Neurofunctional Correlates of Geometry and Feature Use in a Virtual Environment Across the Lifespan

by

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Abstract

There are mixed results regarding the differentiation of neurofunctional correlates of spatial abilities. To help elucidate the existing mixed findings, three experiments were conducted. In Experiment 1, college-aged participants completed a virtual navigation task in which they learned the relationship between landmarks, environmental features, and a goal. The goal was a distinct landmark, or feature, consistently situated in one corner, or a geometric cue, of a rectangular room. Test trials varied the relationship of featural and geometric cues allowing insight into navigational strategies when using these cues. Results showed participants learned the task rapidly, and utilize both landmark and environmental geometry strategies to locate the goal; preferring the feature-based strategy. These results allowed for confidence to transfer the task into the 7 Tesla (T) Magnetic Resonance (MR) scanner in Experiment 2 with a similar sample. This experiment was conducted using functional Magnetic Resonance Imaging (fMRI) to determine neurofunctional correlates of environmental geometry and feature strategies. Behavioral results mimicked Experiment 1. Functional results showed activations in various navigationally relevant regions, such as the parahippocampus and caudate across strategies. Experiment 3 employed the same task with older adults (36-59 years old) to explore age differences in behavior or neurofunction. Behavioral results showed no differences across ages. Functional results revealed similar activations in navigationally relevant regions during the task. A comparison of neurofunction across ages was conducted to examine age differences. One finding was differential activation of the

parahippocampus across trial types and ages. Finally, volumetric comparisons were conducted on the hippocampus and caudate across ages. These results add to the knowledge of the neural function of these regions and the stability of the human navigation network across ages, and may inform our understanding of abnormal aging.

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Chapter 1: Introduction to Spatial Navigation

Imagine you have been hiking all day, and now have to return to your car. How will you get back to your starting position? There are many methods that can be used to reach your goal: follow the trail back, recall the locations of spatial cues you passed on your way up the trail, head east, etc. Many people will utilize many cues that are available (e.g., a distinct tree, some old ruins, a stream they crossed, how far they walked) to ensure they are following the correct trail and do not get lost. This activity of finding a location using features present in the environment is the process of spatial navigation (Brown & Terrinoni, 1996). The question of how humans and animals are able to recall locations with precise accuracy has been posed by many researchers (e.g., Gibson & Kamil, 2001; Kamil & Cheng, 2001). These questions have led to knowledge of landmark use (Sturz, Brown & Kelly, 2009), the ability to use bearing and distance of these landmarks to the goal (Forloines, Bodily & Sturz, 2015), and the influence of environmental geometry on successful navigation (Cheng, 1986).

Research on spatial navigation has involved a variety of animals in an attempt to determine their ability to successfully navigate to and away from their home, safety, or food. Many animals use landmarks to aide in navigation. A landmark can be defined as any object, natural or man-made, that is used to guide search to a specific location (e.g., a food cache, home, or place of safety; Brown & Terrinoni, 1996). An example of landmark use in animals was shown in the digger wasp. When a digger wasp nest was surrounded by a circular array of pinecones the wasps learned the association between the

pinecones and the entrance of their nest in the ground. When the circle of pinecones was shifted to another location close to, but not surrounding their nest, wasps would search in the center of the pinecone circle to locate their nest. These results suggest that digger wasps are able to encode and rely upon landmarks in their environment to locate their nest, and when this landmark array was displaced the wasps searched according to the landmarks (Tommasi & Laeng, 2012). Though experiments in the natural setting are the most ecologically valid forms of studying spatial abilities, most research is performed in the laboratory to control for any form of extraneous variable, and allow for an in-depth understanding of what animals are capable of using to navigate their environments.

This paper will discuss the ability for animals to utilize landmarks and geometric features in order to locate a hidden goal. Specifically, the wealth of research investigating the use of landmarks in animals (mainly humans) will be discussed. Successful landmark use is directly related to various features of the landmarks. In particular, landmark stability, predictiveness of the goal location, and whether the landmark is part of an array will influence animals' reliance to locate a goal. Further, there will be a discussion on how environmental features can be used in the absence of stable landmarks to guide search. This portion will elaborate on when environmental geometry will be preferred over landmark features and how this geometry can assist in goal localization. An in depth analysis on the differences in landmark and geometry use across ages ranging from childhood through adulthood will be presented. This analysis will lead into a summary of the differences in neural development and natural degeneration that could be a mechanism behind the differences in spatial navigation seen across the ages.

Landmark Use

The use of landmarks in navigation across a variety of experiments have expanded the knowledge of how and when animals will use these landmarks. This section will explore how animals have shown the ability to rely on single or multiple landmarks that denote specific goals (Chamizo, Rodrigo & Mackintosh, 2006), learn patterns of landmarks to locate specific goals (Brown & Terrinoni, 1996), treat distal and proximal landmarks different when locating a goal (Chamizo & Rodrigo, 2004), and the ability to judge precise distances and directions from landmarks to goal locations (Kamil & Cheng, 2001). Throughout the study of landmarks and their role in successful goal location, various factors that predict the usefulness of specific landmarks have been identified (Biegler & Morris, 1996; Forloines et al., 2015; Gibson & Kamil, 2001).

Location of a single goal is the most ecologically valid, however animals often rely on various pieces of environmental information to locate multiple previously stored caches (Gibson & Kamil, 2009). When training with multiple locations as goals, animals can learn to search in a pattern to locate the hidden goals. Rats trained in a room with a matrix of 25 bins in which four contained hidden food learned a pattern that denoted where hidden goals were located. Specifically, rats trained with a square or straight-line pattern of hidden goals would search the room for the first of four goals and subsequently show few errors when locating the next three goal locations. These results suggest that rats are capable of learning the pattern and are not searching the arena randomly (Brown & Terrinoni, 1996). Similarly, humans can also learn a pattern of four goal locations guided by landmarks as seen using both real and virtual environments (Sturz et al., 2009; Sturz, Kelly & Brown, 2010). Sturz and colleagues (2009; 2010) investigated whether

uniquely colored bins or landmarks placed at the center of a square or diamond shaped pattern would aid in participants' ability to locate the four bins that created the pattern. When using uniquely colored bins to signify the goal locations of a square pattern, participants showed greater accuracy overall as compared to those that were trained with uniformly colored bins (Sturz et al., 2009). Further, when participants were trained with one landmark in the center of a diamond pattern, uniquely colored bins, or uniformly colored bins, accuracy decreased as the cues that signified the location of the goal were removed. Specifically, search accuracy was greatest when the bins were uniquely colored. When the landmark was in the center of the square or diamond shape participants showed less search errors compared to when the bins were uniformly (Sturz et al., 2010).

In a cache and recovery procedure with only one goal, Watanabe (2005) trained western scrub jays to cache food in a tray that was denoted by a specific cue and positioned in a consistent location. At test, the training tray was moved to a different location and a new tray with a different cue was placed in the training location. This allowed for a cue competition test in which the training location and the distinct cues were in conflict. In another test trial type, the tray was moved to an alternate location with another distinctly cued tray in a location different from training, allowing for a non-competitive test trial where the training location was vacant. The question of interest was whether birds recalled the location of the cache, the distinct cue of the training tray, and what information they would use to recover caches. In the first competitive test trial, the majority of birds searched in the same location as training, essentially ignoring the cue; however, by the second competitive test trial birds searched at chance level between the

two tray locations. When there was no competition between location and tray cues, birds searched according to the correct cue. Overall, these results suggest that birds are capable of using local cues to guide search when the trained location of cache sites is unavailable, although they appear to prefer using location cues to guide search (Watanabe, 2005).

Importantly, the location of the landmarks relative to the goal can determine the success in goal localization. Clark's nutcrackers were trained to locate a hidden goal using landmark arrays that were consistently positioned in relation to the goal (Gibson & Kamil, 2001). During testing trials, the location of the landmarks and goals were shifted in the environment and the birds had to recall the landmark-to-goal relationship in order to find the hidden food. Various landmark arrays were presented such that some of the landmark arrays included the goal location within the array, while others were positioned with the goal outside of the array. Results showed that when the array contained the goal, the nutcrackers were more accurate in goal localization than when the goal was outside of the array. These results suggest that the relative goal position is an important aspect that will influence the birds' ability to use the landmark array to locate the goal.

In summary, the results show an ability to learn patterns of goal locations in order to locate multiple hidden goals (Brown & Terrinoni, 1996). Further, search accuracy will increase when landmarks or cues to signify the goal are present though patterns can be learned in the absence of specific cues (Sturz et al., 2009; 2010). Landmark arrays that denote single goal locations can be learned and when these are shifted during testing, animals can adjust search appropriately to locate the goal (Gibson & Kamil, 2001). However, various alternate factors will determine the reliability and ability to utilize

specific landmarks.

The following section will discuss what factors will influence the animals' ability to rely on specific landmarks to guide search. Two major factors, the stability and proximity to the goal, which will greatly change the predictiveness of the landmark-to-goal relationship, will be explored.

Landmark Stability and Proximity to the Goal

When landmarks are used for navigation, they can be used as single predictors of goal locations or as an array that signifies where a goal location is hidden. As mentioned, the location of the goal in relation to the landmarks or a landmark array will influence the usefulness of the landmarks in successful goal localization (Gibson & Kamil, 2001). In an experiment that required birds to rely only on landmarks, Sutton (2002) investigated whether birds could rely on multiple landmarks or only a subset of a landmark array to locate food. Pigeons were trained to find two goal locations denoted by distinct landmark configurations, and results showed that the birds reliably located the goals using the distinct configurations. In another experiment, two configurations were trained and then individual landmarks from each configuration were shifted toward the goal location during test trials. Pigeons were able to reliably locate the goal despite the shift in three of the five landmarks. Of note, when the two largest landmarks were shifted, search error increased suggesting these landmarks were weighted more than the smaller landmarks during search. The authors interpreted these results as suggesting that pigeons were locating the goal using information from multiple landmarks, but relied more heavily on the largest landmarks (Sutton, 2002).

The stability of landmarks and their relation to the goal can affect animals'

reliance on the unstable landmarks. Landmark stability has been examined in pigeons (Spetch, Rust, Kamil & Jones, 2003; Sturz & Katz, 2009) and humans (Forloines et al., 2015). When landmarks maintain a constant bearing or distance to the goal location but shift along the alternate dimension, pigeons and humans are able to locate a hidden goal. Specifically, if pigeons are trained that a hidden goal is located equidistant from two landmarks, and the landmarks are shifted either toward or away from the goal location, pigeons will search in the centroid of the two landmarks, adjusting their search to account for the novel position (Sturz & Katz, 2009). Humans, when trained with various landmark presentations, will show greater search accuracy when the bearing is held constant as compared to when distance is constant; however, humans are generally precise when locating the hidden goal (Forloines et al, 2015). The reliance on unstable landmarks in goal location suggests that although landmarks appear unreliable in predictability of the goal they are reliable in terms of where the goal location appears.

Research investigating the influence of spatial proximity to a goal has been conducted to determine the effects of landmark-to-goal distance in successful goal location. In order to test this, rats were placed into a Morris Water Maze using one landmark positioned either directly above the platform, on the wall near the platform, or on the wall farther from the platform (Chamizo & Rodrigo, 2004). When comparing results from the near and above landmark placements, rats were faster to locate the platform with the landmark above the platform than with the landmark near the platform. When comparing latencies to locate the platform using the near or far landmark placement, results showed that rats were quicker to escape using the near landmark as compared to the farther one. Importantly, all rats searched in the quadrant of the platform

with greater accuracy as compared to chance regardless of which landmark was present, but were quicker to escape the pool in the presence of the proximal landmarks than the more distal landmarks (Chamizo & Rodrigo, 2004).

Rats trained to locate a platform in a Morris Water Maze using proximal and distal landmarks added further evidence that proximal landmarks are more reliable predictors of goal locations than distal landmarks. Of note, the placement and stability of these landmarks varied across trials. When the more distal landmark was stable, rats relied on the distal, rather than the proximal landmark (Timberlake, Sinning & Leffel, 2007). Biegler and Morris (1996) found similar results when testing the influence of stability and proximity to a goal location and the subsequent learning that can occur. Rats were unable to reliably locate a goal if tested with a landmark that was unstable in its relation to the goal during training.

In sum, proximal landmarks that are more predictive of goal locations are more likely to be relied on than distal landmarks (Timberlake et al., 2007). Alternately, when proximal landmarks are unstable in their position relative to the goal, they are less likely to be relied on as indicators of goal location (Biegler & Morris, 1996). However, if landmarks are consistently predictive in one aspect in relation to the goal, such as consistent bearing to the goal, humans (Forloines et al, 2015) and birds (Sutton, 2002) can rely on them to find hidden objects. Landmarks, while good indicators of goals, are not the only feature that can guide successful navigation. The next section will discuss how the environment itself can also be utilized to locate a hidden goal to the same extent as landmarks.

The Environment as a Cue

Watanabe (2005) showed evidence that the spatial location of a food cache in the environment could be used to guide cache recovery. In nature, animals are reliant on the spatial location of previously stored caches in order to precisely guide search. This idea led researchers to attempt to determine the role of environmental features when animals are searching for a goal. The assumption is that environmental geometry can be used as a cue to guide search. Cheng and Newcombe (2005) reviewed the evidence and proposal of a geometric module of spatial orientation. Creation of this module originated from a variety of experiments in which animals were trained in distinctly shaped enclosures and then tested with all non-geometric features removed. Results showed (similar to that of Watanabe, 2005) that animal are able to rely on the geometry of their environments to locate a goal using a view-based matching strategy. Importantly, the geometric information in this module is not necessarily learned by associative mechanisms, but rather is learned incidentally. In other words, the geometric information allows animals to determine if the egocentric view they perceive is correct based on the presence or absence of specific environmental features. An example of this was shown in rats that completed a reorientation task in which they were trained in a rectangular room with distinctly colored walls with food hidden in one corner. During tests, the walls were uniformly colored and the rats had to reorient themselves within the environment to locate the food goal. The errors seen were rotational errors based on the relative wall lengths of the original training procedure. For example, if the goal was located in relation to a long wall on the left and a short wall on the right during training, when the colored walls were uniform in test, the rat searched in either the correct location or in the

rotational equivalent using the long wall-short wall relationship (Cheng, 1986).

Though this theory seemed to explain how animals use geometric information, the findings of associative phenomena such as blocking and overshadowing suggested that the geometric information was also learned via an associative mechanism. As a result, Miller and Shettleworth (2007) proposed that geometry is treated like any other associative cue and could be influenced by factors such as saliency and predictability of the goal location. Unlike the geometric module assumptions, environmental information is not learned in a different way than other spatial information; geometric information could be overshadowed by featural cues, which disagrees with the geometric module (Cheng 2008).

In order to further the knowledge of the role of geometric information, Della Chiesa, Speranza, Tommasi and Vallortigara (2006) trained chicks to locate a goal using four landmarks creating a square shape equidistant from a hidden goal inside of a square-shaped enclosure. During tests, the landmarks were expanded to twice the distance from the goal, contracted to half the distance to the goal, or positioned in a rectangle. Chicks used both the environmental geometry and landmarks to guide their search based on the result of concentrated search near the center of the environment independent of landmark movements. In order to determine if the chicks were searching in the center of the landmark array or the enclosure, the researchers tested search behavior by shifting the landmark array toward one corner of the enclosure. Results showed that chicks were likely to search in the center of the landmark array rather than the center of the arena during this test. Chicks were able to encode the landmark features independently of the environmental cues, however when the landmarks were shifted in either an outward or

inward direction, chicks appeared to use the environmental information to guide search (Della Chiesa et al., 2006).

In another experiment examining the role of environmental geometry on search behavior, Sturz and Kelly (2009) employed a rectangular three-dimensional virtual environment in which humans were trained to locate a goal in a specific corner. The corners contained uniquely colored bins in which only one was rewarded. During testing, all bins were colored black, and the room size was varied in either an expanded or contracted rectangle, or a square. These test trials investigated whether humans encoded the environmental geometry of the rewarded corner, even though it was irrelevant during training. Results showed that human participants were able to locate the correct or rotationally equivalent corner well above chance in the expansion and contraction tests (Sturz & Kelly, 2009).

Previous research has shown that the use of geometry is based on encoding the particular wall lengths and corner angles (Della Chiesa et al., 2006; Sturz & Kelly, 2009), but the question as to how and when the geometric features will be used persisted. In particular, researchers manipulated the amount of consistent geometric features to determine how these manipulations would affect goal localization (Kelly, McNamara, Bodenheimer, Carr & Reiser, 2008; Sturz, Forloines & Bodily, 2012). One experiment was employed to determine if a principle axis of space could be assisting participants locate the goal (Sturz, Forloines & Bodily, 2012Participants were expected to visit the correct and geometrically correct corners in a rectangular shaped enclosure. The question was if they were dividing the room into two symmetrical halves and travelling to the correct corner based on this axis (see Figure 1). In order to test this, participants were

trained to visit the top right corner in a trapezoid shaped room, and test trials would determine what corner they would visit when presented with either a rectangular room or a parallelogram room. This parallelogram shape allowed for two correct corner angles, but no corner that matched the principle axis (i.e., participants would have to shift preference from the principle axis for environmental features). The rectangular room allowed participants to abide by the principle axis of space as no corners shared similar angles to the trained trapezoid room. This manipulation allowed for a test of participants' use of the principle axis of space as compared to the correct corner angles. Results showed that in the rectangular room, choices were made based on the principle axis of space. Alternately, when the correct corner angles were present in the parallelogram room, participants chose to visit the correct corner angles. These results showed that although participants learned that the rewarded corner was present in the top right portion of the principle axis of space (as seen in the rectangular test), when presented with similar corner angles (as seen in the parallelogram test) they relied on the visible environmental features rather than features that would have been correct according to the principle axis of space.

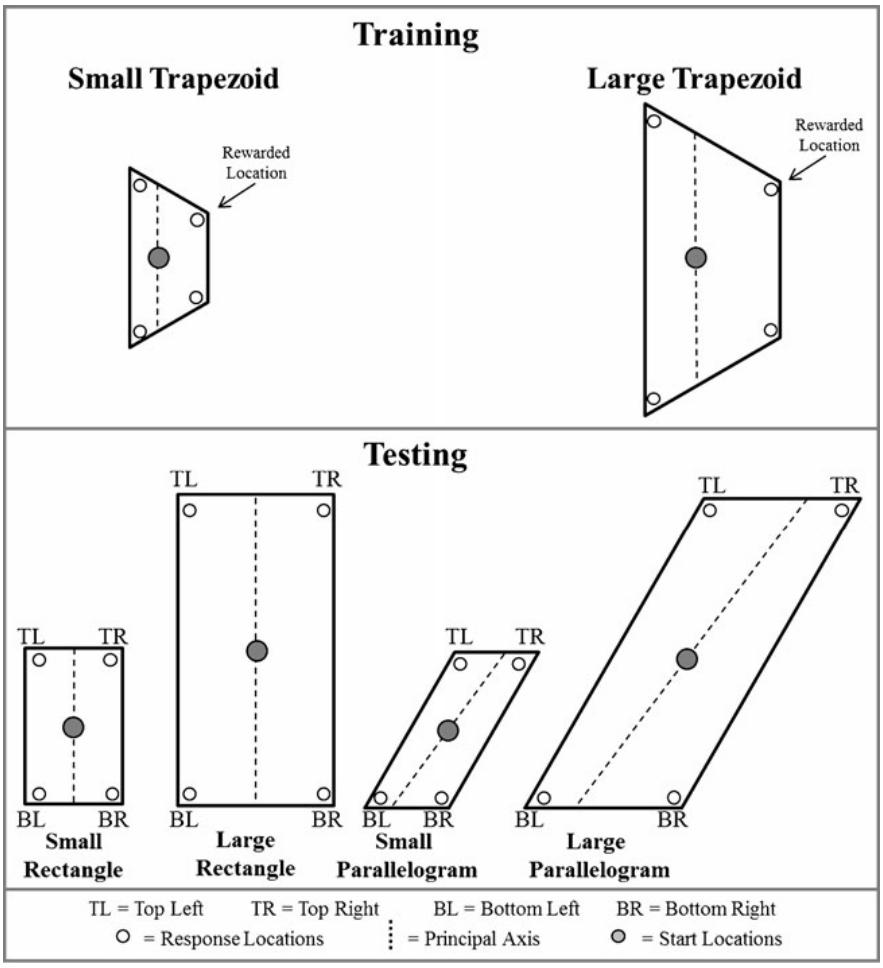

Figure 1. Experimental design from Sturz et al., 2013. The dotted line signifies the principle axis of space in training and testing rooms.

Another experiment challenged participants' ability to use the environmental features in a virtual environment by training them to locate a specific pillar in a circular formation in different shaped environments. Kelly and colleagues (2008) progressively increased environmental cues by using a circular room, square room, rectangular room, and trapezoid room that each contained the circular pillar formation and provided participants with varying degrees of geometric information. Participants were shown a specific pillar and told to recall the location of the pillar. While walking to the pillar, the walls disappeared (Experiment 1) or were changed while the participant was looking the

other direction (Experiment 2) and participants had to locate the to-be-remembered pillar. When the walls disappeared during testing, participants were able to use the stored image of the room geometry to locate the pillar, but took significantly longer paths when the room was circular and provided no geometric frame of reference. When the room features changed while the participant was facing the opposite direction, path lengths to locate the pillar were similar to that of the circular room results. The authors point out that even when the environmental features are removed during pillar localization, the geometric features allow for encoding of a stable frame of reference when locating a goal.

Together these results show that environmental features can be associated with the goal location to the same extent as the landmarks that are paired with the goal location. Environmental features that were assumed to be learned implicitly according to the geometric module (Cheng, 1986) are instead learned through an associative process and are able to be blocked and overshadowed by featural information (Miller & Shettleworth, 2007). Further, geometric features are preferred over a principle axis of space when these features are in conflict (Sturz et al., 2012), and geometric features can provide a stable frame of reference for goal localization even when the geometric features are removed, so long as they remain consistent throughout testing (Kelly et al., 2008).

Variations in Spatial Navigation Abilities Across the Lifespan

The ability to use landmarks and environmental geometry across the lifespan has been studied in depth. When placed into a room in which geometric and landmarks can be used to locate a goal, children and adults differ in the strategies they employ. The difference in strategies is thought to be dependent on the developmental trajectories

during maturation and natural neural degeneration (Newcombe, Huttenlocher, Drummey & Wiley, 1998; Rodgers, Sindone III, & Moffat, 2012). The following section will discuss the developmental differences across the lifespan beginning with children's ability to utilize landmarks and geometry and concluding with variations in strategy use by young and older adults.

In a task comparing college aged adults and children ranging from 18-24 months, Hermer and Spelke (1994) employed the reorientation task in which both groups were required to locate a hidden goal. When in a rectangular room, the children and adults are both able to use geometric information when the room is similarly colored. But when there is one blue wall that serves as a feature, children tended to search as they would in the featureless room, making selections to both geometrically correct corners, seemingly ignoring the landmark. When the researchers added toys as landmarks, children still searched at the geometrically correct corners and failed to rely on the landmarks to locate the hidden object. The researchers noted that children tended to choose the corner that was within their field of view after being disoriented regardless of the landmark or feature wall.

Learmonth, Newcombe and Huttenlocher (2001) replicated Hermer and Spelke's (1994) experiment and found similar results: children can rely on geometric information to locate a goal. Importantly, the experimental room was twice the size of the room in Hermer and Spelke's experiments, which may have allowed for greater exploration of the enclosure. The young children (17-24 months) chose the correct or geometrically correct corners more often than the geometrically incorrect corners. When using two large immovable landmarks in opposite corners of the room (bookcase and the experimental

room door), children were able to locate the hidden goal when it was hidden either near the landmark or far from the landmark. Rarely did the children choose the geometrically correct corner (but not the correct location) when searching for the hidden object when the landmarks were present. When testing with only one landmark placed in the center of one short wall, children were able to locate the goal and when they made errors, they were to the geometrically correct corner. During a replication of the portion of Hermer and Spelke (1994) in which the room included one wall covered by a blue curtain, Learmonth and colleagues found that the children were able to locate the hidden toy by using the blue curtain for reorientation. This result was evidenced by children's preference of the correct corner more often than the geometrically correct corner. The overall result points out that children are able to use geometric information to locate hidden objects in a rectangular environment. Of note, the children were able to use landmarks that were relatively immovable and larger than those in Hermer and Spelke's experiments. This difference may be the reason that the children were able to use this information to guide search. Further, the difference in room size (twice the size of Hermer and Spelke's room) may have contributed to the children's reliance on the landmarks as well as the geometric features of the environment.

Children's ability to utilize the environmental geometry when landmarks are unavailable has been shown in children age as young as 24 months (Hermer & Spelke, 1994; Learmonth, Newcombe, & Huttenlocher, 2001). Huttenlocher, Newcombe and Sandberg (1994) have also shown that children as young as 16 months code geometric information about the location of a hidden goal. However, Newcombe and colleagues (1998) found that children were more accurate with landmarks than when they were

unavailable. The authors suggest that children who are under 21 months are unable to use an external frame of reference (i.e., distal landmarks); they performed worse with distal landmarks than older children. This timeframe corresponds to the age at which children start to walk and this skill may require them to use more information from the environment to locate objects (Huttenlocher et al., 1994). This result was validated in a comparison of children (2nd and 6th grade) and adults (23-36 years old) using a virtual environment maze in which multiple different landmarks were present and could aid in maze completion. Tests involved the same maze with landmarks removed. Second graders made the most errors with the landmarks removed and walked longer distances than sixth graders or adults (Jansen-Osmann & Wiedenbauer, 2004). Overall, children ranging from 16-24 months are capable of using environmental geometry (Huttenlocher et al., 1994; Newcombe et al., 1998), however when placed in a small room which included small landmarks, children tended to rely on the environmental geometry rather than the landmarks or colored wall (Hermer & Spelke, 1994). Further, when landmarks are available in a virtual maze, children perform better than when they are unavailable (Jansen-Osmann & Wiedenbauer, 2004).

When comparing adults of varying ages in spatial tasks, younger adults are faster to complete mazes, make fewer errors, and appear to use a different strategy to complete the spatial tasks compared to older adults (Moffat, Zonderman & Resnick, 2001; Rodgers et al., 2012). In a maze task, Moffat and colleagues (2001) participants younger than 45, between 45 and 65, and older than 65 years of age, where distinctly colored walls acted as landmarks within the maze. Results showed younger participants were faster to complete the maze than both groups of older participants, and older participants made

more errors (i.e., went to the wrong place and/or backtracked). When looking at the first through the fifth trial, the majority of younger participants were able to complete the maze without errors on the final trial, half of the middle aged group were able to complete the final trial without error, and only a quarter of participants in the older group were able to complete the maze without error. In a virtual water maze task that included three age groups of young (20-39), middle (40-59), and older adults (> 60) showed a linear decrease in spatial abilities across maturation. Specifically, as the age of the participants increased, latency to locate the hidden platform increased. Another finding was that the oldest participants spent much less time searching and traveled less distance (Driscoll, Hamilton, Yeo, Brooks, & Sutherland, 2005).

These results were confirmed with men (20-30 and 60-69) trained to walk on a treadmill while immersed in a virtual reality art museum and required to locate a specific place or asked to replace certain paintings in the environment (Lövdén, Schellenbach, Grossman-Hutter, Krüger & Lindenberger, 2005). Younger men walked less distance than older men, regardless of condition (either with or without stability support on the treadmill, or the straight versus jagged hallways). Further, the older men required more trials to complete the task without errors or stopping. In addition to the decrease in distance traveled and trials to complete the maze, the younger men did not appear to be as affected by the task of walking on the treadmill as the older men. This was apparent by the variations in posture of the older men compared to the younger men. The authors point out that walking itself draws attentional control away from task completion and may add to the reason that older adults decline in navigational abilities.

Rodgers and colleagues (2012) tested older (55-85) and younger adults (18-35) in virtual Y-Maze and a virtual water maze. The researchers wanted to determine if participants varied in their use of an allocentric versus egocentric strategy for relocation. If participants were using an allocentric strategy they would be using an external frame of reference based on a cognitive map. For an egocentric strategy, they would be using a frame of reference based on themselves by using a self-referent route. Results showed that overall, older adults took longer to complete the Y-maze and the virtual water maze. Further, the older adults made more repeat visits to incorrect locations in the Y-maze. In the Y-maze older adults preferred an egocentric strategy while there was a slight preference for an allocentric strategy in younger adults. In the virtual water maze task, older adults showed no preference for strategy, but younger adults were using different strategies amongst the group. The younger adults that preferred an allocentric strategy were quicker to find the platform location than if they preferred an egocentric strategy. This study adds to the evidence that in mazes, older adults tend to use an egocentric strategy. The authors speculated that the allocentric strategy relies on the hippocampus and surrounding areas – areas that show degeneration with age – and that the egocentric strategy relies on non-hippocampal areas such as the caudate.

In summary, spatial navigation abilities change over the lifespan in several ways. In children, as young as 18 months, the use of geometric features is consistently shown. When landmarks are large and relatively immovable, young children can rely on these landmarks to find a hidden toy (Learmouth, et al., 2001). However, when the landmarks are rather small, or are in a smaller room, children tend to rely on the geometric features (Hermer & Spelke, 1994). Of note, elementary school aged children make less errors in a

virtual maze when landmarks are present as compared to when they are absent (Jansen-Osmann & Wiedenbauer, 2004). In adulthood, younger adults complete mazes faster than older adults while making fewer errors (Lövdén et al., 2005). The differences across ages are thought to be due to different neural maturation trajectories. The following section will discuss the various neural mechanisms involved in spatial navigation beginning with animal studies of spatial navigation that lead to much of the research in human navigation.

The Role of the Hippocampus and Medial Temporal Lobes in Spatial Navigation

In order to discuss the research on human navigation and the neural structures involved, a brief discussion of the nonhuman animal studies of spatial navigation is necessary. Much of the nonhuman spatial studies elucidated neural regions employed during navigation. These results have been used as templates for research into human navigational abilities. Specifically, the hippocampus has been shown to be involved in a variety of memory tasks, but mostly studied in non-human spatial tasks. The involvement of the hippocampus and surrounding areas have been implicated in spatial navigation since O'Keefe and Nadel (1978) showed that rats with hippocampectomies showed impaired navigation in a water maze task as compared to sham lesion rats. Importantly, the larger the lesion to the hippocampus, the less able rats were to successfully locate a hidden platform.

Another study looked at the connection between the entorhinal cortex and the hippocampus - specifically, the area of the hippocampus that connects to the medial temporal lobe and the hippocampus in rats (Remondes & Schuman, 2004). Rats were split into three groups of sham, hippocampal lesion or entorhinal cortex lesion and then

trained to find a platform in a water maze (see Figure 2 for the experimental design). The rats were then tested after 24 hours, and were able to reliably find the platform.

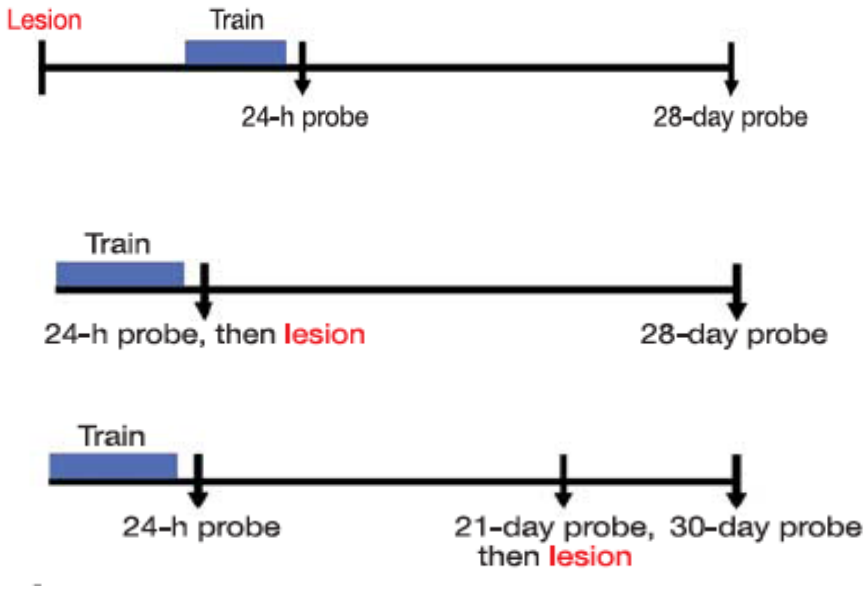

Figure 2. Experimental design from Remondes and Schuman, 2004. Each row denotes the timeline of lesion and test of spatial knowledge by group.

However, when the hippocampus was lesioned, rats showed decreased ability to locate the goal. Rats with the entorhinal cortex lesion were not different from sham lesion rats suggesting that the entorhinal cortex did not require input from the hippocampus to locate the platform. To test the relative input of the entorhinal cortex on spatial memory, the authors trained the rats to locate the platform, then lesioned the entorhinal cortex either the following day, or 21 days later and finally tested memory at either 28 or 30 days, respectively. This difference in lesion delay was to determine if memories were able to acquire permanence in the cortex across delays. The results showed that the entorhinal cortex lesion rats showed greater latencies than sham rats in the immediate lesion (24 hours) as compared to the delayed lesion group (28 days). This suggests that the

connection between the hippocampus and the entorhinal cortex is necessary for memory consolidation and retrieval at the onset of learning, but this process is complete within the 28 days and the lesion of the entorhinal cortex did not impair recall.

