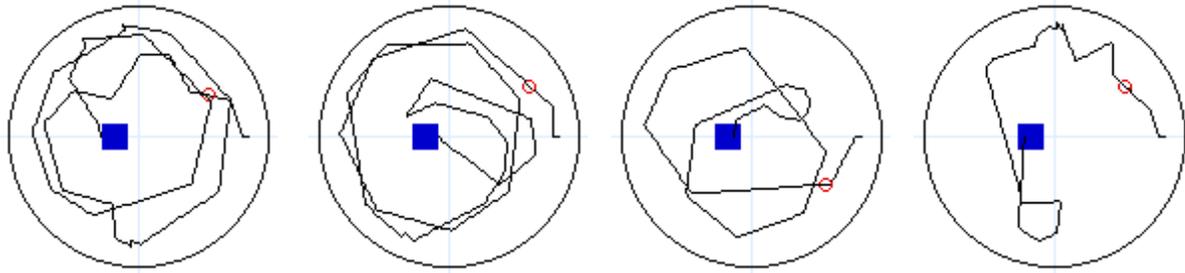
Man
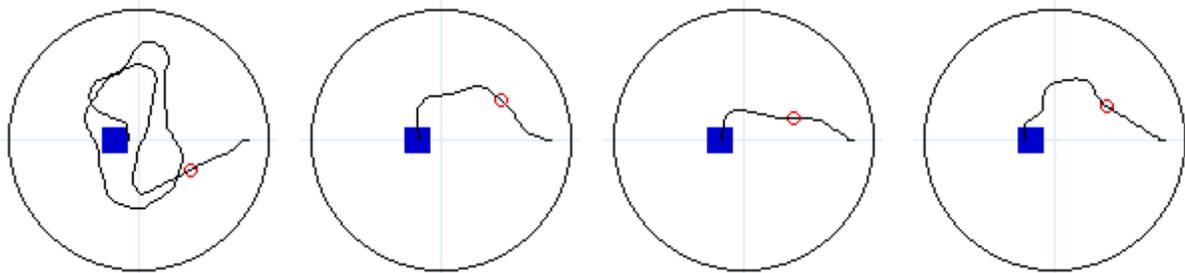
| TRIAL 1 | TRIAL 2 | TRIAL 3 | TRIAL 4 |

Figure 10. Representative Swim Paths of Trial block 2 of Experiment 3. Note the environment changed between trials 2 and 3.

<u>Limitations of the Current Studies and Suggestions for Future Research</u>

Admittedly, the presented experiments had several limitations. The condition of the participants such as mood, hunger, physical or mental health was not known at the time of testing. It was unknown if the participants were on any sort of medications that may have improved or hindered their vMWM performance. Brown et al. (2000a, 2001) have shown chronic nicotine to improve MWM performance in rodents. It was not known if any of our participants were smokers. Furthermore, we were unaware of any hormonal influences that may have affected participants' performance such as steroid use or menstrual cycle. As previously mentioned, the effects of testosterone and estrogen have had varying effects on spatial ability (Galea et al., 2000; Roof, 1993; Tropp & Markus, 2001). Interestingly, in a personal

communication, Hamilton finds no gender differences in the place version of the vMWM in honors students given no extra credit for participation. Intelligence measures were not taken in this study, nor did we ask the participants' GPAs. It would be interesting to see if there is a correlation between GPA and vMWM performance in future research.

The present findings are the first to indicate a significant gender difference on a working memory version of the vMWM. Specifically, these results indicate that men are better able to adapt to changing environmental conditions in cognitive mapping situations than are women. For this reason, this research makes a contribution to the accumulating virtual water maze literature. Acknowledgement of gender differences in a working memory spatial task should facilitate researchers' future analyses of spatial learning and working memory. Researchers should be aware of gender differences on this task when using it to test different populations. Future research should focus on the factors affecting virtual water maze performance such as strategy differences, stress, and spatial navigation experience. Specifically, participants could rate anxiety levels before and after testing to determine if anxiety could be affecting performance in either gender. Similarly, participants could be asked about activities that would lend to spatial navigation experience.

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