

# Environment Schema-Like Influences in Spatial Navigation: An fMRI Study

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# Environment Schema-Like Influences in Spatial Navigation: An fMRI Study

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# TABLE OF CONTENTS

<b>ACKNOWLEDGEMENTS .....</b>	<b>III</b>
<b>LIST OF TABLES .....</b>	<b>VI</b>
<b>LIST OF FIGURES.....</b>	<b>VII</b>
<b>LIST OF ABBREVIATIONS.....</b>	<b>VIII</b>
<b>SUMMARY.....</b>	<b>IX</b>
<b>CHAPTER 1. INTRODUCTION.....</b>	<b>1</b>
<b>CHAPTER 2. BACKGROUND .....</b>	<b>5</b>
2.1 TRADITIONAL SCHEMA THEORY .....	5
2.2 THE EFFECT OF CONGRUENCY AND FAMILIARITY ON BRAIN CONNECTIVITY.....	8
2.3 APPLYING SCHEMAS TO SPATIAL NAVIGATION .....	9
<b>CHAPTER 3. RESEARCH QUESTIONS AND PREDICTIONS.....</b>	<b>12</b>
<b>CHAPTER 4. METHOD .....</b>	<b>16</b>
4.1 PARTICIPANTS .....	16
4.2 MATERIALS.....	16
4.3 PROCEDURE .....	17
4.3.1 fMRI Task.....	19
4.4 FMRI PARAMETERS AND ANALYSES.....	21
<b>CHAPTER 5. BEHAVIORAL RESULTS.....</b>	<b>24</b>
5.1 THE FRÉCHET DISTANCE METHOD .....	24
5.2 NAVIGATION STRATEGIES .....	26
5.3 BEHAVIORAL EVIDENCE FOR SCHEMA-LIKE REPRESENTATIONS.....	29
<b>CHAPTER 6. FMRI RESULTS.....</b>	<b>32</b>
6.1 UNIVARIATE FMRI APPROACH .....	32
6.1.1 Does the hippocampus contribute differently from mPFC regions during planning of a route compared to actively navigating the route?.....	32
6.1.2 Does the shift in route directionality affect how the hippocampus and mPFC regions process navigation periods? .....	35
6.1.3 Does a relationship exist between navigation strategy and extent of planning? Within-subjects approach .....	37
6.1.4 Does a relationship exist between navigation strategy and extent of planning? Between-subjects approach .....	38
6.2 MULTIVARIATE FMRI APPROACH .....	39
6.2.1 Do representations (as opposed to activity levels) in the hippocampus and mPFC discriminate between forward and backward trials?.....	39
6.2.2 Is there a schema/identity representation for environments? .....	43
6.2.3 Does how strongly an environment identity is represented predict an individual’s performance? ...	44

<b>CHAPTER 7. DISCUSSION .....</b>	<b>47</b>
7.1 BREAKING DOWN THE FINDINGS.....	48
7.2 FUTURE ANALYSES.....	53
7.3 CONCLUSION.....	54
<b>APPENDIX A .....</b>	<b>57</b>
MAP LAB INFORMATION FORM.....	57
<b>APPENDIX B .....</b>	<b>60</b>
MAP LAB SUPPLEMENTAL DEMOGRAPHICS .....	60
<b>APPENDIX C .....</b>	<b>61</b>
Y-MAZE TASK.....	61
<b>APPENDIX D .....</b>	<b>63</b>
ENVIRONMENT ITEMS + LURES.....	63
<b>APPENDIX E .....</b>	<b>66</b>
QUESTIONNAIRE ON SPATIAL REPRESENTATION (QSR) .....	66
<b>APPENDIX F .....</b>	<b>68</b>
PEARSON’S CORRELATIONS COMPUTED IN JASP.....	68
<b>REFERENCES .....</b>	<b>71</b>

## LIST OF TABLES

Table 1	Experimental ROIs and Masks	23
Table 2	Assigned – Assigned: Forward FD & Within-town RSA	68
Table 3	Assigned – Assigned: Backward FD & Within-town RSA	68
Table 4	Midroute – Midroute: Forward FD & Within-town RSA	69
Table 5	Midroute – Midroute: Backward FD & Within-town RSA	69
Table 6	Assigned – Midroute: Forward FD & Forward RSA	70
Table 7	Assigned – Midroute: Backward FD & Backward RSA	70

## LIST OF FIGURES

Figure 1	Visualization of cognitive maps as metric, graph-like, and schematic representations of our environment	6
Figure 2	Dual-Solution task	20
Figure 3	Visualization of ROI mask locations	23
Figure 4	Fréchet Distance	24
Figure 5	Probe strategy preference	28
Figure 6	Assigned – Midroute activity contrasts	33
Figure 7	Assigned – Arrived activity contrasts	34
Figure 8	Navigate – Midroute activity contrasts	35
Figure 9	Assigned – Midroute (forward vs. backward) activity contrasts	36
Figure 10	Assigned – Midroute activity correlated with Fréchet Distance	39
Figure 11	Across-town similarity during the planning period	40
Figure 12	Evidence of town-specific coding during the planning period	41
Figure 13	Similarity of representations between planning and midroute navigation	42
Figure 14	Evidence of environment identity representations during the planning period	44
Figure 15	Within-town similarity during planning correlated with Fréchet Distance	45
Figure 16	Within-town similarity during midroute navigation correlated with Fréchet Distance	46
Figure 17	Within-town similarity between planning and midroute navigation correlated with Fréchet Distance	46
Figure 18	The Y-Maze task	61
Figure 19	Sample Y-Maze environment	61
Figure 20	Sample item test prompts	63
Figure 21	"Animal" target items (circled in RED) and lures	63
Figure 22	"Face" target items (circled in RED) and lures	64
Figure 23	"Other" target items (circled in RED) and lures	65

## LIST OF ABBREVIATIONS

ACC	Anterior Cingulate Cortex
ANOVA	Analysis of Variance
BA	Brodmann Area
dmPFC	Dorsomedial Prefrontal Cortex
FD	Fréchet Distance
FFA	Fusiform Face Area
fMRI	Functional Magnetic Resonance Imaging
HP	Hippocampus
IFG	Inferior Frontal Gyrus
MFG	Middle Frontal Gyrus
MP RAGE	Magnetization-Prepared Rapid Gradient Echo
mPFC	Medial Prefrontal Cortex
MTL	Medial Temporal Lobe
MVPA	Multi-Voxel Pattern Analysis
PPA	Parahippocampal Place Area
pvmPFC	Posterior-Ventromedial Prefrontal Cortex
ROI	Region of Interest
RSA	Representational Similarity Analysis
SFG	Superior Frontal Gyrus
SLIMM	Schema-Linked Interactions Between Medial Prefrontal and Medial Temporal Regions
SPM	Statistical Parametric Mapping
TR	Repetition Time
vmPFC	Ventromedial Prefrontal Cortex

## SUMMARY

Studies on spatial schemas have primarily come from rodent studies examining the development of task representations in the animal's brain. Such studies provide support for accelerated learning of novel spatial associations when prior associations already exist, and notably, there seems to be rapid disengagement of the hippocampus when encoding new experiences within an existing cognitive map. Research has set out to test whether existing spatial knowledge can also benefit novel learning in humans, and if there are similar neural characteristics during prospective planning and recall of memories related to existing spatial knowledge. The present study tested healthy young adult participants across two days in a virtual navigation task and used fMRI to examine complementary views of how the medial temporal lobe and medial prefrontal cortex (mPFC) contribute to route planning and navigation. Univariate and multivariate fMRI analyses revealed: 1) Functional differences in subdivisions of the mPFC, sometimes agreeing, but other times responding differently across various stages of navigation (e.g., planning vs. goal arrival), and differing in how they explain individual differences in navigation behavior. 2) Broad agreement between when and how the hippocampus (right hemisphere in particular) and mPFC (posterior-ventral mPFC in particular) are engaged for task stages, represent environments, and track participant differences – a finding which aligns well with their anatomical interconnections, but may contradict the competitive view from models of schema memory.

## CHAPTER 1. INTRODUCTION

Navigating our environment is a ubiquitous aspect of our daily lives, but doing this efficiently and effectively can be a lot more challenging than it seems. Knowing what information to pay attention to and how we encode these stimuli is key for becoming better navigators, but in order to understand *how* we do this we need to understand the neural framework behind these abilities.

While navigating, there is a constant stream of information available to us as we are tasked with paying attention to landmarks, road signs, and perhaps even your GPS screaming at you to “TURN RIGHT!”. All of these incoming pieces of information are in themselves important, but when grouped together into a meaningful knowledge structure, they may facilitate the navigation process for a particular event (e.g., driving to work). But what happens when we encounter a different event in which the knowledge structure shares similar features to another (e.g., driving to a grocery store you’ve never been to before, but can make good inference about its location by thinking about the existing spatial relationships in your knowledge structure of the environment)? Can we utilize schematic structures to facilitate our memory for semantically related events (instances and/or features of navigational experiences that can be meaningfully associated with one another)? For this thesis, I define a spatial “schema” as a knowledge network that represents an understanding of space and the connections/associations within it that could be, but don’t have to be, rigidly tied to specific geometric proportions at the global scale.

To help answer these types of questions, the current study applied the use of naturalistic navigation contexts in conjunction with advanced neuroimaging techniques to simulate realistic environments and capture behaviors one would experience in the real world. A common concern

with conducting neuroimaging research is that studying memory often uses simple or discrete stimuli (e.g., responding with a button to if an object or a face is familiar or not) and we are unable to generalize results to the complex multi-featured format of real-world memory and memory-guided behavior. The current study addresses this limitation by using virtual navigation tasks, which are both immersive and provide continuous stimuli to our memory systems. One outstanding question in the field that such virtual navigation tasks can address is: How are complex episodic events (e.g., continuous experiences of stimuli that make up a route) integrated together into memory to guide decisions?

In order to capture the diverse and changing characteristics of the real world, we adopt the theory that humans utilize schema-like structures as memory aids during navigation. In the traditional sense of the term, a “schema” is defined as an organized mnemonic “network” of information that is based on associative connections across memories of experiences, and into which novel experiences can be integrated as we continue to acquire new knowledge about our world (Bartlett, 1932). In this framework, new and already-existing information come together, as opposed to each experience developing isolated representations, and this allows us to make predictions when encountering new situations (for example, in navigation, one might have an expectation for what one may encounter down a side street or around a corner based on experiences with other parts of the environment or with similar environments).

People tend to form complex temporal schema “scripts” (highly elaborate structured schemas of how events tend to play out in episodes), and there is research showing that brain regions such as the medial prefrontal cortex (mPFC) are particularly sensitive to the structure of the script – scrambling the “storyline” (events played out differently than expected based on one’s schema) disrupts responses in this region (Baldassano, Hasson, & Norman, 2018). Like in life, the

current study does not pre-set a script for one to utilize when encountering novel experiences. Often, a script consists of seemingly incongruent pieces of information that don't carry much significance until schematized together (in a navigation setting, for example, distinct routes and landmarks in an environment – what do gasoline and burgers have to do with one another? Perhaps nothing until we learn how they tend to be paired at rest stops and appear at regular intervals along highways). We often tend to replay such scripts, modifying them as we go through life as we encounter new experiences that both use our schema knowledge but also provide information we use to amend our schema.

Schema theory is complex and there are many open questions about how schemas affect learning and behavior. In particular, the neural “implementation” of schemas is an active area of debate. Briefly, as noted above and discussed more below in the *Background*, non-spatial research emphasizes the role of the mPFC and suggests it competes with hippocampal “episodic” memory (van Kesteren et al., 2010); however, rodent research often associates the hippocampus with spatial schemas (McKenzie et al., 2013; McKenzie et al., 2014), and as discussed in section 2.1, cognitive maps may be thought of as schema-like structures for how environments are organized (Maxim & Brown, 2023). From this debate, when it comes to spatial navigation, there are two open questions I address in my thesis: 1) How does the hippocampus compare to mPFC contributions during human schema-like navigation? 2) How do spatial schemas contribute to planning vs. active navigation? For example, one prediction I test which speaks to the hippocampus vs. mPFC debate, is that we may rely on hippocampal memory processes to simulate or plan (Spiers & Maguire, 2006; Brown et al., 2016), but during active navigation, when prefrontal-dependent working memory and decision-making mechanisms are needed, we may increase reliance on the mPFC. This is because its putative function in schema memory is to integrate current cues and experiences

with internal memories, which may aid active navigation by helping us continually update our position relative to our schema.

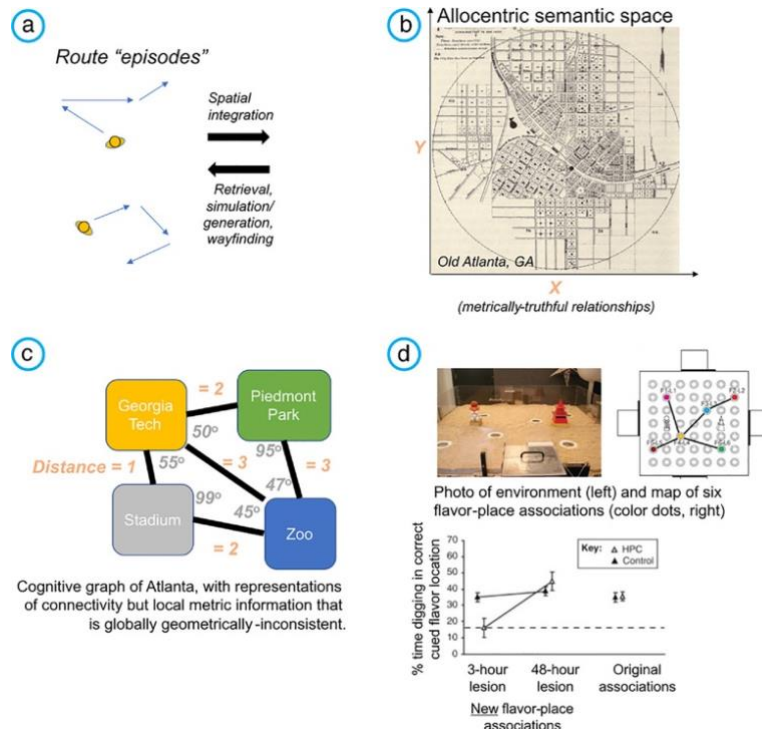
The present study examined these questions, and sought to test the effect of retrieving schematic representations of distinct navigational instances (i.e., individual events while navigating different routes) and how we utilize these schema-like structures to solve novel routes. This study incorporated the use of an immersive virtual reality task designed by (Brown, Gagnon, & Wagner, 2020) and we measured neural activity during navigation using advanced functional magnetic resonance imaging (fMRI) techniques. My aim was to provide novel insight into the neural mechanisms (particularly in the medial prefrontal and medial temporal regions) that are active throughout planning, mid-route, and goal periods of navigation. I set out to examine how these networks utilize schematic structures and when one might rely on these “schemas” across a navigation event (e.g., planning vs. active navigation) and between navigation events (e.g., when taking novel routes based on prior knowledge, vs. repeating a previously-learned route).