As the role of the hippocampus and surrounding medial temporal lobe structures were found to be involved in spatial navigation, researchers began to look for specific cells in these regions that accounted for various portions of spatial navigation. As such, researchers discovered certain cells that were activated while animals were facing specific directions or heading along a path (O'Keefe & Dostrovsky, 1971). In particular, these place cells in the hippocampus of rats were found to respond to specific places in an environment.

Research into the neural structures involved in spatial navigation led to the discovery a human navigation network (HNN; Maguire, et al., 1998). Throughout testing in a complex virtual environment task, researchers were able to determine specific regions that are active across various aspects of navigation, such as heading direction, planning, recalling locations, way-finding (navigation without guidance), and trail following. When participants were following arrows, the left hippocampus showed significant activation. During way-finding, the right hippocampus and right inferior parietal cortex were active. Importantly, as accuracy in way-finding increased so did activation in the right hippocampus. The researchers posited that the differential activation in the right and left hippocampi are related to distinct aspects of navigation: the right hippocampus allows for an episodic memory of the travelled space, while the left hippocampus allows for an allocentric representation of space. Another region activated during way-finding was the right inferior parietal cortex, which was inferred to be related

to correct body movements in an egocentric navigational strategy and heading direction. When participants were required to navigate a novel map that required taking a detour, there was activation in the left frontal regions: specifically, the left middle and superior fontal gyri. The researchers pointed out that this area is active during many tasks involving task switching. Finally, the right caudate nucleus was found to be active when the speed of travel was adjusted. In sum, the human navigational network requires input from the left and right hippocampus depending on the type of navigation, the inferior parietal cortex for an egocentric navigational strategy, the left frontal regions when faced with a conflict, and the right caudate nucleus when the speed of travel shifts. The discovery of a human navigation network has allowed researchers to focus on these areas when investigating spatial navigation across contexts.

In addition to the human navigation network, specific regions have been implicated that can aide in successful navigation. Specifically, Epstein and Kanwisher (1998) discovered the parahippocampal place area (PPA) that responds selectively to passively viewing scenes that depict places, but not individual objects. When viewing images of intact scenes, the PPA was more active than when the participants viewed faces or objects. The intact scenes consisted of either empty rooms, furnished rooms, or landscapes. The PPA is bilateral in the parahippocampal structure, but not included in the hippocampus proper (specifically including an area that straddles the collateral sulcus, the posterior tip of the parahippocampal gyrus, and adjacent regions of the fusiform gyrus) (Epstein & Kanwisher, 1998). Importantly, activation of the parahippocampal gyrus can be seen when objects that are relevant to navigation are presented in isolation. Research has shown that, after only one presentation of a maze that includes objects that

are relevant and not relevant to successful navigation, the parahippocampal gyrus exhibits greater activation to navigation relevant objects. These results suggest that even if the objects are seen in a non-spatial context, they will bring forth a representation of the spatial context that activates the parahippocampal gyrus to a greater extent than objects that are not required for successful navigation (Janzen & van Turennout, 2004).

In another line of research that has been built from the aforementioned nonhuman animal research was the discovery of place cells in the rodent hippocampus. These findings stemmed from the initial studies in which rodent hippocampi and surrounding regions were lesioned to determine what portions were required for navigation (O'Keefe & Nadel, 1978). Location of specific cells in the hippocampus that were active during single moments during navigation were called place cells and shed light onto how nonhuman animals navigate their environments. Recently, the role of place cells in humans has been seen in path integration (Chen, He, Kelly, Fiete, & McNamara, 2015) and cells that specifically respond to spatial locations and landmarks (Ekstrom et al., 2003). In spatial navigation, cells that responded specifically to places (separated from the environment) were mainly located in the right hippocampus (Ekstrom et al., 2003). Unlike the place cells discovered in rats, place cells in the hippocampus of humans in this experiment did not appear to be specific to directionality. When looking at views of spatial layouts, cells in the parahippocampal region were active. The authors point out that the dissociation with place and view dependent cells illuminates the distinction that the hippocampus is more likely to activate with specific places, while the parahippocampal region is more likely to activate when viewing spatial layouts.

In agreement, Miller and colleagues (2013) had participants complete a virtual environment maze task in which they were required to recall the location of specific items in the maze. They found similar place cells that activated when participants were in a specific place in the environment, and that a majority of these cells were in the hippocampus with only a few located in the entorhinal cortex, amygdala, and anterior medial temporal lobe. Importantly, the authors found that many of the place cells were direction dependent. In other words, when the participant was facing a specific direction in a certain place in the environment the cells were more likely to activate than if they were facing an alternate direction. Of note, when participants were asked to recall the location of items from the environment, similar activation was found to when the participant was in the environment. This spatial context reinstatement suggests that participants were recalling the location of the item, which was reactivating the same cells that were activated as when they were traversing the maze. The authors suggest that the reinstatement of context when recalling the location of intramaze items is evidence that the place cells found in the medial temporal lobe regions carry contextual information when retrieving an episodic memory of the place.

Along with cells in the parahippocampal region, cells in the entorhinal cortex have been investigated for their role in navigation. Cells in the entorhinal cortex have shown differential activation when participants are turning in specific directions (path cells) and when participants are facing specific directions (place cells). In order to identify these cells, Jacobs, Kahana, Ekstrom, Mollison, and Fried (2010) placed participants that had previously been fitted with electrodes for epileptic seizure treatment into a virtual navigation task. When participants were navigating the maze, they were

required to make clockwise or counterclockwise turns and visit specific locations in the maze. At intersections where participants made turns, path cells that related to the direction the participant was facing and which way they were turning activated. These cells were mainly located in the entorhinal cortex but were also found in the hippocampus, parahippocampus, and frontal regions. Path cells in the entorhinal cortex were active at the moment of making the turns, whereas the other regions' cells were active in relation to specific headings not specific to turning. Alternately, place cells located in the hippocampus, entorhinal cortex, parahippocampal gyrus, and amygdala activated only when participants were facing a location originating from a specific direction, leading to a more view-dependent activation pattern. Place cells found in the hippocampus were more location-dependent than cells in alternate regions (Jacobs et al., 2010). Path and place cells in the hippocampus and surrounding regions and their role in navigation have been compared to the animal studies that have shown place and path cells in similar regions. The discovery of cells that activate during specific moments in navigation has allowed for a more in depth understanding of how these specific regions are involved in spatial navigation.

The role of the hippocampus, parahippocampus, and surrounding medial temporal lobes has been investigated across various manipulations. In particular, based on work completed with rodents (O'Keefe & Nadel, 1978), researchers have identified regions that are active during navigation which collectively form the human navigation network. Specifically, the left hippocampus is involved in allocentric reorientation and guided navigation, whereas the right hippocampus is involved in episodic recollection and unguided navigation. When participants are faced with a conflict, activation is found in

left frontal regions. Finally, when the speed of travel is adjusted the caudate nucleus is activated (Maguire et al., 1998). Further, the parahippocampal gyrus activates when viewing items that were relevant for navigation (Janzen & van Turennout, 2004) and the PPA activates when viewing specific places in the environment (Epstein & Kanwisher, 1998). Place cells, similar to those discovered in rodent hippocampi, have been found in humans. In the right hippocampus place cells have been identified that respond to previously visited places when facing specific directions. Of note, these cells respond to items that were seen in environmental contexts when those items are removed from the context, suggesting that the hippocampal place cells can be activated when there is a context reminder of the space (Miller et al., 2013). The parahippocampus responds to specific layouts in space as seen through activation of view-dependent cells - cells that respond when the participant is facing a specific direction viewing a certain spatial layout (Janzen et al., 2010). These regions and cells have allowed for the identification of a precise network of structures that are involved in spatial navigation, and have guided research into the physiological mechanisms that underlie successful spatial navigation. The following section will cover a subset of research investigating these regions and how they are employed during spatial navigation tasks, specifically, in virtual environments. The focus will include the small amount of studies that have specifically manipulated the use of features and geometry in the environment.

Doeller, King, and Burgess (2008) trained participants in a virtual environment task in which they were required to recall the position of a pylon in order to test for neurophysiological differences when using environmental geometry versus features. In test trials, participants were required to replace the pylon with respect to the distal

environmental. Functional MR scanning results showed a distinction between the hippocampus and right dorsal striatum during the two types of encoding. Specifically, if the participant was encoding the location of a landmark, the dorsal striatum (mainly in the caudate head) was more likely to be active. Alternately, if the participant was learning boundary related locations, the posterior hippocampus was more likely to be active. The authors suggest that the boundary related activation of the hippocampus and the landmark related activation of the caudate in the dorsal striatum is evidence that these areas are distinct in terms of different portions of navigation.

Sutton, Twyman, Joanisse, and Newcombe (2012) pointed out that the distal cues in Doeller et al. (2008) could have added to the hippocampal activation seen. In a task similar to Cheng (1986), five wall conditions were created: 1) a walls only rectangular room, 2) a room with pillars but an extended horizon creating no environmental geometry, 3) a room where the floor texture extended up the wall a bit, 4) a room with a square flush to the floor was placed in one corner, and 5) a square room with one beacon. In each room, there was a to-be-remembered pylon, and in the testing phase participants had to replace the pylon where it was originally found. Behavioral results showed the same pattern of results as Cheng (1986) - participants placed the pylon in the correct or geometrically correct corner more than would be expected by chance in the rectangular rooms. Imaging results showed that during the pillars condition, more hippocampal and parahippocampal activation occurred compared to the other conditions. The PPA was more active when comparing the flush floor object room to the walls only room. This agrees with Epstein and Kanwisher (1998) and PPA activation with spatial places. Importantly, PPA activation was greatest when the room features were vertical versus

those that were flush to the floor. Further, the results showed activation in the left superior temporal and left supramarginal gyri when the geometry conditions were compared to the square beacon room. The authors posit that this could be due to using a verbal coding system to recall the geometric information, as these areas are often active when perceiving auditory speech. Importantly, the majority of these results do not agree with the results found in Doeller and colleagues (2008). The pillar condition showed a large amount of hippocampal activation whereas Doeller and colleagues showed greater activation in the caudate for landmark based localization. In a similar object replacement task, Kaplan, Horner, Bandettini, Doeller, and Burgess (2014) found that when objects were novel, parahippocampal and hippocampal activation was prevalent along with cingulate and anterior gyri activation. When participants were responding to geometric features, greater posterior hippocampus activation was found, while the anterior hippocampus responded to both novelty and geometry.

In a study that attempted to determine the neural structures involved when participants use environmental features without environmental geometry available to locate a goal. Wegman, Tyborowska, and Janzen (2014) asked participants to locate a specific place in a virtual environment denoted by an array of blocks as landmarks while in an MR scanner. The blocks provided the participants with two distinct pieces of information across trials that would denote the goal location: one was a shadow that provided directional information and the other was the relative placement of each block in relation to the goal. During scanning, these two pieces of information were separated across trials such that one trial would include one block with its shadow, another trial would include blocks without shadows, and a control trial would include both pieces of

information with the goal location visible. This separation of spatial information allowed for multiple contrasts to determine the neural structures involved when presented with each type of information. When comparing no shadow trials with shadow trials, there was activation of the bilateral hippocampi and the left superior occipital gyrus. When navigating using a single landmark (i.e., no shadow trial), the caudate was more active than during the other trials. When comparing the no shadow and shadow trials to the control trials, similar activations were found across experimental trials. Specifically, activations were seen in the the right hippocampus, right parahippocampal gyrus, caudate, and thalamus, and parietal, occipital, frontal, and occipital lobes as compared to control trials. The authors' attempt to remove geometry from the environment may have been thwarted during the no shadow conditions when the participants had to recall the location of the missing landmarks. This inference is drawn from the greater activation of the hippocampus during the no-shadow trials compared to the shadow trials such that the participants were imagining a spatial configuration that could similarly activate the hippocampus in the same way environmental geometry does. Further, the lack of increased activation of the caudate during these trials suggests that the participants are not solely relying on single landmarks.

Combined, these results show that the type of task, strategies used, and placement of landmarks or geometric information can greatly affect functional imaging results. Specifically, when using very distal landmarks that cannot be used for navigation (Doeller et al., 2008) the dissociation between the hippocampus and dorsal striatum (specifically the caudate head) appears to be opposite of results seen when either the landmarks are reliable for navigation or are proximal to the goal (Kaplan et al., 2014;

Sutton et al., 2012). However, the influence of the hippocampus, PPA, and surrounding regions appear to be important in successful navigation (see Table 1 and Figure 3 for a summary of neural structures employed during spatial navigation).

Table 1.

Neural Structures Involved in Spatial Navigation		
Area	**Related Behaviors/Processes**	**Feature/ Geometry**
Left Hippocampus*	Guided Navigation Allocentric Strategies	
Right Hippocampus*	Way-finding Episodic Memories	 Both
Bilateral Hippocampus	Place Cells Boundaries (posterior) Novelty and Geometry (anterior) Novel Objects	Both Geometry Geometry Feature
Parahippocampus	Viewing Scenes (PPA) Viewing Navigationally Relevant Objects (PPA) Place Cells Landmarks Novel Objects Vertical Walls	Geometry Feature Both Feature Feature Geometry
Left Superior Temporal Lobe & Left Supramarginal Gyrus	Boundaries	Geometry
Cuneus, Precuneus, and PCC*	Encoding locations	Both
Entorhinal Cortex	Path Cells Place Cells	Both
Right Inferior Parietal Cortex*	Body Movements Egocentric Strategy Heading Direction	Both
Frontal Cortex (Left Middle and Left Superior Frontal Gyri)*	Taking Detours	
Caudate	Landmarks	Feature
Right Caudate Nucleus*	Speed of Travel	
*Denotes the HNN Structures (Maguire et al., 1998)		

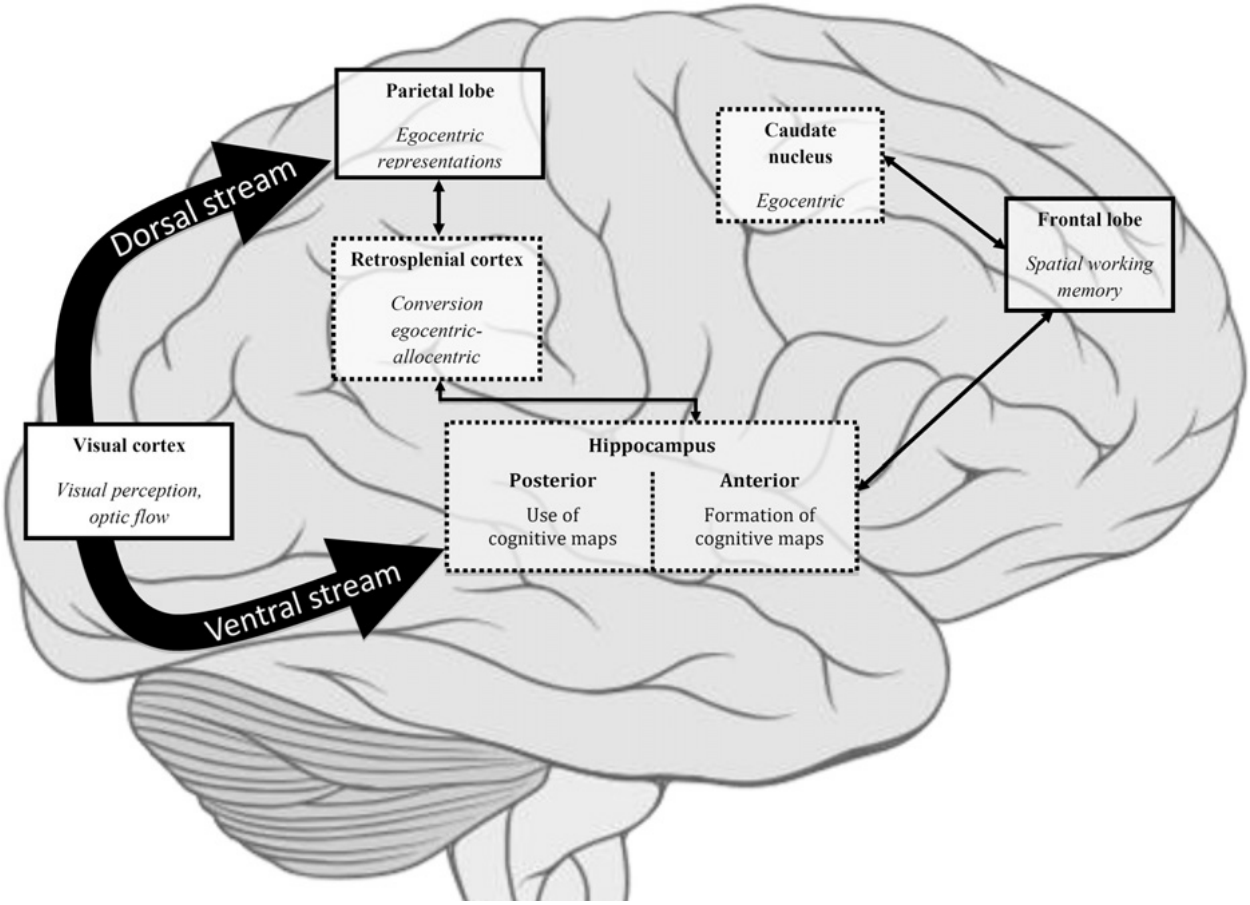

Figure 3. Structures involved in spatial navigation from Lithfous et al., 2013.

Spatial Navigation and Neural Structures Across the Lifespan

When investigating spatial navigation across adulthood, the research on healthy aging is sparse. Much of the focus is on the differences between disease states and healthy aging to determine potential behavioral markers for diagnosis (e.g., Jack et al., 1997; Lithfous, Dufour & Després, 2013). However, there are only a few studies that have employed spatial tasks using functional imaging in young and older healthy participants, and these studies focus on a dichotomous split of ages (Moffat, Elkins & Resnick, 2006; Moffat, Kennedy, Rodrige & Raz, 2007), potentially leading to a partial

picture of the subtle changes across ages. As will be explored, there are neurophysiological changes that occur with healthy aging (Driscoll et al., 2003; Erickson & Barnes, 2003; Raz et al., 2005) which could explain differences seen with behavioral tasks across young and older adults (e.g., Lövdén et al., 2005). These studies will be discussed in detail in the following section.

As the neural structures change across development, it is expected that these changes will impact success in navigational tasks. Pine and colleagues (2002) compared adolescents (12-16) and adults (25-38) in a virtual reality city. The participants either were guided by arrows or had to navigate using memory to locate specific places in the environment. Adolescents were able to find more locations than adults, but adults were able to label locations after scanning to a greater extent than adolescents, suggesting they were using an allocentric strategy. Subjects that found more locations, regardless of age, were likely to have greater activation in the right medial temporal regions at the amygdala-hippocampal junction than those that found fewer locations. Further, activations that correlated with greater location of places were the cerebellum, BA 8 and 47 in the frontal lobes, the posterior cingulate gyrus, basil ganglia, and thalamus. When navigating using memory (without guiding arrows), the left hemisphere showed differential activation, specifically in the temporoparietal junction, the cerebellum, the posterior cingulate, parahippocampus, and posterior hippocampus. When controlling for allocentric strategy and task success, adolescents showed greater activation overall than adults: specifically, in the temporoparietal junction, frontal cortex, posterior parietal cortex, and cerebellum, brainstem, and thalamus. The authors suggest that as humans age (at least to age 38), they are more likely to use an allocentric strategy as seen in the

ability for adults to recall a greater amount of locations after scanning. Further, the increased right medial temporal lobe activation agrees with previous studies showing the right regions are activated during navigation. Interestingly, the left regions were more activated in the younger participants. This is consistent with previous research showing left-sided maturation of the temporoparietal cortex, which supports the development of using abstract representations across development.

In a study that explored trends across adulthood, Moffat and colleagues (2006) compared younger (21-39) and older (60-78) participants during encoding of a virtual environment maze task. Results showed that in younger adults, the right hippocampus, bilateral parahippocampal gyrus, cuneus, precuneus, bilateral parietal lobe, retrosplenial cortex, and posterior cingulate gyrus were active. Importantly, these areas comprise what is known as the human navigational network. Older adults showed a shift in activations with reduced activity in the posterior hippocampus, and posterior parahippocampal gyrus, the retrosplenial cortex of the posterior cingulate gyrus. The older adults showed increased activation in the medial frontal gyrus and anterior cingulate gyrus. The reduced hippocampal, parahippocampal activation in older adults may account for age-related declines in navigational abilities. These results suggest that the older adults may be compensating for reduced activity in the hippocampal and parahippocampal regions by employing more frontal structures. These differences in activated regions during a spatial task across adulthood require further investigation to determine what degeneration is characteristic of normal aging. Similar results were found in a follow-up study that included a volumetric analysis of regions that have been implicated in spatial navigation (Moffat et al., 2007). Regions that showed decreased volume in older patients were the

lateral prefrontal cortex, hippocampal complex, caudate, and the cerebellum. Of note, larger volume of the prefrontal white and gray matter was correlated with better maze completion performance regardless of age, suggesting that successful navigation requires input from the prefrontal cortex. Additionally, the volume of the caudate nucleus was also positively correlated with successful navigation.

The healthy aging process includes neural degeneration throughout many brain regions. These changes lead to some pronounced behavioral differences, such as memory deficits, and the aforementioned spatial decrements. For example, participants aged 15-74 who are asked to complete a task which required them to recall locations of objects in a museum exhibit showed a sharp decrease in recall accuracy after the age of 60 that consistently declined to the age of 74 (Uttl & Graf, 1993). Because spatial memory (or the ability to recall previously seen items), is reliant on the hippocampus, there is evidence to assume that the degeneration of the hippocampus across healthy aging may be contributing to the decrease in spatial performance (Erickson & Barnes, 2003).

Natural degeneration of the hippocampus has been examined through the use of volumetric analyses. In a comparison of healthy adults from 20-39 and 60-85, a decrease in volume of bilateral hippocampus was found. Although there was degeneration found in both the anterior and posterior hippocampus, the anterior hippocampus suffered from less degeneration than the posterior hippocampus. The participants in this study were also performing a virtual water maze task in order to correlate performance with neural degeneration. As would be expected, better performance correlated with larger hippocampal volume (Driscoll et al., 2003). Of note, the development of the hippocampus shows a steady total volume between the ages of 4 and 25. However, the

portions of the hippocampus vary throughout development. The posterior hippocampus gradually gains size over time, while the anterior half decreases over time (Gogtay et al., 2006).

The variability seen between subjects and across time causes some difficulty in determining the trajectory of hippocampal volume across the lifespan. In a study examining the volume of this structure across five age groups ranging from 18-85, researchers found that there was as much variability in hippocampal size in the youngest group as there was in the oldest groups; albeit steadily decreasing around the age of 45. This variability showed that some of the youngest participants has similarly sized hippocampi as participant in the oldest group (Lupien et al., 2007). In a post mortem investigation of hippocampal volume across ages, a reduction in CA1 neurons in the hippocampus amongst the older group (ages 75-99). Further, there was a total volume loss in the hippocampus as compared to younger subjects (ages 16-52; Simic, Kostovic, Winbald, & Bogdanovic, 1997).

The hippocampus is not the only navigationally relevant structure to suffer from normal aging related degeneration, various other regions show a decrease in volume (Raz et al., 2005). In this study, participants ranging from 20-77 at the first scan were followed up with after five years in order to determine the differences in various brain regions across ages. As was previously mentioned, there is a great amount of variability across participants in development and degeneration across ages. By looking at the same participants' differences in regional brain volumes, and then comparing these difference scores across participants, the researchers were able to better understand structural changes over time. The largest volumetric decreases found were in the caudate and

cerebellum. There were also decreases in the hippocampus and to a lesser extent in the entorhinal cortex, and prefrontal white matter. Importantly, the decrease in volume showed the greatest decline at the age of 50 and a sharp acceleration of degeneration after this age (Raz et al., 2005). Further, Sowell and colleagues (2003) looked at gray matter density between the ages of 7 and 87, and found that the dorsal areas of the parietal lobes reached the lowest density by the age of 50 while the frontal lobes reached the lowest density by the age of 60. The decrease in density of the posterior and inferior parietal lobes occurred bilaterally, but moreso on the left hemisphere (Sowell et al., 2003).

In sum, there are very few studies that have looked at aging and spatial abilities while participants are undergoing functional imaging, and this leaves room for much needed follow-up research. Results from these studies show that when comparing adolescents and participants from early adulthood, successful navigation is correlated with right medial temporal lobe and amygdala-hippocampal junction activation regardless of age. Further, when participants are not required to navigate a maze using memory there is greater activation in the left hemisphere structures than the right hemisphere (Pine et al., 2002). When comparing young adults with older adults in a virtual water maze, younger adults show activation that corresponds with the HNN (see Table 1 and Figure 3). Alternately, older adults show greater posterior hippocampal and parahippocampal activation as well as greater frontal activation (Moffat et al., 2006), and total white and gray matter volume is correlated with better navigation (Moffat et al., 2007). There are various structures that suffer volume loss that have been implicated in spatial navigation (see Table 2).

Table 2.

Neural Structures Involved in Spatial Navigation that Degenerate with Normal Aging

Area	Approximate Age	Reference
Bilateral Hippocampus*	60	Moffat et al., 2007
	60	Driscoll et al., 2003
	45	Lupien et al., 2007
	Sharp decline starting at 50	Raz et al., 2005
Anterior Hippocampus*	60	Driscoll et al., 2003
Entorhinal Cortex	Linear from 20-77	Raz et al., 2005
Cerebellum	60	Moffat et al., 2007
	Linear from 20-77	Raz et al., 2005
Lateral Prefrontal Cortex	60	Moffat et al., 2007
Caudate*	60	Moffat et al., 2007
	Linear from 20-77	Raz et al., 2005

*Denotes the HNN structures

In particular, the total volume of the hippocampus, specifically the posterior portion (Driscoll et al., 2003), lateral prefrontal cortex (Moffat et al., 2007), caudate, cerebellum, and entorhinal cortex (Raz et al., 2005) show degeneration that corresponds with normal aging. Further, gray matter density decreases in the dorsal parietal lobes around age 50 and the frontal lobes around age 60 (Sowell et al., 2013).

Limitations of Previous Research

Many of the previous spatial tasks that have been used as a comparison across age groups have employed complex environments that require more of the participants than simply locating a goal. For example, when participants are traversing a maze, they are required to remember objects in the environment (Lövdén et al., 2005), recall the path they have taken, or encounter a detour that requires a change in course (Maguire et al., 1998). While these studies have allowed for a large amount of information to be gained,

the complexity of these environments and tasks may create confounds that could have led to differences due to various other psychological factors such as attentional control, working memory, or problems with decision making. It is for this reason that the current study will employ a sparse environment where participants will only experience environmental geometry and landmarks. This will allow for a more complete determination of the neural structures involved when participants across ages use each of these environmental features to navigate and what occurs when these environmental cues are in conflict or absent.

As has been described, much of the previous research on spatial navigation and the neural structures involved have focused on determining the precise structures involved in successfully locating or recalling locations in environments. While this has allowed for a wealth of knowledge into these structures, there is a lack of research on what happens across the lifespan. The few imaging studies looking at normal aging differences in spatial abilities examine a binary split (Moffat et al., 2006; 2007; Pine et al., 2002). Volumetric studies of the natural degeneration of brain structures shows that there are changes that occur at the ages of 50 and 60 (Raz et al., 2005; Sowell et al., 2003). It is for this reason that the current research proposal will include four age groups that will allow for a greater understanding of potentially subtle changes in spatial abilities that can occur immediately prior to and following these ages. This analysis is of great importance given that research has shown that spatial abilities decline in some degenerative diseases (such as Alzheimer's disease). Comparisons of spatial navigation success across healthy and patients with these degenerative diseases have been completed (Jack et al., 1997) based on the fact that the structures employed in spatial navigation

show degeneration in these diseases. Another aspect of the proposed research that can add to the understanding of structural changes and how they may relate to navigational abilities is a volumetric analysis across these ages of the caudate and hippocampus. These regions have been implicated as a part of the HNN and are employed when utilizing landmarks and environmental geometry respectively (Maguire et al., 1998). If there is a greater understanding of the precise normal age related declines in spatial performance and the structures involved, then there could be a supplemental diagnostic measure for these degenerative diseases based on which aspect of navigation is suffering. The proposed research will allow for a psychological and neurological baseline for future research with patients suffering with degenerative diseases.

Chapter 2: Methods of the Current Experiments

Three experiments were designed to determine the role of the hippocampus, parahippocampus, and surrounding medial temporal lobes during a simplistic spatial reorientation task based on Cheng (1986). The previous imaging studies investigating spatial navigation tasks have employed dynamic real-world virtual environment tasks (Doeller et al., 2008; Kaplan et al., 2014; Sutton et al., 2012). These experiments have each found results that could be due to potential confounds such as very distal landmarks, the added active learning component of encoding and replacing objects in the environments, or the richness of the environment. As such, the current experiments have been simplified in order to determine the role of neural structures when presented with various environmental features and room shapes.

Experiment 1 was designed with two goals in mind. 1) To ensure that the simplified experimental task elicited the same results as found in the prior research (Cheng, 1986; Sturz & Kelly, 2009). 2) To determine the time required for participants to complete the task to allow for the scanning sequences of Experiment 2 to be created. Experiment 2 consisted of the same task (with minor differences due to the experimental apparatus) which college aged participants completed while undergoing functional brain imaging in a 7 Tesla Magnetic Resonance (MR) scanner. The purpose of the second experiment was to examine the functional correlates of environmental geometry and features. Finally, Experiment 3 was conducted with participants aged 35 and older. This allowed for a comparison of functional and structural differences within and across age

groups permitting a greater examination of what regions are involved in this type of spatial task and what changes occur across ages.

Chapter 3: Experiment 1

During Experiment 1, participants will complete a virtual environment analogue of the reorientation task (Cheng, 1986) on a laptop computer. This task will require participants to navigate the environment to locate the one location (a predetermined corner denoted by a specific landmark) that will transport them to the next trial. The experiment will be split into two seamless phases consisting of training (Training Phase) and testing (Testing Phase). The Training Phase will introduce participants to the task and allow for participants to reach an asymptotic level of performance. The Testing Phase will introduce blocks of test trials interspersed with training trials. Participants will experience three types of test trials (eight presentations of each test type) that will differ in cue availability. Specifically, test trial manipulation varied the presence or absence of the landmarks, location of the correct landmark in relation to the correct geometry, and a lack of geometric information.

It was hypothesized that participants would learn the task relatively quickly which will be shown as a sharp decrease in errors and latency to locate the goal during training. Test trials will test whether participants can rely on landmarks, or environmental geometry alone, to locate the goal (or the rotational equivalent) with little error. When the environmental geometry and landmarks are in conflict, it was hypothesized that participants will rely on the landmarks moreso than the geometry, but will chose one of these features to a greater extent than the alternate choices.

Participants

Sixteen undergraduates (7 males: mean age 20.14, range 18-26; 9 females: mean age 20.88, range 18-31) completed the virtual environment reorientation task. Participants were awarded class credit or extra credit for their participation.

Methods

Apparatus. The task used was based on Cheng's (1986) reorientation task. Participants used a personal Dell laptop computer to complete the three-dimensional (3D) virtual environment task, which was created using Valve Hammer Editor based on the Half-Life Team Fortress Classic game platform. The game is a 3-D virtual environment that participants experience in first-person perspective consists of a rectangular room (429vu x 1200vu x 352vu [1vu (virtual unit) = ~2.54cm]) with uniformly colored blue walls, a light green floor, and a grey ceiling. Inside the room at each corner stands a uniquely colored pillar (32vu x 16vu x 128vu) to differentiate the potential goal locations (see Figure 4). The pillars are colored green, teal, yellow, and red. Participants navigated the environment using a Logitech trackball mouse.

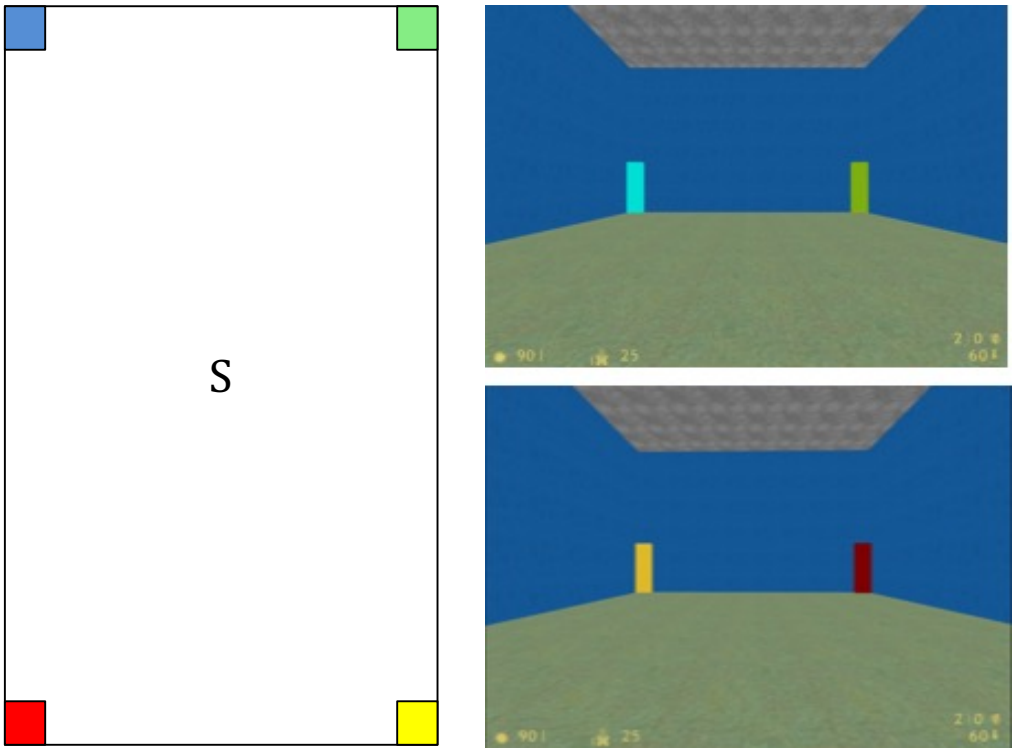

Figure 4. Left panel. Bird's eye view of the training room. "S" represents the start position. Participants were randomly assigned to one of the four corners. Right panel. Participant's view of the virtual environment from the starting position facing north (top) and south (bottom).

Training Phase. Participants were brought to the lab seated in front of a laptop computer and shown an instructions screen. The instructions stated:

> "Your goal is to locate the place in the environment that takes you to the next trial. Please use the trackball mouse to move around the environment. If you are correct, you will see "CORRECT!!". When you are finished, you will see a score screen. This will say "0". Please come get the researcher. Thanks for your participation!"

The researcher asked if the participant understood the instructions and the experiment began. Participants were randomly assigned to one of four corners as correct, and the

room was darkened and the researcher left the room. Upon completion, the participant saw a "Finished" screen and let the researcher know they were finished. The participants were debriefed and credit was assigned.

A session consisted of 87 trials. The first 15 trials were training trials. Participants start by facing one of four random directions in each trial (North, South, East, or West), and were required to move their player (32vu x 32vu x 72vu) to the correct corner via a trackball mouse to make a selection of that corner as the goal location. A selection is made if the participant walks into that corner. If the participant chose the correct corner, they saw "CORRECT!!!" on the screen, and were immediately transported to the next trial. If the participant chose the incorrect corner, no feedback was given, and they could continue searching. The intertrial interval (ITI) consisted of a black screen for 10s before the next trial began.

Testing Phase. The testing phase consisted of 72 trials constructed from 24, three trial test blocks. Each test block contained one test trial and two baseline (training) trials. There were three test trial types: No Landmark, Square, and Conflict. Each test trial type was tested eight times (see Figure 5 for test types). Each trial type occurred once within three consecutive test blocks and was pseudorandomized so that a test trial type did not occur on successive test blocks. The test trials differed across landmark removal (No Landmark), environment shape (Square), and landmark placement (Conflict). Each test trial allowed for different analyses of what had been learned and which features of the environment were used when features are changed or removed. Any choice to a corner was recorded and started the 10s ITI. No feedback was given during test trials.

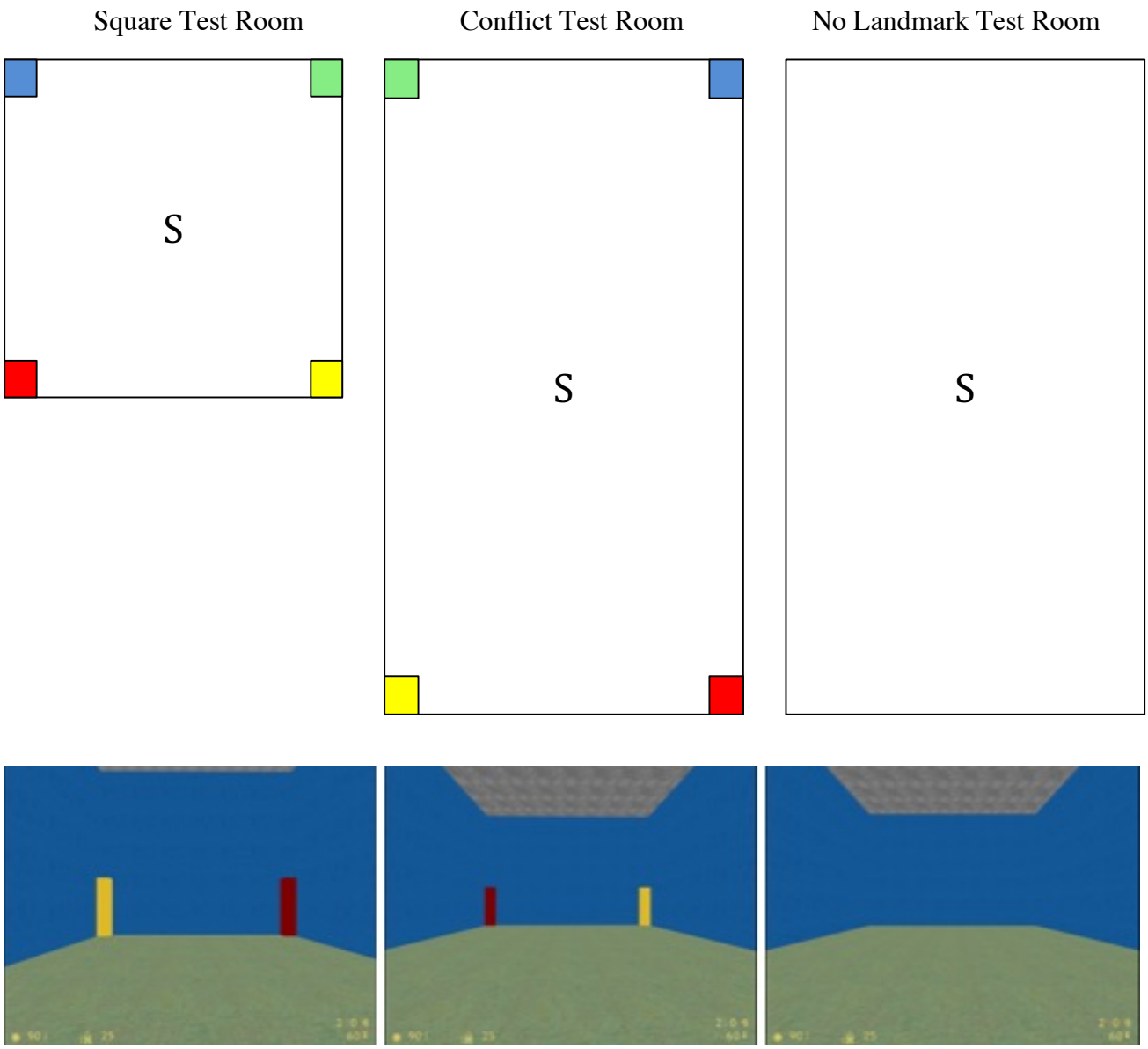

Figure 5. Top Panel. Bird's eye view of each testing room. Left. Square test room. Middle. Conflict test room. Right. No Landmark test room. "S" represents the start position. No feedback was given during these test trials. Bottom panel. Participant's view of the testing rooms. Square test room (left) is viewed from the opposite wall, Conflict (middle) and No Landmark (right) test rooms are viewed from the start position.

The No Landmark test trial consisted of removal of the landmarks that previously denoted the goal location. Corner choices were compared such that the choices to the geometrically correct corners were compared to the choices to the geometrically incorrect

corners. Further, these averages were compared to chance. Specifically, if participants made more than 50% of their choices to the geometrically correct corners, the assumption is that they learned about the geometric relationship. The Square test room (418vu x 418vu x 352vu) trial consisted of a change in the environmental geometry and requires participants rely only on the landmark feature. This test determined if participants have learned the correct landmark and allowed for an analysis of stable learning of the landmarks across the experiment. The final test was the Conflict test trial in which the landmarks and geometry were conflict; specifically, the landmarks were switched with the landmark nearest. This test determined which element of the environment participants prefer to use when these features are in conflict: landmark or environmental geometry.

Results

Training Results. An analysis of training trials was completed to determine if participants learned the location of the landmark that denotes the goal location based on proportion of correct choices across the 15 training trials. In order to determine if participants were learning the task to an asymptote level, a Two-Way Repeated Measures ANOVA was conducted on number of errors with trial (1-15) and gender (male, female) as factors. As can be seen in Figure 6 (top panel), the number of errors decreased rapidly across the first three trials. The ANOVA revealed a significant main effect of trial F (14, 196) = 14.669, $p < .001$ with no interaction between trial and gender F (14, 196) = 1.449, $p > .05$. There was no effect of gender F (1, 14) = 4.536, $p > .05$. Bonferroni's pairwise comparisons revealed that trials 1-3 had a greater number of errors than the remaining training trials ($ps < .05$).

A Two-Way Repeated Measures ANOVA with trial (1-15) and gender (male, female) as factors was conducted on latency to complete each training trial. As shown in Figure 6 (bottom panel), the average time to complete each trial decreased as training progressed. The results showed a main effect of trial F (14, 196) = 15.071, $p < .001$, an interaction between trial and gender, F (14, 196) = 2.0, $p < .05$, but no effect of gender, F (1, 14) = 3.246, $p > .05$. Bonferroni's pairwise comparisons revealed that trial 1 took significantly longer to complete than the remaining trials ($p < .05$). The interaction was due to females taking longer than males on the first 3 trials of training, but females were equivalent to males from trials 4-15, as supported by the following analyses. A Two-Way Repeated Measures ANOVAs was conducted with trial (1-3) and gender (male, female) as factors. This test revealed an effect of trial F (2, 28) = 12.495, $p < .05$, an effect of gender F (1, 14) = 4.627, $p < .05$, and no interaction (F (2, 28) = 2.357, $p > .05$). When conducting a similar analysis on trials (4-15), there was no main effect of trials, F (11, 154) = .820, $p > .05$, gender, F (1, 14) = .058, $p > .05$, or interaction (F (11, 154) = .706, $p > .05$. In, sum participants reached asymptotic performance levels by the end of the training phase.

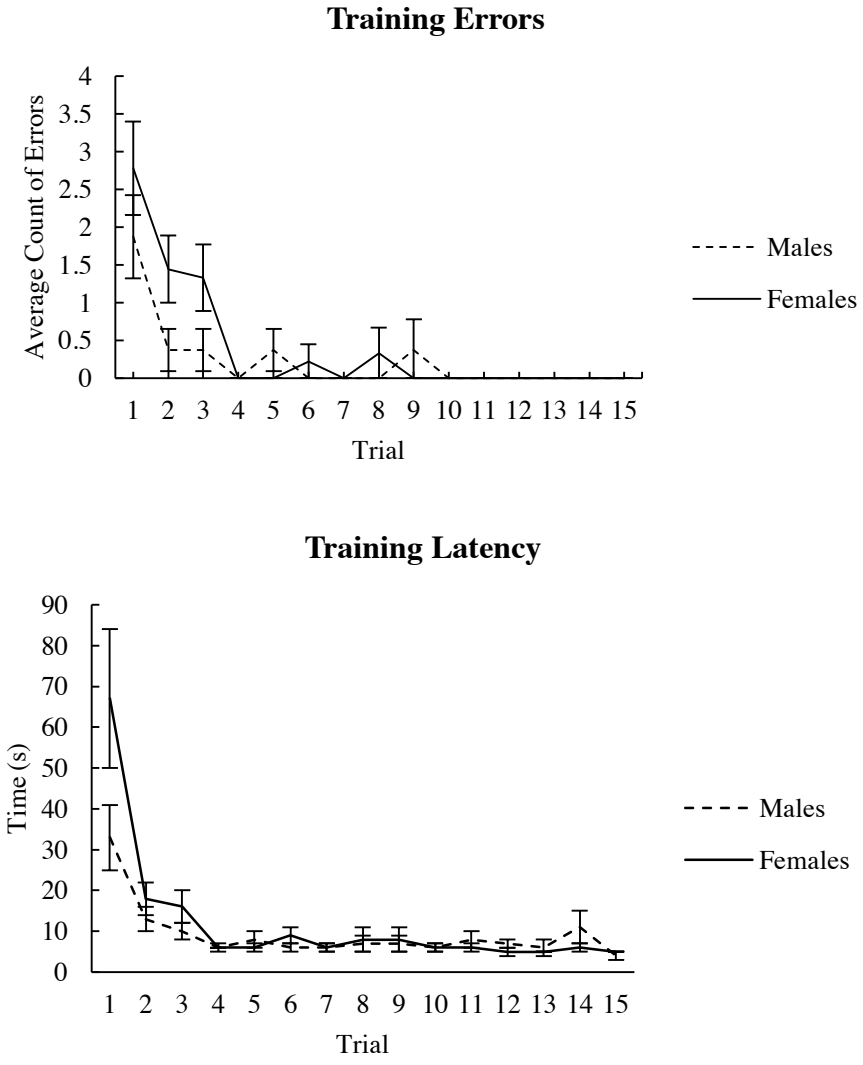

Figure 6. Experiment 1. Top panel. Training errors across training trials. Bottom panel. Latency to complete each training trial. Error bars represent *SEMs*.

Test Results. In order to determine stability across testing for each test type (Square, No Landmark, Conflict), separate Two-Way Repeated Measures ANOVAs on test type across trials (1-8) and gender (male, female) were conducted on proportion of choices made to the correct location to determine accuracy in goal localization. During the Square test trials, participants showed stable performance across testing, F (7, 98) =

1.376, $p > .05$. There was no interaction between trial and gender $F(7, 98) = 1.123$, $p > .05$, or effect of gender $F(1, 14) = .004$, $p > .05$. *A* one-sample *t*-test was conducted to determine if participants were choosing the correct corner more than would be expected by chance (.25). The test showed that participants chose the correct corner ($M = .84$, $SEM = .06$) more often than chance $t(15) = 10.108$, $p < .05$ (see Figure 7, bottom panel). This result shows that participants learned the landmark they were assigned, and selected that landmark greater than the other landmarks. In fact, as seen in the bottom panel of Figure 7, participants rarely chose the incorrect corners. Although, choice performance did not change over testing, first trial performance was also examined. During the first presentation of the Square test, no choices were made to alternate landmarks than the one assigned (Figure 7, top panel).

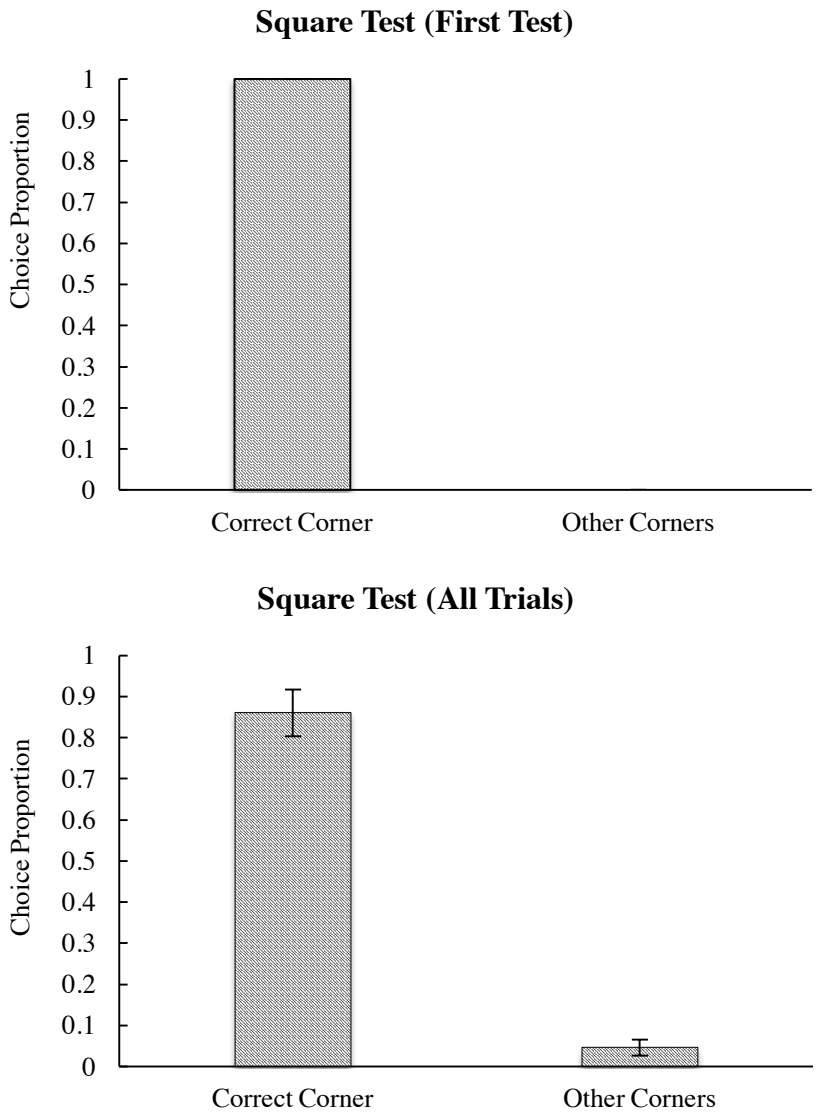

Figure 7. Experiment 1. Top panel. Proportion of choices for the first presentation of the Square test. Bottom panel. Proportion of choices for all presentations of the Square test. Error bars represent *SEMs*.

For the No Landmark test trials, a Two-Way Repeated Measures ANOVA on trial (1-8) and gender (male, female) was conducted to examine stability across testing. Participants showed stable performance across testing, $F\,(7, 98) = .997, p > .05$. There was no interaction between trial and gender $F\,(7, 98) = 1.354, p > .05$, or effect of gender, $F\,(1, 14) = .004, p > .05$. A one-sample *t*-test was conducted to determine if

participants were choosing the correct or geometrically correct corners greater than would be expected by chance (.5). Results showed that participants chose the correct or geometrically correct corners (M = .79, SEM = .05) greater than would be expected by chance, t (15) = 6.195, p < .05 (see Figure 8, bottom panel). Although choice performance did not change over testing, first trial performance was also examined. As can be seen in Figure 8 (top panel), participants rarely chose the geometrically incorrect corners during the first test presentation. These result shows that participants were choosing the correct or geometrically correct corner to a greater extent than the incorrect corners.

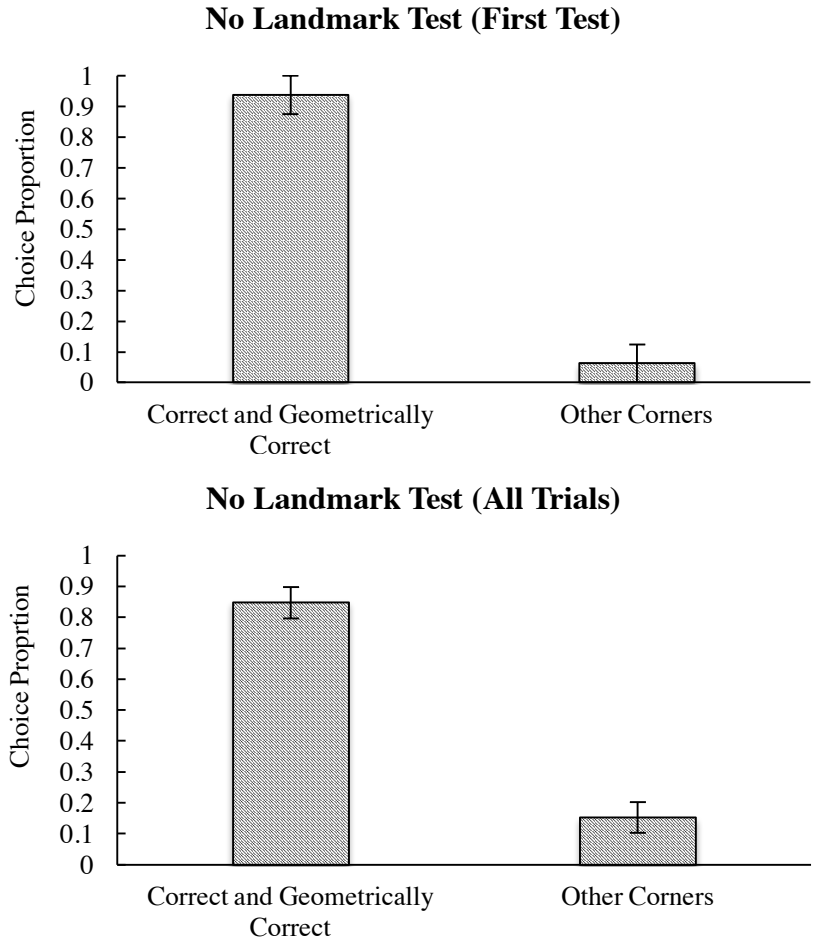

Figure 8. Experiment 1. Top Panel. Proportion of choices for the first presentation of the No Landmark test. Bottom panel. Proportion of choices for all presentations of the No Landmark test. Error bars represent *SEMs*.

For Conflict trials, a Two-Way Repeated Measures ANOVA on test trial (1-8) and gender (male, female) were conducted to determine stability across testing. Participants showed stable performance across testing, $F\ (7, 98) = .629, p > .05$, and there was no interaction $F\ (7, 98) = .629, p > .05$, or effects of gender $F\ (1, 14) = .089, p > .05$. A one-sample *t*-test was conducted to determine if participants were choosing the correct corner or correct landmark greater than would be expected by chance (.5). This test

revealed that participants were choosing the correct landmark or corner (M = .95, SEM = .03) greater than would be expected by chance, t (15) = 15.97, $p < .05$ (Figure 9, bottom panel). This result shows that participants were choosing the correct landmark more often than the correct corner, but these choices were greater than choices to the alternate corners. Although choice performance did not change over testing, first trial performance was also examined. As can be seen in the top panel of Figure 9, there were no choices to either the correct corner or to the alternate corners during the first test, all choices were made to the correct landmark.

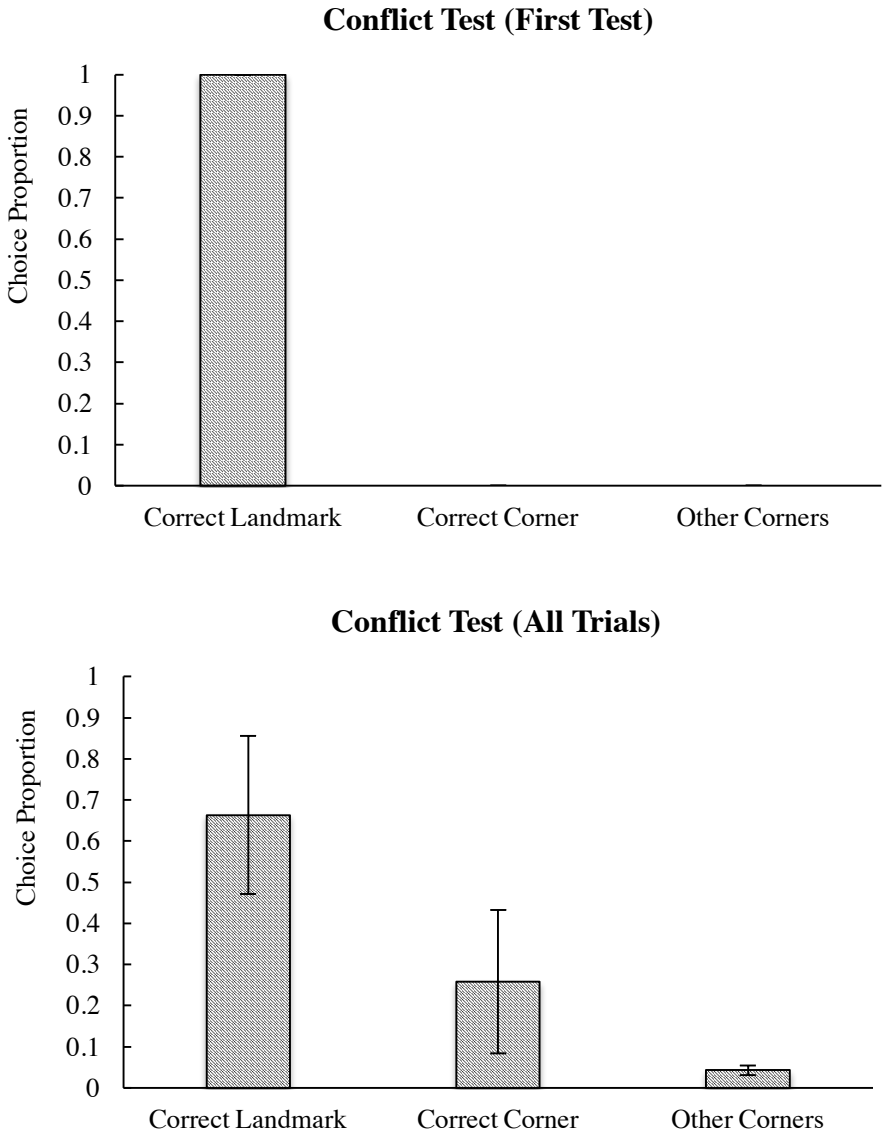

Figure 9. Experiment 1. Top panel. Proportion of choices for the first presentation of the Conflict test. Bottom panel. Proportion of choices for all presentations of the Conflict test. Error bars represent *SEMs*.

Discussion

The results of Experiment 1 show that participants can quickly learn the location of a hidden goal using colored landmarks in a rectangular room. During tests, participants showed reliance on the landmark when the geometry was unavailable and that the landmark was a more salient feature than the geometry when the two were in

conflict. Of note, the results also showed that when the landmark was unavailable, they could rely on the environmental geometry to locate the goal. These results are consistent with previous studies (Cheng, 1986; Sturz & Kelly, 2009). Across training, participants showed a marked decrease in time to complete the trial and accuracy when choosing which landmark was correct. During tests, when participants were placed in the Square testing room, they consistently chose the correct landmark to a greater extent than the alternate corners. This result is evidence that participants learned the specific landmark-goal relationship. In the Conflict test, participants initially chose to visit the correct landmark, but over the eight test trials divided their choices between the correct corner and the correct landmark to a greater extent than the alternate options. Importantly, when the landmarks were removed in the No Landmark test, participants visited the correct or geometrically correct corner. This suggests that although participants preferred the correct landmark to the correct geometric information (as seen in the initial Conflict test trials), they learned about the geometric information provided by the environment and were capable of using this information for successful goal localization.

As these results are consistent with previous findings, the second experiment employed the same task in the 7T MR scanner to determine what neural structures are involved in goal localization across the three test types. As noted in Experiment 1, participants showed asymptotic performance by the third training trial and stable performance across test trials. These results allow for confidence that during Experiment 2 and 3, participants across ages will be able to learn the task within the pre-scanner training trials, and show similar stable performance across all testing trials. This stable

performance should allow for reliable and consistent activations across training and testing trials.

Chapter 4: Experiment 2

Experiment 1 demonstrated that the reorientation task can be rapidly learned. The same procedure from Experiment 1 was used in Experiment 2 but implemented in the 7T MR scanner. The purpose of Experiment 2 employed the same procedure to determine which neural structures are involved when using environmental geometry, landmarks, and when these environmental cues are in conflict. The simplicity of the virtual environment will allow for investigation of which structures are active when participants are using features, geometry, or when the two are in conflict.

Behaviorally, participants should perform similarly to Experiment 1. Participants receive 15 training trials before entering the scanner then again upon entering the scanner prior to the testing phase. Pre-scanner training errors and latency (time to find the goal location) should decrease over the initial training trials and rapidly reach asymptotic performance (as in Experiment 1). In regard to errors, there should be little difference between the end of pre-scanner and the start of in-scanner training (baseline) trials, as the participants have already learned the task upon entering the scanner. Functionally, there should be various navigationally relevant regions active throughout the task. It is expected that there will be greater activation of the caudate when using landmarks to locate the goal as compared to when the landmarks are unavailable. When the landmarks and geometry are in conflict, it is expected that the frontal cortex will show greater activation as compared to baseline and the other test trials.

Participants

A total of 20 right handed participants (7 male, 13 female) ranging from 19 to 26 ($M = 22$, $SD = 2.2$) were included. Participants' education ranged from sophomore in college to graduate education (2 with a Master's and 5 currently in PhD programs). All participants completed the same task as in Experiment 1 while undergoing functional scans. All participants underwent the standard safety screening protocol for entering the MR scanner per the institutional policy and were paid ($40.00) for their participation.

Methods

Training. Participants experienced 15 initial training trials outside of the MR scanner. To ensure that participants learned the task, the training trials had a criterion of the stable performance across the final eight trials to enter the scanner. This criterion was chosen because as of trial 10 in Experiment 1, participants showed stable performance in both latency and number of errors (see Figure 6).

fMRI task. Following this, participants completed the full task as explained in Experiment 1. A session consisted of 87 trials. A session began with 15 baseline (pre-scanner training trials) followed by three 24 trial testing blocks (same as Experiment 1). The only difference between the experimental presentation in Experiment 1 and 2 was that the task was split into 3 separate runs. As the average time to complete the full task in Experiment 1 was 25 minutes, each run in the scanner was 13 minutes long. This ensured that participants could complete all trials for that run. This extra time allowed for any participant to complete the required trials per run even if they were not familiar with a trackball, video games, or they were unaccustomed to the scanning environment.

Image Acquisition. All fMRI acquisition was completed at the Auburn University MRI Research Center using a Siemens 7Tesla MR Scanner (Siemens Healthcare, Erlangen, Germany) and a 32-channel head coil by Nova Medical (Wilmington, MA). The head coil was equipped with two mirrors that allow the participant to look at a projection screen (Silent Vision Projector, Avotec Incorporated) at the rear end of the scanner bore. The virtual environment was displayed through the projection system using a Dell computer. Participants used an MR compatible trackball mouse (Current Designs, Inc.), like that used in Experiment 1, to navigate the environment.

Prior to functional scanning, an anatomical scan was completed using a T1-weighted MPRAGE (256 slices, voxel size = 0.6mm^3, TR/TE 2200/3.05ms, 7° flip angle, base/phase resolution 384/100, collected in an ascending fashion, acquisition time = 7:39) 2200ms TR, 3.05ms TE) for an ultra-high field anatomical image. The event related experimental design was used to estimate blood oxygenation level dependent (BOLD) signal changes using a gradient echo, echoplanar imaging sequence (40 slices, voxel size = .90 x .90 x 1.5mm^3, TR/TE 3200/28ms, 70° flip angle, base/phase resolution 234/100, collected in an interleaved fashion, iPAT GRAPPA acceleration factor = 3, 244 timepoints, acquisition time = 13:10).

Results

Training Results. Figure 10 (top panel) shows the average number of errors for pre-scanner and scanner training. All participants rapidly learned the reorientation task across two contexts (pre-scanner, in-scanner) and acclimated well to the scanner environment, as confirmed by the following analyses. A Two-Way Repeated Measures

ANOVA was conducted on the average number of errors with trial (1-15) and context (pre-scanner, in-scanner) as factors. There was a main effect of trial, F (14, 532) = 14.363, $p < .05$, and a main effect of context, F (1, 38) = 18.439, $p < .05$. Further there was a trial x context interaction, F (14, 532) = 8.577, $p < .05$. The interaction was due to a greater number of errors during the pre-scanner trials as compared to the in-scanner trials during trial 1 and 2 (paired *t*-tests, *ts* (19) > 2.62, $p < .05$), but the remaining trials did not differ from each other (*t*s < 1.453, *ps* > .05). A Two-Way Repeated Measures ANOVA was conducted on number of errors with trial (8-15) and context (pre-scanner, in-scanner) to ensure participants had reached the criterion of stability in performance during the final eight trials of training. There was no effect of trial, F (7, 266) = .862, $p >$ .05, no effect of context, F (1, 38) = 2.021, $p > .05$, and no trial x context interaction, F (7, 266) = .862, $p > .05$. Figure 10 bottom panel shows that the time required to complete trials decreased across training trials. Latency stabilized quickly during the training trials in both pre-scanner and in-scanner training. A Two-Way Repeated Measures ANOVA was conducted on latency with trial (1-15) and context (pre-scanner, in-scanner) as factors. There was a main effect of trial, F (14, 518) = 25.228, $p < .05$[1], and a main effect of context, F (1, 37) = 12.908, $p < .05$. Further, there was a trial x context interaction, F (14, 518) = 6.131, $p < .05$. The interaction was due to longer pre-scanner latency for trial 1, t (19) = 4.777, $p < .05$, as compared to faster latency during this trial in-scanner.

To determine consistency in latency across the final eight trials, two One-Way Repeated Measures ANOVAs were conducted on the final eight trials of training across context. During pre-scanner training, there was no main effect of trial, F (7, 126) = 1.452,

[1] Due to a recording error, one participant's training time for trial 1 was not recorded.

$p > .05$. Alternately, during in-scanner training, there was a main effect of trial, F (7, 133) = 5.372, $p < .05$. A trend analysis was conducted to determine linearity across these trials. Latency decreased across these final eight trials as confirmed by a significant linear component, F (1, 19) = 28.954, $p < .05$ from a trend analysis. The overall difference in latency across context (pre-scanner, in-scanner) could be due to the experimental apparatus; using the trackball mouse in the scanner as compared to the pre-scanner trackball mouse, is physically different. Participants are accustomed to moving a mouse in a seated position, but not in a supine position. Further, the mice were calibrated as closely as possible, but the in-scanner mouse was less sensitive than the pre-scanner mouse.