## CHAPTER 2. BACKGROUND

### 2.1 Traditional Schema Theory

There is little research that has applied principles of schema theory to human navigation. However, I believe that there are schema-like mechanisms that operate on spatial memory. In order to support this application, we must first understand the connection between schema formation and cognitive maps and how they might confer “schema-like” influences on memory and navigation. Cognitive maps are essentially associative structures that allow one to generalize memories of individual episodes (e.g., routes) to form maps, eventually extrapolating information from one map to another. From a spatial navigation point of view, one’s cognitive map is made up of linked representations of routes in an environment, which can all be associated together via their allocentric relation to landmarks within that environment. As we form these relationships, we can utilize this structure to help us continue to form new connections, allowing for new route information to be processed as “congruent” with our current cognitive map. Strictly speaking, cognitive maps are traditionally defined as Euclidean maps – however, in reality, experimental work has shown our spatial memory is often error-prone and fragmented by barriers in the environment and thus fails to meet that definition (see Maxim & Brown, 2023 for review). As one’s spatial knowledge becomes fragmented, it is likely that our memories may no longer fit this traditional definition of a cognitive map, and rather become more compartmentalized and episode-oriented. Spatial knowledge can be derived from allocentric or egocentric navigational experiences, sometimes even in parallel (Iglói et al., 2009; Ishikawa & Montello, 2006). Recent research (Chrastil & Warren, 2015; Warren et al., 2017) has questioned whether “cognitive maps” in these instances truly represent Euclidean space, or if they more closely resemble “cognitive

graphs” (a network of connections between places with local metric information that is inconsistent/geometrically inaccurate on a more global scale; Figure 1). This evidence that people actually form cognitive graphs rather than Euclidean maps is, in my view, more true to the traditional sense of the term “schema”. However, the term schema may be more accurate for explaining situations where we solve new routes, plan, take shortcuts, etc., because a graph still represents what you know from the past, but a spatial “schema” reflects how well one can infer new relationships from fragmented spatial knowledge. This knowledge can be generalized from one map to another, where environments may share similar features and the navigator might predict probable relationships from said schema. In this Master’s work, my focus is on such novel route planning and shortcutting, rather than just measures of previously-learning spatial relationships.



**Figure 1 | Visualization of cognitive maps as metric, graph-like, and schematic representations of our environment**

**Figure 1 (continued)** | Figure and legend reproduced from Maxim & Brown (2023). Consistent with conceptualizations of schemas in non-spatial literature, individual navigational episodes (a) can become integrated into memory (b) to form associative maps, from which we can plan or simulate future experiences (bidirectional arrows). Recent data suggest many maps may fail to convey true Euclidean representations of space and instead resemble labeled graphs (c) that emphasize topology/connectivity and local metric relationships. Seminal work in animals (d) has demonstrated that evidence of cognitive maps in simple environments can convey schema-like benefits to memory. For example, having been trained extensively on relationships for multiple flavor-place associations (top panel), rodents rapidly consolidate new flavor-place associations learned in a single shot in the same environment. Shown here, hippocampal (HPC) lesions 48 h after one-shot flavor-place learning yielded no long-term memory deficit for that association, compared to sham lesion controls and well-learned original associations. This hippocampal independence was not evident for immediate lesions 3 h after new learning, but rodents that had not learned an original schema did not exhibit the same rapid consolidation of new associations (not depicted). Fig. 1d reproduced with permission from van Kesteren et al. (2012).

Research supports that humans, like animals, can encode novel information better when it can be related to an existing knowledge structure (van Kesteren, et al., 2012), and consistent with our view of cognitive mapping, this has been shown in a recent study to apply to human spatial memory (van Kesteren, Brown, & Wagner, 2018). This schematic network of representations can also help more rapidly consolidate new information (Tse et al., 2007). As I discuss in my recent review (Maxim & Brown, 2021), one might look at Tse et al.’s rodent cognitive map as a schema, where the animal has formed associative representations between stimuli and its experiences at various times and locations in an environment. Important for my fMRI predictions in this current thesis work, one non-spatial framework for understanding how past experiences and new memories interact is the “schema-linked interactions between medial prefrontal and medial temporal regions” (SLIMM) model (van Kesteren et al., 2012). According to this model, the processing of novel information is determined by medial temporal lobe (MTL) – medial prefrontal cortex (mPFC) interactions. One of their important arguments is that the mPFC accelerates direct neocortical learning independent of the MTL, particularly when the incoming novel information is congruent with existing associative relationships in memory. This predicts opposing roles of the mPFC and MTL for memory function depending on how novel/incongruent it is with existing

schemas (e.g., how well it fits what has been learned about a map, in my spatial navigation framework).

## **2.2 The Effect of Congruency and Familiarity on Brain Connectivity**

The SLIMM model holds that during retrieval prior to consolidation, experiencing a familiar representation will lead to reactivation of the existing schema. One's schematic memory captures this re-encountering overtime, leading to greater resonance, higher mPFC activity, and further strengthening of the schema. However, novel information that is incongruent to one's existing schema is encoded separately via the MTL, rather than integrated into an existing memory (van Kesteren et al., 2013). Nonetheless, the ability of information to evoke, or "resonate" with existing knowledge leads to greater mPFC activity, thus increasing direct potentiation between neocortical representations and enough re-exposure and offline replay can eventually lead to effective long-term memory storage.

As alluded to in the *Introduction*, there is debate when it comes to schemas over the disengagement of the hippocampus during memory retrieval (Moscovitch et al., 2006). On one hand, research supports the rapid acquisition of declarative memory and learning independent of the hippocampus (Sharon, Moscovitch, & Gilboa, 2011), and that mPFC activity might actually *inhibit* MTL activity (Laroche, Davis, & Jay, 2000; van Kesteren et al., 2010). On the other hand, although we might expect higher mPFC activity when replaying a particular schema of an environment, we still expect high hippocampal activity when differentiating between *several* schemas due to overlapping similarities, thus requiring selective differentiation of the representations from one another (Brown et al., 2010; Hulbert & Norman, 2015). Additional support for this "facilitative" interaction between hippocampal activity and schemas is shown in

research looking at scene-item pair mates, with findings indicating that prior learning helps decrease representational overlap of such pair mates in the hippocampus, but not in regions such as the parahippocampal place area (PPA) (Favila, Chanales, & Kuhl, 2016).

Additional studies suggest that there is increased MTL-mPFC coupling during encoding for *less congruent* information in relation to the strength of the schema (van Kesteren et al., 2010). More specifically, a stronger schema is associated with less hippocampal-ventromedial prefrontal cortex (vmPFC) connectivity. This suggests that this joint network seems to form/cooperate when novel information is particularly difficult to integrate during the encoding process. Changes across the hippocampal-vmPFC circuitry could therefore help infer the strength of the relationships between these new and old memories (Zeithamova, Dominick, & Preston, 2012). Further support suggests that the vmPFC generates a confidence signal important for functions like strategic retrieval for preventing memory confabulations, forming contextually relevant schemas, and mnemonic decision-making (Hebscher & Gilboa, 2016). This is important for helping predict the importance of the mPFC during “schema-based” navigation, particularly when we need to make strategic choices about an instance and how it relates to our prior memories of that instance (e.g., arriving at a previously encountered intersection during a novel attempt at taking a shortcut).

### **2.3 Applying Schemas to Spatial Navigation**

Despite decades of work strongly associating the hippocampus with spatial memory, navigation research has consistently suggested that the hippocampus is *not* required for taking detours in highly familiar environments (Maguire et al., 1998; Spiers & Maguire, 2006; Spiers & Gilbert, 2015). Data show that storage of spatial knowledge relies more on the posterior parahippocampal cortex rather than the hippocampus proper, and from the literature in the

preceding section, the decision-making component of navigation from heavily schematized environments may depend critically on prefrontal subdivisions. Thinking about SLIMM and the debate in the literature on when the hippocampus is more strongly recruited, the hippocampus may be more important for taking detours when navigating in learned but *less* familiar environments (e.g., ones learned in a relatively restricted way where people haven't been able to explore all side streets extensively and repeatedly; Brown, Gagnon, & Wagner, 2020). The hippocampus is known to aid with detailed episodic and spatial memories (Moscovitch et al., 2006; Rosenbaum et al., 2004) and episodic memories typically require replay of experiences for better recall. This may be particularly important when recalling environments for which we don't already have an existing network of routes, forcing one to depend more on simulation (as opposed to simple retrieval) of possible routes from recent experiences for things like shortcuts or detours.

Reviewed in Maxim and Brown (2021), studies on spatial schemas have primarily come from rodent studies (Tse et al., 2007, McKenzie et al., 2013; McKenzie et al., 2014;) showing development of task representations in the animal's brain. Such studies provide support for accelerated learning of novel spatial associations when prior associations already exist, and notably, there seems to be rapid disengagement of the hippocampus when encoding new experiences within an existing cognitive map. More recent research has set out to test whether existing spatial knowledge can also benefit novel learning in humans and if there are similar neural characteristics during prospective planning and recall of memories related to existing spatial knowledge (van Kesteren, Brown, & Wagner, 2018). Prior spatial associations seem to predict learning of new cognitive map information with the hippocampus important for navigational planning, yet a strong spatial schema reduced this activity for retrieving newer memories. Importantly, consistent with the schema literature in the preceding sections above, other human

navigation studies have also shown support for increased mPFC activity for maintaining memory of goal locations during navigation (Ciaramelli, 2008; see Patai & Spiers, 2021 for further review) and this region may facilitate learning of novel routes through one's cognitive map (putatively, helping elaborate/expand the schema) (Brown & Stern, 2013).

In a related study conducted by Brown et al. (2020), researchers set out to test prospective navigational planning while manipulating psychological stress in young adults. They found that participants who performed planning under stress showed disrupted neural activity necessary for mnemonic retrieval and mental simulation. These participants also showed reduced navigation of shortcuts over the familiar routes. This was indirectly tied to reduced activity in both the hippocampus and prefrontal cortices during a “planning period” in the task. More direct links to the role these areas play, and whether they play similar roles during subsequent active navigation of the space, remain to be tested.

Influenced by these findings, my thesis study aimed at analyzing these regions important for mnemonic retrieval (mPFC and hippocampus) and examine whether there was any overlap with one's flexibility in drawing upon schema-like representations during navigation. A key difference in my experiment is that participants did not undergo any experimental stressors, with the intention of focusing on the key neural mechanisms involved in these spatial memory processes during attentive and undisturbed navigation. Furthermore, my analyses focused on how memories of environments are represented in the hippocampus and mPFC at different navigational stages.

### **CHAPTER 3. RESEARCH QUESTIONS AND PREDICTIONS**

The above literature begs several questions: 1) Do we generally process spatial memories via the hippocampus, simply because we have it? Or are there certain elements of navigation (i.e., planning, mid-route, goal) where hippocampal mechanisms are more important than others? 2) Are these hippocampal mechanisms dissociable to some degree from prefrontal correlates of performance, as argued by the non-spatial schema literature? Perhaps a major differentiator is when planning or active navigation are more closely aligned to prior experiences (schema-like memory) of the environment or depend more on novel inferences.

The current study asks such questions by providing a generalizable simulation of how humans perceive a stream of information (in this case, different routes and distinct landmarks) and bind these seemingly “incongruent”, or semantically-distinct, pieces of information into a single representation to aid during planning and wayfinding. One reason my research focuses on neural representation and the use of a “schema” during different periods of navigation is that different regions (in this case, hippocampus and mPFC) may play different roles at different stages. Moreover, there may be opposing relationships between cognition across different periods which could influence the relative engagement of hippocampal and mPFC mechanisms. For example, more planning of a route before navigation might result in less need to make real-time decisions during navigation – two possible moments in the task where one brain region may be more important than the other. In particular, if one is planning a more novel route to a novel goal, this would be putatively more hippocampal-dependent according to the literature above. But if planning a route more closely aligned with prior experience, this may draw on the putative functions of mPFC as a node for relating current experiences or goals to past experiences and

outcomes. My task was designed to test this contrast, and this is particularly interesting because it illustrates how strategy (what we choose to do – e.g., take a familiar route or shortcut, as was implemented in my task design) and execution (how well or efficiently a person implements that strategy) are not equivalent. Especially in the context of continuous experiences like navigating a route, a person’s decision at one point can influence what types of decisions they need to make later on, and they can also change their strategies as memory cues come and go (all of which may differentiate relative contributions of the hippocampus vs. mPFC).

More generally, my research assess how having a schema-like representation of one’s environment can modulate behavioral/cognitive effects and their associated neural activity. Furthermore, as noted above, I propose this memory structure also supports map-like memory integration for navigating *across* different environments. Perhaps when people have formed a stronger schematic representation from prior learning, this could allow them more flexibility to alter route navigation, such as taking a detour from the familiar route, or a “shortcut”, based on experiences had in other environments.

An important aspect of schema theory that has not been thoroughly tested in spatial navigation is that, although a schema made up of distinct episodes could facilitate new learning and planning, it comes at the cost of episodic specificity – we begin to lose detail of each individual episode as memories continue to build, leading to increased interference across environments (van Kesteren & Brown, 2014; van Kesteren, Brown, & Wagner, 2016). Our lab recently showed behavioral evidence that greater map memory of a route was associated with greater episodic interference between memories (He et al., 2021), however, the neural bases for this has not been directly defined. Based on the literature reviewed above, one of my predictions was that individuals with a strong within-town representational similarity (evident of a strong schema-like

representation for the environment) would show a tendency for taking more shortcuts than someone with high similarity between-towns and unable to discriminate across environments. I predicted this environment-level coding would depend most on mPFC regions, particularly during navigation as someone would need to utilize their environment schema to more efficiently reach the goal. Furthermore, I predicted to find that participants who have a more difficult time discriminating between environments, would depend more heavily on the hippocampus in order to recall specific episodes from their past experiences navigating the towns to help guide them along the environment. Furthermore, I predicted this would also manifest at the within-subject level, such that environments that show behavioral indicators of being less “schematized” would be associated with greater hippocampal activity for navigating those distinct routes.