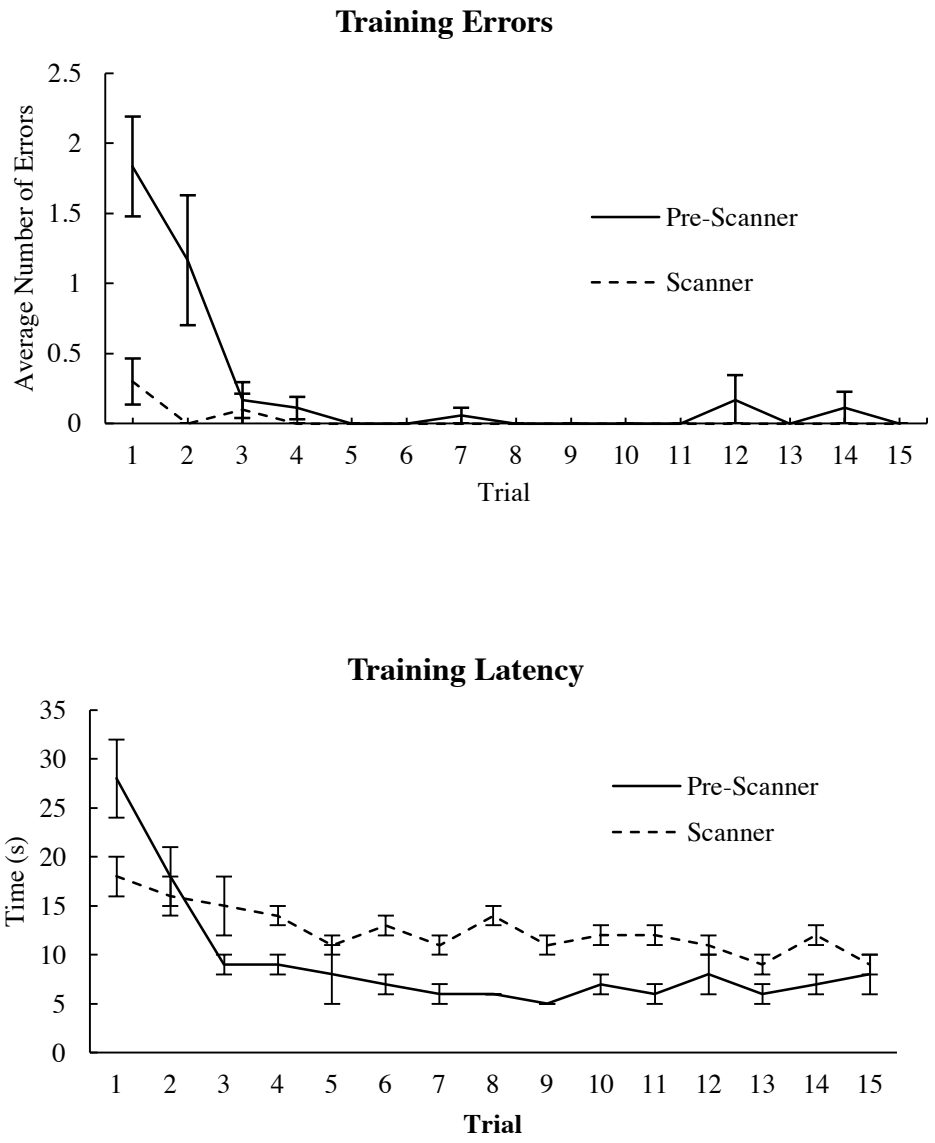

Figure 10. Top panel: Average number of errors during pre-scanner and in-scanner context by trial. Bottom panel: Average latency during pre-scanner and in-scanner context by trial. Solid line represents the pre-scanner context, while the dashed line represents in-scanner context trials. Error bars represent SEM.

Test Results. In order to determine stability across testing for each test type (Square, No Landmark, Conflict), separate One-Way Repeated Measures ANOVAs for each test type across test presentation (1-8) were conducted on proportion of choices made to the correct location to determine accuracy in goal localization. Performance for

all test types was stable across testing, Fs (7, 133) < 2.8, ps > .05. As performance did not differ across testing trials, these trials were averaged together for each test type.

Square Test. Figure 11 (bottom panel) shows the average proportion of choices across the eight presentations of the Square test. A one-sample *t*-test was conducted to determine if participants were choosing the correct corner, or the rotational equivalent, more than would be expected by chance (.25) on each trial. Results showed that participants were choosing the correct corner (M = .91, SEM = .03) more often than chance, t (19) = 21.0, p < .05 (Figure 11; bottom panel). This result shows that participants learned the landmark they were assigned, and selected that landmark greater than the other landmarks. In fact, as seen in the bottom panel of Figure 11, participants rarely chose the incorrect corners. Although, choice performance did not change over testing, first trial performance was also examined. During the first presentation of the Square test, no choices were made to the incorrect corners (Figure 11; top panel).

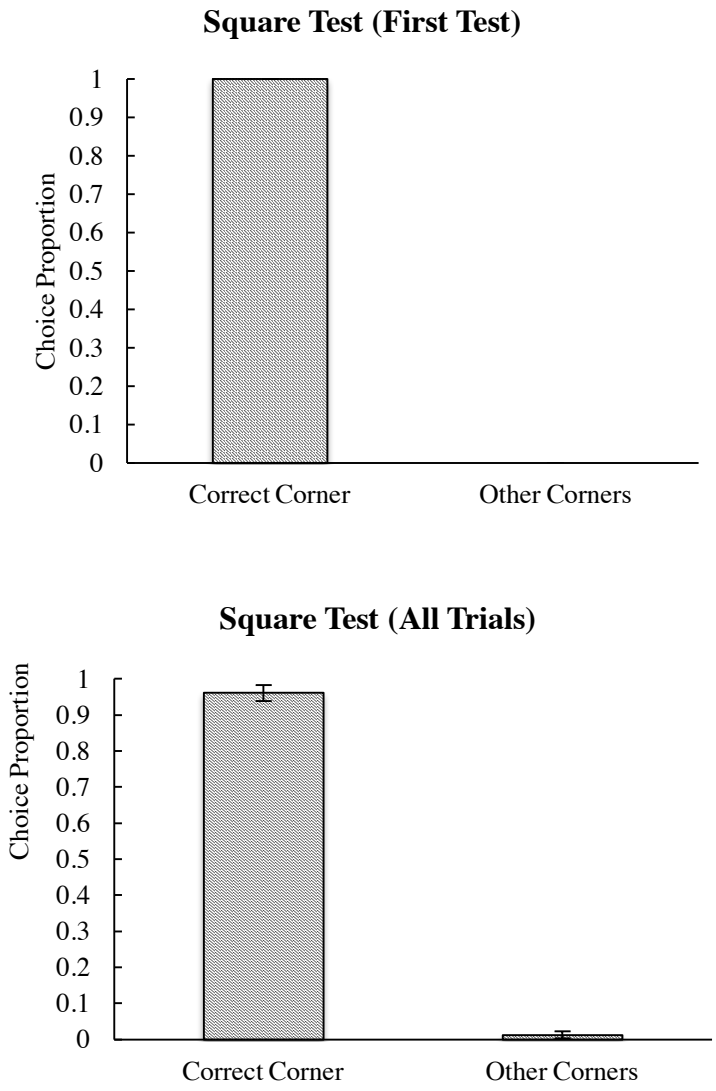

Figure 11. Experiment 1. Top panel. Proportion of choices for the first presentation of the Square test. Bottom panel. Proportion of choices for all presentations of the Square test. Error bars represent *SEMs*.

No Landmark Test. Figure 12 (bottom panel) shows the average proportion of choices across the eight presentations of the No Landmark test. A one sample *t*-test was conducted to determine if participants were choosing the correct corner or geometrically correct corner more than would be expected by chance (.5). Results showed that participants chose the correct corner ($M = .9$, $SEM = .04$) more often than chance, $t\,(19) = 9.963$, $p < .05$ (Figure 12, bottom panel). This result shows that in the absence of the

landmarks, participants can rely on environmental geometry to guide search. Although choice performance did not change over testing, first trial performance was also examined. During the first presentation of the No Landmark test showed no choices to incorrect corners (Figure 12, top panel).

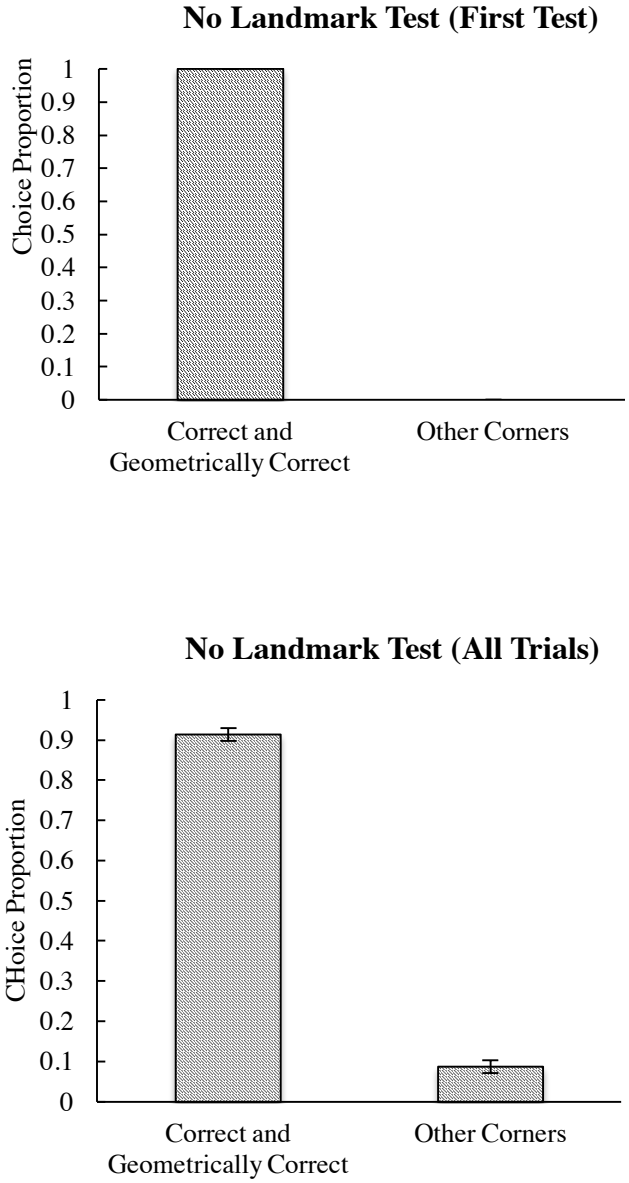

Figure 12. Experiment 1. Top panel. Proportion of choices for the first presentation of the No Landmark test. Bottom panel. Proportion of choices for all presentations of the No Landmark test. Error bars represent *SEMs*.

Conflict Test. Figure 13 (bottom panel) shows the average proportion of choices across the eight presentations of the Conflict test. A one sample *t*-test was conducted to determine if participants were choosing the correct corner or correct landmark greater than would be expected by chance. Results showed that performance was above chance (.5). Results showed that participants chose the correct corner ($M = .04$, $SEM = .09$) or correct landmark ($M = .91$, $SEM = .20$) more than chance, $t\ (19) = 17.490$, $p < .05$. Though performance was stable over testing, first trial performance was analyzed. During the first presentation, majority of choices were made to the correct corner ($M = .9$, $SEM = .06$) or correct landmark ($M = .05$, $SEM = .05$) as compared to chance, $t\ (19) = 9$, $p < .05$ (Figure 13, top panel). These results show that participants prefer the correct landmark to a greater extent than the correct corner, $t\ (19) = 13.225$, $p < .05$, but both are chosen to a greater extent than the incorrect locations.

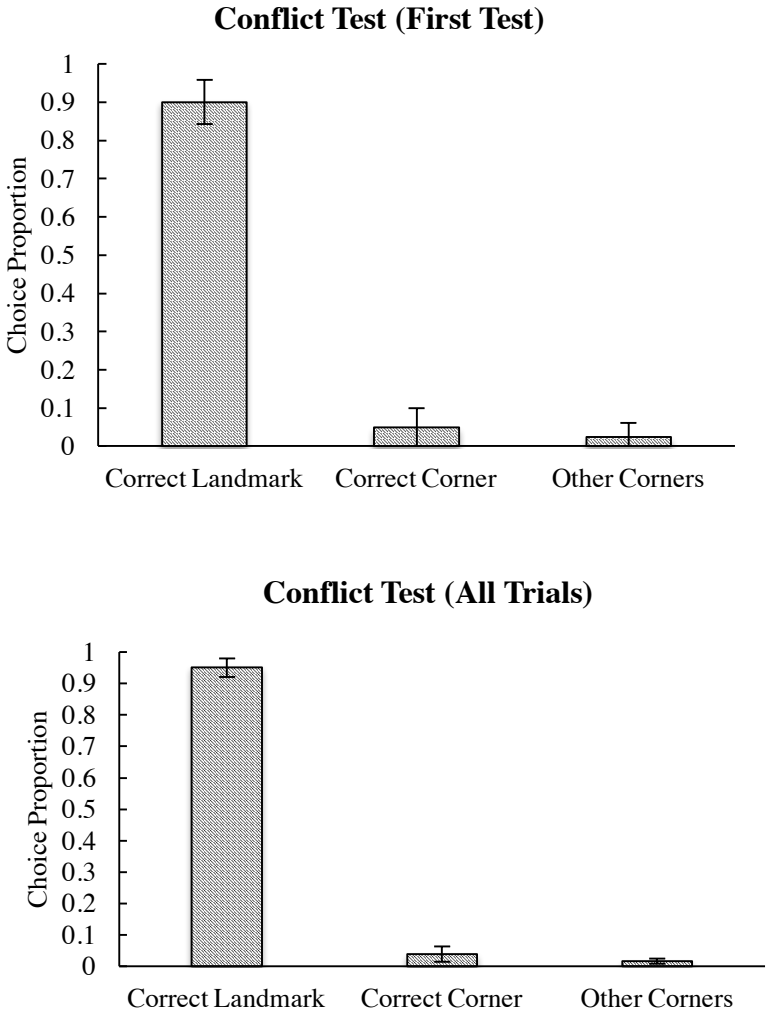

Figure 13. Experiment 1. Top panel. Proportion of choices for the first presentation of the Conflict test. Bottom panel. Proportion of choices for all presentations of the Conflict test. Error bars represent *SEMs*.

Imaging Analysis. Preprocessing of images was completed using FMRIB Software Library (FSL; Woolrich et al., 2009). This included brain extraction using FSL's brain extraction tool (BET) to remove the skull and non-brain tissue to facilitate coregistration. Motion correction was performed using two methods, 1) a script using FSL Motion Outliers which removes any timepoint with excessive motion prior to

analyses, and 2) Motion Correction in FMRIB's Linear Image Registration Tool (MCFLIRT). Neuroimaging data analysis was carried out using FSL's FMRI Expert Analysis Tool (FEAT) v6.00 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Coregistration of each participants' structural and functional images with the Montreal Neurological Institute (MNI) 2mm brain for use in the functional analysis was completed using FMRIB's Linear Image Registration Tool (FLIRT). Slice timing correction for interleaved acquisition was performed, and spatial smoothing was conducted with a 5mm kernel. *Z* (Gaussianised T/F) statistic images were created by contrasting different trial types to elucidate any differences. Gender was included as a variable of no interest in all contrasts. All functional maps were thresholded using clusters determined by $z > 2.3$ and a (corrected) cluster significance threshold of $p < 0.05$ (Worsley 2001). All coordinates are presented in MNI space. Activated regions by trial type are listed in individual tables according to trial type (Tables 3-12).

Imaging Results. The results from the imaging analysis will be discussed as they relate to the previously denoted navigationally relevant structures by the four trial types (baseline, conflict testing, square testing, no landmark testing), however all activations will be listed in individual tables by trial type. Following this, activation comparisons across trial types will be discussed.

In these analyses, the 87 trials were grouped by baseline (63 trials) and testing trials (24 trials). Various structures revealed a consistent pattern of activation during baseline compared to testing (e.g., Baseline > Testing). In particular, two HNN structures showed activations; the left middle and superior frontal gyri and the cuneus, precuneus, and posterior cingulate cortex during the training trials (Table 3; Figure 14). These

regions, as a part of the HNN, have been shown to be active when encountering boundaries and encoding locations, respectively.

Table 3.

Baseline > Testing

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
7	4.6	42	4	52	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.58	44	12	28	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 9
	4.48	34	2	46	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.32	52	16	30	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 9
	4.31	50	10	34	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
	4.21	52	14	36	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
6	4.38	48	-60	36	Right	Parietal Lobe	Angular Gyrus	BA 39
	4.26	0	-74	46	Left	Parietal Lobe	Precuneus	BA 7
	4.25	60	-56	20	Right	Temporal Lobe	Superior Temporal Gyrus	BA 22
	4.18	40	-70	48	Right	Parietal Lobe	Superior Parietal Lobule	BA 7
	4.17	62	-56	28	Right	Temporal Lobe	Superior Temporal Gyrus	BA 39
	4.14	-54	-54	42	Left	Parietal Lobe	Inferior Parietal Lobule	BA 40
5	4.24	30	-44	-18	Right	Anterior Lobe	Culmen	*
	4.14	-26	-74	-14	Left	Posterior Lobe	Declive	*
	4.11	-12	-88	-8	Left	Occipital Lobe	Lingual Gyrus	BA 18
	3.96	16	-84	-12	Right	Posterior Lobe	Declive	*
	3.93	12	-84	-12	Right	Posterior Lobe	Declive	*
	3.85	-14	-98	4	Left	Occipital Lobe	Cuneus	BA 17
4	4.27	-30	18	-6	Left	Sub-lobar	Claustrum	*
	4.21	-30	16	-14	Left	Sub-lobar	Extra-Nuclear	BA 13
	4.19	-56	14	0	Left	Frontal Lobe	Precentral Gyrus	BA 44
	3.82	-38	12	-16	Left	Sub-lobar	Extra-Nuclear	BA 13
	3.54	-36	12	-20	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 13
	2.93	-36	20	-26	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 47
3	4	46	24	-18	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.93	30	18	-6	Right	Sub-lobar	Claustrum	*
	3.65	52	36	-16	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.61	44	32	-14	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.35	54	38	-20	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.29	36	16	-16	Right	Sub-lobar	Extra-Nuclear	BA 13
2	4.21	64	-52	-14	Right	Temporal Lobe	Inferior Temporal Gyrus	BA 20
	3.78	60	-28	-16	Right	Temporal Lobe	Middle Temporal Gyrus	BA 21
	3.41	60	-42	-14	Right	Temporal Lobe	Middle Temporal Gyrus	BA 20
	3.36	50	-34	-12	Right	Temporal Lobe	Fusiform Gyrus	BA 20
	3.33	64	-32	-18	Right	Temporal Lobe	Inferior Temporal Gyrus	BA 20
	3.25	54	-40	-10	Right	Temporal Lobe	Fusiform Gyrus	BA 37
1	4.46	-24	56	24	Left	Frontal Lobe	Superior Frontal Gyrus	BA 9
	3.59	-32	60	-4	Left	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.31	-22	44	36	Left	Frontal Lobe	Superior Frontal Gyrus	BA 8
	3.24	-36	54	14	Left	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.15	-22	64	18	Left	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.09	-44	56	-2	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 10

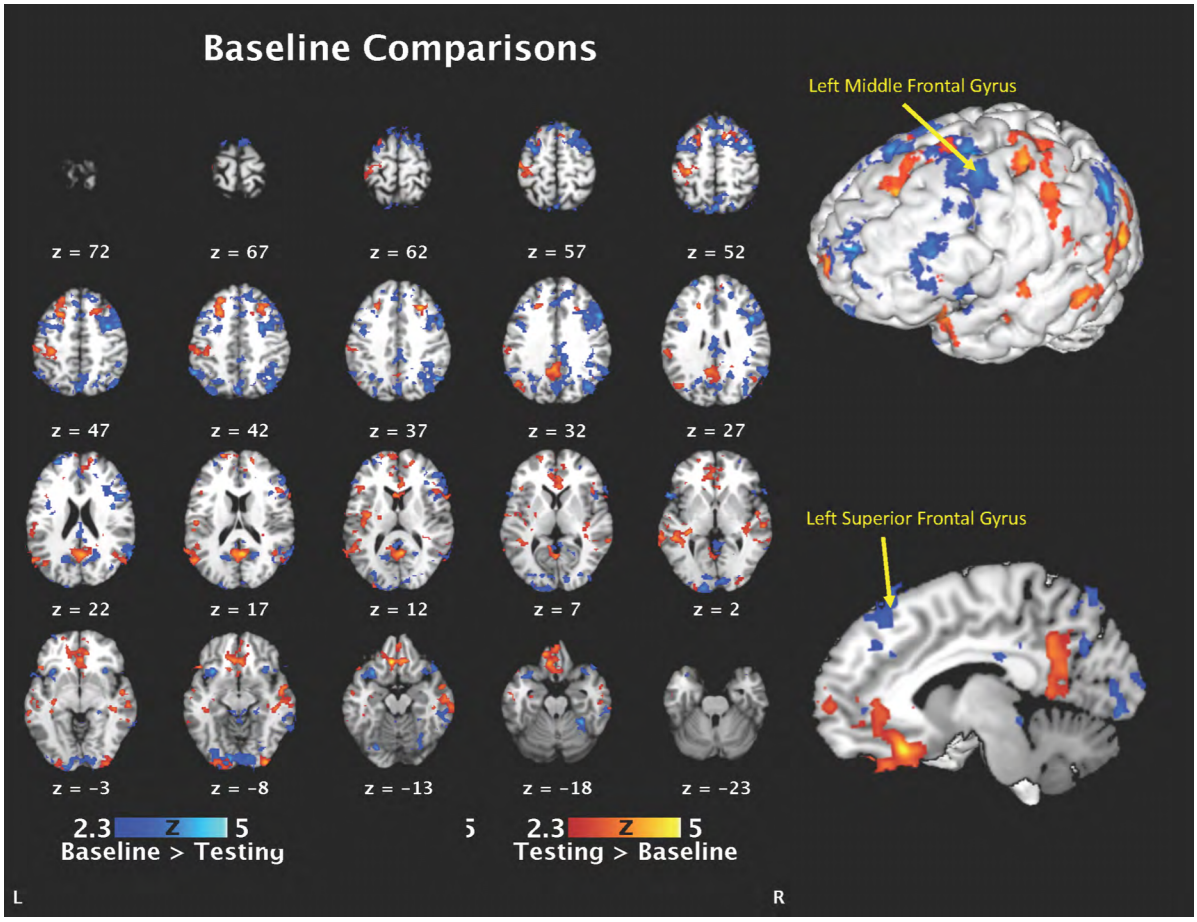

Figure 14. Activations found during the Baseline trials when subtracting the Testing trials (Blue/Light Blue), and activations found during the Testing trials when subtracting the Baseline trials (Red/Yellow).

The next set of contrasts investigated the neurofunctional correlates of each test type as compared to baseline. When subtracting activations during the baseline trials from the Square test trials (Square > Baseline), the left middle and superior frontal gyri, the cuneus and precuneus, and caudate tail showed activations (Table 4; Figure 15). These results agree with previous findings that the caudate activated in relation to landmarks (Doeller et al., 2008).

Table 4.

Square > Baseline

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
12	4.99	-8	30	-14	Left	Limbic Lobe	Anterior Cingulate	BA 24
	4.39	0	20	-24	Left	Frontal Lobe	Medial Frontal Gyrus	BA 25
	4.28	-4	24	-26	Left	Frontal Lobe	Medial Frontal Gyrus	BA 25
	4.07	6	30	-12	Right	Limbic Lobe	Anterior Cingulate	BA 24
	4.06	2	32	-4	Right	Limbic Lobe	Anterior Cingulate	*
	3.99	-10	38	-20	Left	Frontal Lobe	Medial Frontal Gyrus	BA 10
11	4	-32	-30	2	Left	Temporal Lobe	Caudate	Caudate Tail
	3.99	-66	-34	0	Left	Temporal Lobe	Middle Temporal Gyrus	*
	3.95	-48	-36	2	Left	Temporal Lobe	Superior Temporal Gyrus	BA 22
	3.92	-56	-64	20	Left	Occipital Lobe	Middle Temporal Gyrus	BA 19
	3.87	-42	-68	24	Left	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.73	-46	-64	34	Left	Temporal Lobe	Middle Temporal Gyrus	BA 39
10	4.72	4	-56	16	Right	Limbic Lobe	Posterior Cingulate	BA 23
	3.97	-2	-48	32	Left	Limbic Lobe	Cingulate Gyrus	BA 31
	3.91	0	-58	8	Left	Limbic Lobe	Posterior Cingulate	BA 30
	3.61	2	-54	34	Left	Parietal Lobe	Precuneus	BA 31
	3.6	-10	-52	32	Left	Parietal Lobe	Precuneus	BA 31
	3.59	-8	-48	6	Left	Limbic Lobe	Posterior Cingulate	BA 29
9	4.18	50	-8	-6	Right	Temporal Lobe	Superior Temporal Gyrus	BA 22
	3.81	58	-12	-16	Right	Temporal Lobe	Middle Temporal Gyrus	BA 21
	3.74	58	-24	-2	Right	Temporal Lobe	Superior Temporal Gyrus	BA 21
	3.73	58	-22	2	Right	Temporal Lobe	Superior Temporal Gyrus	BA 41
	3.68	50	-6	2	Right	Sub-lobar	Insula	BA 13
	3.65	44	-26	-10	Right	Sub-lobar	Insula	BA 13
8	4.21	-20	28	28	Left	Frontal Lobe	Medial Frontal Gyrus	BA 9
	4.19	-22	18	44	Left	Frontal Lobe	Superior Frontal Gyrus	BA 8
	3.92	-26	26	44	Left	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.91	-22	34	44	Left	Frontal Lobe	Superior Frontal Gyrus	BA 8
	3.59	-24	26	34	Left	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.44	-20	28	54	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
7	4.58	28	26	38	Right	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.81	12	18	50	Right	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.73	20	22	48	Right	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.49	36	28	40	Right	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.3	16	18	44	Right	Frontal Lobe	Medial Frontal Gyrus	BA 32
	3.2	26	12	54	Right	Frontal Lobe	Superior Frontal Gyrus	BA 6
6	3.33	52	-62	24	Right	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.26	42	-54	16	Right	Temporal Lobe	Superior Temporal Gyrus	BA 22
	3.16	44	-58	26	Right	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.07	52	-56	14	Right	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.02	56	-64	14	Right	Occipital Lobe	Middle Temporal Gyrus	BA 19
	2.94	44	-60	34	Right	Temporal Lobe	Middle Temporal Gyrus	BA 39
5	3.92	-44	24	10	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 45
	3.63	-48	24	-6	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.03	-50	18	-20	Left	Temporal Lobe	Superior Temporal Gyrus	BA 38
	3.03	-46	18	16	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 45
	2.9	-54	28	-14	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	2.88	-42	14	28	Left	Frontal Lobe	Middle Frontal Gyrus	BA 9
4	4.38	-20	62	16	Left	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.82	-18	60	10	Left	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.49	-8	60	12	Left	Frontal Lobe	Medial Frontal Gyrus	BA 10
	3.49	-20	56	0	Left	Frontal Lobe	Medial Frontal Gyrus	BA 10
	3.26	-4	64	14	Left	Frontal Lobe	Medial Frontal Gyrus	BA 10
	3.26	-16	58	-4	Left	Frontal Lobe	Medial Frontal Gyrus	BA 10
3	3.58	-28	-92	-10	Left	Occipital Lobe	Inferior Occipital Gyrus	BA 18
	3.53	-24	-92	-10	Left	Occipital Lobe	Inferior Occipital Gyrus	BA 18
	3.43	-28	-94	12	Left	Occipital Lobe	Middle Occipital Gyrus	BA 18
	3.22	-18	-98	-8	Left	Occipital Lobe	Inferior Occipital Gyrus	BA 17

	3.07	-22	-100	-2	Left	Occipital Lobe	Lingual Gyrus	BA 18
	2.86	-10	-94	-8	Left	Occipital Lobe	Inferior Occipital Gyrus	BA 17
2	3.67	48	20	16	Right	Frontal Lobe	Middle Frontal Gyrus	BA 46
	3.57	60	12	12	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 44
	3.44	42	22	8	Right	Sub-lobar	Insula	BA 13
	2.95	46	28	10	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 45
1	4.16	32	-92	-10	Right	Occipital Lobe	Inferior Occipital Gyrus	BA 18
	3.08	36	-88	-2	Right	Occipital Lobe	Inferior Occipital Gyrus	BA 18
	2.97	32	-84	-2	Right	Occipital Lobe	Middle Occipital Gyrus	BA 18

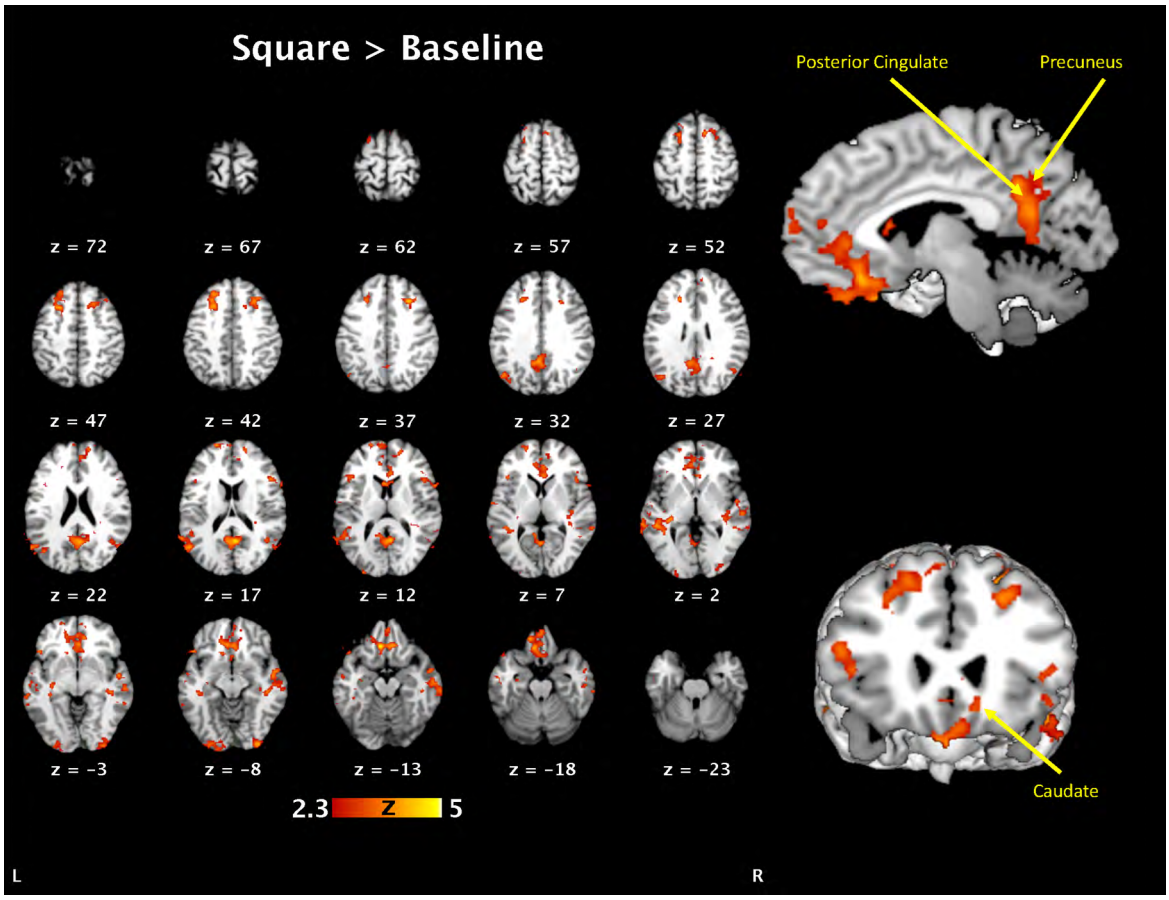

Figure 15. Activations found when subtracting the Baseline from the Square testing trials.

When subtracting the baseline activations from the Conflict testing trials (Conflict > Baseline), no previously denoted navigationally relevant regions were active (Table 5;

Figure 16). During the No Landmark test trials, there were no activations that reached significance when subtracting the baseline activations.

Table 5.

Conflict > Baseline

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
1	4.21	-32	-26	50	Left	Frontal Lobe	Precentral Gyrus	BA 4
	3.9	-50	-28	44	Left	Parietal Lobe	Postcentral Gyrus	BA 2
	3.88	-36	-10	12	Left	Sub-lobar	Insula	BA 13
	3.87	-42	-18	56	Left	Parietal Lobe	Postcentral Gyrus	BA 3
	3.54	-52	-18	18	Left	Parietal Lobe	Postcentral Gyrus	BA 43
	3.49	-42	-20	14	Left	Sub-lobar	Insula	BA 13

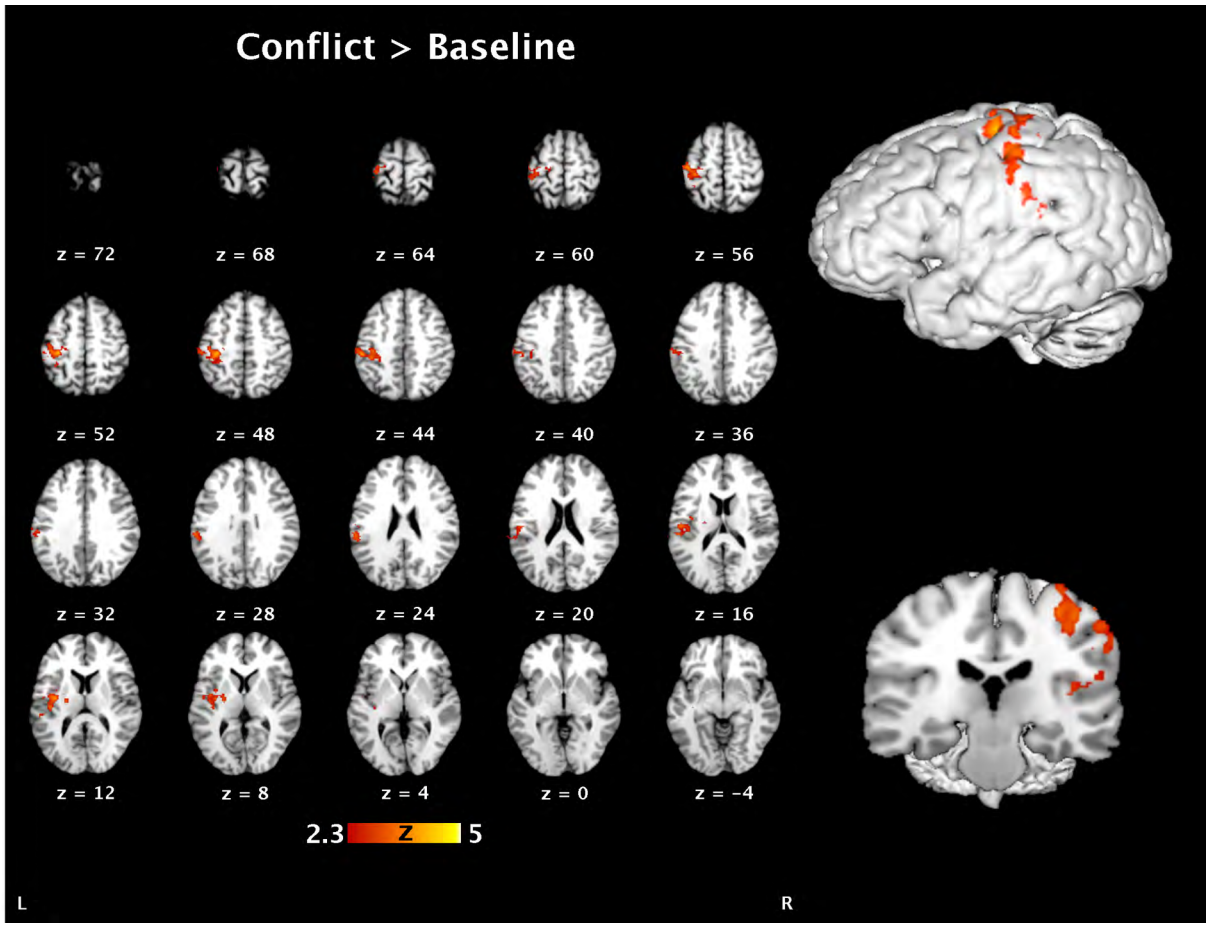

Figure 16. Activations found when subtracting the Baseline from the Conflict testing trials.

In the following analyses, activations from the individual test trial types were subtracted from the baseline trial (63 trials) activations. There were no activations that reached significance during the baseline trials when subtracting the Square test trials (Baseline > Square). Alternately, when subtracting activations during the No Landmark trial from the baseline trials (Baseline > No Landmark) the left middle and superior frontal gyri, and the cuneus and posterior cingulate cortex showed activations (Table 6; Figure 17). The frontal regions have been implicated in taking detours (Maguire et al., 1998) which would agree with activations seen here. Participants are facing an environment in which they have a less salient cue (environmental geometry) to locate the goal. When subtracting activations during the Conflict trials from the baseline trials (Baseline > Conflict), no activations reached significance.

Table 6.

Baseline > No Landmark

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
10	5.13	40	16	50	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.54	48	38	14	Right	Frontal Lobe	Middle Frontal Gyrus	BA 46
	4.48	6	32	58	Right	Frontal Lobe	Superior Frontal Gyrus	BA 6
	4.48	58	18	12	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 44
	4.42	52	16	32	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
	4.4	52	38	12	Right	Frontal Lobe	Middle Frontal Gyrus	BA 46
9	5.51	42	-54	34	Right	Temporal Lobe	Superior Temporal Gyrus	BA 39
	5.02	50	-60	40	Right	Parietal Lobe	Angular Gyrus	BA 39
	4.68	56	-54	30	Right	Temporal Lobe	Superior Temporal Gyrus	BA 39
	4.53	54	-58	28	Right	Temporal Lobe	Middle Temporal Gyrus	BA 39
	4.49	-2	-74	44	Left	Parietal Lobe	Precuneus	BA 7
	4.47	58	-54	22	Right	Temporal Lobe	Superior Temporal Gyrus	BA 22
8	4.76	-54	-54	42	Left	Parietal Lobe	Inferior Parietal Lobule	BA 40
	4.55	-34	-60	40	Left	Parietal Lobe	Angular Gyrus	BA 39
	4.28	-38	-64	46	Left	Parietal Lobe	Inferior Parietal Lobule	BA 39
	4.15	-36	-72	44	Left	Parietal Lobe	Precuneus	BA 19
	4.02	-36	-64	52	Left	Parietal Lobe	Superior Parietal Lobule	BA 7
	3.81	-32	-74	42	Left	Parietal Lobe	Precuneus	BA 19
7	4.79	38	42	-14	Right	Frontal Lobe	Middle Frontal Gyrus	BA 47
	4.67	42	50	-12	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 10
	4.43	22	62	8	Right	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.95	40	58	0	Right	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.67	48	48	-22	Right	Frontal Lobe	Middle Frontal Gyrus	BA 11
	3.6	40	50	-22	Right	Frontal Lobe	Superior Frontal Gyrus	BA 11
6	4.13	-30	18	60	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.06	-30	12	60	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.04	-44	8	30	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 9
	3.91	-28	6	62	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.9	-40	24	30	Left	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.79	-48	26	28	Left	Frontal Lobe	Middle Frontal Gyrus	BA 9
5	3.9	-2	-32	22	Left	Limbic Lobe	Posterior Cingulate	BA 23
	3.86	12	-46	34	Right	Limbic Lobe	Cingulate Gyrus	BA 31
	3.74	14	-38	30	Right	Limbic Lobe	Cingulate Gyrus	BA 31
	3.6	10	-28	28	Right	Limbic Lobe	Posterior Cingulate	BA 23
	3.13	10	-18	30	Right	Limbic Lobe	Cingulate Gyrus	BA 23
	3.02	8	-12	28	Right	Limbic Lobe	Cingulate Gyrus	BA 23
4	4.12	-32	56	-4	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	4.06	-36	58	-10	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.66	-22	62	16	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.64	-24	50	-10	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.61	-26	52	0	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.32	-30	54	6	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
3	4.81	30	16	-12	Right Cerebrum	Sub-lobar	Claustrum	*
	4.33	36	16	-20	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.39	24	28	-18	Right Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 11
	3.12	48	22	-22	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.06	24	6	-20	Right Cerebrum	Frontal Lobe	Subcallosal Gyrus	BA 34
	2.66	24	4	-16	Right Cerebrum	Sub-lobar	Lentiform Nucleus	Putamen
2	3.98	68	-38	-10	Right Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 21
	3.98	64	-50	-14	Right Cerebrum	Temporal Lobe	Inferior Temporal Gyrus	BA 20
	3.79	66	-28	-18	Right Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 21
	3.62	60	-30	-14	Right Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 21
	3.52	56	-38	-14	Right Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 20
	2.63	48	-42	-20	Right Cerebrum	Temporal Lobe	Fusiform Gyrus	BA 37
1	4.65	-30	16	-12	Left Cerebrum	Sub-lobar	Extra-Nuclear	BA 13
	3.24	-42	12	-8	Left Cerebrum	Sub-lobar	Insula	BA 13
	2.79	-34	14	-22	Left Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47

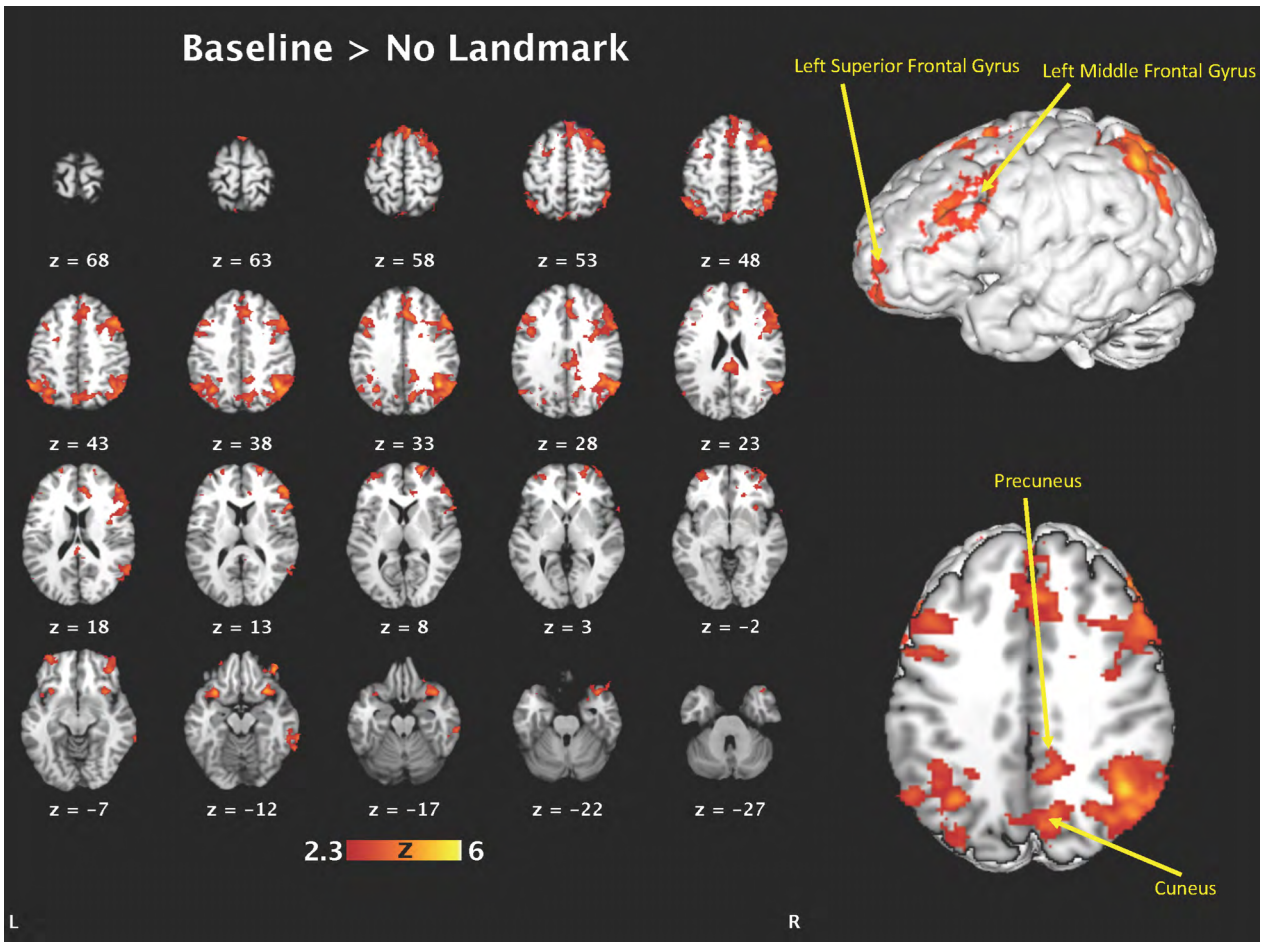

Figure 17. Activations seen during the Baseline trials when subtracting the No Landmark trials.

Next, test trial type activations were compared against each other and baseline to determine differences when placed in differing environments and when participants were required to utilize different cues. Contrasts including the Square test trials subtracting activations during the No Landmark (Square > No Landmark) test trials showed activations in the left middle and superior frontal gyri, the right inferior parietal lobule, and the caudate (Table 7; Figure 18). Further, the right inferior parietal cortex has been implicated in the HNN and was found to be active when participants are utilizing an

egocentric strategy and in relation to heading direction (Maguire et al., 1998). As the Square test does not necessarily require a global view of the environment, participants could be utilizing a view based matching strategy to locate the correct landmark. When subtracting the Conflict test trial activations from the Square test trial activation (Square > Conflict), the left middle frontal gyrus was active. These regions could be expected to show activations as the environment is shifted (mimicking a detour situation), and participants must reliably choose the landmark when in these test trials (Table 8; Figure 18). Of note, the square test trials showed greater activation than all other trial types in the left superior temporal lobe, which was found to activate in relation to boundaries in Sutton et al. (2012). Of note, there was no activation found in the left supramarginal gyrus during any trial type as was found in Sutton et al. (2012).

Table 7.

Square > No Landmark

Cluster	*Z*	x	y	z	Hemisphere	Lobe	Region	Area
9	4.03	44	-48	28	Right	Temporal Lobe	Superior Temporal Gyrus	BA 13
	3.92	52	-36	52	Right	Parietal Lobe	Inferior Parietal Lobule	BA 40
	3.89	42	-44	52	Right	Parietal Lobe	Inferior Parietal Lobule	BA 40
	3.67	56	-56	38	Right	Parietal Lobe	Supramarginal Gyrus	BA 40
	3.47	52	-40	56	Right	Parietal Lobe	Inferior Parietal Lobule	BA 40
	3.45	52	-50	42	Right	Parietal Lobe	Inferior Parietal Lobule	BA 40
8	4.56	30	8	62	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.1	30	14	58	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.95	18	-2	54	Right	Frontal Lobe	Medial Frontal Gyrus	BA 6
	3.28	24	-4	52	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.17	14	14	64	Right	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.12	16	20	60	Right	Frontal Lobe	Superior Frontal Gyrus	BA 6
7	4.64	2	44	28	Left	Frontal Lobe	Medial Frontal Gyrus	BA 9
	4.12	-6	52	34	Left	Frontal Lobe	Medial Frontal Gyrus	BA 8
	4.02	-4	46	40	Left	Frontal Lobe	Medial Frontal Gyrus	BA 8
	3.45	4	52	22	Right	Frontal Lobe	Medial Frontal Gyrus	BA 9
	3.09	-12	52	30	Left	Frontal Lobe	Superior Frontal Gyrus	BA 9
	2.99	6	50	32	Right	Frontal Lobe	Medial Frontal Gyrus	BA 6
6	3.95	16	54	12	Right	Frontal Lobe	Medial Frontal Gyrus	BA 10
	3.59	30	58	8	Right	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.32	24	48	18	Right	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.25	14	60	16	Right	Frontal Lobe	Superior Frontal Gyrus	BA 9
	3.1	32	64	4	Right	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.05	18	60	4	Right	Frontal Lobe	Medial Frontal Gyrus	BA 10
5	3.94	38	22	32	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.66	46	26	22	Right	Frontal Lobe	Middle Frontal Gyrus	BA 46
	3.63	44	20	38	Right	Frontal Lobe	Precentral Gyrus	BA 9
	3.43	42	22	24	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.37	52	24	22	Right	Frontal Lobe	Middle Frontal Gyrus	BA 46
	3.35	56	24	22	Right	Frontal Lobe	Inferior Frontal Gyrus	BA 9
4	3.95	22	-4	-2	Right	Sub-lobar	Lentiform Nucleus	Lateral Globus Pallidus
	3.76	30	-24	8	Right	Sub-lobar	Thalamus	Pulvinar
	3.6	26	-14	2	Right	Sub-lobar	Lentiform Nucleus	Lateral Globus Pallidus
	3.41	32	-6	6	Right	Sub-lobar	Lentiform Nucleus	Putamen
	3.28	30	-4	-2	Right	Sub-lobar	Lentiform Nucleus	Putamen
	3.26	38	-4	-6	Right	Sub-lobar	Claustrum	*
3	3.69	-36	2	58	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.54	-36	20	50	Left	Frontal Lobe	Superior Frontal Gyrus	BA 8
	3.38	-30	4	58	Left	Frontal Lobe	Sub-Gyral	BA 6
	3.33	-28	-2	48	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.18	-26	14	48	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.11	-36	8	60	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
2	4.14	2	42	-6	Right	Limbic Lobe	Anterior Cingulate	*
	3.88	6	44	2	Right	Limbic Lobe	Anterior Cingulate	BA 32
	3.04	-2	42	-14	Left	Limbic Lobe	Anterior Cingulate	BA 32
	2.6	6	50	-6	Right	Limbic Lobe	Anterior Cingulate	BA 32
	2.5	-4	48	12	Left	Frontal Lobe	Medial Frontal Gyrus	BA 9
1	3.97	-60	-40	6	Left	Temporal Lobe	Middle Temporal Gyrus	BA 22
	3.79	-64	-34	4	Left	Temporal Lobe	Middle Temporal Gyrus	BA 22
	2.9	-66	-28	4	Left	Temporal Lobe	Superior Temporal Gyrus	BA 22
	2.88	-52	-40	12	Left	Temporal Lobe	Superior Temporal Gyrus	BA 22

Table 8.

Square > Conflict

Cluster	*Z*	x	y	z	Hemisphere	Lobe	Region	Area
2	4.41	38	22	32	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.7	42	22	26	Right	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.45	46	26	24	Right	Frontal Lobe	Middle Frontal Gyrus	BA 46
	3.32	40	32	20	No Gray Matter found	Frontal Lobe	Middle Frontal Gyrus	
	3.31	30	16	36	Right	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.3	20	24	44	Right	Frontal Lobe	Superior Frontal Gyrus	BA 8
1	3.76	12	58	14	Right	Frontal Lobe	Superior Frontal Gyrus	BA 9
	3.66	24	48	16	Right	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.45	20	52	10	Right	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.17	28	58	14	Right	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3	28	56	2	Right	Frontal Lobe	Superior Frontal Gyrus	BA 10
	2.92	38	54	8	Right	Frontal Lobe	Middle Frontal Gyrus	BA 10

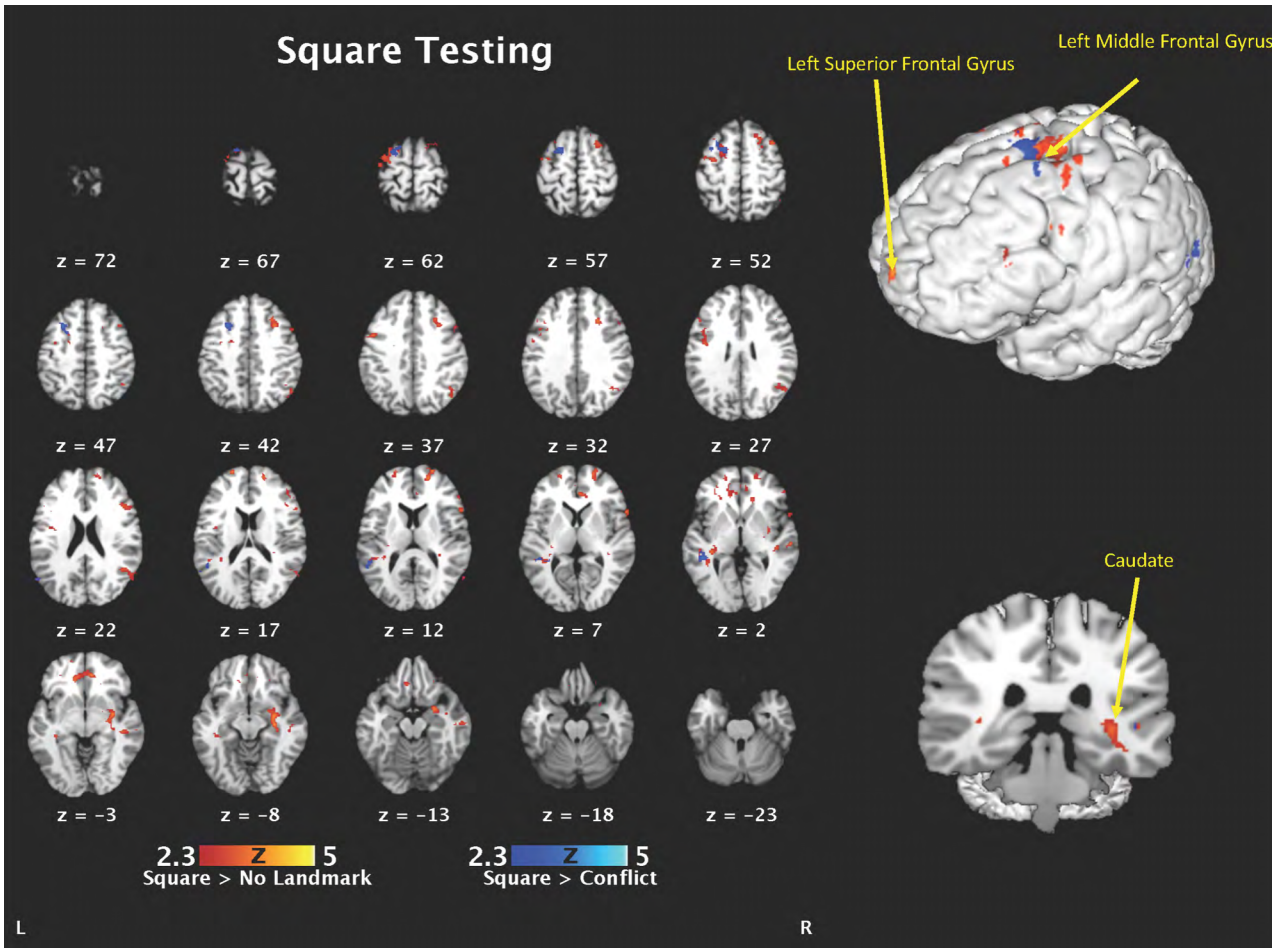

Figure 18. Activations seen during Square trials when subtracting the No Landmark test trials (Red/Yellow) and the Conflict test trials (Blue/Light Blue).

There were no activations during the No Landmark trials that reached significance when subtracting the other trial types. When subtracting the No Landmark test trials from the Conflict test trials (Conflict > No Landmark), activation was seen in the right inferior parietal cortex (Table 9; Figure 19). No other differences were seen when subtracting trial types from the Conflict trials.

Table 9.

Conflict > No Landmark

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
1	3.81	42	-52	34	Right	Temporal Lobe	Superior Temporal Gyrus	BA 39
1	3.71	50	-60	40	Right	Parietal Lobe	Angular Gyrus	BA 39
1	3.48	44	-56	50	Right	Parietal Lobe	Inferior Parietal Lobule	BA 40
1	3.33	58	-66	10	Right	Temporal Lobe	Middle Temporal Gyrus	BA 37
1	3.13	48	-66	36	Right	Parietal Lobe	Angular Gyrus	BA 39
1	3.11	46	-52	46	Right	Parietal Lobe	Inferior Parietal Lobule	BA 40

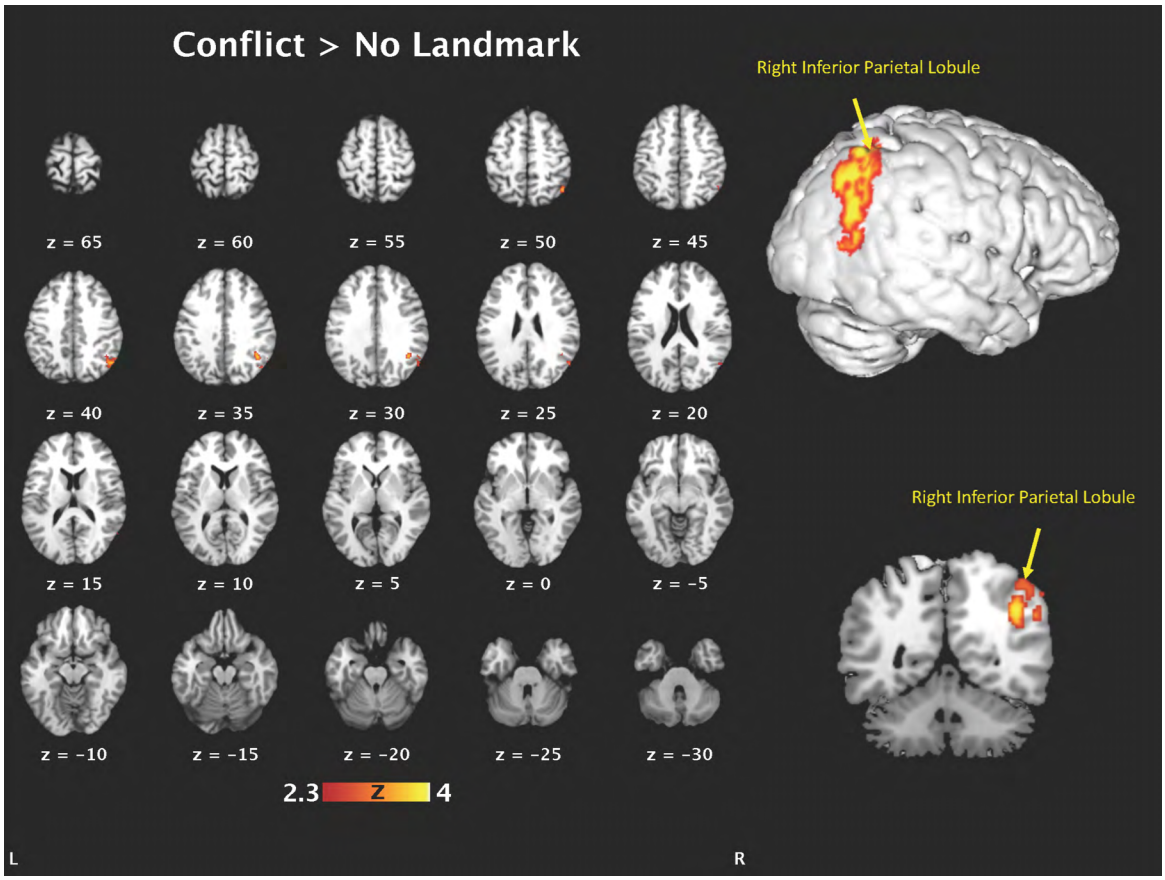

Figure 19. Activations seen during Conflict trials when subtracting the No Landmark trials.

Finally, activations from each test trial type were compared to all other trials (testing and baseline) to further elucidate activations in each trial type. Square testing trials where compared to all other trials (Square > All). During the Square testing trials, there was activation seen in the parahippocampus and the left middle and superior frontal gyri (Table 10; Figure 20). The parahippocampus is related to various navigationally relevant actions (e.g., using landmarks and encountering novel objects) but was not included in the HNN (Kaplan et al., 2014). Next, No Landmark testing trials where compared to all other trials (No Landmark > All). During the No Landmark trials, the only previously denoted region that showed activations was the parahippocampus (Table 11; Figure 20). Finally, Conflict testing trials where compared to all other trials (Conflict > All). During the Conflict trials the only navigationally relevant regions active were the cuneus, precuneus, and posterior cingulate cortex (Table 12; Figure 20).

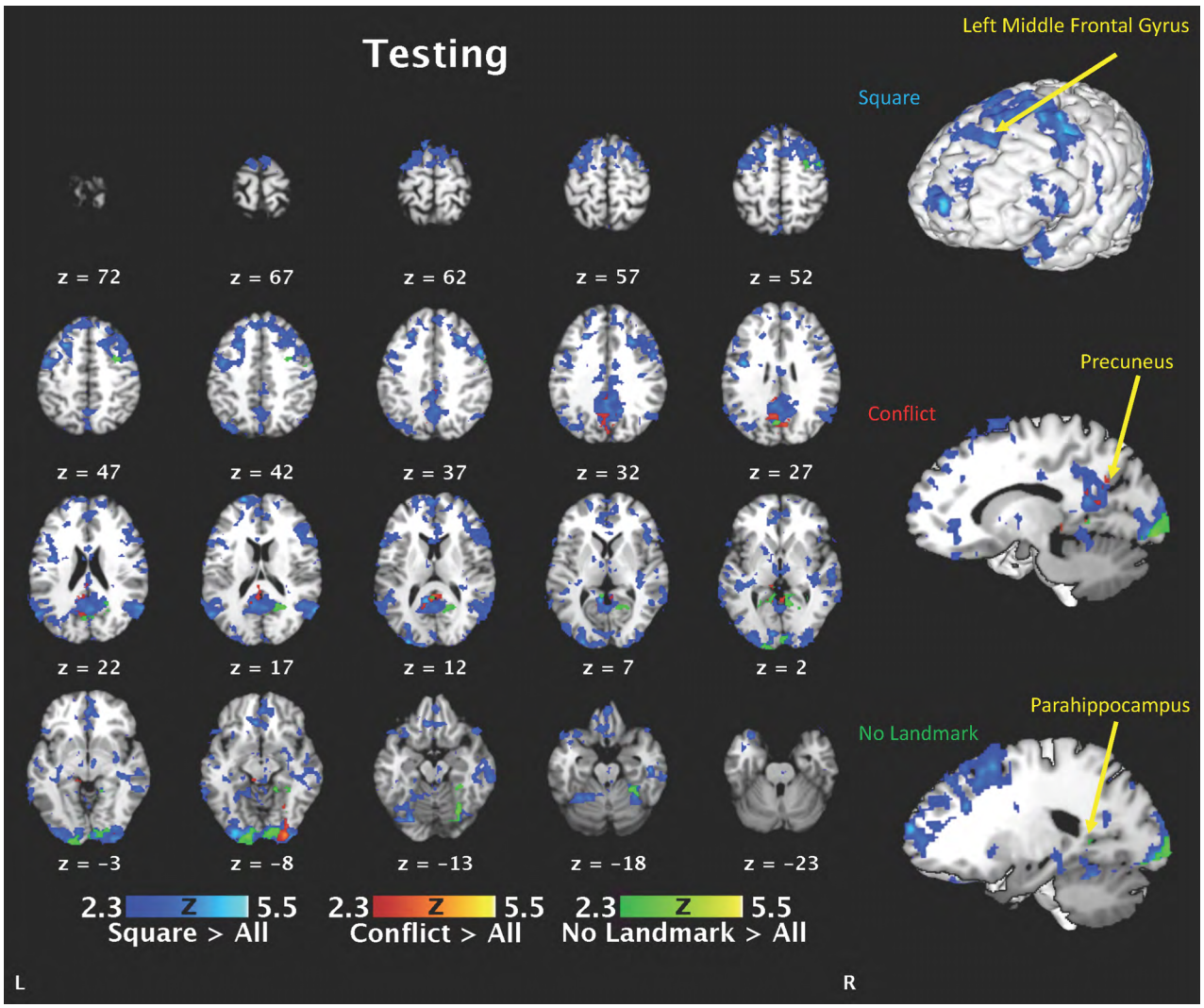

Figure 20. Activations found when subtracting all other trial types (Baseline and Testing) from each test type. Blue/Light Blue represents Square > All, Red/Yellow represents Conflict > All, and Green/Lime represents No Landmark > All.

Table 10.

Square > All

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
3	5.17	-40	-2	26	Left	Frontal Lobe	Precentral Gyrus	BA 6
	4.87	-18	62	16	Left	Frontal Lobe	Superior Frontal Gyrus	BA 10
	4.77	-22	26	30	Left	Frontal Lobe	Cingulate Gyrus	BA 32
	4.65	-26	16	46	Left	Frontal Lobe	Middle Frontal Gyrus	BA 6
	4.64	50	10	36	Right	Frontal Lobe	Precentral Gyrus	BA 6
	4.53	-32	22	-28	Left	Frontal Lobe	Inferior Frontal Gyrus	BA 47
2	4.98	-28	-94	10	Left	Occipital Lobe	Middle Occipital Gyrus	BA 18
	4.92	-30	-88	-10	Left	Occipital Lobe	Fusiform Gyrus	BA 19
	4.78	10	-90	-10	Right	Occipital Lobe	Lingual Gyrus	BA 18
	4.75	30	-92	-10	Right	Occipital Lobe	Inferior Occipital Gyrus	BA 18
	4.67	-8	-48	12	Left	Limbic Lobe	Posterior Cingulate	BA 29
	4.62	-8	-48	6	Left	Limbic Lobe	Posterior Cingulate	BA 29
1	4.65	60	-58	18	Right	Temporal Lobe	Superior Temporal Gyrus	BA 22
	4.54	48	-20	-18	Right	Limbic Lobe	Parahippocampal Gyrus	BA 36
	4.08	54	-64	16	Right	Occipital Lobe	Middle Temporal Gyrus	BA 19
	4.03	58	-22	2	Right	Temporal Lobe	Superior Temporal Gyrus	BA 41
	4.02	54	-62	24	Right	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.96	62	-30	-12	Right	Temporal Lobe	Middle Temporal Gyrus	BA 21

Table 11.