Building on the points raised above, a theoretically impactful feature of this study was that it asked how often and to what extent we may “bypass” the hippocampus when retrieving memories. The SLIMM model claims that the MTL captures new experiences, but is inhibited by the mPFC if the novel information is strongly associated with an existing schema (referred to as “congruent” in their model). As discussed below, because my fMRI data targeted post-consolidation memory retrieval in service of navigation, I postulated that retrieval in navigation would primarily be more mPFC-dependent (and less hippocampal engaging) when individuals chose to navigate in a manner more consistent with their prior familiar experiences. Complementing the hippocampal predictions above, in cases where people navigated routes more strongly aligned to their prior knowledge, we predicted that mPFC activity would be correlated with reactivation of the existing knowledge structure already formed (e.g., familiar route information). While I expected this opposing relationship between the hippocampus and mPFC with what people *plan* to do, based on the SLIMM theory, I believed the strength of mPFC

involvement would be particularly valuable *during* navigation. Namely, as people transition from simulating navigation during planning to actually following a route, I predicted the hippocampus becomes progressively disengaged, and we begin to rely more on our prefrontal circuitry, particularly the mPFC, to maintain our current goal and relate our position continuously to our “schema” of the environment as new cues become available (e.g., turning a corner and seeing a familiar landmark) (Ciaramelli, 2008).

## **CHAPTER 4. METHOD**

### **4.1 Participants**

This study recruited 19 healthy young adult participants (ages 18-28) from the Georgia Institute of Technology. Of the sample, there were 12 females, 16 were right-handed, and 13 of the participants identified as Asian, five as White, and one as Hispanic/Latino. All participants underwent a rigorous health screening process to determine eligibility. Individuals were excluded from the study if they met any one of the exclusionary criteria consisting of (but not limited to) heart disease, diabetes, use of anxiety/depression medications, illegal drug use and excessive alcohol use. Health information collected for screening purposes was not kept for our records. This study followed strict guidelines for handling sensitive information and maintaining participant safety throughout the experiment in accordance with the Georgia Tech Institutional Review Board. Participants were compensated with \$20 per hour of their time across both experiment days.

### **4.2 Materials**

Participants were asked to provide demographic information at the beginning of the study, including details such as age, sex, handedness, years of education, and quality of sleep (Appendix A and B). Participants were asked to complete two different tasks aimed at measuring navigation strategy and execution: 1) a dual-solution task (experimental task, described below) to reveal different types of navigational strategies and provide a measure of efficacy, and 2) the Y-maze task (Rodgers, Sindone, & Moffat, 2012) to provide insight into how their strategy choices in the complex environments of the dual-solution task relate to a person's preference for more flexible landmark-based or more rigid familiar-response-based behavior. Prior to starting the experimental task, participants were asked to complete the Y-maze task (Appendix C). Lastly, prior to starting

the experiment, participants were given a concise version of *Ishihara's Tests for Colour Deficiency* (Ishihara, n.d.) in order to control for individual differences in navigation due to differences in perception of an environment.

Throughout the primary “dual-solution” navigation task (Figure 2; described in detail below), participants were given memory tests for the various items they encountered in each environment (a famous face, an animal, and a food or a tool). For the item test, participants were given three item “cheat sheets” for the three object category types. Each sheet consisted of the encountered items of that type, along with lure items that were never shown to the participant in any of the environments (Appendix D). This item test is important for helping track how well participants know key landmark items and was used to measure planning and thought during environment navigation. After having completed all navigation tasks on the second and final day of the experiment, participants were asked to respond to the *Questionnaire on Spatial Representation (QSR)* (Pazzaglia et al., 2000; Appendix E).

### **4.3 Procedure**

Prior to starting the navigation task for the experiment, participants were asked to complete the Y-maze task for five different environments (specifically designed for the Y-maze task and unrelated to the environments for the experiment). For this task, participants were given vague directions to follow the path until they reached a fork in the road and had to choose which direction to take (right or left). They knew whether they chose the correct path if they heard a guitar chord sound or an incorrect path if they heard an alarm buzzer. However, there were also objects at the ends of each path. On the last run through of each environment, the map rotated, leading to a location change of the objects on the screen. This task allowed us to observe whether individuals

chose to continue traveling along the previously cued path, or whether they chose to travel towards the new location of the objects.

For this experiment, participants were tasked with navigating throughout six computerized virtual environments in this modified version of the task used by Brown et al. (2020). Participants were asked to navigate and learn the environment routes throughout this two-day experiment. Each environment simulated a different “town” with distinct routes, buildings and objects. Participants navigated through a network of streets following a delineated route which was strictly enforced for training purposes on Day 1. In each of the six environments, participants encountered three categorically-distinct items throughout the town along the trained route. The items differed for all six towns, resulting in 18 total items encountered. Items were visible along the navigated route and participants were tested on which three items belonged to what environment.

On the first day (the encoding phase) of this two-day study, participants repeatedly navigated all six towns using the keyboard arrow keys corresponding to “forward”, “left” and “right” movements. Backward movements were not possible. First, the participants navigated the towns following red arrows on the ground leading along the correct path. There were four arrow-guided trials throughout the six towns followed by four additional unguided trials to help strengthen the memory of the trained route. For every new trial, environment order was pseudo-randomized and participants were placed in a different starting location for each town. The three items were visible along the trained route in order to allow for the participant to integrate these items into a single organized schema-like memory structure corresponding to each specific town.

Across the 8 trials occurring on Day 1, participants were given three item recognition tests in which three screenshots of the same town appeared on the screen and the participant was asked

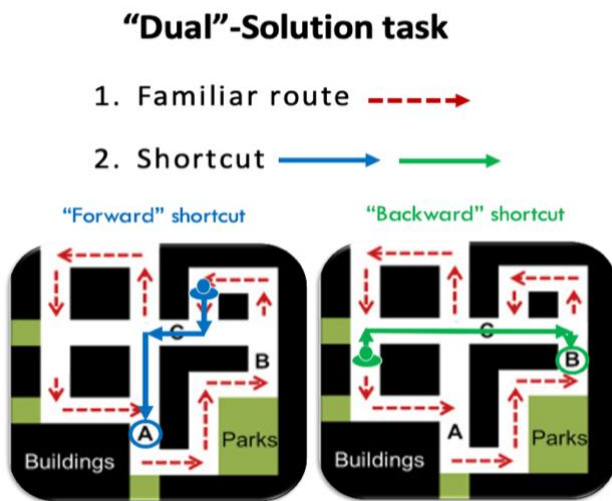
to correctly indicate which items were located in the town shown, in no particular order (see Appendix D). The goal for this task was for the participant to correctly identify the correct target item in each sheet corresponding to the given environment. The fourth and final item memory test was an item recall instead of a recognition test. This time, participants were not given the item sheets and had to retrieve the correct items for each town from memory.

#### *4.3.1 fMRI Task*

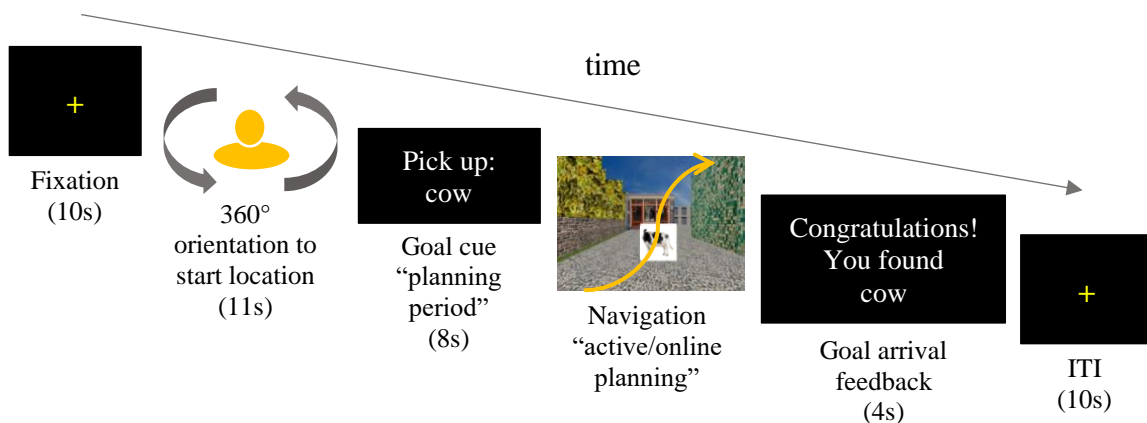
The second day (the retrieval phase) occurred approximately 24 hours later to allot enough time for memory consolidation of the environment schemas, consisting of the three items presented per town during the initial encoding phase. For Day 2, participants were placed inside the MRI scanner to complete their navigation tasks. During part one of the retrieval phase, participants were asked to complete one unguided trial of the six towns to determine a baseline of how well they recalled the trained route from the day prior for all of the six maps. For part two of the retrieval phase, participants were given the aforementioned “dual-solution” task (Figure 2) – an unguided memory probe game intended to have participants correctly identify the location of specific target items rather than reaching the finish line in the environment. The premise behind this task was for participants to use their own strategy rather than stick to the trained familiar route to locate these items. The probe locations were designed such that there was a “shortcut” option to reach the target item, however participants were not explicitly told this information. Instead, they were simply told to use whatever strategy they’d like to get to the goal. This task allowed them to veer off the trained route for the first time since navigating the environments. How quickly the participant reached the target item depended on how well they learned the environment and location of each item throughout the town. Participants were not given a time stressor, but were asked to get to the goal “as quickly and as efficiently as possible”.

The possible shortcuts consisted of a path that either followed the trained forward direction (probe 1), but for some goals, the optimal route would require the participant to backtrack the familiar route in some way (probe 2) – a novel direction along the environment (Figure 2). For this probe task, participants were asked to navigate each environment twice, with the first round target being the “animal” goal and the second round target the “face” goal. The animal goal was optimally reached via the forward direction route and the face was most quickly reached via backtracking.

A



B



**Figure 2 | Dual-Solution task**

**Figure 2 (continued)** | (A) The participant is given the freedom to navigate to the goal using a chosen strategy. Solution 1 involves following along the trained familiar route (red). Solution 2 involves taking an optimal shortcut route to the goal. The shortcut direction depends on the trial. In the first trial, the optimal shortcut lies roughly along the direction of the familiar route (blue; goal = animal), and in the second, the optimal shortcut requires back-tracking the familiar path along the environment (green; goal = face). It is up to the navigator to determine the best route for each specific goal item. (B) fMRI probe trial structure. Participants are oriented to their starting location for the given trial and are then cued to navigate to a target item. This is the “planning period” where the participant is expected to strategize their trajectory following either the familiar route or a shortcut. Participants who do not use their planning period might end up planning “online” on their way to the goal. Participants are shown three towns, followed by a brief check-in and then continue on with the remainder of the towns. Maps adapted from Brown et al. (2020).

#### 4.4 fMRI Parameters and Analyses

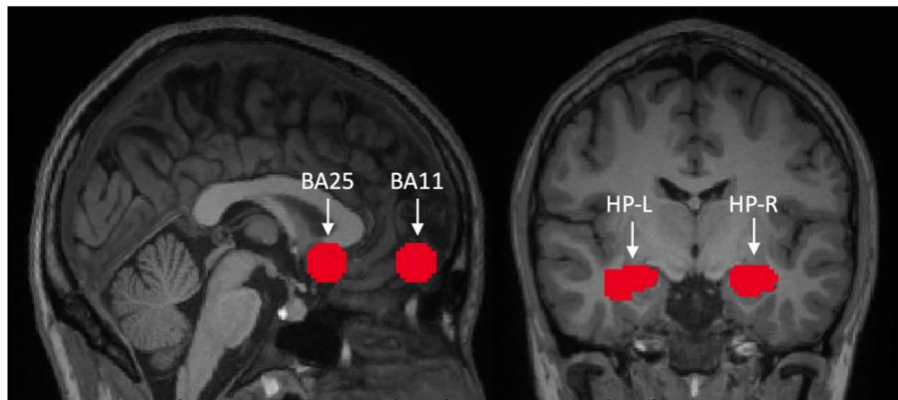
Day 1 of the experiment was conducted in a controlled lab setting while sitting down in front of a computer as the participant was tasked with navigation the virtual desktop environments. On Day 2, participants were placed inside a Siemens 3T MRI scanner where they remained inside for approximately 1 hour as they completed the navigation tasks. Participants underwent a T1-weighted MP RAGE structural scan of their brain and a T2\*-weighted functional scan during the experiment. We utilized a 20-channel head coil and collected functional data of 2x2x2mm voxels across an interleaved oblique slice acquisition sequence with a 2s repetition time (TR).

There were four scanning runs of the probe task that made up the linear model being tested, each with five experimental regressors plus six motion regressors. The main regressors consisted of the five different stages of the task: 1) Orient [12s duration] – the participant is rotated 360 degrees to view the environment from their starting location, followed by a black screen indicating the target goal item. 2) Assigned [8s duration] – the participant is shown a blank black screen and is given 8s to plan their route to the goal. 3) Navigate [2s duration] – captures the participant’s brain activity at the initial start to navigating the environment. 4) Midroute [2s duration] – captures the participant’s brain activity at the exact midpoint location in the environment based on coordinates, not time. 5) Arrived [2s duration] – the participant’s arrival to the target goal item in

the environment. A plethora of univariate analyses were conducted on the functional data to target my research questions. We conducted 10 different activity contrasts comparing different periods of our main dual-solution navigational task. We expanded on these results by conducting parametric modulations and between-subjects correlations using a metric known as Fréchet Distance (described below), comparing this value for the main probe task to the assigned (“planning”) period. For these analyses, we applied a significance threshold of .001 and corrected for multiple comparisons using SPM’s cluster extent significance (based on random field theory) of  $p < .05$ , to ensure we reported statistically-meaningful activity clusters across the board. Lastly, we ran a representational similarity analysis (RSA) for our primary periods of interest which again included the assigned period as well as the midroute period of navigation. The RSA analyses were designed to address my more specific mechanism predictions about how memories were represented (e.g., evidence of an environment schema-like representations being brought to mind during different stages of navigation in the hippocampus vs. the mPFC). These two conditions were analyzed across four anatomically-defined brain regions of interest (see Table 1 and Figure 3 below): right hippocampus, left hippocampus, ventromedial prefrontal cortex (vmPFC – BA11), and posterior-ventromedial prefrontal cortex (pvmPFC – BA25). Both vmPFC and pvmPFC were analyzed separately because of their extensive associations with non-spatial studies of schema and hippocampal function and prospective navigation planning (van Kesteren et al., 2010; Brown et al., 2016). Thus I considered that I might discover differentiable ways of representing the task in these two subdivisions.