No Landmark > All

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
3	3.89	-4	-68	26	Left	Occipital Lobe	Precuneus	BA 31
	3.82	26	-66	-12	Right	Posterior Lobe	Declive	*
	3.59	18	-84	-12	Right	Posterior Lobe	Declive	*
	3.56	10	-88	-6	Right	Occipital Lobe	Lingual Gyrus	BA 18
	3.55	28	-38	-12	Right	Limbic Lobe	Parahippocampal Gyrus	BA 36
	3.49	26	-60	-12	Right	Posterior Lobe	Declive	*
2	3.83	-14	-92	-10	Left	Occipital Lobe	Lingual Gyrus	BA 18
	3.6	-22	-102	-6	Left	Occipital Lobe	Inferior Occipital Gyrus	BA 17
	3.38	-20	-100	-2	Left	Occipital Lobe	Lingual Gyrus	BA 18
	3.01	-20	-84	-12	Left	Occipital Lobe	Fusiform Gyrus	BA 19
	2.5	-2	-90	-10	Left	Occipital Lobe	Lingual Gyrus	BA 18
1	3.45	32	4	46	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.32	28	4	50	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.25	40	2	54	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6
	2.94	52	2	38	Right	Frontal Lobe	Precentral Gyrus	BA 6
	2.88	56	0	38	Right	Frontal Lobe	Precentral Gyrus	BA 6
	2.86	30	-2	52	Right	Frontal Lobe	Middle Frontal Gyrus	BA 6

Table 12.

Conflict > All

Cluster	Z	x	y	z	Hemisphere	Lobe	Region	Area
3	3.63	-4	-46	12	Left	Limbic Lobe	Posterior Cingulate	BA 29
	3.55	0	-44	12	Left	Limbic Lobe	Posterior Cingulate	BA 29
	3.26	-10	-48	2	Left	Anterior Lobe	Culmen	*
	3.23	-8	-32	-6	Left	Sub-lobar	Thalamus	*
	3.21	-10	-54	14	Left	Limbic Lobe	Posterior Cingulate	BA 30
	3.04	0	-48	2	Left	Anterior Lobe	Culmen	*
2	3.66	-6	-60	28	Left	Parietal Lobe	Precuneus	BA 31
	3.41	6	-70	28	Right	Parietal Lobe	Precuneus	BA 31
	3.11	10	-64	26	Right	Parietal Lobe	Precuneus	BA 31
	3.05	10	-60	34	Right	Parietal Lobe	Precuneus	BA 7
	3.05	-4	-66	34	Left	Occipital Lobe	Cuneus	BA 7
	3.02	0	-76	32	Left	Occipital Lobe	Precuneus	BA 31
1	4.19	26	-92	-10	Right	Occipital Lobe	Fusiform Gyrus	BA 18
	3.34	20	-90	-10	Right	Occipital Lobe	Lingual Gyrus	BA 18
	3.15	14	-90	-10	Right	Occipital Lobe	Lingual Gyrus	BA 18
	3.14	28	-82	-8	Right	Occipital Lobe	Lingual Gyrus	BA 18
	3.12	30	-66	-16	Right	Posterior Lobe	Declive	*
	2.95	26	-62	-10	Right	Occipital Lobe	Fusiform Gyrus	BA 19

Discussion

Experiment 2 was conducted in order to determine the neurofunctional correlates of geometry and feature learning in a virtual environment in college-aged participants. Behaviorally, participants performed at a maximal level. During the pre-scanning training, participants showed a marked decrease in errors and latency to complete training trials across these initial training trials. This performance showed an asymptotic level of performance prior to entering the scanner and as such, ensured that the confound of learning while acquiring neurofunctional images was eliminated.

Test trials revealed a similar pattern of consistency as was seen in Experiment 1. Across all test trial types, participant choices were consistent across each presentation. Performance in the Square test trials revealed that participants reliably chose the correct landmark as compared to the alternate landmarks. This result suggests that the assigned landmark was a salient and reliable feature of goal localization. When in the No

Landmark environment, participants reliably chose the correct or geometrically correct corner. Participants learned the geometric relationship between the assigned landmark and its position in the environment. Finally, when presented with the Conflict test trials, participants chose the correct landmark to a greater extent that the correct corner. This result demonstrates that the landmark was a much more salient feature of the environment than the geometric cue, although participants chose the correct and geometrically correct corner in the absence of landmarks.

These results are similar to Experiment 1 and previous research (Cheng, 1986; Sturz & Kelly, 2009). Because performance was stable and reliable across training and test trials, functional results can be interpreted with confidence; the potential confound of errors or participant confusion during the task will not be of concern in interpreting the imaging results. As was hypothesized, there were many activations found in navigationally relevant regions. The caudate was found to be active during the Square trials when the use of landmarks was required for successful goal localization. This is in agreement with previous research from Doeller et al. (2008). The parahippocampus was found to be active in two trial types, Square and No Landmark. These trials include landmarks alone and novel environments respectively, which agrees with previous research (Epstein & Kanwisher, 1998). When subtracting activations found in the No Landmark trials from the Square and Conflict trials, activations were located in the right inferior parietal cortex, a part of the HNN. This region is related to an egocentric strategy (Maguire et al., 1998). In relation to this task, participants could be using an egocentric, or view-based matching, strategy to locate the goal. Of note, during the Conflict trials participants rarely chose the correct corner, which would agree with an egocentric

strategy rather than a global or allocentric strategy. Another HNN structure that was found to be active during the Baseline and Square trials was the left middle and superior frontal gyri. Maguire et al. (1998) noted that this region was active when participants were faced with a detour. This result does not align with the hypothesis that the frontal regions would be more active when landmarks and geometry were in conflict. However, this region may also be related to using reliable landmarks as these trials share the common feature of landmarks positioned in the same spatial relation. Finally, the cuneus, precuneus, and posterior cingulate cortex showed activations during all trial types. As a part of the HNN, these regions were implicated in encoding of locations. These regions may also be involved in recalling previously encoded locations.

Of note, there were regions that were expected to show activations, but not found in this task. In particular, there was no hippocampal activations found in any of the trial contrasts. This does not imply that the hippocampus is not related to navigation, only that this task does not engage this region to a level of significance. Further, previous research from Doeller et al. (2008) using a similar task reported hippocampal activation during geometry trials. However, participants were learning boundary related locations when the hippocampal activations were found. Similarly, Sutton et al. (2012) reported left supramarginal gyrus activation when participants were utilizing geometry to locate a goal. Of note, the authors posited this region (and the left temporal gyrus) was activated due to participants using a verbal strategy to solve these trials. In line with this, the current experiment activated the left temporal gyrus and the lingual gyrus during various trials which agrees with the idea that participants use a verbal strategy to solve the No Landmark trials.

Taken together, this current task is robust in that it allows for an investigation of how college-aged participants use features and geometry to locate a goal. Further, this task elicits various navigationally relevant structures and structures that have not previously been implicated in navigation. Specifically, many HNN structures were found to be activated in this simple environment which strengthens the evidence that these regions are important during navigation. One aspect of the current experiment was to resolve previous mixed findings in similar simple environments. In agreement with Sutton et al (2012), the parahippocampus was activated in trials that included landmarks, but also in trials in which landmarks were removed. However, the posterior hippocampus and supramarginal gyrus activations reported in that experiment were not replicated in the current experiment. It is not the position of the author that this nullifies the importance of this region, only that the current task does not elicit this activation. Also in agreement with Doeller et al. (2008), caudate activation was found during the Square trials in which participants have to rely on landmarks to locate the goal.

The inclusion of many navigationally relevant regions and partial consistencies with previous similar environments ensures that this task is a good method to test for navigational abilities across ages. As such, Experiment 3 was conducted to determine the stability of task performance across aging in both behavioral and functional terms. The following experiment includes participants that are older than college age and uses the same task for comparison purposes.

Chapter 5: Experiment 3

Experiment 3 was a preliminary examination to determine if participants of different ages will show similar or different activation in the structures involved in spatial navigation (see Table 1; Figure 3) when completing this task. Due to the small sample size, and the exploratory nature of this experiment, the results of this study should be taken as preliminary. As previous research has shown, there are various changes in spatial abilities throughout the lifespan (Lövdén et al., 2005; Moffat et al., 2006; 2007; Pine et al., 2002) that could potentially be explained by neuroanatomical structural differences (Raz et al., 2005; Sowell et al., 2003). Specific hypotheses are as follows. First, an analysis of age groups' behavioral performance of the reorientation task will allow for insight into any differences that occur across the lifespan. It is hypothesized that all participants will complete the task similar to Experiment 2, but older participants may show more errors than their younger counterparts. Alternately, the possibility exists that participants of older ages may perform similarly to their younger counterparts behaviorally due to the simplicity of the environment. If so, the functional differences or similarities may shed light onto the process of healthy aging, and how age affects the use of features and environmental geometry.

Another purpose of this experiment is to conduct a volumetric analysis on the hippocampus and caudate nucleus, which have been implicated in both geometry and feature learning (Kaplan et al., 2014; Sutton et al., 2012; Wegman et al., 2014). Due to this, the volumetric analysis will potentially allow for a greater understanding of any

behavioral decrements in the task. The greatest volumetric differences should be seen in the youngest and oldest participants with a decline occurring across the lifespan.

The age range was chosen first, to get a snapshot of the subtle changes across the lifespan, and second due to natural neural degeneration across the lifespan (Raz et al., 2005), and to elucidate what occurs behaviorally and structurally prior to, and after the structural changes seen in previous volumetric studies. Specifically, it is hypothesized that increased age will be associated with a linear decline in caudate volume, whereas there should be a significant difference in hippocampal volume between the youngest and oldest participants.. In line with the volumetric decreases, it is hypothesized that participants in the young group will have the greatest success in the navigational task as compared to the older participants. There should be a decrease in success with landmarks across the aging due to the decreased caudate volume. Finally, it is hypothesized that the older participants should show the greatest impairment during the No Landmark test as the hippocampal volume is predicted to decrease.

Participants

As this was a preliminary study, a small sample size was used. Ten participants aged 36-57 (mean age 46.6, *SD* = 7.5; 8 males, 2 females) were included in Experiment 3. All but 1 participant was right handed. Participant's education level included 7 PhD's, 2 with Master's Degrees, and 1 with an undergraduate degree). All participants underwent the standard protocol for entering the MR scanner per the institutional policy, and paid $40.00 for their participation.

Methods

Data collection and image acquisition were identical to Experiment 2.

Results

Training. Figure 21 (top panel) shows average number of errors for pre-scanner and scanner training. All participants rapidly learned the reorientation task before entering the scanner and acclimated well to scanner environment.

An analysis of training trials was completed to determine if participants learned the location of the landmark that denotes the goal location based on the number of errors across the 15 pre-scanner and in-scanner training trials. A Two-Way Repeated Measures ANOVA was conducted on errors with trial (1-15) and context (pre-scanner, in-scanner) as factors. There was a main effect of trial, F (14, 252) = 8.682, $p < .05$, a main effect of context, F (1, 18) = 12.126, $p < .05$, and a Trial x Context interaction, F (14, 252) = 3.919, $p < .05$. The interaction is due to a greater number of errors during the pre-scanner trials as compared to the in-scanner trials during trial 1, t (9) = 2.751, $p < .05$. The remaining trials did not differ from each other ($ps > .05$) suggesting that participants quickly learn the task across the first two trials. A Two-Way Repeated Measures ANOVA was conducted on number of errors with trial (8-15) and context (pre-scanner, in-scanner) to ensure participants had reached criterion of stability in performance during the final eight trials of training. There were no main effects across trials, F (7, 126) = .825, $p > .05$, and context, F (1, 18) = 2.143, $p > .05$, and no Trial x Context interaction, F (7, 126) = .825, $p > .05$.

Figure 21 (bottom panel) shows that the time required to complete trials decreased across training trials. Latency stabilized quickly during the training trials in both pre-scanner and in-scanner training. A Two-Way Repeated Measures ANOVA was conducted on latency to complete trials with trial (1-15) and context (pre-scanner, in

scanner) as factors. There was a main effect of trial, F (14, 238) = 9.957, $p < .05$[2], a main effect of context, F (1, 17) = 4.479, $p < .05$, and a Trial x Context interaction, F (14, 238) = 2.101, $p < .05$. The interaction was due to an increase in latency to complete the in-scanner trials as compared to the pre-scanner trials during some trials ($ps < .05$). To determine consistency in latency across the final eight trials, a Two-Way Repeated Measures ANOVA was conducted on the final eight trials of training. There was no main effect of trial, F (7, 119) = 1.336, $p > .05$, no Trial x Context interaction, F (7, 199) = 1.268, $p > .05$, but a main effect of context, F (1, 17) = 17.639, $p < .05$. In-scanner training trials (M = 5.833, SEM = .722) took longer to complete than pre-scanner trials (M = 10.012, SEM = .685). As mentioned in Experiment 2, this difference is likely due to the participants' familiarity with using a mouse in the supine position or the differences in sensitivity across mice.

[2] Due to a recording error, one participant's training time for trial 15 was not recorded.

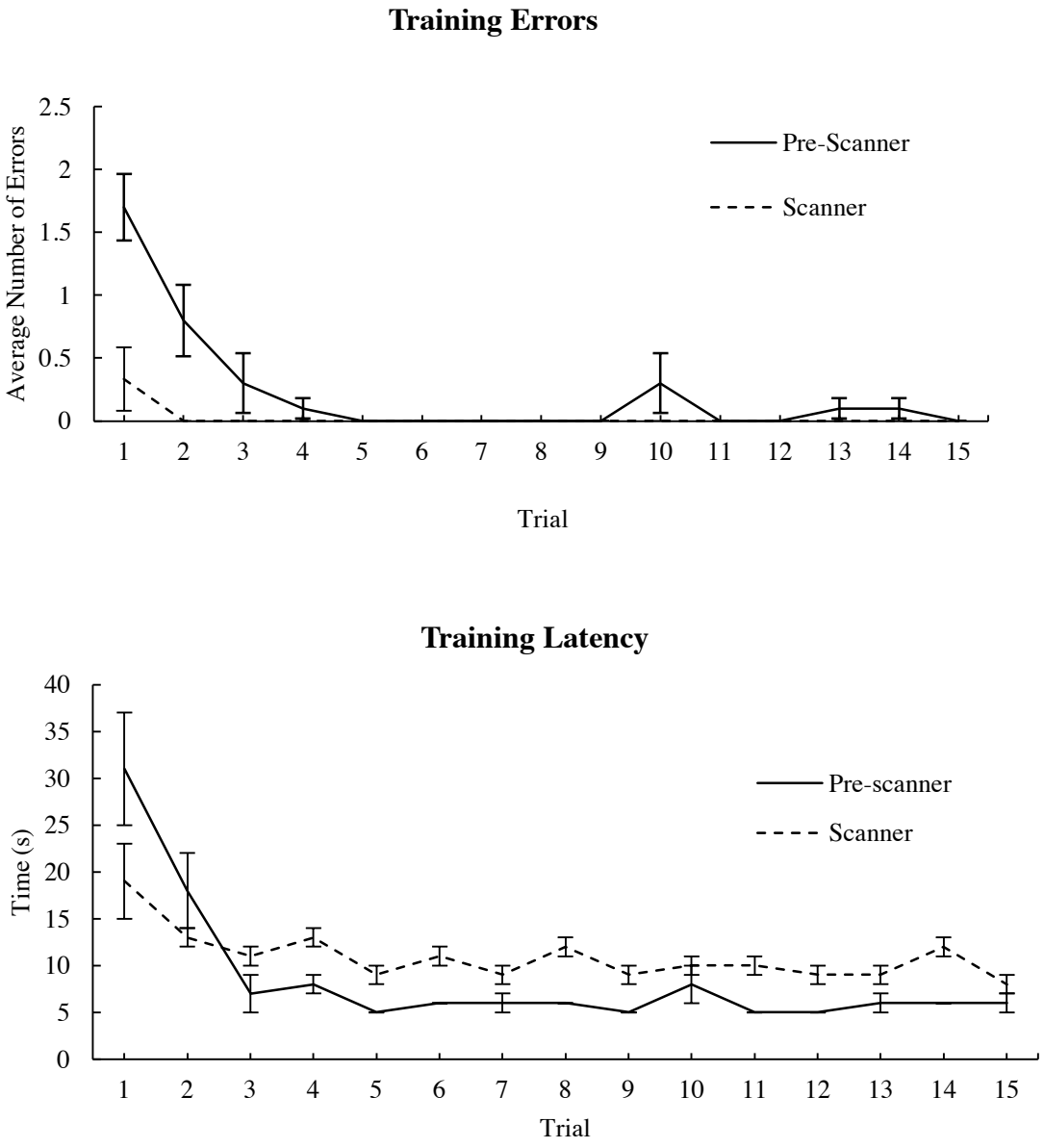

Figure 21. Top panel: Average number of errors during pre-scanner and in-scanner context by trial. Bottom panel: Average latency during pre-scanner and in-scanner context by trial. Solid line represents the pre-scanner context, while the dashed line represents in-scanner context trials. Error bars represent SEM.

Test Results. In order to determine stability across testing for each test type (Square, No Landmark, Conflict), separate One-Way Repeated Measures ANOVAs on test type across test presentation (1-8) were conducted on proportion of choices made to

the correct location to determine accuracy in goal localization. Performance for all test types was stable across testing, Fs (7, 63) <.783, ps > .05. As performance did not differ across testing trials, these trials were averaged together for each test type.

Square Test. Figure 22 (bottom panel) shows the average proportion of choices across the eight presentations of the Square test. A one-sample *t*-test was conducted to determine if participants were choosing the correct corner more than would be expected by chance (.25) on each trial. Results showed that participants were choosing the correct corner (M = .93, SEM = .042) more often than chance t (9) = 15.885, p < .05 (Figure 22; bottom panel). This result shows that participants learned the landmark they were assigned, and selected that landmark greater than the other landmarks. In fact, as seen in the bottom panel of Figure 22, participants rarely choose the incorrect corners. Although, choice performance did not change over testing, first trial performance was also examined. During the first presentation of the Square test, no choices were made to the incorrect corners (Figure 22; top panel).

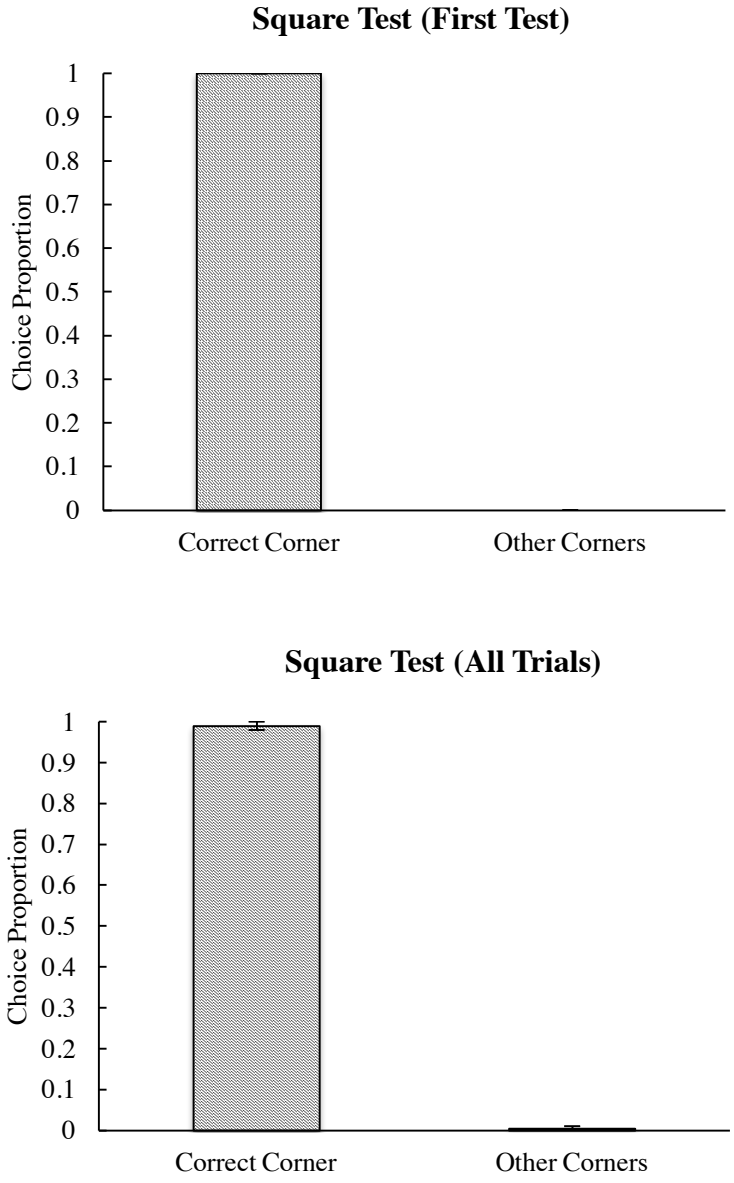

Figure 22. Experiment 1. Top panel. Proportion of choices for the first presentation of the Square test. Bottom panel. Proportion of choices for all presentations of the Square test. Error bars represent *SEMs*.

No Landmark Test. Figure 23 (bottom panel) shows the average proportion of choices across the eight presentations of the No Landmark test. A one sample *t*-test was conducted to determine if participants were choosing the correct corner or geometrically

correct corner more than would be expected by chance (.5). Results showed that participants were choosing the correct corner (M = .88, SEM = .056) more often than chance t (9) = 4, p < .05 (Figure 23, bottom panel). This result shows that in the absence of the landmarks, participants can rely on environmental geometry to guide search. Although choice performance did not change over testing, first trial performance was also examined. During the first presentation of the No Landmark test, no choices were made to the incorrect corners. (Figure 23; top panel).

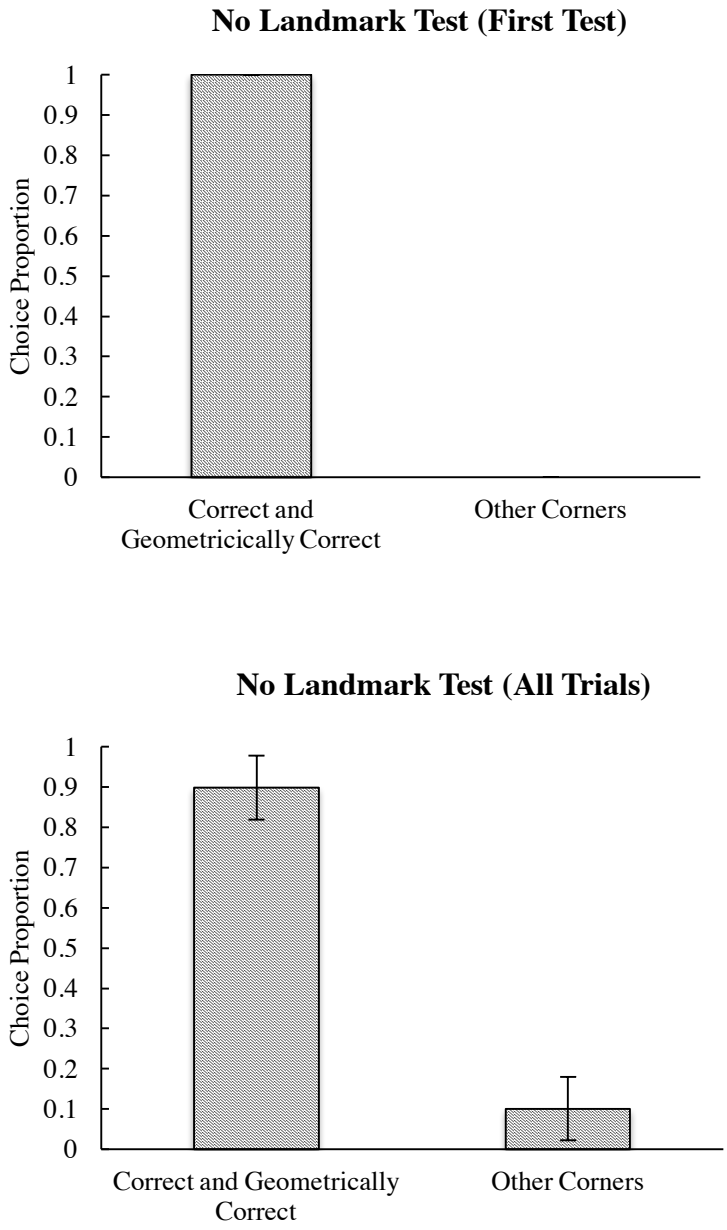

Figure 23. Experiment 1. Top panel. Proportion of choices for the first presentation of the No Landmark test. Bottom panel. Proportion of choices for all presentations of the No Landmark test. Error bars represent *SEMs*.

Conflict Test. Figure 24 (bottom panel) shows the average proportion of choices across the eight presentations of the Conflict test. A one sample *t*-test was conducted to determine if participants were choosing the correct landmark greater than would be

expected by chance. Results showed that performance was above chance (.25). Results showed that participants were choosing the correct landmark (M = .85, SEM = .08) more than chance, t (9) = 7.060, p < .05. Though performance was stable over testing, first trial performance was analyzed. During the first presentation, no choices were made to either the alternate corners (Figure 24, top panel).

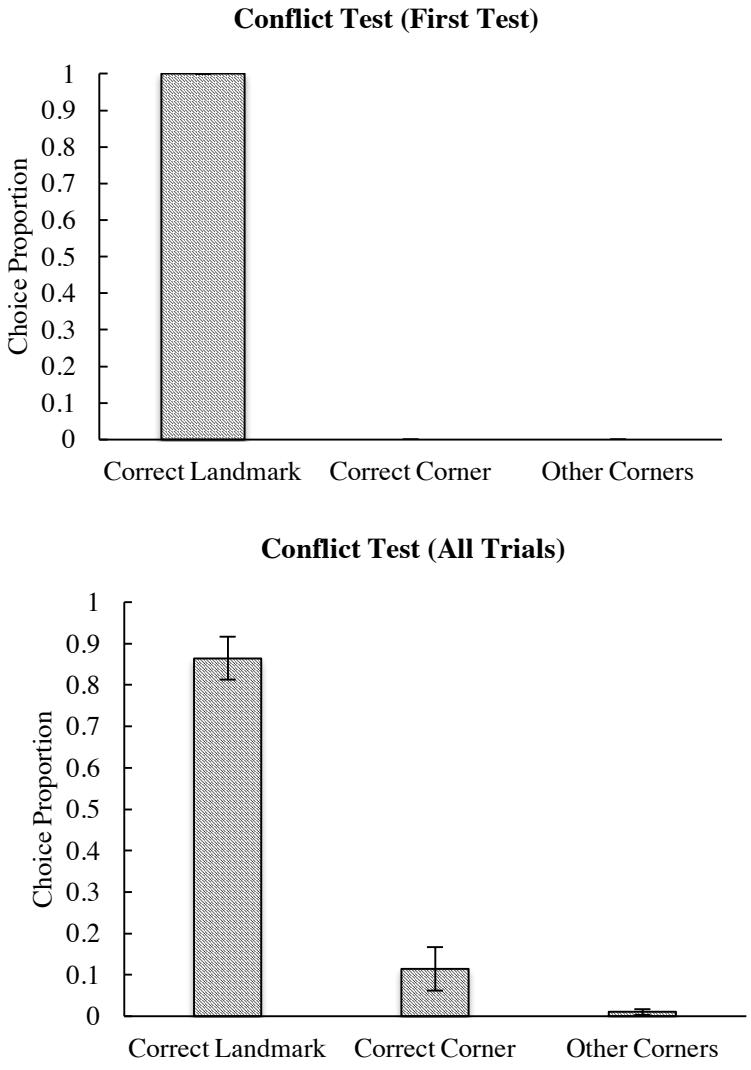

Figure 24. Experiment 1. Top panel. Proportion of choices for the first presentation of the Conflict test. Bottom panel. Proportion of choices for all presentations of the Conflict test. Error bars represent *SEMs*.

Imaging Analysis. Imaging analyses was identical to Experiment 2. An added variable of age was included in the age comparisons. To accomplish this, age was mean centered across all participants ($M = 33$), and included as a variable of interest in the analyses. This allowed for participants' activations in the younger group to be subtracted from participants' activations in the older group. This analysis technique results in a report of activations found in the older group as compared to the younger group. This was included in all contrasts in the age comparison analyses to elucidate any age differences across trial types. Activated regions by trial type are listed in individual tables according to trial type (Tables 13-16).

Imaging Results. Because of the small sample size, many of the contrasts that were conducted in the previous experiment did not reveal areas of activation to the level of significance. As such, contrasts were conducted on individual trial types without subtracting the remaining trials, and trial types were compared to activations during the ITI to determine any functional activity throughout the task. Unfortunately, these analyses did not reveal activations that reached threshold during the Square or No Landmark trials. However, it is important to note that various navigationally relevant structures were found to be active throughout the experiment and will be discussed below.

During the baseline trials, there was activation found in HNN regions; the left middle frontal gyrus and the left supramarginal gyrus (Figure 25; Table 13), and the parahippocampus, cuneus when subtracting ITI activation (Figure 26; Table 14). Of note, in Experiment 2 there was similar activation in the cuneus and left middle frontal gyrus in younger participants.

Table 13.

Baseline

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
8	3.71	-44	-42	54	Left Cerebrum	Parietal Lobe	Inferior Parietal Lobule	BA 40
	3.63	-36	-32	34	Left Cerebrum	Parietal Lobe	Postcentral Gyrus	BA 2
	3.59	-56	-52	32	Left Cerebrum	Parietal Lobe	Supramarginal Gyrus	BA 40
	3.58	-38	-24	68	Left Cerebrum	Frontal Lobe	Precentral Gyrus	BA 4
	3.55	-48	-36	62	Left Cerebrum	Parietal Lobe	Inferior Parietal Lobule	BA 40
	3.53	-58	-28	44	Left Cerebrum	Parietal Lobe	Postcentral Gyrus	BA 2
7	3.56	-40	-8	20	Left Cerebrum	Sub-lobar	Insula	BA 13
	3.47	-34	-18	-4	Left Cerebrum	Sub-lobar	Lentiform Nucleus	Putamen
	3.46	-32	-6	12	Left Cerebrum	Sub-lobar	Claustrum	*
	3.46	-44	-2	2	Left Cerebrum	Sub-lobar	Insula	BA 13
	3.33	-8	-26	2	Left Cerebrum	Sub-lobar	Thalamus	Pulvinar
	3.24	-30	-6	-10	Left Cerebrum	Sub-lobar	Lentiform Nucleus	Putamen
6	3.48	44	-40	40	Right Cerebrum	Parietal Lobe	Supramarginal Gyrus	BA 40
	3.21	54	-40	34	Right Cerebrum	Parietal Lobe	Supramarginal Gyrus	BA 40
	3.16	48	-56	32	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.07	46	-54	28	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.03	50	-44	40	Right Cerebrum	Parietal Lobe	Supramarginal Gyrus	BA 40
	2.98	46	-58	40	Right Cerebrum	Parietal Lobe	Angular Gyrus	BA 39
5	3.68	8	-6	44	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 24
	3.36	0	2	38	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 24
	3.29	12	-2	38	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 24
	3.17	-6	-10	50	Left Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 6
	3.14	-6	-20	46	Left Cerebrum	Frontal Lobe	Paracentral Lobule	BA 31
	3.13	-2	-10	44	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 24
4	3.66	-40	28	36	Left Cerebrum	Frontal Lobe	Precentral Gyrus	BA 9
	3.62	-42	32	34	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.24	-38	36	24	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 9
	3.1	-40	32	44	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.02	-36	18	34	Left Cerebrum	Frontal Lobe	Precentral Gyrus	BA 9
	2.98	-36	40	34	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 9
3	4.21	12	-52	-22	Right Cerebellum	Anterior Lobe	Fastigium	*
	3.98	6	-58	-24	Right Cerebellum	Anterior Lobe	Fastigium	*
	3.56	4	-64	-24	Right Cerebellum	Anterior Lobe	Culmen	*
	3.24	24	-52	-24	Right Cerebellum	Anterior Lobe	Culmen	*
	3.24	22	-56	-22	Right Cerebellum	Anterior Lobe	Culmen	*
	2.77	0	-52	-26	Left Cerebellum	Anterior Lobe	Culmen	*
2	4.35	-44	46	-18	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 11
	3.18	-50	36	-20	Left Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	2.75	-48	38	-10	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 47
	2.58	-32	46	-18	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 11
1	3.42	2	-76	2	Left Cerebrum	Occipital Lobe	Lingual Gyrus	BA 18
	3.12	-8	-78	-2	Left Cerebrum	Occipital Lobe	Lingual Gyrus	BA 18
	2.98	2	-76	-6	Left Cerebellum	Anterior Lobe	Culmen	*
	2.95	2	-70	0	Left Cerebellum	Anterior Lobe	Culmen of Vermis	*
	2.95	-4	-70	-4	Left Cerebellum	Anterior Lobe	Culmen	*
	2.92	0	-72	-4	Left Cerebellum	Anterior Lobe	Culmen	*

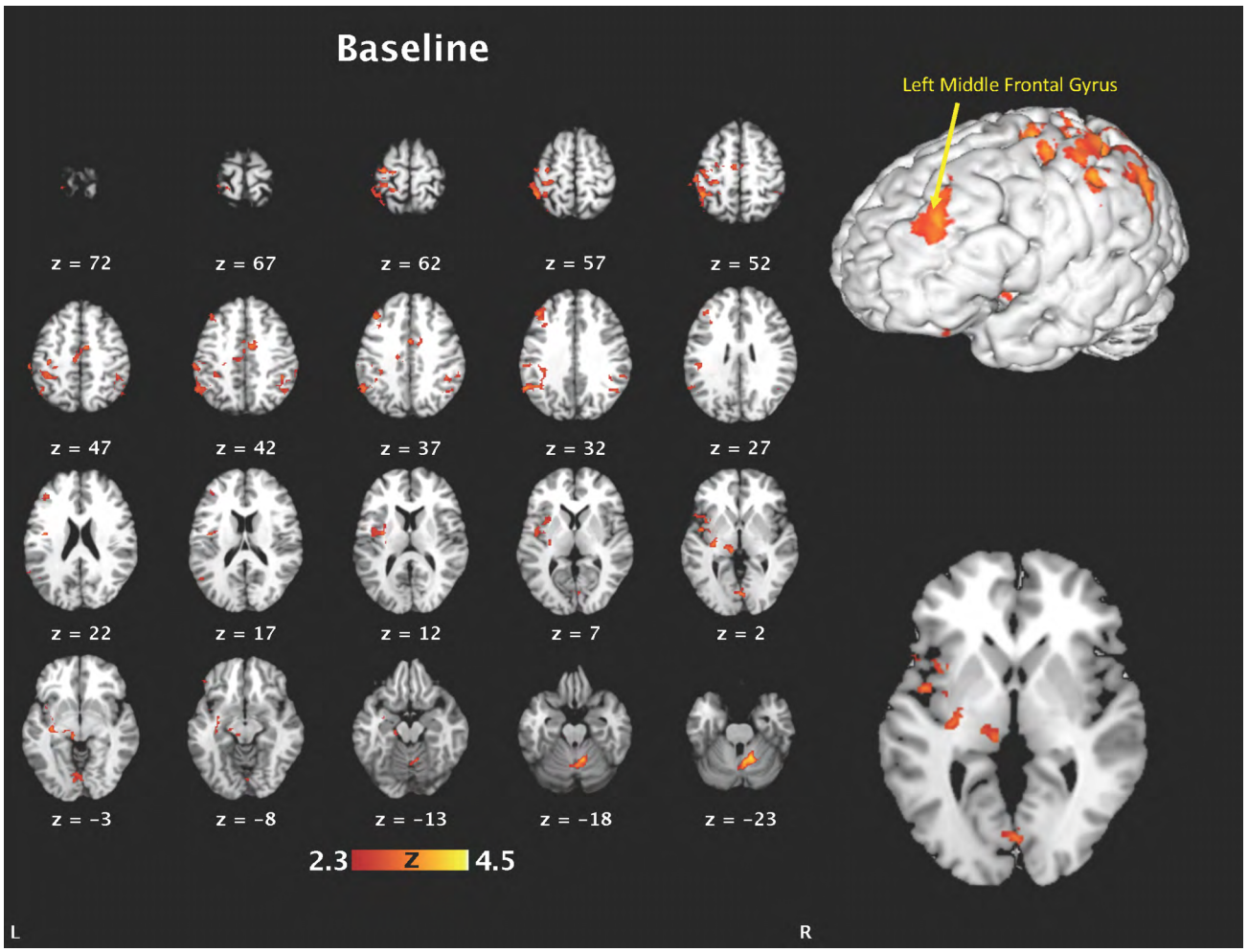

Figure 25. Activations seen during the Baseline trials.

Table 14.

Baseline > ITI

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
1	3.84	-2	-70	12	Left Cerebrum	Occipital Lobe	Cuneus	BA 30
	3.84	-10	-74	24	Left Cerebrum	Occipital Lobe	Cuneus	BA 18
	3.62	-20	-62	-4	Left Cerebrum	Limbic Lobe	Parahippocampal Gyrus	BA 19
	3.46	-18	-74	24	Left Cerebrum	Occipital Lobe	Precuneus	BA 31
	3.2	-12	-70	-2	Left Cerebrum	Occipital Lobe	Lingual Gyrus	BA 18
	3.03	-24	-72	2	Left Cerebrum	Occipital Lobe	Lingual Gyrus	*

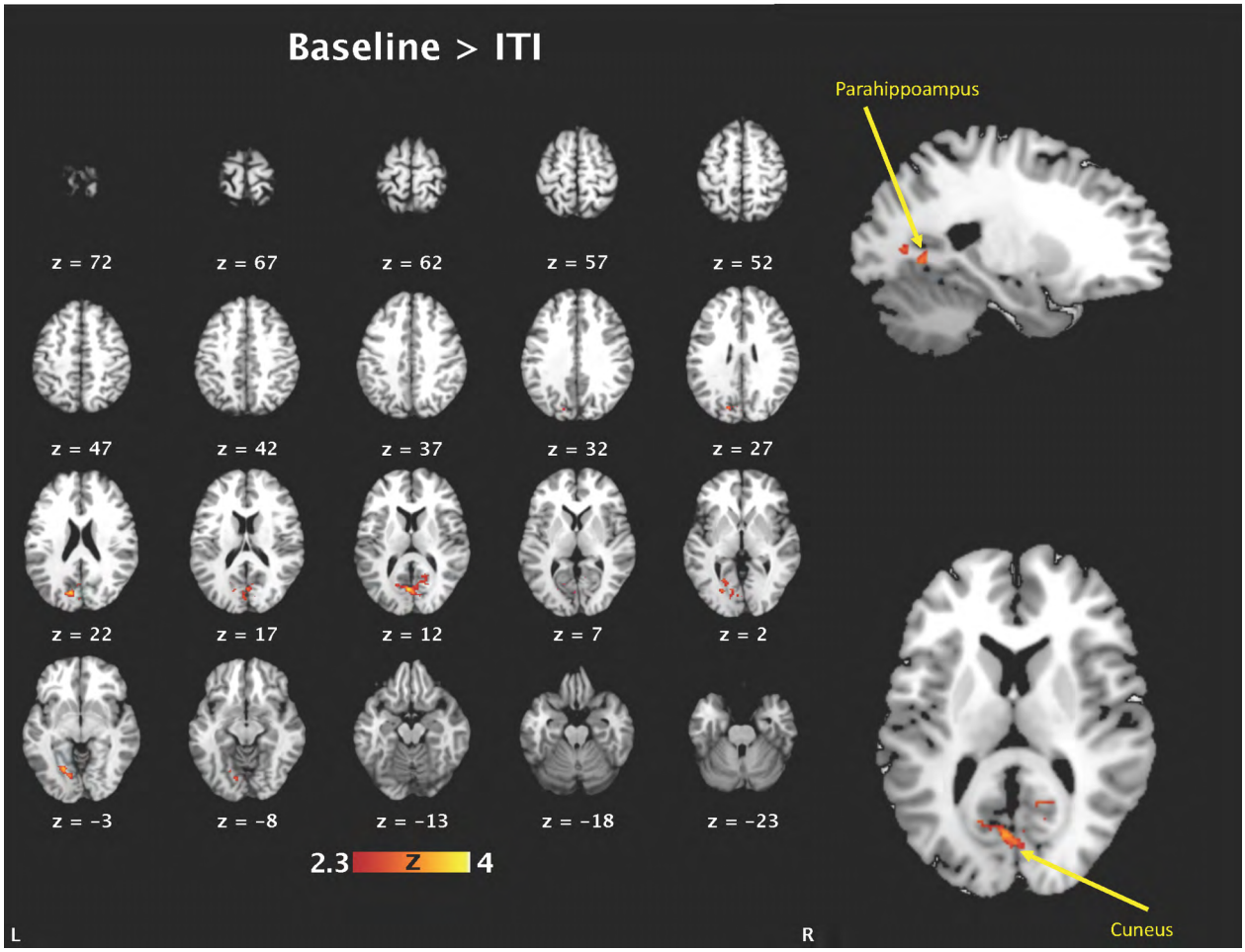

Figure 26. Activations seen during the Baseline trials when subtracting the ITI activations.

In the Conflict trials, activations were seen in the left superior temporal lobe and the left supramarginal gyrus as was found in Sutton et al. (2012; Figure 27; Table 15). There was also activation located in HNN structures such as the left middle and superior frontal gyri and the precuneus when subtracting activations seen in the ITI (Figure 28; Table 16).

Table 15.

Conflict

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
5	4.15	-40	-54	30	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.8	-56	-52	32	Left Cerebrum	Parietal Lobe	Supramarginal Gyrus	BA 40
	3.6	-54	-58	26	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.5	-48	-54	30	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.3	-56	-58	18	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 22
	3.29	-52	-52	42	Left Cerebrum	Parietal Lobe	Inferior Parietal Lobule	BA 40
4	3.92	-42	46	-20	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 11
	3.69	-38	60	4	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.55	-38	48	-16	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 11
	3.41	-28	4	10	Left Cerebrum	Sub-lobar	Lentiform Nucleus	Putamen
	3.34	-40	8	-6	Left Cerebrum	Sub-lobar	Insula	BA 13
	3.28	-46	14	0	Left Cerebrum	Sub-lobar	Insula	BA 13
3	3.31	-4	38	16	Left Cerebrum	Limbic Lobe	Anterior Cingulate	BA 32
	3.25	-8	36	24	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 32
	3.16	-8	38	4	Left Cerebrum	Limbic Lobe	Anterior Cingulate	BA 32
	3.13	-4	36	36	Left Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 6
	2.88	-10	34	44	Left Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 8
	2.74	-12	32	14	Left Cerebrum	Limbic Lobe	Anterior Cingulate	BA 32
2	3.26	44	-54	26	Right Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.16	56	-56	30	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.02	52	-56	32	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	2.59	60	-52	40	Right Cerebrum	Parietal Lobe	Inferior Parietal Lobule	BA 40
	2.56	56	-58	40	Right Cerebrum	Parietal Lobe	Inferior Parietal Lobule	BA 40
	2.55	52	-60	44	Right Cerebrum	Parietal Lobe	Inferior Parietal Lobule	BA 40
1	3.47	-40	26	44	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.19	-46	22	42	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 8
	3.08	-38	36	32	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 9
	2.88	-36	26	48	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 8
	2.8	-36	18	38	Left Cerebrum	Frontal Lobe	Precentral Gyrus	BA 9
	2.79	-32	30	50	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 8

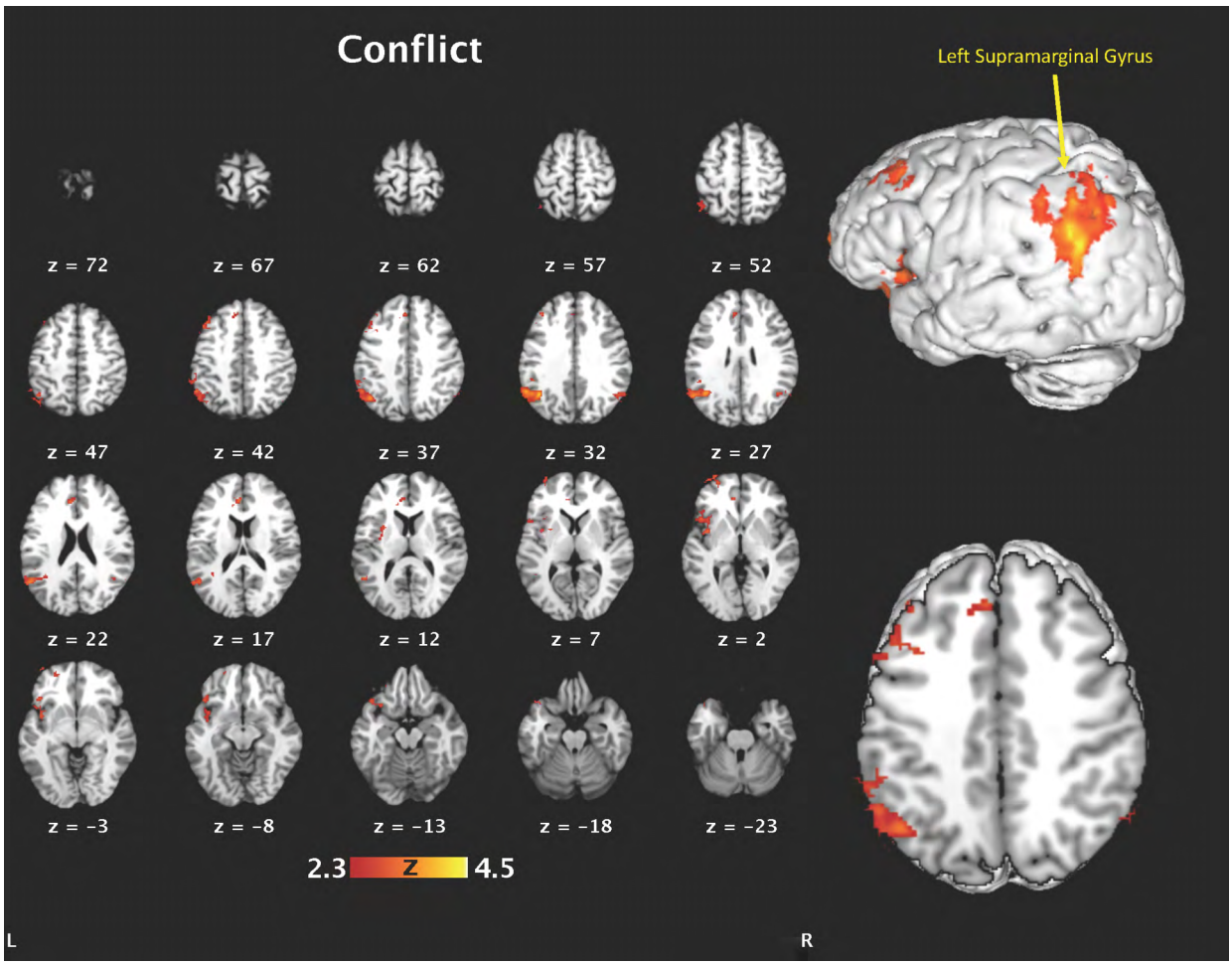

Figure 27. Activations seen during the Conflict trials.

Table 16.

Conflict > ITI

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
2	3.23	-14	-44	30	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	3.05	-10	-46	34	Left Cerebrum	Parietal Lobe	Precuneus	BA 31
	2.79	-4	-52	32	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	2.77	6	-62	24	Right Cerebrum	Occipital Lobe	Precuneus	BA 23
	2.75	12	-60	28	Right Cerebrum	Parietal Lobe	Precuneus	BA 31
	2.73	8	-64	28	Right Cerebrum	Parietal Lobe	Precuneus	BA 31
1	4.23	-40	-56	30	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.27	-54	-56	28	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	2.7	-46	-62	36	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	2.39	-58	-58	18	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 22

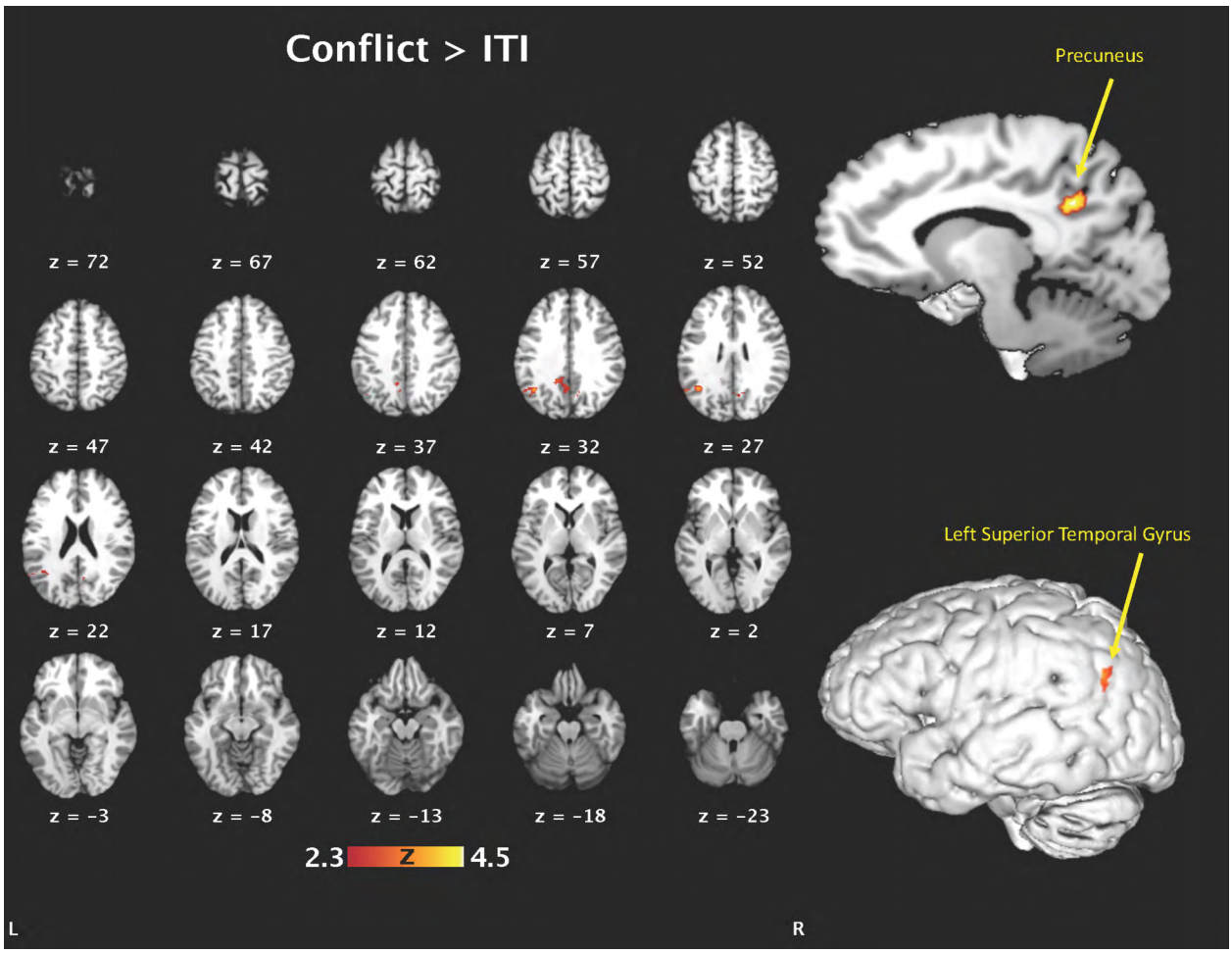

Figure 28. Activations seen during the Conflict trials when subtracting the ITI activations.

Discussion

Experiment 3 was conducted to perform a preliminary assessment of how older adults use geometry and features to guide navigation in a virtual environment, and the neurofunctional correlates of such behavior. Behavioral results show that older adults perform the task at an optimal level. Errors and latency to complete trials decreased across pre-scanner training. During the test trials, participants showed stable and consistent performance across test trials. When presented with the Square test,

participants relied on the landmark. When the landmark was unavailable in the No Landmark tests, older adults regularly chose the correct and geometrically correct corners. Finally, when the correct landmark and corner were in conflict, older adults chose the landmark to a greater extent than the alternate options.

In regards to functional results, while the lack of power is a limitation, it was still possible to gain insight into what regions activated across two of the four trial types. During the training trials and Conflict test, various navigationally relevant regions showed activations. In particular, the parahippocampus, cuneus, and left middle and superior temporal gyri. Of note, there was activation found in the left supramarginal gyrus in both trial types. Previous research (Sutton, et al., 2012) has reported this region relates to geometry use, while these trials do not require participants utilize this cue, it is available.

One main function of Experiment 3 was to determine similarities and differences across healthy aging. The next section will compare performance in Experiment 2 and 3 across age groups to investigate any age-related changes. Further, volumetric comparisons will be discussed, but are jeopardized by the same limitations as the functional results were.

Chapter 6: Age Comparisons

Behavioral Comparisons. Due to the large range in participant ages (36-57), the following comparisons were conducted across three groups to attempt to determine any age related behavioral differences. The older group was split into two smaller groups of 5 people for further comparisons; 36-44 years old and 49 to 57 years old. The split was chosen in order to potentially illuminate any behavioral differences that may occur across adulthood.

Figure 29 (top panel) shows the average number of errors during the pre-scanner training across age groups. A Two-Way Repeated Measures ANOVA investigating errors across the 15 pre-scanner training trials was conducted and revealed there was a significant effect of trial $F\ (14, 28) = 11.454, p < .05$. However, there was no main effect of group $F\ (2, 27) = .866, p > .05$, or Trial x Group interaction, $F\ (14, 378) = .583, p > .05$ (Figure 29; top panel). Figure 28 (bottom panel) shows the average time to complete pre-scanner training across age groups. Similarly, a Two-Way Repeated Measures ANOVA was conducted on time to complete these training trials which revealed a main effect of trial $F\ (14, 28) = 17.786, p < .05$, but no effect of group $F\ (1, 25) = .483, p > .05$, and no Trial x Group interaction, $F\ (14, 350) = .540, p > .05$ (Figure 29; bottom panel).

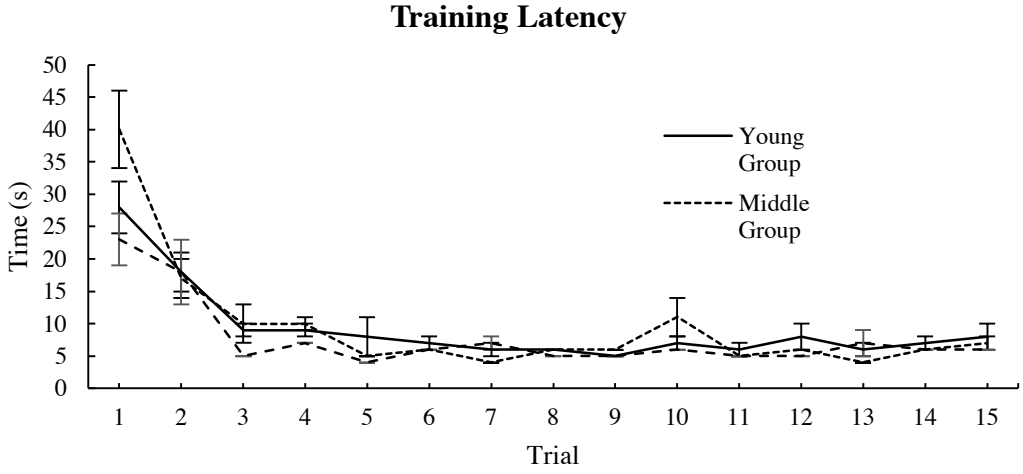

Figure 29. Top panel: Average number of errors during pre-scanner training by trial. Individual lines represent groups. Bottom panel: Average latency during pre-scanner training by trial. Individual lines represent groups. Solid line represents the young group, dotted lines represent the middle group, while the dashed line represents the older group. Error bars represent SEM.

Figure 30 shows a comparison of age groups across the three test types. A Repeated measures ANOVA was conducted with group (older, middle, young) and trial type (Square, No Landmark, Conflict) as factors to determine if there were differences in performance across test type. As the previous analyses in Experiment 2 and 3 showed consistency in performance during these trials, the 8-trial average for each test type was used in this ANOVA. There was no main effect of test type, $F\,(2, 52) = .733, p > .05$, no main effect of group, $F\,(2, 26) = .270, p > .05$, nor was there a Test x Group interaction, $F\,(4, 52) = 1.027, p > .05$. This result shows that participants of all ages performed this task to a similar level behaviorally.

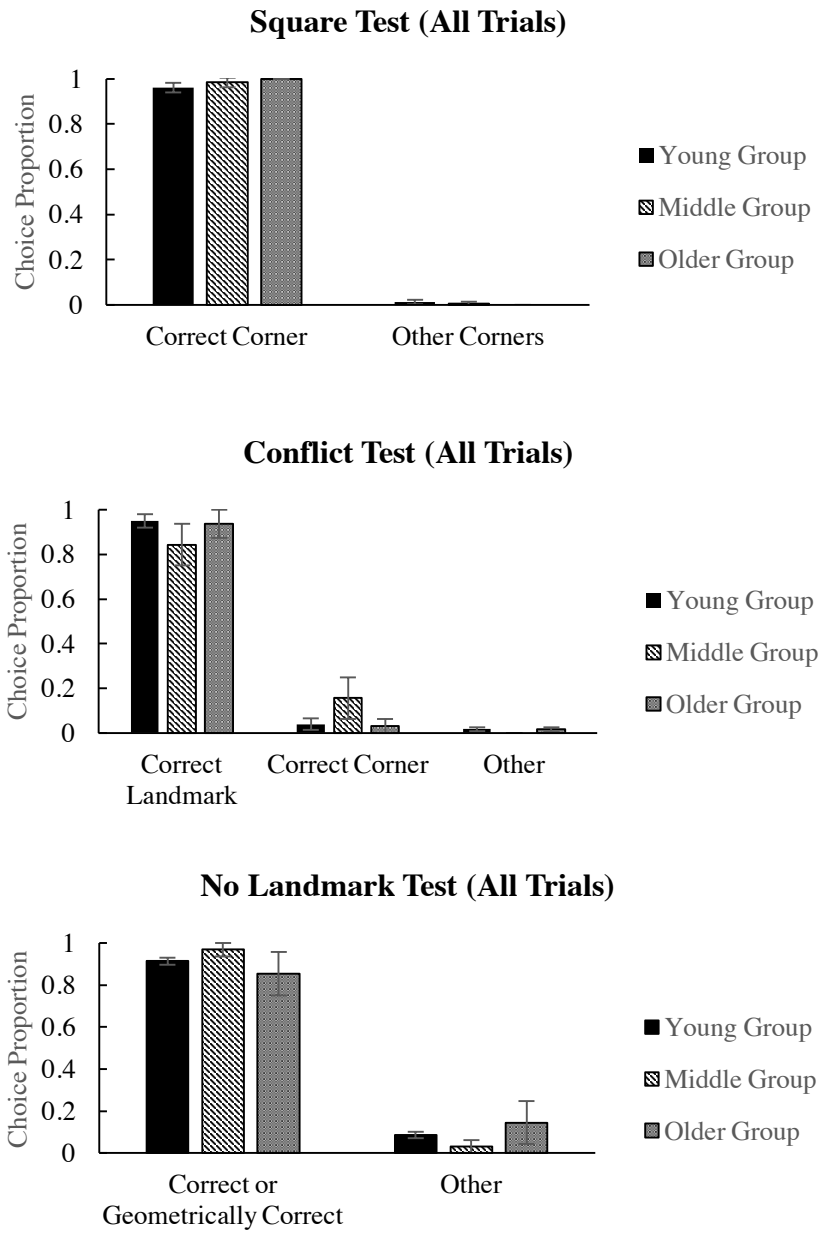

Figure 30. Choices made to each corner type across three test trial types. Solid bars represent the young group, diagonal lined bars represent the middle group, while stippled bars represent the older group. Error bars represent SEMs.

Age Related Functional Changes. Even though there was a lack of significant activations in the older group due to the small sample size, when adding age into the analyses there were some functional differences across ages. Analyses were conducted as in Experiment 2 and 3, however age was mean centered and added to the equation as described in the methods. As such, results presented represent changes with older age.

During the Baseline trials when considering the differences that occur across ages, there were navigationally relevant regions that increased in activation in older adults. Specifically, the posterior cingulate cortex, the left superior temporal gyrus, and the left supramarginal gyrus (Figure 31; Table 17). The posterior cingulate cortex is included in the HNN and was found to be related to encoding locations (Maguire, et al., 1998). The left superior temporal and left supramarginal gyrus was reported in Sutton et al. (2012) and was related to when participants were utilizing boundaries. It is worth noting that in the younger group's results, there was no evidence of left supramarginal gyrus activation.

Performance in the Square trials revealed activations when subtracting activations during the ITI and when considering the effect of age. Regions included in the HNN were found to have more activation in older adults than younger adults in the posterior cingulate cortex, cuneus, and precuneus (Figure 32; Table 18). When inspecting the Conflict trials accounting for age, a similar pattern of greater activation in the older adults in the posterior cingulate cortex, and the left middle temporal and supramarginal gyrus were found. Of note, two HNN structures implicated in encountering detours showed greater activation in older adults; the left middle and superior frontal gyri (Figure 33; Table 19). While this region was found in the younger adults during the Conflict trials, one can postulate that the older adults may be more affected by the difference in environments than their younger counterparts. In agreement, the No Landmark trials when accounting for age revealed a similar pattern of activations; the precuneus and posterior cingulate cortex, left superior and middle frontal gyri, and the left superior temporal gyrus (Figure 34; Table 20).

Table 17.

Baseline + Age

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
3	3.42	-6	-50	24	Left Cerebrum	Limbic Lobe	Posterior Cingulate	BA 30
	3.15	0	-58	8	Left Cerebrum	Limbic Lobe	Posterior Cingulate	BA 30
	3.07	18	-46	26	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	3.04	-2	-42	32	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	2.91	12	-44	30	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	2.85	0	-54	16	Left Cerebrum	Limbic Lobe	Posterior Cingulate	BA 23
2	4.02	32	38	12	No Gray Matter found			
	3.6	44	24	0	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 45
	3.58	38	34	12	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 46
	3.47	44	30	6	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 13
	3.41	36	42	4	Right Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.22	44	30	-10	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
1	3.5	-48	-58	-4	Left Cerebrum	Temporal Lobe	Inferior Temporal Gyrus	BA 19
	3.21	-42	-52	10	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.19	-50	-52	8	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.08	-62	-52	24	Left Cerebrum	Temporal Lobe	Supramarginal Gyrus	BA 40
	3.07	-52	-62	16	Left Cerebrum	Occipital Lobe	Middle Temporal Gyrus	BA 19
	3.04	-56	-62	16	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39

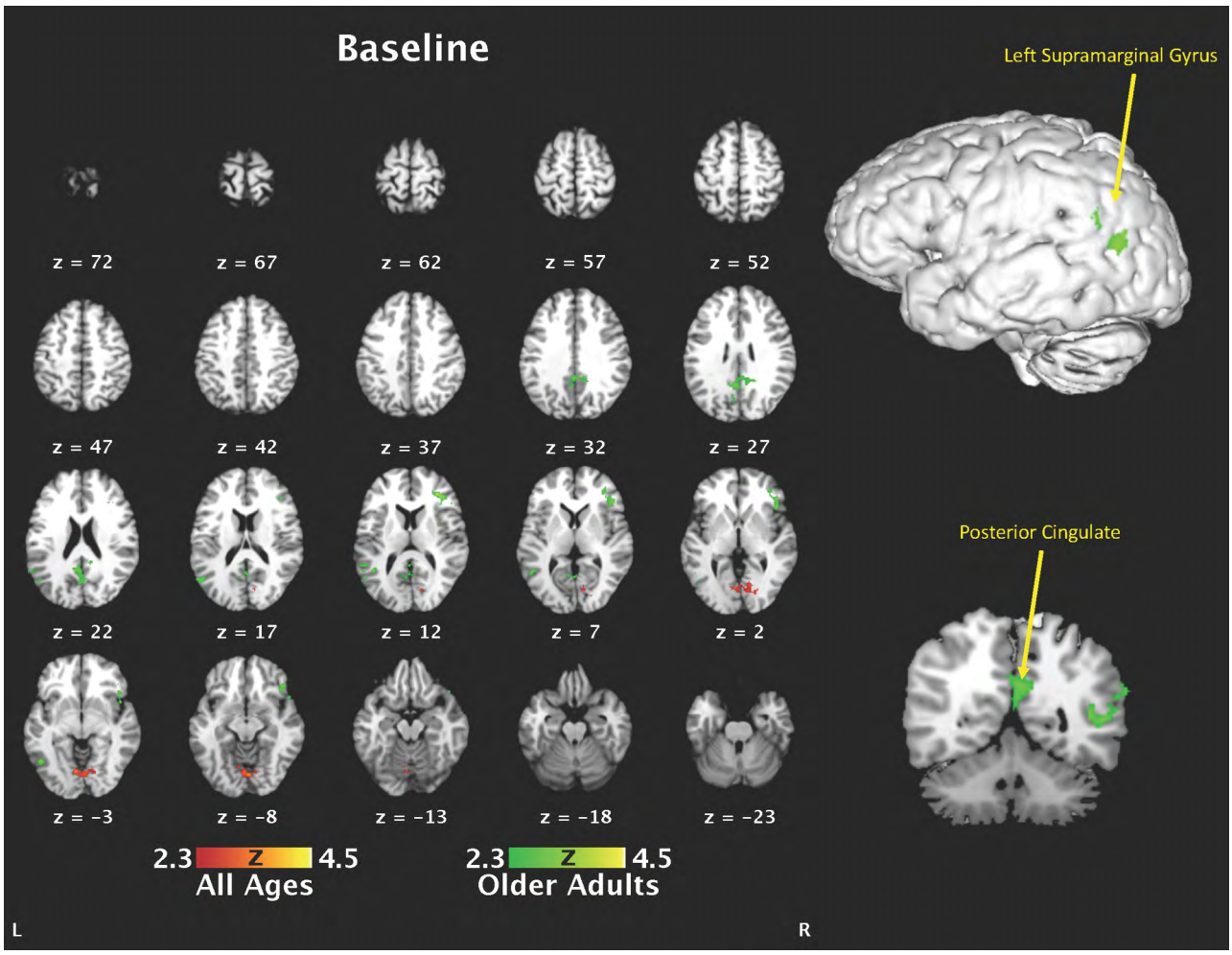

Figure 31. Activations seen during the Baseline trials when accounting for age. Green represent the areas activated with increasing age, while the red represents mean activation across ages.