**Table 1 | Experimental ROIs and Masks**

<b>Regions of Interest (ROI)</b>	<b>ROI Mask</b>
Hippocampus – Right (HP-R)	Obtained from the WFU PickAtlas (AAL)
Hippocampus – Left (HP-L)	Obtained from the WFU PickAtlas (AAL)
Ventromedial prefrontal cortex (vmPFC – BA11)	Obtained from Brown et al., 2016 xyz = -2, 56, -10
Posterior-ventromedial prefrontal cortex (pvmPFC – BA25)	Obtained from Brown et al., 2016 xyz = -5, 16, -11



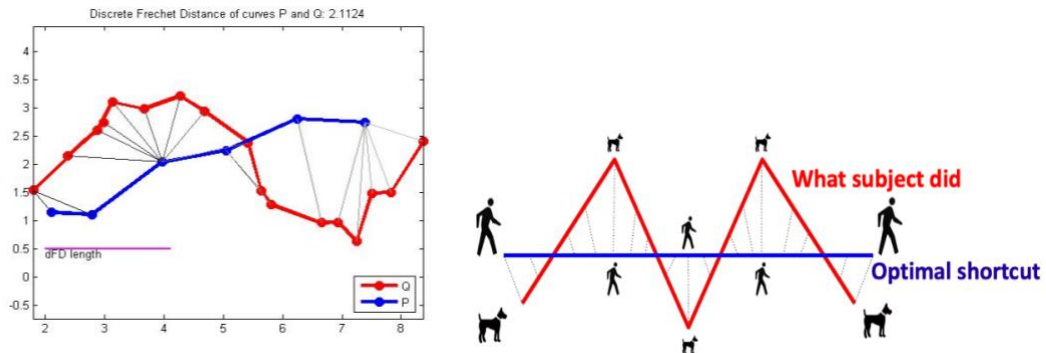
**Figure 3 | Visualization of ROI mask locations**

# CHAPTER 5. BEHAVIORAL RESULTS

## 5.1 The Fréchet Distance Method

While participants navigated the “dual-solution” task, they could have taken either the familiar route, the optimal shortcut, or some shorter version of the familiar route to get to the goal. Path length cannot fully capture this range of attempts because sub-optimal shortcuts could require similar path lengths as taking the familiar route, and some attempts at novel routes could more closely hug the familiar route or the optimal shortcut respectively. In order to quantify in a continuous way whether one person was more of a response-based familiar route taker, vs. a shortcut-route taker, we adopted a measure known as “Fréchet Distance”. The Fréchet Distance (FD) is a mathematical way to describe how one route deviates from another (Danziger, 2020), with a lower FD value indicating little deviation between routes (Figure 4).

A



B

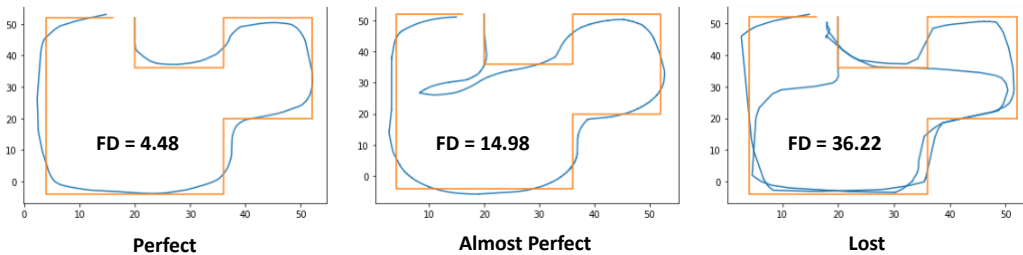


Figure 4 | Fréchet Distance

**Figure 4 (continued)** | (A-left) Visual representation of Fréchet Distance showing distances between points on two separate lines,  $p$  and  $q$ . (A-right) The “dog-walker” example (based on Alt & Godau, 1995). To illustrate the use of FD for the current study, labeled are the “dog” and “walker” trajectories as the supposed route the subject followed compared to the optimal shortcut for a given environment, respectively. (B) Three examples of the same environment when different participants were asked to navigate the familiar trained route (unguided) at the start of Day 2. The more exact they were in their trajectory of the trained route, the lower their FD value (B-left). The more lost they were in the environment, the further they were from a perfect trajectory, thus the higher their FD value (B-right).

This Fréchet Distance measure is a continuous measure, with the FD values ranging from approximately 4-48. These values were derived from comparing the perfect midpoint along a route to wherever the participant went. A value of zero would signify the route was navigated perfectly, without deviating from the midpoint (think military-like march). However, this is simply not how humans naturally traverse an environment, instead cutting corners and sticking to one side of the “road”. Thus, a “perfect” trajectory means following the route without skipping sections or circling around, an “almost perfect” route means there were one or two mistakes made, but the main route was mostly followed, and if there were several mistakes made and the participant clearly did not follow the route then this meant they were “lost”. In this way, we can categorize a participant’s behavior and observe route similarities and differences between a route of interest and what the participant actually did. Traditional measures of path length are subject to the same considerations (e.g., the improbability of walking a truly 100% optimal path length) but are insensitive to whether behaviors more closely align with the familiar or optimal shortcut. Indeed, it’s entirely probable that an imperfect attempt at a shortcut has the same path length as a familiar route, but Fréchet Distance can at least reveal the critical difference between strategy and execution discussed above.

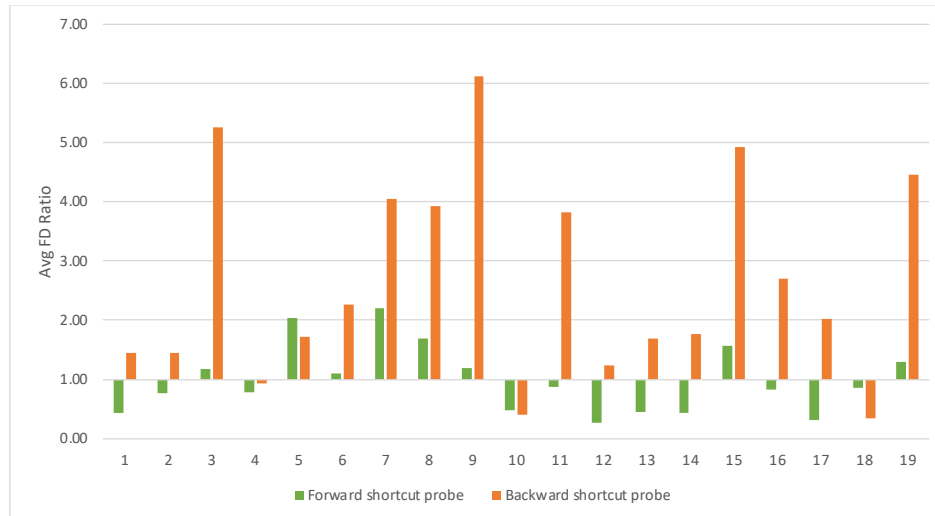
## 5.2 Navigation Strategies

Before analyzing the participant's navigation strategy choices during the probe task on Day 2, it was important to address the question of whether their performance was dependent on their overall memory of the familiar-route from Day 1. Establishing this baseline for how well they retained knowledge of the trained route was necessary for understanding why a subject may choose to use one strategy or another. Using the Fréchet Distance method outlined in Figure 4B, we looked at how well the participant retraced the trained route (completely unguided) at the start of Day 2. Based on the findings from Brown et al., 2020, we predicted participants would perform well on this unguided familiar route task, even after only a few hours of navigation training the day prior. As predicted, performance on this task was impressive, with the highest FD (averaged across the six towns) at just 18.06, meaning participants were making very few mistakes, if any (see Figure 2B for a frame of reference). Approximately 58% of the participants were within an FD of 10 on average, virtually a perfect trajectory of the trained route keeping in mind the natural deviations from the true midpoint of the path that both FD and other metrics like path length would pick up on.

Learning that participants remembered the trained route from Day 1 was important in order to clearly compare novelty to genuine familiarity of a route when analyzing navigation strategy choices during the dual-solution probe task on Day 2. I then asked whether a participant was more prone to taking shortcuts or more comfortable following the familiar route during the probe task. Across subjects, the total average FD value across probe runs was 18.78; however a paired samples t-test confirmed a significant difference ( $p=.002$ ) between probe types, with navigation of the “forward shortcut” probe runs ( $M=14.98$ ,  $SD=4.81$ ) following the optimal shortcut more closely than “backward shortcut” probe runs ( $M=22.58$ ,  $SD=7.10$ ) – those where the optimal route would

have been to back-track direction in the environment relative to the familiar route. Because routes could fall anywhere in between optimal shortcut and familiar route paths, I also ran a calculation to look at a ratio of how close, on average, these participant trajectories were to the optimal compared to the familiar route. This showed further support for route strategy differences between the two probes ( $p < .001$ ), with data indicating that for the runs where backtracking was optimal, participants chose to more closely follow the familiar (forward-moving) route. However the ratio was shifted in runs where the optimal shortcut already followed along the forward direction (i.e., more closely mapping to the optimal shortcut route than the familiar for “forward” runs). These data suggest that directionality may be a critical factor for when and how well we take shortcuts (Figure 5).

Why did participants choose to more closely follow the familiar path for the backtracking probe as opposed to the forward-direction probe? One interpretation is that participants are clearly confident in the familiar routes they trained on during Day 1 (as was suggested above by their performance in the familiar route test 24 hours after training). While both probe trials provide a novel goal (and potential strategy), it's possible the participants preferred to follow this exact familiar route more often when the alternative was not only novel, but came with an additional challenge of potentially having to backtrack past global and local cues in the environment in an unfamiliar direction.



**Figure 5 | Probe strategy preference**

**Figure 5** | Illustrated are the ratios of the familiar vs. shortcut FD values for the dual-solution probe task on Day 2. We divided the optimal shortcut FD by the familiar route FD per environment, then calculated the average FD across the 6 environments for each participant. These values indicate whether the participant’s routes were closer to the optimal route or the familiar route. Higher scores indicate a greater distance from the optimal shortcut than the familiar route.

These findings are quite interesting on their own, suggesting participants are thinking about the situation in relation to their prior knowledge of these environments and thus making a different choice based on the probe trial’s demands. What I wanted to gather was whether these results were accompanied by differences in neural activity across our main regions of interest: the hippocampus and mPFC. Given the debate in the field on their respective contributions to spatial schemas and navigating more or less-novel situations where connections to prior knowledge are more or less clear and effortful, this could mean neural activity in these regions may therefore be weighted differently when it comes to route directionality.

Similarly, I wanted to test how participant navigation during the Day 2 probe task compared to their Y-maze performance from the beginning of Day 1. Though not a primary part of the experiment (these data were collected partly in service of a bigger cognitive aging study),

these Y-maze task data could enable me to see if strategy preferences in the Y-maze predict how people respond to the forward vs. backward shortcutting problems in the more complex and naturalistic task. Research has consistently shown that young adults are typically more allocentric navigators, centering their attention and actions on other people or things rather than their own perspectives (Rodgers, Sindone, & Moffat, 2012). Because of this, we anticipated similar Y-maze results, which should support lower FD values in the dual-solution task for the optimal shortcut. Our Y-maze data showed that on average, participants chose allocentric (“place”) based navigation 55% of the time. When grouping across the five Y-maze trials, 58% of participants were primarily place-based navigators. Though our results are in line with prior findings, participants did not significantly choose this strategy over a more egocentric (response) based one. Furthermore, we found no evidence that Y-maze task preference results in taking a particular route during the forward ( $t=.99$ ,  $p=.337$ ) or backward ( $t=.24$ ,  $p=.812$ ) probe trials (e.g., a more place-based navigator during the Y-maze task did not have smaller FD values during the probe task), further begging the question of whether strategy preference is dependent on route complexity and directionality.

### **5.3 Behavioral Evidence for Schema-Like Representations**

While the above tests using Fréchet Distance were able to help validate cognitive map learning from the experimental task in general (e.g., showing successful familiar route memory and differences in strategy between forward and backward probes), I wanted to test if participants were successfully forming associations between landmark items encountered along the route and correctly remembering what towns these groupings belonged to. It is important to note that the landmarks presented to the participants were not meaningfully related to one another and were paired at random (making it harder to group together), and not based systematically on prior

semantic associations before learning our task. Take for example one of the six environments of which a participant navigated throughout both days. In this environment, participants came across the following three items – *Face*: Oprah Winfrey, *Animal*: Giraffe, *Other*: Hammer. In order to successfully form a schematic representation of the environment from events with these items during training, a participant would have likely had to invoke some strategy to remember that these items belong together. Unfortunately, the design of this study did not question participants on their thought process regarding how they went about forming these associations, however, the quantitative data derived from the item tests performed on Day 1 can still help inform on this matter.

As predicted based on no prior associations, participants scored drastically lower on the first item test (which occurred after only one pass-through of each environment) compared to every other test performed later in the experiment. On the first item test (block 1), the participants scored an average of 26%. Just two more rounds of the environments later, participants scored an average of 92% by the second test! Group accuracy reached ceiling at 96% for block 3, with equal performance for block 4. These data are important background for interpreting the fMRI as well as probe trial behavior, because it made clear that participants had found an effective way of associating these novel arbitrary triplets of items with their specific towns before the scanning task. The constant replay of their pairings over the course of the training routes could allow for the formation of schema-like knowledge of each environment made up of individual item representations.

Interestingly, it wasn't just the item test accuracy showing important results for interpretation of the main behavioral and fMRI datapoints. Response frequency/timing data in the item tests showed that of the three landmarks, participants tended to respond with the "face" item

first, followed by the remaining two items (even though face was not disproportionately encountered first along routes when learning). Even on the first item test, where participants had only been exposed to each item one time, 74% of the first item responses provided were of faces. As mentioned above, accuracy was quite low for this first block so it is very likely that many of the face guesses were incorrect, nevertheless, it was the item category most commonly guessed first. As participants gained confidence in their memory of the other items in each town, this percentage eventually dropped throughout the item test blocks. In the final item test, where participants were only able to recall the items without a memory cue sheet as an aid, 56% of participants jotted the face landmark as their initial response of the three. This suggests that, despite the faces not taking any precedence in the presentation of the task, participants were “thinking of each town” according to the face item that belonged there (e.g., this is “Oprah’s town”). For the purposes of my study, which emphasizes questions surrounding schema theory, this suggests that non-spatial identities (particularly the faces of people) were being used to relate and distinguish environments and their landmarks more than the environment’s other structural features (unique textures, layout, etc.). Combined with the ability of taking a novel shortcut in an environment, it’s clear that participants are able to “fill in the blanks” with spatial and non-spatial information – an ability made possible if one has *some* schematic representation of an environment, further than what the individual was trained on.