Table 18.

Square > ITI + Age

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
2	3.73	12	-70	-14	Right	Posterior Lobe	Declive	*
	3.11	34	-52	-12	Right	Occipital Lobe	Fusiform Gyrus	BA 37
	3.05	26	-62	-10	Right	Occipital Lobe	Fusiform Gyrus	BA 19
	3	26	-68	-6	Right	Occipital Lobe	Fusiform Gyrus	BA 19
	2.91	16	-64	-16	Right	Posterior Lobe	Declive	*
	2.83	22	-52	-16	Right	Anterior Lobe	Culmen	*
1	3.87	20	-66	20	Right	Limbic Lobe	Posterior Cingulate	BA 31
	3.55	12	-68	26	Right	Occipital Lobe	Precuneus	BA31
	3.48	20	-62	16	Right	Limbic Lobe	Posterior Cingulate	BA 30
	2.39	20	-72	12	Right	Occipital Lobe	Cuneus	BA 30

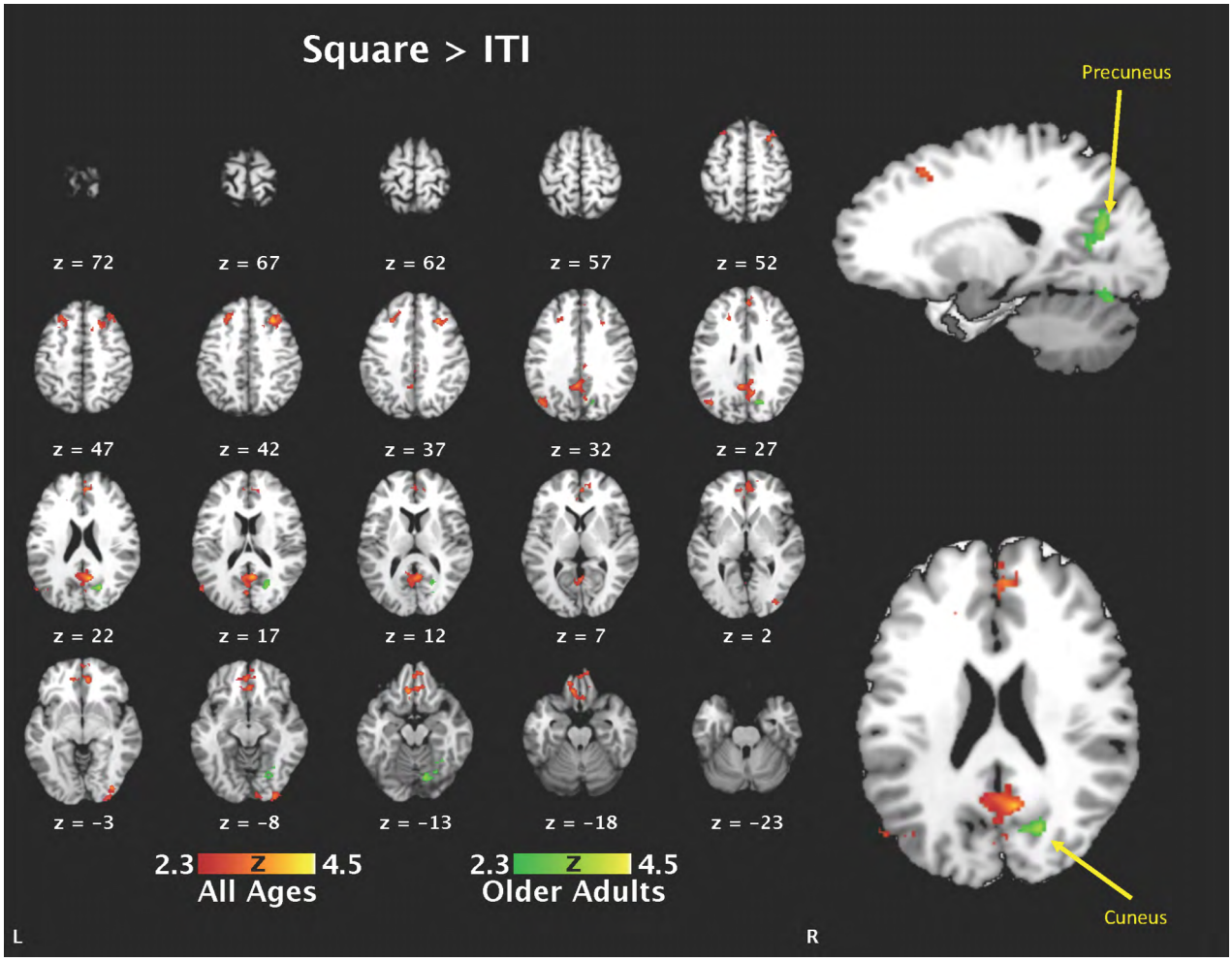

Figure 32. Activations seen during the Square trials when subtracting the activations during the ITI when accounting for age. Green represent the areas activated with increasing age, while the red represents mean activation across ages.

Table 19.

Conflict + Age

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
8	3.73	-50	-52	10	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.58	-60	-52	28	Left Cerebrum	Temporal Lobe	Supramarginal Gyrus	BA 40
	3.49	-54	-58	32	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.09	-42	-52	8	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.09	-50	-58	16	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	2.95	-58	-60	16	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
7	3.85	-38	20	4	Left Cerebrum	Sub-lobar	Insula	BA 13
	3.45	-40	24	0	Left Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 45
	3.34	-36	16	-28	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 38
	3.26	-32	8	-4	Left Cerebrum	Sub-lobar	Claustrum	*
	3.19	-48	14	-2	Left Cerebrum	Sub-lobar	Insula	BA 13
	3.18	-32	18	-14	Left Cerebrum	Frontal Lobe	Extra-Nuclear	BA 47
6	3.48	4	-18	32	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 23
	3.43	14	-18	34	No Gray Matter found			
	3.36	8	-2	34	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 24
	3.27	8	-8	42	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 24
	3.1	6	-10	48	Right Cerebrum	Frontal Lobe	Paracentral Lobule	BA 31
	3.06	8	-12	32	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 23
5	3.69	10	42	-6	Right Cerebrum	Limbic Lobe	Anterior Cingulate	*
	3.68	6	46	-4	Right Cerebrum	Limbic Lobe	Anterior Cingulate	BA 32
	3.27	8	44	30	Right Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 9
	3.07	16	42	34	Right Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 8
	3.04	0	48	-2	Left Cerebrum	Limbic Lobe	Anterior Cingulate	BA 32
	3.02	-4	48	6	Left Cerebrum	Limbic Lobe	Anterior Cingulate	BA 32
4	3.32	-6	-50	26	Left Cerebrum	Limbic Lobe	Posterior Cingulate	BA 23
	3.15	18	-46	28	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	3.13	10	-50	28	Right Cerebrum	Limbic Lobe	Posterior Cingulate	BA 23
	2.94	-4	-42	34	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	2.85	8	-40	34	Right Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	2.69	-14	-46	28	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
3	4.2	40	12	34	Right Cerebrum	Frontal Lobe	Precentral Gyrus	BA 9
	3.38	48	10	34	Right Cerebrum	Frontal Lobe	Precentral Gyrus	BA 9
	3.26	36	2	48	Right Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.13	38	4	42	Right Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 6
	2.97	50	4	34	Right Cerebrum	Frontal Lobe	Precentral Gyrus	BA 6
	2.79	42	4	50	Right Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 6
2	3.2	44	30	4	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 13
	3.14	38	28	-4	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.1	46	30	-10	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
	3.06	46	24	-2	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 45
	2.95	40	14	-8	Right Cerebrum	Sub-lobar	Insula	BA 13
	2.69	46	20	-14	Right Cerebrum	Frontal Lobe	Inferior Frontal Gyrus	BA 47
1	3.48	-8	32	60	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.33	-12	24	60	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.29	-14	20	60	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 6
	3.21	0	28	58	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.15	-18	14	66	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.13	0	36	56	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6

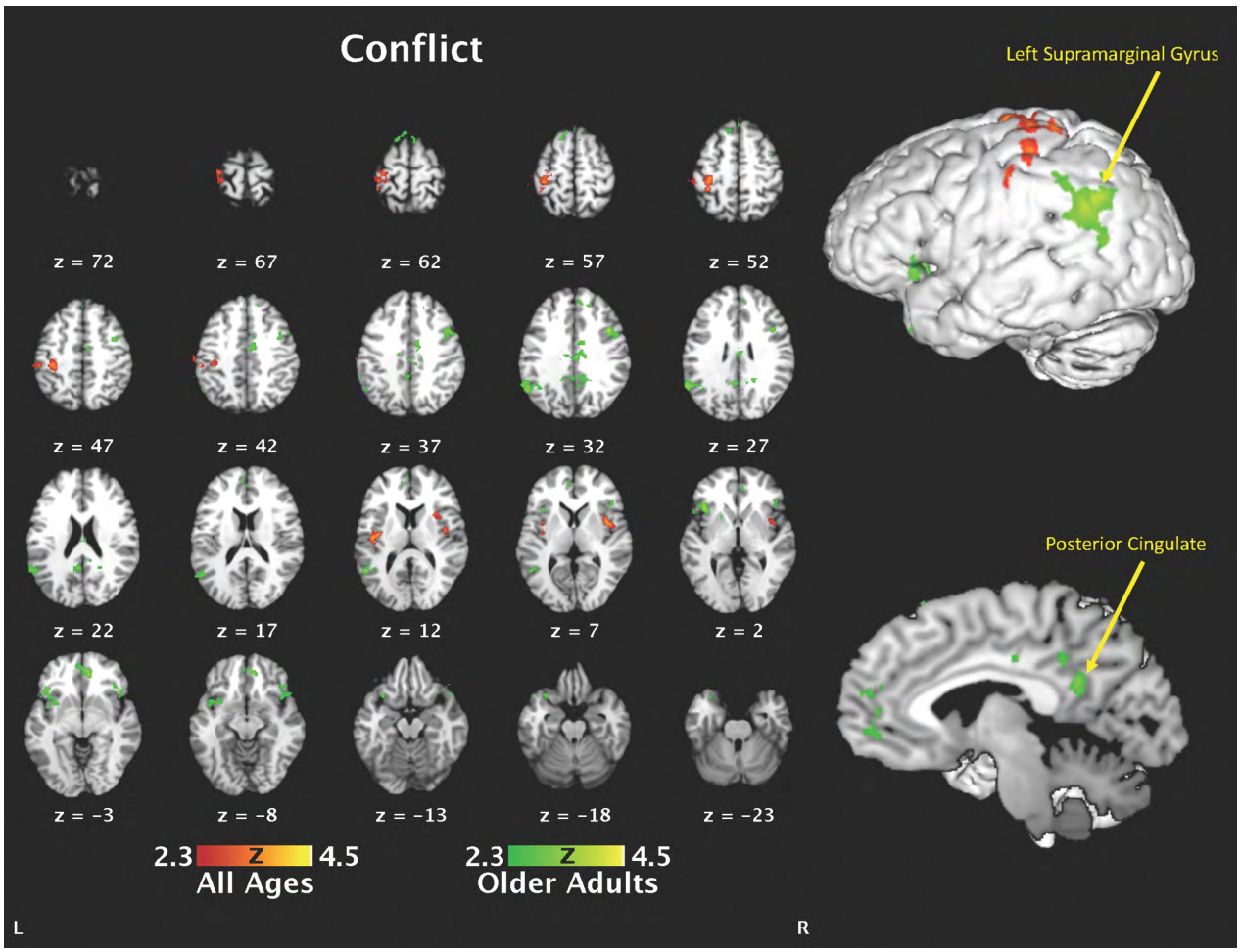

Figure 33. Activations seen during the Conflict trials when accounting for age. Green represent the areas activated with increasing age, while the red represents mean activation across ages.

Table 20.

No Landmark + Age

Cluster Index	Z	x	y	z	Hemisphere	Lobe	Region	Area
6	3.71	-2	-70	30	Left Cerebrum	Parietal Lobe	Precuneus	BA 31
	3.47	-2	-66	32	Left Cerebrum	Occipital Lobe	Precuneus	BA 31
	3.31	0	-42	34	Left Cerebrum	Limbic Lobe	Cingulate Gyrus	BA 31
	3.23	0	-66	24	Left Cerebrum	Occipital Lobe	Precuneus	BA 23
	3.17	0	-44	12	Left Cerebrum	Limbic Lobe	Posterior Cingulate	BA 29
	3.13	10	-48	26	Right Cerebrum	Limbic Lobe	Posterior Cingulate	BA 23
5	3.93	8	42	30	Right Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 9
	3.45	-2	36	58	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.3	4	40	56	Right Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 6
	3.28	12	32	40	Right Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 8
	3.26	-2	46	34	Left Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 6
	3.23	-20	48	34	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 9
4	3.83	48	-56	20	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.39	56	-62	24	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.08	46	-60	38	Right Cerebrum	Parietal Lobe	Angular Gyrus	BA 39
	3.02	48	-60	34	Right Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	2.99	58	-58	16	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 22
	2.97	52	-52	30	Right Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
3	3.52	-44	-52	16	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
	3.47	-50	-60	16	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.19	-50	-56	18	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 22
	3.18	-52	-64	24	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.05	-50	-64	28	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	2.98	-52	-58	36	Left Cerebrum	Temporal Lobe	Superior Temporal Gyrus	BA 39
2	3.44	-22	60	14	Left Cerebrum	Frontal Lobe	Middle Frontal Gyrus	BA 10
	3.37	-22	56	22	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 10
	3.03	-10	58	10	Left Cerebrum	Frontal Lobe	Medial Frontal Gyrus	BA 10
	2.96	-14	54	18	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 9
	2.94	-10	56	16	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 9
	2.66	-26	48	16	Left Cerebrum	Frontal Lobe	Superior Frontal Gyrus	BA 10
1	3.4	-32	-74	30	Left Cerebrum	Occipital Lobe	Superior Occipital Gyrus	BA 19
	3.24	-34	-70	36	Left Cerebrum	Temporal Lobe	Middle Temporal Gyrus	BA 39
	3.2	-38	-74	42	Left Cerebrum	Parietal Lobe	Precuneus	BA 19
	2.87	-32	-70	48	Left Cerebrum	Parietal Lobe	Precuneus	BA 19
	2.52	-26	-70	46	Left Cerebrum	Parietal Lobe	Precuneus	BA 7

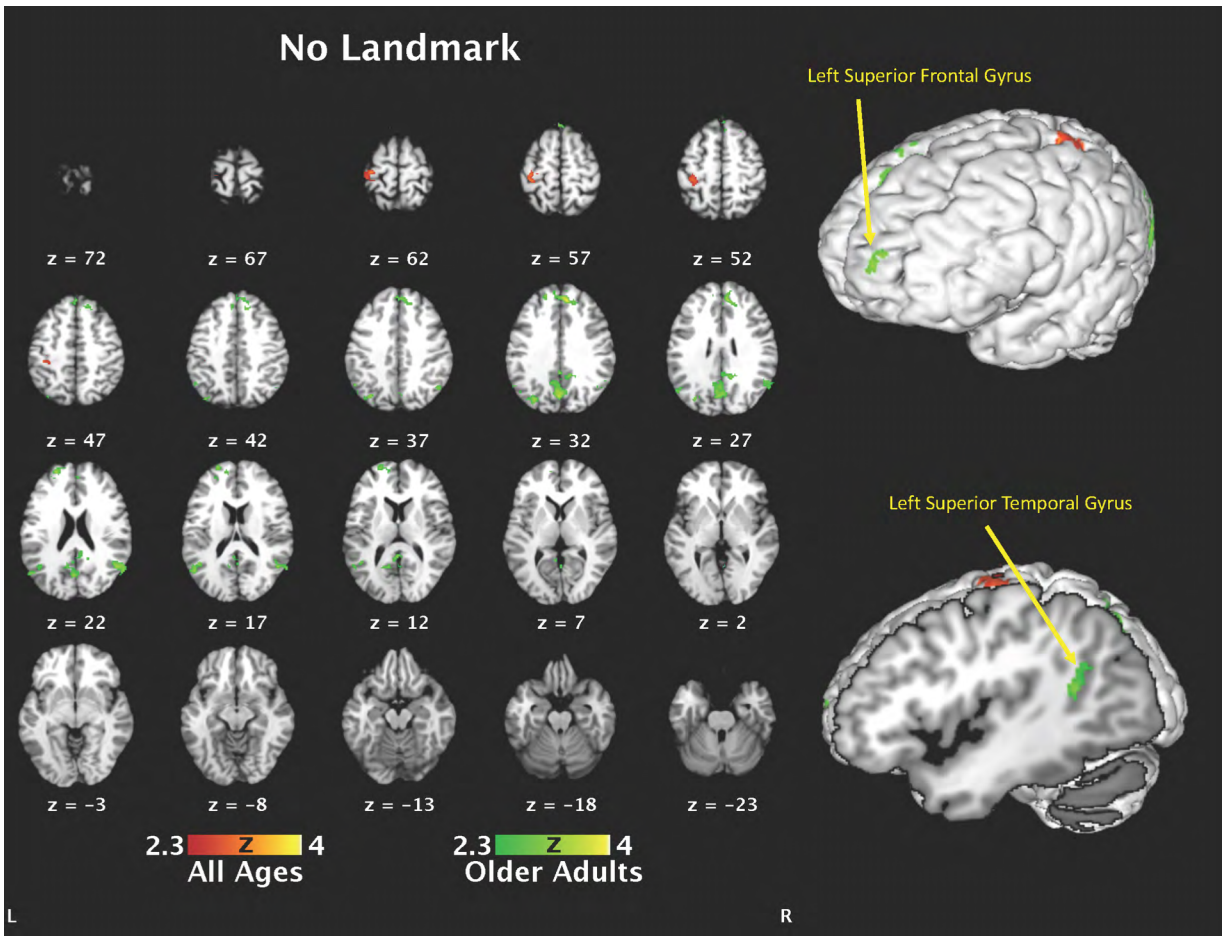

Figure 34. Activations seen during the No Landmark trials when accounting for age. Green represent the areas activated with increasing age, while the red represents mean activation across ages.

Volumetric Comparisons. Volumetric data was collected by utilizing the high resolution structural scans from each participant. Cortical and subcortical segmentation was performed with freesurfer's automated segmentation tools, which is available for download online (http://surfer.nmr.mgh.harvard.edu/).

Correlations of age and volume of the left and right hippocampus and caudate were completed. Volumes were transformed using a proportion of total intracranial volume to normalize individual data for comparison purposes. Of the four structures compared, the left caudate was positively correlated with age $r = .39, p < .05$. The

remaining structures were not correlated with age. It is worth noting that there was a nonsignificant trend for hippocampal volume to be negatively correlated with age (Figure 35).

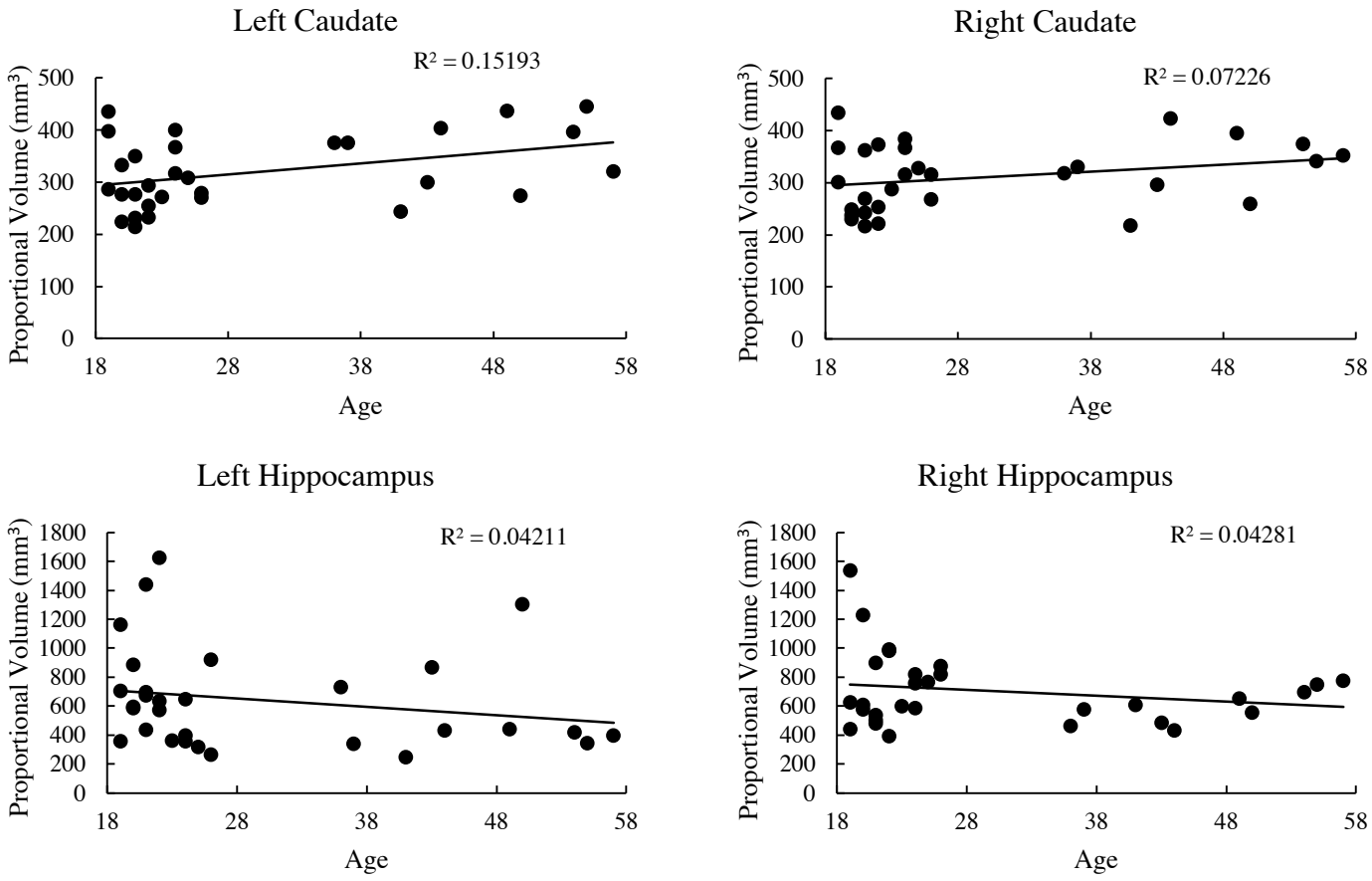

Figure 35. Volumes plotted by age presented in mm^3. Top panel shows the volume of the left and right caudate across ages. Bottom panel shows the volume of the left and right hippocampus across ages. Trend lines represent R^2.

Discussion

The age comparisons were completed to elucidate any changes in behavior, function, or structural volume across the lifespan. As this was a preliminary investigation, these data should be taken as such. Small sample size and sample characteristics in the older group allow for initial conclusions regarding behavioral data,

but the lack of statistical power in the imaging data does not allow for complete inferences to be drawn. That said, the findings do allow for an initial framework of geometry and feature use in a virtual environment.

Behaviorally, older adults did not differ from their younger counterparts overall. All participants could reliably locate the goal given the available cues. There was not an increase in variability in choices to incorrect landmarks during the training or test trials. While this does not mimic the hypotheses stated, this is not a complete detriment to the task itself. The purpose of the preliminary data collection is to hopefully translate this task for patients with MCI and probable AD. As this task does not elicit notable behavioral changes across ages, it is possible that this stability would be a good mechanism to test the abnormal aging process.

Functionally, there were various navigationally relevant structures that were found to have greater activation in older adults (> 30 years old). Across training and Square trial types, participants in the older group had activations in the left supramarginal gyrus. This region was reported in Sutton et al. (2012) and was suggested to relate to participants utilizing a verbal strategy to solve the task. As younger participants did not reveal this activation, it is possible that older adults were more inclined to verbally recall the goal location. Other HNN structures that relate to encoding locations and taking detours were found to have greater activations in older adults than younger adults. Across all trial types, older adults showed greater posterior cingulate cortex activation which relates to encoding locations as per the HNN (Maguire et al., 1998). However, as can be recalled from the interpretation of Experiment 2's data, it may be that the posterior cingulate cortex, precuneus, and cuneus may be more related to recalling locations across

time rather than simply encoding locations. In the No Landmark trial, greater activations were found in the left superior frontal gyrus in older adults than younger adults. This region, a part of the HNN, has been related to taking detours, or more specific for the current experiment, encountering an environment without the most salient cues.

In younger adults, there was activation seen in the parahippocampus across the Square and No Landmark trials. In older adults, there was no parahippocampal, hippocampal, or caudate activation seen. The lack of hippocampal activation is not surprising as was previously discussed, but the lack of parahippocampal and caudate activation in the older adults or the age comparison suggests that older adults may be functionally solving this task differently. Unfortunately, the sample size limitation does not allow for this assumption to be fully tested.

The volumetric results revealed an unexpected significant result in which the left caudate was positively correlated with age, and a nonsignificant trend towards an expected negative correlation with hippocampal volume. The low sample size in the older group allowed for a large amount of variability within the older participants. There is a large amount of inter-age variability in volume size in these two structures (Raz et al., 2005), and as such a larger sample size across ages may be necessary to elucidate these structural changes. It is also possible that sample characteristics could have influenced the results; the young participants were college-aged students that were in the process of obtaining their undergraduate degrees. Alternately, the older group was well educated with at the least a Master's degree. While there is little to no evidence that education level and type of education influences brain size, the disparate nature of the samples could have confounded the volumetric findings.

Chapter 7: Conclusions

This project's purpose was to examine the previous mixed findings in similar simple environments. This objective was achieved through multiple components. First, the implementation of the reorientation task which is robust, simple, and elicited few errors for use in the MR scanner ensured the similar task simplicity. Next, to determine the neurofunctional correlates of environmental geometry and feature use in a young population to compare to previous results. Finally, an age comparison was intended to determine if this task is sensitive to previously reported changes across healthy aging. To do this, age comparisons were conducted behaviorally, functionally, and structurally. While the results in the age comparison portion of the experiment did not reveal many differences, the task did allow for some insights into healthy aging.

Experiment 1 showed that the task developed by Cheng (1986) and repeated in a virtual environment by Sturz and Kelly (2009) was successful in the participant population at Auburn University. Specifically, this experiment showed that training errors decreased rather quickly across the first 15 trials of the task. Participants reliably chose the correct landmark when presented with the Square test trials, suggesting they learned the relationship between the landmark and the goal. When the landmarks were removed, participants showed that the geometric information provided by the location of the trained landmark was indeed learned, and could be used to locate the goal. Finally, when the landmarks were in conflict, participants showed that the landmark was the more salient, or at the least, preferred cue to locate the goal. These results allowed for

confidence that this task would be a dependable measure for implementation in the MR Scanner in Experiment 2.

The second experiment employed the task in the MR Scanner using a similar participant population as Experiment 1. Behaviorally, results from Experiment 2 revealed a similar pattern as was seen in the Experiment 1. Imaging results revealed many navigationally relevant structures were activated by this task. Multiple HNN structures, such as the parahippocampus, cuneus, precuneus, and posterior cingulate cortex, right inferior parietal cortex, left middle and superior frontal gyri and the caudate were active across test trials. These activations highlight the role of these structures in navigational tasks (Maguire et al., 1998).

Mixed results from two previous studies that employed similar simplistic environments were tested in this experiment. Doeller et al. (2008) found that when participants were utilizing geometric cues, there was activation in the caudate. The results from the current study found activations in the caudate when participants were in the Square trials in which the only available cue was the landmarks. This finding agrees with previous research. Another reported finding in Doeller et al. (2008) was activation in the posterior hippocampus when participants were using environmental geometry. The current experiment does not agree with this finding, however, experimental differences may be the cause of this. Participants were learning the location of objects in relation to environmental boundaries in the previous experiment, whereas in the current experiment, the environment was changed and required no encoding for future trials.

Another similar experiment found activations that did not agree with Doeller et al. (2008). Sutton et al. (2012) found hippocampal and parahippocampal activation when

participants were utilizing landmarks to locate a goal. The results of the current experiment revealed that when participants were in the Square test trials, the parahippocampus was active which agrees with Sutton et al. (2012). Of note, there was parahippocampal activation during the No Landmark test trials which agrees with the findings from Maguire et al. (1998) which suggested this region was related to novelty. In complete disagreement, the current study found activation in the left superior temporal gyrus when participants were in the Square test trials. Sutton et al. (2012) found this region correlated to when participants were faced with geometry. Importantly, the authors suggested this region and the left supramarginal gyrus, not active in the current study, were linked to participants potentially using a verbal strategy to solve the task. It is possible that in the current experiment this may also be the case.

There were interesting activations that have not previously been implicated in navigational tasks. Many cerebellar activations were reported - the culmen and declive. The culmen has been reported in tasks that relate to location detection (Pennick & Kana, 2011), emotional interference of goal-directed behavior (Mitchell et al., 2007), and stroop interference tasks (Woodward, Ruff & Ngan, 2006). The declive has been implicated in spatial memory, but in relation to saccade accuracy rather than a working memory process (Geier, Garver & Luna, 2007). The cerebellar structures, while reported in multiple tasks, appear to be under researched and may be more important to these tasks than is currently known. Additionally, the fusiform and lingual gyri were found to relate to all trial types. These regions have been implicated in face recognition, (e.g., McCarthy et al., 1997) and across-session familiarity (Gauthier et al., 1999) in the fusiform gyrus, and visual attention (e.g., Fink et al., 1996) in the lingual gyrus. These regions appear to

be related to navigation in small scale environments and should be further investigated and included in future neural navigational models.

Experiment 3 was a replication of Experiment 2 and intended to compare younger participants with their older counterparts. It should be noted that the sample size is a limitation when it comes to comparing the older and younger groups. There were 20 participants in Experiment 2, and only 10 in Experiment 3. While this does create a potential confound due to lack of statistical power, the results start to shed light onto potential differences.

Behaviorally there were few differences found, and the sparse differences appeared to be due to single trial variability between participants. This does not agree with previous research that older adults show an increase in time to complete mazes and errors in older participants (e.g., Lövdén et al., 2005). However, this could be due to the simplicity of the task and the comparatively young range of participants. For example, in Lövdén et al. (2005), participants in the older group were 60-69 years old.

Functionally, there were similar navigationally relevant regions activated as reported in the younger group, albeit during different trial types. One such activation that differed across ages was the parahippocampus. In older adults this region was correlated to training trials, but in younger adults it correlated to the No Landmark and Square trials. This suggests that this region is related to navigation, but the function of this region may differ across healthy aging. Of note, there was activation found in the left supramarginal gyrus in the older adults during the Conflict and training trials, but not in the younger adults. As Sutton et al. (2012) posited, this region could have related to a verbal coding strategy. Older adults may be more inclined to verbally solve the task. Another region

that showed greater activation in older adults as compared to younger adults was the superior frontal gyrus during the No Landmark trials. This region is a part of the HNN and is said to relate to an egocentric strategy (Maguire et al., 1998). Older adults could be using a matching-based strategy to solve the No Landmark task to a larger extent than younger adults.

Finally, one aspect of the current experiment was an attempt to supply a post hoc explanation of why older adults switch from allocentric to egocentric strategy use across normal aging. Specifically, if the left hippocampus showed a greater decrease in volume across ages this could potentially add insight into the switch in strategies as this area has been shown to be active during alloecentric navigation whereas egocentric strategies rely on input from the right inferior parietal cortex (Rodgers et al., 2012). Specifically, the older adults showed a trend in decreased hippocampal volume, albeit non-significant. However, the aforementioned increase in frontal activations and a trend toward decreased hippocampal volume suggests that Rodgers' et al. (2012) supposition that the structural changes could explain strategic changes. However, this area will require a larger sample size and greater statistical power to answer.

In conclusion, the current set of experiments allowed for an initial investigation into what structures are related to geometry and feature use in a simplistic virtual environment. This task elicited many previously identified navigationally relevant structures, as well as some structures (i.e., cerebellar and posterior cortex) that deserve a more in depth investigation as it relates to navigation. While there were limitations in the older group, the findings are still informative. The lack of behavioral differences across ages leaves the potential for this task to be a good tool for investigating abnormal aging

as it relates to degenerative dementias. If this task is robust across healthy aging, it may be a good tool to determine subtle changes in abnormal aging.

Future research should implement similar simple tasks to determine the neural correlates of individual cues that are used in successful navigation in order to understand the nuances of spatial navigation. These tasks should be implemented in older adults to determine what structures are related to simplistic navigational tasks and in abnormal aging to elucidate subtle differences across these two aging processes.

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