## CHAPTER 6. FMRI RESULTS

I conducted a mix of univariate and multivariate analyses to help address 1) how the hippocampus and mPFC respectively contribute to navigation, 2) do these patterns of neural activity differ across regions when route directionality is at play, and 3) whether this differs depending on what a person's strategy may be (a shortcut vs. a familiar route); which can be considered as relying more on new inferred relationships from schematic knowledge or replicating past experiences. I examined these neural questions at different phases of the navigation process (planning, navigation, midroute, goal arrival) and during different trials of the experimental task (forward vs. backward), because this was particularly valuable for understanding when these different areas predict behaviors based on prior memories of one's navigation experiences and whether they are more schema-aligned or not.

### 6.1 Univariate fMRI approach

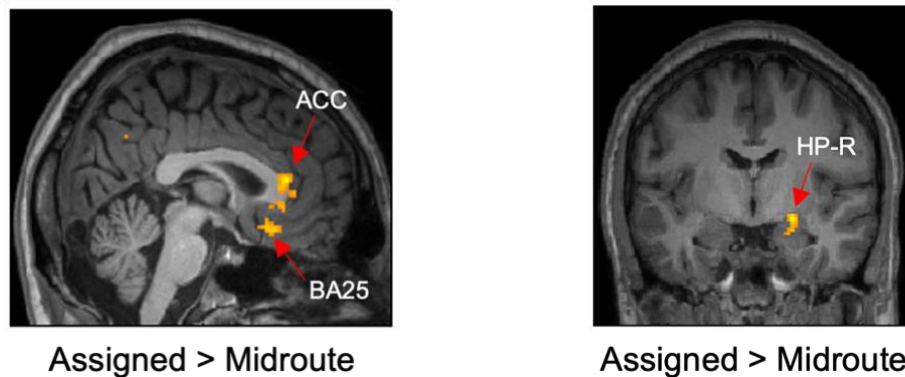
#### 6.1.1 *Does the hippocampus contribute differently from mPFC regions during planning of a route compared to actively navigating the route?*

To answer this question, I tested for differences in activity across the planning period ("assigned") compared to the midpoint of the navigated route ("midroute"), as well as responses to the goal arrival ("arrived") period (when planning next steps is no longer needed for the trial, but reward and "retrospective" thought could instead occur).

##### 6.1.1.1 Assigned – Midroute

First, analysis of my four main regions of interest showed there was more activity during the planning period than midroute in the left hippocampus ( $t=2.34$ ,  $p=.031$ ), right hippocampus

( $t=2.67$ ,  $p=.016$ ) and BA25 ( $t=5.42$ ,  $p<.001$ ). However, the vmPFC (BA11) was not more significant during the planning period in comparison to the midroute period. A whole-brain analysis showed there were significant clusters of activity that included the ACC [cluster peak: (0, 30, 8),  $k=250$ ,  $t=6.49$ ,  $p<.001$ ], right hippocampus [(22, -8, -12),  $k=56$ ,  $t=5.13$ ,  $p=.011$ ], and left IFG [(-46, 30, 20),  $k=107$ ,  $t=4.91$ ,  $p=.001$ ]. When examining the inverse of this contrast (active navigation activity greater than planning), only the primary visual cortex was more active, which was to be expected given the participant was receiving perceptual information as opposed to staring a black screen during the planning period.

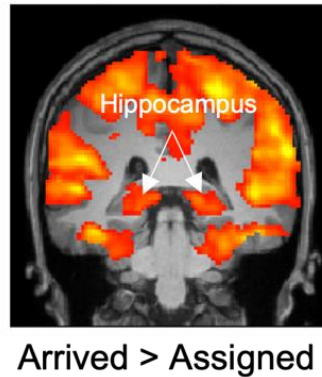


**Figure 6 | Assigned – Midroute activity contrasts**

#### 6.1.1.2 Assigned – Arrived

When comparing the planning period to neural responses at goal arrival, my ROI analyses showed that all four regions were significantly more active for arrived than for assigned: left hippocampus ( $t=-5.18$ ,  $p<.001$ ), right hippocampus ( $t=-5.50$ ,  $p<.001$ ), BA11 ( $t=-4.68$ ,  $p<.001$ ), and BA25 ( $t=-2.26$ ,  $p=.037$ ). At the whole-brain level, when comparing the planning period to the goal arrival, no significant clusters were observed in my regions of interest for assigned activity > arrived activity. In the reverse contrast (goal > planning) there was a significant cluster of activity

that included the SFG  $[(-12, 32, 56), k=261, t=6.02, p<.001]$ , and although not a suprathreshold cluster, we did see greater activity in the left and right hippocampus.

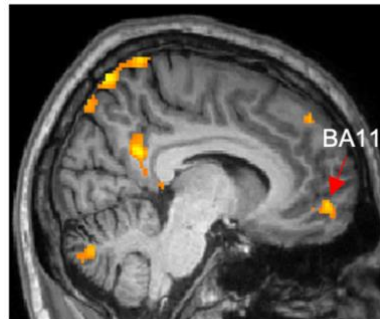


**Figure 7 | Assigned – Arrived activity contrasts**

#### 6.1.1.3 Navigate – Midroute / Navigate – Arrived

After conducting the above mentioned contrasts, it became clear that the visual stimulation from seeing and navigating through the environment elicited more suprathreshold activity than any mental imagery processes while simply staring at a black screen during planning. Because of this I decided to conduct an additional exploratory analysis comparing activity of the start of navigation (immediately after the prescribed planning period) to midroute activity. This was interesting to me because both are moments of navigation throughout the environment which should invoke plenty of visual stimulation, but it was possible some planning occurs/continues at the outset of navigation from the immediate preceding planning period (since now the environment is visible to help cue additional memory details). When contrasting the start of navigation to midroute, we saw greater fusiform activity (not a suprathreshold cluster). However, for midroute > navigation start, we found greater activity in BA11  $[(10, 56, -8), k=186, t=5.03, p<.001]$  as well as extensive SFG activity  $[(20, 40, 48), k=235, t=6.32, p<.001]$ . When comparing the navigate

period to the goal arrival and vice-versa, we saw widespread fusiform and IFG/MFG activity, particularly for goal arrival > navigation.



Midroute > Navigate

**Figure 8 | Navigate – Midroute activity contrasts**

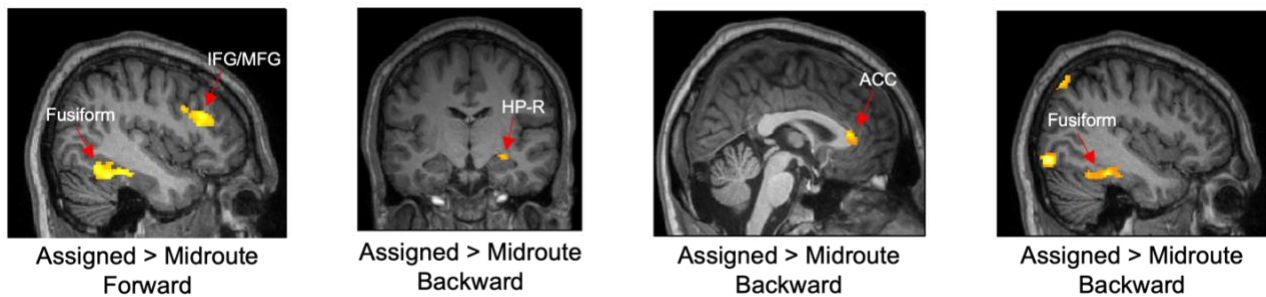
6.1.2 *Does the shift in route directionality affect how the hippocampus and mPFC regions process navigation periods?*

The question of directionality for the shortcut probes became of particular importance after learning the participants behaved differently when the optimal route to the goal involves potentially backtracking one's environment. The novelty of this direction switch adds a new layer of complexity to the task, that became evident by these behavioral findings. Given that both my mPFC and hippocampal ROIs were engaged in planning more-so than active navigation on average (above results), I then tested for neural differences between our two primary time points of interest during the task (planning and midroute) as a function of subdividing probe trials based on directionality.

6.1.2.1 Assigned – Midroute (forward vs. backward)

Testing in my *a priori* ROIs showed that BA25 was the only region significantly more active during the planning period compared to midroute for forward shortcut trials ( $t=3.85$ ,

$p=.001$ ). In comparison, on the backtracking shortcut trials, we found that all regions except BA11 ( $t=.32$ ,  $p=.754$ ) were significantly more active for the planning period over the midroute: left hippocampus ( $t=2.33$ ,  $p=.032$ ), right hippocampus ( $t=2.82$ ,  $p=.011$ ), and BA25 ( $t=3.70$ ,  $p=.002$ ). Whole-brain analyses showed that for the forward shortcut trials, when comparing the planning period to the midroute period, we found more planning activity in the left IFG/MFG [ $(-42, 26, 26)$ ,  $k=327$ ,  $t=5.10$ ,  $p<.001$ ] and the left fusiform area [ $(-48, -56, -20)$ ,  $k=318$ ,  $t=6.71$ ,  $p<.001$ ]. The inverse contrast simply resulted in extensive visual activity. When comparing the planning to the midroute period in backward shortcut trials, we found higher activity for planning in the fusiform [ $(-40, -38, -22)$ ,  $k=174$ ,  $t=6.08$ ,  $p<.001$ ], the ACC [ $(2, 30, 10)$ ,  $k=89$ ,  $t=5.56$ ,  $p=.001$ ], and in the right hippocampus [ $(28, -14, -12)$ ,  $k=51$ ,  $t=4.49$ ,  $p=.011$ ]. The inverse contrast for the backtracking trials also showed some increased activity in the fusiform and SFG.



**Figure 9 | Assigned – Midroute (forward vs. backward) activity contrasts**

#### 6.1.2.2 Assigned – Arrived (forward vs backward)

The ROI analysis for forward trials showed that all regions but BA25 ( $t=-1.47$ ,  $p=.159$ ) were significantly more active for the goal arrival period than for the planning period: left hippocampus ( $t=-3.66$ ,  $p=.002$ ), right hippocampus ( $t=-4.79$ ,  $p<.001$ ), and BA11 ( $t=-3.68$ ,  $p=.002$ ). These same regions – again except for BA25 ( $t=-1.79$ ,  $p=.09$ ) – similarly resulted in more activity for arrived than for assigned during the backward trials: left hippocampus ( $t=-4.41$ ,  $p<.001$ ), right

hippocampus ( $t=-4.47, p<.001$ ), and BA11 ( $t=-3.37, p=.003$ ). At the whole-brain level, particularly for the backward instance of the task, we saw greater activity in the primary visual cortex, right MFG, and cuneus/precuneus areas for goal arrival > planning, though these clusters were not significant clusters per our threshold settings.

### 6.1.2.3 Assigned – Assigned / Midroute – Midroute (forward vs backward)

The above tests examine significant differences between time periods (e.g., assigned vs. midroute) and then examined when these differences were or were not significant for forward vs. backward trials. In order to directly test if there were areas of the brain more active for one time period in one scenario than the other, I also compared forward and backward trials within just the assigned period and did the same forward and backward comparison for the midroute period. There were no suprathreshold clusters for the assigned period, and the midroute period did not exhibit any large cluster outside of the visual cortex for the backward trials, thus we found no significant trial directionality differences within a time period at the whole-brain level to report.

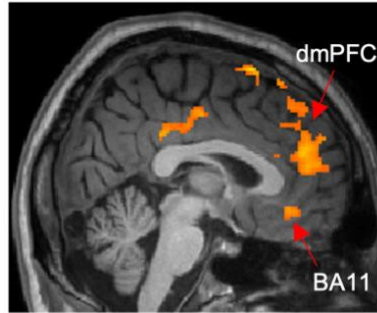
### 6.1.3 *Does a relationship exist between navigation strategy and extent of planning? Within-subjects approach*

The above tests examine differences in average engagement of my regions of interest for different navigation periods/scenarios. I then set out to examine how much engagement of these areas could capture when a participant's routes were actually "pre-planned" vs. solved "online". To do this, I conducted a parametric modulation analysis, by taking the Fréchet Distance value for each probe environment a participant navigated and fitting it as a modulator to the planning period activity. There was no neural activity that met our significance and cluster thresholds, indicating

that any trial-by-trial underlying relationship between planning period activity and strategy preference/performance across probe runs was not strong enough for us to detect in this design.

#### *6.1.4 Does a relationship exist between navigation strategy and extent of planning? Between-subjects approach*

Paralleling the above trial-wise analysis, I also wanted to test whether planning period activity in my ROIs was different for those who were more “shortcut-y” vs. “familiar route-y” in their behavior. I ran a between-subjects analysis for the assigned compared to midroute period for both forward and backward trials by taking the participant’s average shortcut FD values for each probe type. For the forward shortcut trials, I found no activity signifying positive or negative relationships that met our significance and cluster thresholds. However, for the backward trials, there were several regions where the planning period activity was positively associated (greater activity predicted higher FDs) with differences in navigational efficiency. There were several suprathreshold clusters peaking at SFG/MFG and extending medially into the left dorsal medial prefrontal cortex (dmPFC), as well as clusters in the left fusiform gyrus, and a significant cluster that included BA 11 [(10, 38, -10),  $k=90$ ,  $t=5.43$ ,  $p=.001$ ]. There were no instances for the backward trials where planning activity was negatively associated (greater activity predicted smaller FDs), suggesting this activity is really about “effort” or perhaps greater decision-making rather than predicting more efficient navigation.



Assigned > Midroute  
Backward

**Figure 10 | Assigned – Midroute activity correlated with Fréchet Distance**

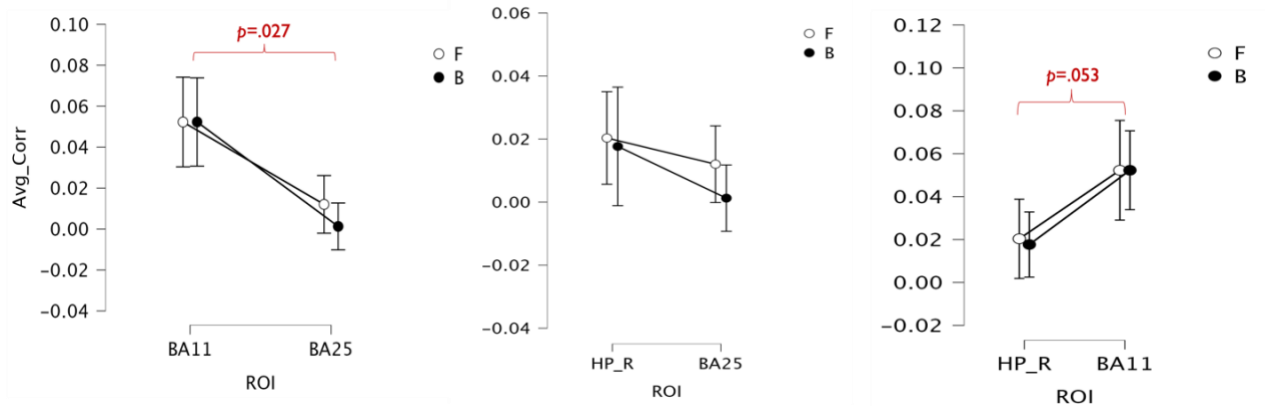
## 6.2 Multivariate fMRI Approach

6.2.1 *Do representations (as opposed to activity levels) in the hippocampus and mPFC discriminate between forward and backward trials?*

### 6.2.1.1 Assigned – Assigned

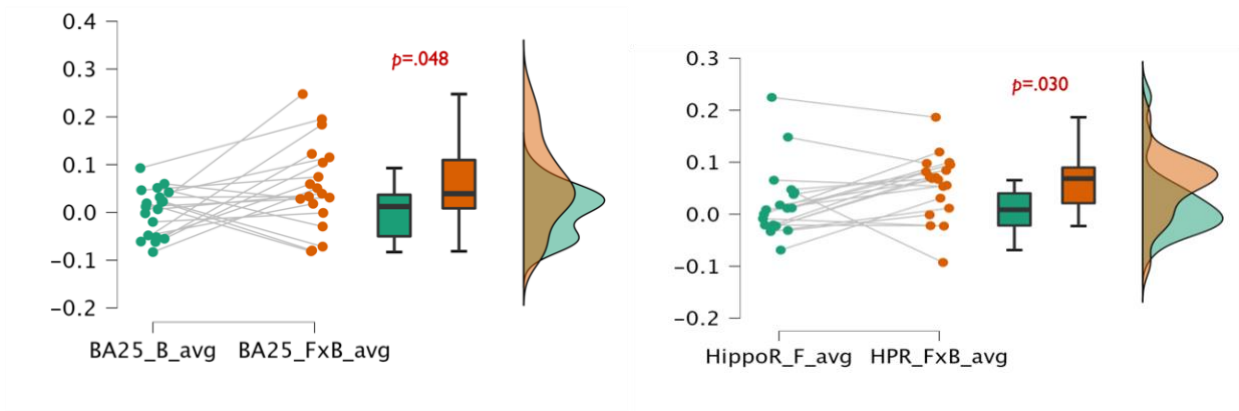
Representational similarity analysis (RSA) allowed me to compare across-town similarity of forward and backward trials (i.e., how similar are the representations of different towns to each other). First, I conducted a 2 (ROI: BA11, BA25) x 2 (Directionality: forward, backward) repeated measures ANOVA to compare coding similarity between mPFC regions for the different probe routes. There was a significant main effect for ROI ( $F=5.80, p=.027$ ) showing BA11 had higher similarity (during planning) for forward and backward trials, but no main effect of directionality ( $F=.11, p=.740$ ) or interaction effect ( $F=.09, p=.774$ ) were found. I ran the same ANOVA comparing the right hippocampus and BA25 and found no main effect of ROI ( $F=.60, p=.448$ ), directionality ( $F=.16, p=.691$ ), or an interaction effect ( $F=.18, p=.673$ ). However, I did find a marginally significant effect of ROI when comparing the right hippocampus to BA11 ( $F=4.31,$

$p=.053$ ) – showing BA11 had higher similarity across towns – but no main effect of directionality ( $F=.004, p=.951$ ) nor an interaction effect ( $F=.005, p=.946$ ).



**Figure 11 | Across-town similarity during the planning period**

The above tests compared coding similarity across towns for different regions and forward vs. backward trials. Critically, I also examined if any of my ROIs exhibited environment-specific coding (which would be seen with higher RSA values between trials involving the same town than between trials involving different towns). Paired samples t-tests unpacking differences for forward and backward trials between towns vs. within a town showed that BA25 had significantly higher similarity within the environment than between environments for the backward trials ( $t=-2.12, p=.048$ ) and marginally significant similarity for forward trials ( $t=-1.80, p=.088$ ), suggesting this area expresses a representation of the specific town a person is in, and does so (qualitatively) more on the demanding backward trials. Similar to BA25, the right hippocampus also exhibited environment-specific coding, however, this was qualitatively more evident for forward trials ( $t=-2.36, p=.030$ ) vs. marginally significant for backward trials ( $t=-1.94, p=.069$ ). BA11 and the left hippocampus did not show significant discrimination between forward/backward, nor between/within towns (i.e., no evidence of environment-specific coding) during the planning period.



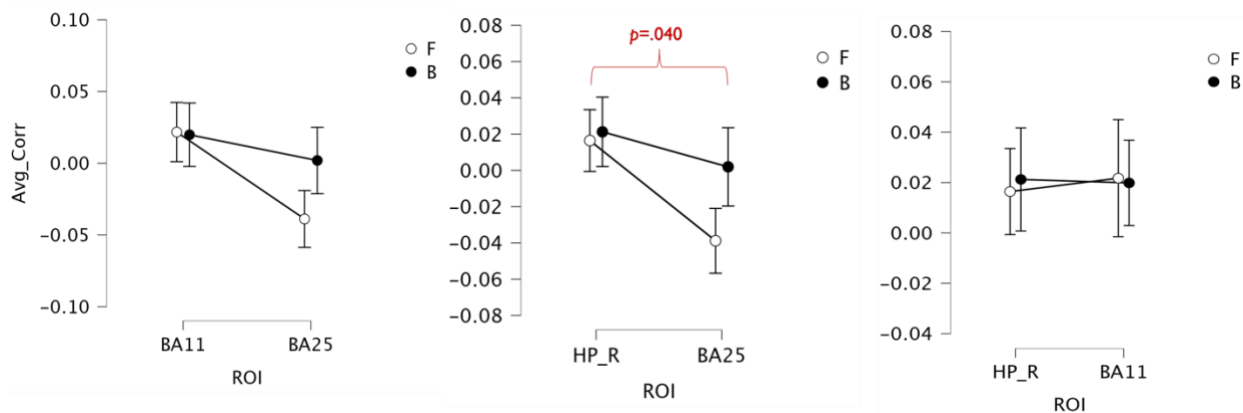
**Figure 12 | Evidence of town-specific coding during the planning period**

### 6.2.1.2 Midroute – Midroute

I ran the same repeated measures ANOVAs looking at ROI and directionality for the midroute period of navigation (for forward and backward trials), once again comparing the two mPFC regions to each other and in relation to the right hippocampus. For BA25 vs. BA11, there was no main effect for ROI ( $F=1.40, p=.252$ ), no main effect of directionality ( $F=.10, p=.760$ ), an no interaction effect ( $F=2.05, p=.170$ ). When comparing the right hippocampus and BA25, we again found no main effects for ROI ( $F=.16, p=.669$ ), directionality ( $F=.25, p=.626$ ) nor an interaction effect ( $F=1.18, p=.291$ ). Comparing the right hippocampus to BA11 also resulted in null findings for the midroute period: ROI ( $F=1.09, p=.310$ ), directionality ( $F=2.81, p=.111$ ), interaction effect ( $F=.027, p=.872$ ). These null results suggest there is no one region (from our ROIs) that codes more or less for across-town similarity of forward and backward trials. When examining if any of my ROIs exhibited environment-specific coding during the midroute period of navigation, paired samples t-tests revealed no significant evidence for discrimination of trial types between or within a town.

### 6.2.1.3 Assigned – Midroute

Lastly, we wanted to compare if midroute representations were similar to those from the planning period for the same trial type (forward or backward) within a town. Once again we ran a 2x2 repeated measures ANOVA for ROI and directionality, only this time the interpretations were applied to similarity between the different stages of navigation (planning vs. midroute). Comparing the mPFC regions to each other resulted in no main effects for ROI ( $F=3.10, p=.095$ ) or directionality ( $F=1.05, p=.320$ ), and no interaction effect ( $F=.87, p=.363$ ). When comparing BA25 to the right hippocampus, there was a significant main effect for ROI ( $F=4.88, p=.040$ ), suggesting BA25 discriminates representations from the planning period to those of the midroute period more than the right hippocampus, but we saw no main effect for directionality ( $F=1.24, p=.281$ ) nor an interaction ( $F=.86, p=.366$ ). The right hippocampus vs. BA11 showed null effects across the board: ROI ( $F=.01, p=.919$ ), directionality ( $F=.01, p=.947$ ), interaction effect ( $F=.04, p=.853$ ).

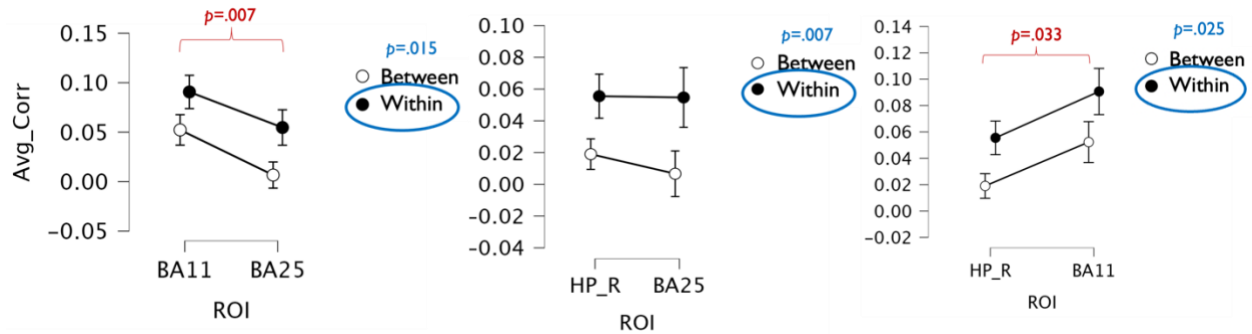


**Figure 13 | Similarity of representations between planning and midroute navigation**

## 6.2.2 *Is there a schema/identity representation for environments?*

### 6.2.2.1 Assigned – Assigned

The above tests showed that, on average, representations within and between towns did not differ for forward vs. backward trials. However, there was some evidence of environment-level coding. To explore this more directly, I computed the average of forward and backward between-town RSA values to create a combined result for each town (not tailored to route directionality) and compared this new between-town RSA value to that of the within-town. I first ran a 2 (ROI: BA11, BA25) x 2 (Identity: between-town, within-town) repeated measures ANOVA comparing both mPFC regions and found a significant main effect for ROI ( $F=9.30$ ,  $p=.007$ ) as well as for identity ( $F=7.23$ ,  $p=.015$ ), but no interaction effect ( $F=.073$ ,  $p=.790$ ). A paired samples t-test revealed that BA25 had a marginally significantly higher similarity within-town than between-towns ( $t=-2.02$ ,  $p=.058$ ). Comparing the right hippocampus to BA25 resulted in a main effect for identity ( $F=9.19$ ,  $p=.007$ ), but no main effect for ROI ( $F=.16$ ,  $p=.696$ ) and no interaction effect ( $F=.20$ ,  $p=.657$ ); a paired samples t-test revealed that, in general, there was higher similarity for within-town representations than between-towns across both regions. An analysis of BA11 vs. right hippocampus showed significant main effects for both ROI ( $F=5.30$ ,  $p=.033$ ) and identity ( $F=5.98$ ,  $p=.025$ ), and no interaction effect ( $F=.006$ ,  $p=.939$ ). Further analysis revealed that the right hippocampus exhibited significantly stronger within-town similarity ( $t=-2.96$ ,  $p=.008$ ). Together, these findings serve as evidence that both the right hippocampus and BA25 can discriminate what town a person is in on a given trial.



**Figure 14 | Evidence of environment identity representations during the planning period**

### 6.2.2.2 Midroute – Midroute

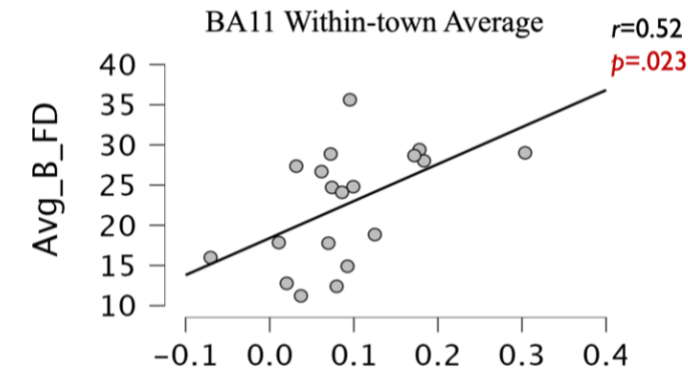
The above ANOVAs were also computed for the midroute period of the task. Comparing BA11 vs. BA25 showed no main effects for ROI ( $F=1.92, p=.182$ ) or identity ( $F=3.25, p=.088$ ), and no interaction effect ( $F=.16, p=.691$ ). Comparing the right hippocampus to BA25 also resulted in null effects for ROI ( $F=.19, p=.665$ ), identity ( $F=.59, p=.454$ ), and the interaction ( $F=.68, p=.419$ ). Results for BA11 vs. right hippocampus showed a marginally significant main effect for ROI ( $F=4.01, p=.061$ ), no main effect for identity ( $F=1.69, p=.210$ ), and no interaction effect ( $F=1.40, p=.252$ ).

### 6.2.3 *Does how strongly an environment identity is represented predict an individual's performance?*

#### 6.2.3.1 Assigned – Assigned

I correlated average Fréchet Distance for the shortcut trials with the strength of town representations in my ROIs (within-town RSA scores) and found that specifically for backward probe trials there was a significant positive correlation ( $r=0.52, p=.023$ ) between FD and BA11 within-town similarity scores – the higher the within-town similarity in BA11 during the planning period, the higher the FD was during backtracking probe trials (i.e., people who did not follow the

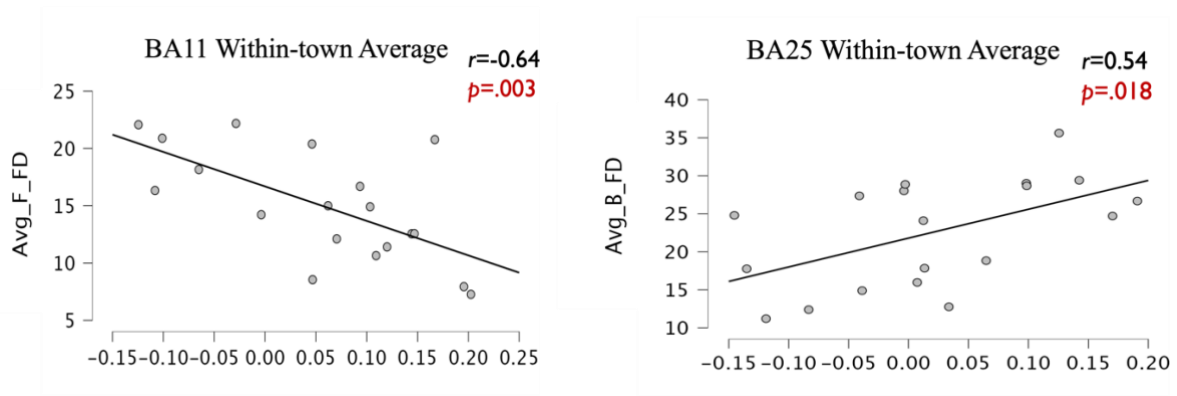
shortcut as much brought stronger representations of the environment to mind in vmPFC during planning). See Appendix F for the complete correlation matrices.



**Figure 15 | Within-town similarity during planning correlated with Fréchet Distance**

#### 6.2.3.2 Midroute – Midroute

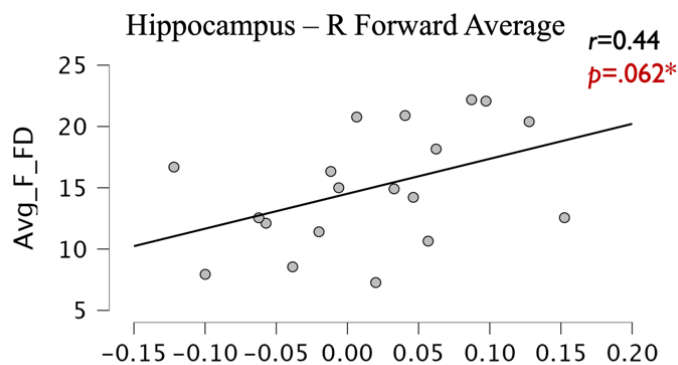
Interestingly, this relationship was flipped during active navigation, for forward trials. During the mid-route period, BA11 was negatively correlated with the average forward FD ( $r=-0.64$ ,  $p=.003$ ) – the higher the within-town similarity in BA11 during the midroute period, the lower the FD was during forward shortcut trials (i.e., people with a stronger environment representation in vmPFC while navigating had more precise shortcutting). We also found a significant opposing pattern in our other medial prefrontal ROI: a positive correlation with BA25 and average backward FD ( $r=0.54$ ,  $p=.018$ ) – the higher the within-town similarity in BA25 during the midroute period, the higher the FD was during backward shortcut trials. See Appendix F for the complete correlation matrices.



**Figure 16 | Within-town similarity during midroute navigation correlated with Fréchet Distance**

### 6.2.3.3 Assigned – Midroute

To address whether changes in how strongly an environment was represented from planning to navigation was related to performance, I also tested if assigned-midroute similarity correlated with FDs. Results showed that the right hippocampus for forward trials was marginally positively correlated with the average forward shortcut FD ( $r=0.44$ ,  $p=.062$ ) – the higher the forward trial similarity between the planning and midroute periods in the right hippocampus, the higher the FD was for forward shortcut trials. See Appendix F for the complete correlation matrices.



**Figure 17 | Within-town similarity between planning and midroute navigation correlated with Fréchet Distance**

## CHAPTER 7. DISCUSSION

By examining the behavioral outcomes and neural mechanisms involved in different stages of navigation, we can tackle debate in the field on how the hippocampus and the mPFC work together – potentially balancing episodic and schematic memories rather than treating memories in the same way. The experimental task tested was designed much like a real-world navigation scenario, where we come across a copious amount of information and have a lot of flexibility in how we use our memories to both plan and process that information online while actively navigating. My data tackled two major regions identified in many navigation studies (hippocampus and mPFC), and which are centered at debate over whether they compete and/or contribute to more episode-specific vs. schema-like knowledge, and tested ideas of how they contribute to navigation in different ways. Knowing what brain regions play a role and *when* over the course of navigation, is valuable in understanding the neural processes behind prospective planning, mid route planning, and goal representations. Moreover, this is a chance to test how schemas (operationalized as map-like knowledge) may play an important role in one’s memory performance and strategy use in the context of spatial navigation.

We know from previous literature that there is evidence of hippocampal dependency during prospective planning (Brown et al., 2016; van Kesteren, Brown, & Wagner, 2018; Brown, Gagnon, & Wagner, 2020; He, Starnes, & Brown, 2022). We also know there is increased prefrontal activity when thinking about semantically related events (van Kesteren et al., 2012), which is also critical to many attempts at planning. The hippocampus and vmPFC are intimately anatomically connected (Barbas & Blatt, 1995), but schema models like SLIMM (van Kesteren et al., 2012) and rodent data focused on the hippocampus (McKenzie et al., 2013; McKenzie et al., 2014) are not aligned

on how these two areas contribute to navigational memory. How the schema-driven memory findings for mPFC apply to spatial navigation, and how the hippocampus and mPFC work together to facilitate different stages of navigation is therefore still an open question and a major focus of this thesis.

My experiment set out to answer several questions regarding the neural mechanisms involved in the binding of distinct navigational events and the mechanisms at play in how we utilize complex cognitive maps of our environment. In the grand scheme of things – no pun intended – my work aimed to understand 1) how the hippocampus and mPFC contribute to navigation and 2) whether these patterns of neural activity differ across regions in situations where behaviors more closely align with or differ from prior experience. To address these questions, I conducted a mix of univariate and multivariate analyses including whole-brain and ROI-extracted activity contrasts, within and between-subjects parametric modulations, and representational similarity analyses to get at the degree to which environment identities are represented and perhaps related across trials.

## **7.1 Breaking Down the Findings**

I first wanted to know what regions were active across the various stages/periods of the navigational task. I predicted greater planning period activity than midroute activity in the hippocampus given this region's involvement in prospective "simulation" and retrieval of prior spatial knowledge to plan novel behaviors (van Kesteren, Brown, & Wagner, 2018). I also hypothesized that someone who might not have pre-planned their route in the environment might have more midroute activity, particularly in mPFC, given the greater demands for online decision-making and continually relating oneself to cues familiar from prior experiences (trying to localize

oneself in their environment “schema”). The midroute period did not display greater activity (aside from the visual cortex) when compared to planning. However an ROI analysis indeed showed greater left and right hippocampal activity, as well as BA25 activity during planning. BA11 was not found to be more active during planning than midroute, though it is likely this null result reflected equal engagement during both periods of navigation (as opposed to neurons in this area being inactive for either stage). All four ROIs were significantly more active for the goal arrival period than for planning, suggesting that both the hippocampus and mPFC regions are important for attending to the goal. In cases where they had taken a novel shortcut (optimal or not) to that novel goal, this could also reflect hippocampal learning mechanisms and the mPFC accessing one’s existing “schema” of the environment and the items (now novel goals) associated with each (e.g., a complementary role for both systems in updating their knowledge structure with new spatial relationships from that experience, such as in cases where there is some incongruence and some resonance with past knowledge in the SLIMM model [van Kesteren et al., 2012]).

Route directionality was not a primary focal point for my study, however it reflects another level of the degree to which experiences more closely align or deviate from prior experiences with the environment (i.e., some shortcuts are even more novel than others), and quickly became a dominant theme throughout the course of my analysis. I became curious as to whether hippocampus and mPFC activity shifted when completing a trial where the optimal route was either following in the forward direction of the familiar route, or having to backtrack. Consistent with the greater degree of novelty/deviation from prior training, ROI extractions showed that BA25 was the only region significantly more active during the planning period compared to midroute (for forward shortcut trials), while all regions except for BA11 were significantly more active for the planning period for backward trials. RSA analysis indicates that compared to BA25,

BA11 has significantly higher similarity for forward and backward trials during the planning period, implying this region is not sensitive to the directionality of the trial; this doesn't mean BA11 isn't coding for directionality at all, rather it could be coding for both in a similar way.

Turning to the comparison between planning and goal arrival stages, all ROIs except for BA25 appeared to be active for goal arrival compared to planning for both forward and backward probe trials. Comparing and contrasting with the planning-midroute results described above, an interesting shift was that BA11 was significantly more active than BA25 for the goal for both forward and backward shortcut trial types (whereas BA25 was identified more clearly as important for planning in terms of both activity contrasts with navigation and in terms of representing the identity of the environment one is planning to navigate).

I show that BA25 is generally more active during planning than midroute navigation, and the same was true when looking at just forward and just backward trials. Further RSA analysis shows that BA25 had higher similarity for forward and backward trials within each town than between environments, meaning this region holds some kind of representation of the town itself (while BA11 and left hippocampus did not). This was an important discovery from my work, because the brain needs such representations – they are useful to have when attempting to plan a route (and not confusing information needed to plan in one environment with that of another), and my data highlight BA25 as more active and representationally-important for planning from prior knowledge. The right hippocampus, which we know was active during planning (for backward trials) and goal arrival in general, also had environment-specific coding during planning for forward and backward trials. This potentially contradicts the competition view from models of schemas like SLIMM, suggesting that both the mPFC and hippocampus are necessary for bringing to mind information about, and discriminating between, towns.

One unique feature of my design was our Fréchet Distance measure, which turned out to be quite telling of a subjects navigation strategy preference and whether this depends more heavily on one brain region than another. I had postulated that if a participant planned a lot, they would have a subsequently low FD value (meaning they were closer to the optimal shortcut for the given probe), while little planning might lead to a higher FD value because they may end up wandering around the environment. Parametric modulations were unable to detect any significant differences that could speak to this postulation, but we did find evidence in general for differences in activity according to strategy.

I had predicted that novel route planning would be more hippocampal-dependent and planning a route drawing from prior experiences might elicit greater mPFC activity. Moreover, I hypothesized that the hippocampus would become less engaged *during* navigation because I would argue this indicates potential use of an existing schematic organization for the environment as opposed to retrieving a specific learned sequence from hippocampal-dependent memory in the case of a familiar route strategy. Forward shortcut trials did not exhibit any significant differences in activity across regions, but we did find evidence for significantly greater BA11 activity during the *planning* period for the backward trials correlated with higher FD values for these trials, suggesting that in fact this area was more engaged when people did not tend to take novel shortcuts. This finding could reflect 1) effort – that people are attempting to use their prior knowledge of the environment rather than simulating a novel route to the goal and 2) more complex relationships between mPFC subregions and FD (revealed by the RSA results which I discuss more below).

We know from the behavioral results that most participants follow the familiar route more closely for the backtracking trials. This is revealed by the complexity of having to not only take a novel shortcut, but have it follow a novel direction along the environment. It is possible that

BA11's lack of representational discriminability between forward and backward trials during planning may have impacted a participant's ability to plan a shortcut in this novel direction, thus encouraging them to fall back to following closer to the familiar route. My correlational analyses nicely supported this theory – because there exists a strong relationship between the backward trial FD and BA11. We also found BA11 to be negatively correlated with the average forward FD during the *midroute* period resulting in lower FD values for the forward shortcut trials. Thus, although BA11 did not show significant town-specific coding overall for the group, the between-subjects analyses revealed that the degree to which it had town-specific coding was a significant factor at various navigational stages for how often/effectively shortcuts were taken.

I had predicted that higher similarity in neural representations within a town would mean having a stronger schema-like structure for the environment, thus more dependent on the mPFC for taking more shortcuts. However, we found that the higher the within-town similarity in BA25 during the midroute period, the higher the FD was during backward shortcut trials. I speculate that when we combine forward and backward representations for a town into an overall identity, or “schema”, for an environment, we may lose out on the helpful discriminability of information associated with route directionality.

Finally, concerning our initial hippocampal predictions, we did find a relationship in the right hippocampus between higher FD values for forward shortcut trials and higher similarity between the planning and midroute stages of the task. This was interesting because this result means that when people have more similar representations in the hippocampus prior to and during navigation, this is associated with subjects taking less optimal shortcut routes. It could be the case that since higher FDs are more aligned with navigating based on past experience rather than taking novel routes, this could mean a) it's easier for people to retrieve the whole route during planning

(since they aren't simulating or making it up), thus what is represented in hippocampal memory during planning is quite similar to what is represented when actually experiencing the route. Or b) maybe its "effort" again – if people have poor map memory they are more likely to take a familiar route, and if they have poor memory they are more likely to be planning “online”, making decisions from start to finish.

## 7.2 Future Analyses

One particularly important analysis for understanding item representations contained in the environment (which make up part of the environment’s identity) would be to train an MVPA algorithm through the use of a localizer task, to decode brain activity associated with different environment items from the regions where they are represented in the cortex. This may allow us to quantify whether the participant thinks about the goal during the *planning* period, or another landmark item *en route* to a goal (e.g., an orange along the shortcut vs. a brown bear along the familiar route). By looking for goal representations during planning, we may be able to determine how prominent a participant’s item associations are, and perhaps which item is most influential in helping bring the environment’s *identity* (in multiple sense of the word) to mind (e.g., high fusiform face area [FFA] activity would indicate more ‘Face’ item representation). This analysis would allow us to quantify whether a planning event might be more aligned, in neural terms, to information from the familiar route or to information along a novel shortcut (since some item types are always positioned along one of these options vs. the other). This could be related to data such as my assigned-midroute representational similarity results presented in this Thesis, and with this, we could test whether more MVPA evidence for one route vs. the other on a given trial is associated with relatively more mPFC or more hippocampal activity in that planning event.

Likewise, asking how something as simple as object memory impacts one's ability to navigate complex environments is important because it can reveal the significance that a specific landmark can have on one's mental visualization of the space. Our behavioral results from the item test during the training day of the experiment explicitly show that participants think about the face item first, often times associating the town to a specific person. With that in mind, future experiments should test the benefits and costs of assigning so much weight to a landmark and how this might impact performance and neural dependency if that landmark were to no longer exist in the environment (e.g., helping us generalize, yet harming episodic specificity for spatial memories). Asking such questions is important for understanding the fundamental science of how we build relational knowledge about our lives from smaller pieces.

It is important to note that the present experiment was not designed with the purpose of challenging the debate of whether we form and utilize cognitive maps or graphs, rather I wanted to focus on understanding how a navigator is able to infer new relationships when navigating novel environments based on prior knowledge of experiences – thus the use of the term “schema”. Future versions of this research could implement design choices stemming directly from the cognitive map and cognitive graph literatures to more directly address whether we utilize one or the other when planning novel or familiar routes along an environment.

### **7.3 Conclusion**

Theories of schema functions in the brain based primarily on human, non-spatial studies present some conflict with animal spatial memory study operationalization of “schemas”. In particular, they raise debate on whether the mPFC and hippocampus respond to and process relational memories in similar or competing ways. Here, I find data that support the fact that both

the hippocampus and medial prefrontal cortex are important for successful navigation. What is key in understanding potentially unique functional differences between the two was examining each region at various stages of navigation. In particular, planning is something that we can *choose* to do if we have enough knowledge to guide our prospective thought. It can encompass planning to follow a familiar route (e.g., to work one morning), but we can also use that knowledge to plan a novel route (stopping by the pharmacy on the way to work). However sometimes we're required to or might opt to plan a novel route "online" while navigating (realizing we've never driven to work from the pharmacy) and as we "wayfind" in this way, the route might become increasingly complex – as we either apply our spatial knowledge at a given step to take a shortcut from the current location, or at other times fall back on what we know and head towards a familiar landmark or route that will eventually get us to work on time. Because of this, routes may often reflect a continuum between a purely habitual route or an optimal route, and examining each stage of the navigation process is important for understanding how brain regions such as mPFC and hippocampus represent or predict route novelty, directionality, and overall complexity.

Furthermore, understanding the neural bases of individual differences such as innate navigation preferences is key for breaking down the differences between hippocampal and mPFC-dependent navigation. Some individuals are naturally more allocentric navigators, placing more weight on place-based strategies compared to a more egocentric and response-based approaches to routes. We know from years of research that young adults are traditionally more allocentric navigators compared to older adults. But even then they vary, and may vary in different situations (I show, for example, in forward vs. backtracking oriented shortcuts). Understanding such individual differences between navigators may provide greater insight to how our reliance on certain brain regions wanes over the course of a route. My experiment is therefore part of a

necessary series of experiments that must be done in order to understand these differences. I find

- 1) functional differences in BA25 and BA11 subdivisions of the mPFC which have previously both been tied to schemas and navigation, with the two sometimes agreeing but other times responding different to, e.g., planning vs. goal arrival, and differing in how they explain individual differences in navigation behavior.
- 2) Broad agreement between when and how the hippocampus (right hemisphere in particular) and mPFC (BA25 in particular) are engaged for task stages, represent environments, and track participant differences – a finding which aligns well with their anatomical interconnections, but may contradict the competitive view from models of schema memory like SLIMM.

It is my hope that findings from the present study can be generalized beyond the young adult population. We know from prior research that aging and neurocognitive disorders such as dementias have significant effects on hippocampal and prefrontal circuitry (for review see Jobson et al., 2021). We must test if the balance between episodic and schema-like memories observed in our study become altered in older adult groups, especially when knowing that aging leads to degraded cognitive map precision, decreased flexibility interacting with spatial memory, and potentially higher loss of spatial configural detail compared to landmark content of a schema (Lester et al., 2017). Building on the foundations from prior and current literature, we need to continue to examine the fMRI correlates in the frontal and MTL circuitry in order to expand our understanding of how individuals shift between familiar route retrieval, novel route planning and exploration, and how these abilities might be impacted as we age.

## APPENDIX A

### MAP Lab Information Form

Name: \_\_\_\_\_ Participant ID: \_\_\_\_\_

E-mail address: \_\_\_\_\_ Phone number: \_\_\_\_\_

Years of Education: \_\_\_\_\_ Age: \_\_\_\_\_ Sex: \_\_\_\_\_ Handedness: \_\_\_\_\_

**Race (check all that apply):**

American Indian/Alaskan       Asian       Pacific Islander

Black/African American       White       Hispanic/Latino

**Is English your first language?**       Yes       No

If no, at what age did you start learning it? \_\_\_\_\_

**Are you Bilingual?**       Yes       No

**Do you have normal (or corrected to normal) vision?**       Yes       No

**If you are participating in an fMRI or EEG study, would you be able to wear contacts for the experiment?**       Yes       No

**Are you colorblind?**       Yes       No

**Do you have normal (or corrected to normal) hearing?**       Yes       No

**How would you rate your general health?**

Poor  Fair  Good  Excellent

1. Are you currently taking any medications or any illegal drugs?  Yes  No

---

2. Do you have a pacemaker, vagus nerve stimulator, or other electrical implant?

Yes  No

3. Do you have a history of head trauma?  Yes  No

4. Have you ever had a seizure?  Yes  No

5. Do you have any speech, sensory, or motor impairments or a learning disability?

Yes  No

6. Have you ever been diagnosed with a psychiatric illness, or seen anyone for emotional or psychiatric problems?  Yes  No

7. Have you ever been on any anti-depressant, neuroleptic, or sedative medications?

Yes  No

Are you currently taking?  Yes  No

8. Have you ever used illegal drugs in the past?  Yes  No

9. Do you have a history of cardiac or other general health-related problems?

Yes  No

**Please respond to the following specific health conditions – write N/A if a condition is not applicable**

- Respiratory Problems?  
+ Medications? \_\_\_\_\_
- Heart Disease?  
+ Medications? \_\_\_\_\_
- High Blood Pressure?  
+ Medications? \_\_\_\_\_
- Low Blood Pressure or Anemia?  
+ Medications? \_\_\_\_\_
- Diabetes?  
+ Medications? \_\_\_\_\_
- Sickle Cell Anemia?  
+ Medications? \_\_\_\_\_
- Parkinson’s/Alzheimer’s?  
+ Medications? \_\_\_\_\_
- Stroke?  
+ Medications? \_\_\_\_\_
- ADD/ADHD?  
+ Medications? \_\_\_\_\_
- Multiple Sclerosis?  
+ Medications? \_\_\_\_\_
- Arthritis (problems with hands or back)?  
+ Medications? \_\_\_\_\_
- Other health problems we haven’t mentioned?  
\_\_\_\_\_

Are you currently ill?      \_\_\_\_\_ Yes                      \_\_\_\_\_ No

**Do you / could you have:**

Rhinovirus / “cold”	_____ Yes	_____ No
Influenza virus	_____ Yes	_____ No
Epstein-Barr virus / “mono”	_____ Yes	_____ No
Type 1 herpes	_____ Yes	_____ No
Strep bacteria	_____ Yes	_____ No
Hepatitis B or hepatitis C	_____ Yes	_____ No
HIV	_____ Yes	_____ No

## APPENDIX B

### MAP Lab Supplemental Demographics

#### DAY 1

Participant ID: \_\_\_\_\_

How many hours of sleep did you get last night? \_\_\_\_\_

Was this sleep restful (circle one)?      **Yes**   -   **No**

Was this sleep different than normal (circle one)?      **More**   -   **Less**

What time did you wake up this morning? \_\_\_\_\_

#### DAY 2

How many hours of sleep did you get last night? \_\_\_\_\_

Was this sleep restful (circle one)?      **Yes**   -   **No**

Was this sleep different than normal (circle one)?      **More**   -   **Less**

What time did you wake up this morning? \_\_\_\_\_

Did you think about the task when you weren't performing the task with us in the lab?

**Yes**   -   **No**

- If yes, how frequently?

\_\_\_\_\_

- In what detail (briefly describe what you thought about or remembered)?

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

# APPENDIX C

## Y-Maze Task

(Rodgers, Sindone, & Moffat, 2012)

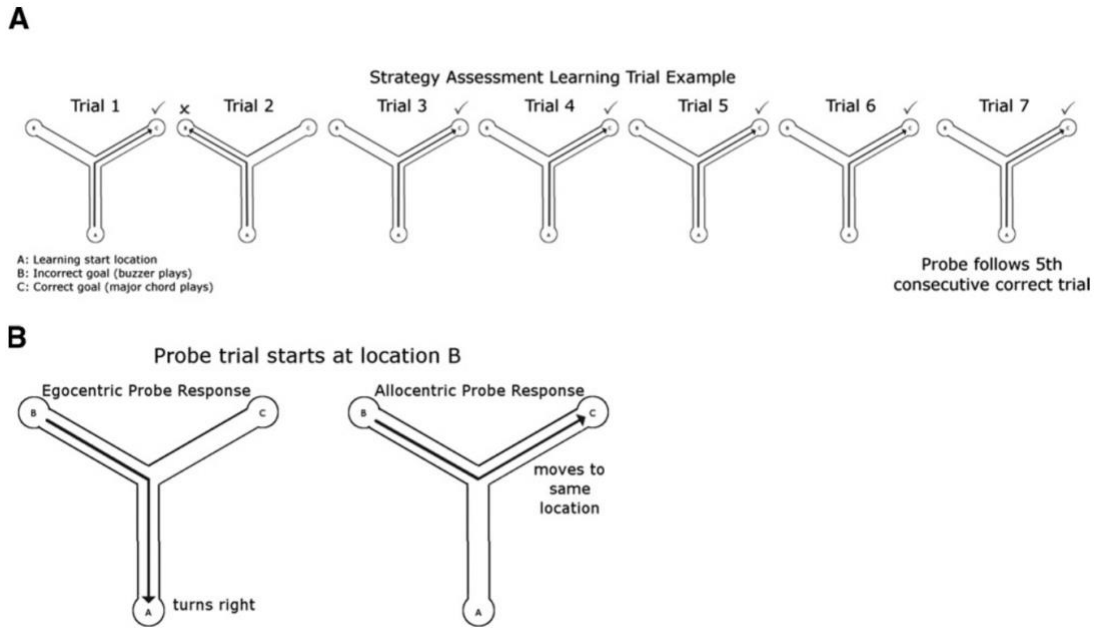
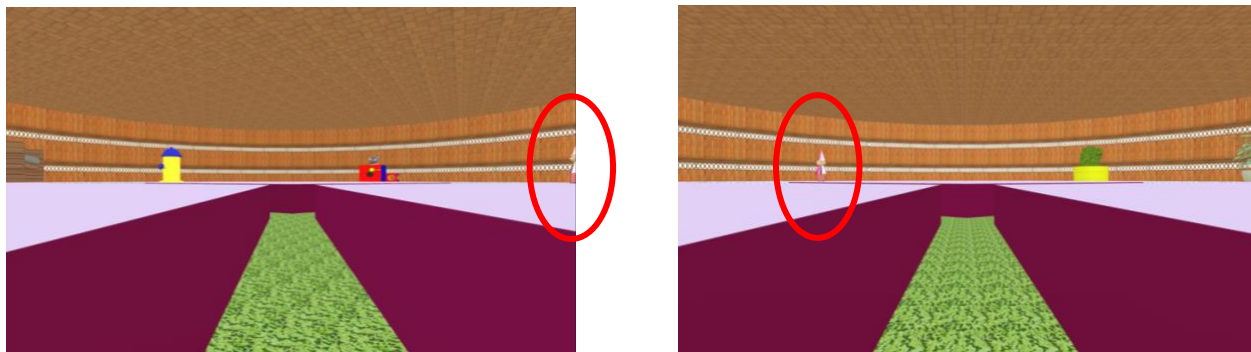


Figure 18 | The Y-Maze task



Sample environment designed by Qiliang He, Ph.D. in the Memory Affect and Planning Lab.  
See task instructions on the next page.

Figure 19 | Sample Y-Maze environment

## **Instructions:**

You will be placed in a 3D environment where your task is to use the arrow keys to move through a corridor and make a choice where to end.

*Keep moving down a hallway until you hear a sound...*

- When you choose correctly, you will hear a guitar chord.
- When you choose incorrectly, you will hear an alarm buzzer.

When you reach the end you will automatically be teleported back to where you started, and the maze will restart.

You will repeat the same environment 5 - 6 times. There will be 5 environments total.

When you complete all of the trials for one environment, the next environment will immediately begin.

# APPENDIX D

## Environment Items + Lures

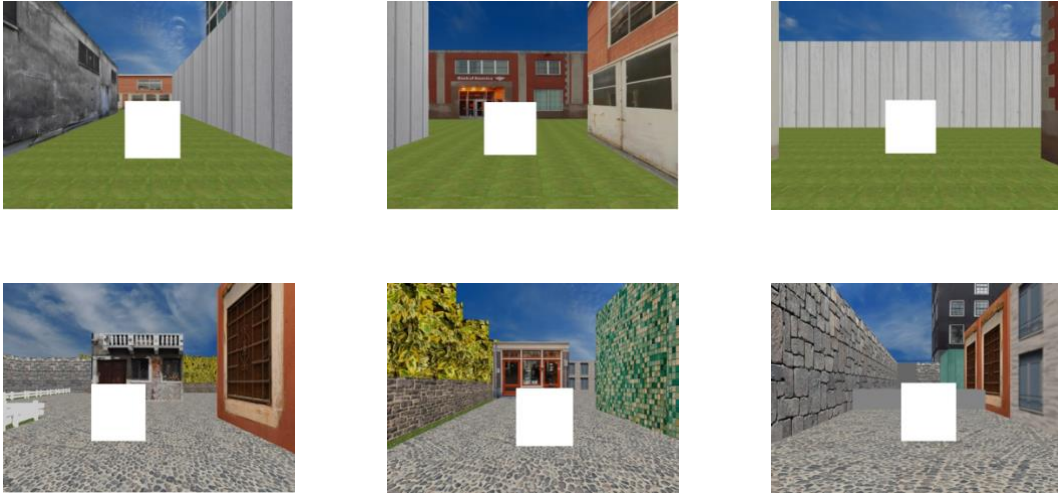


Figure 20 | Sample item test prompts

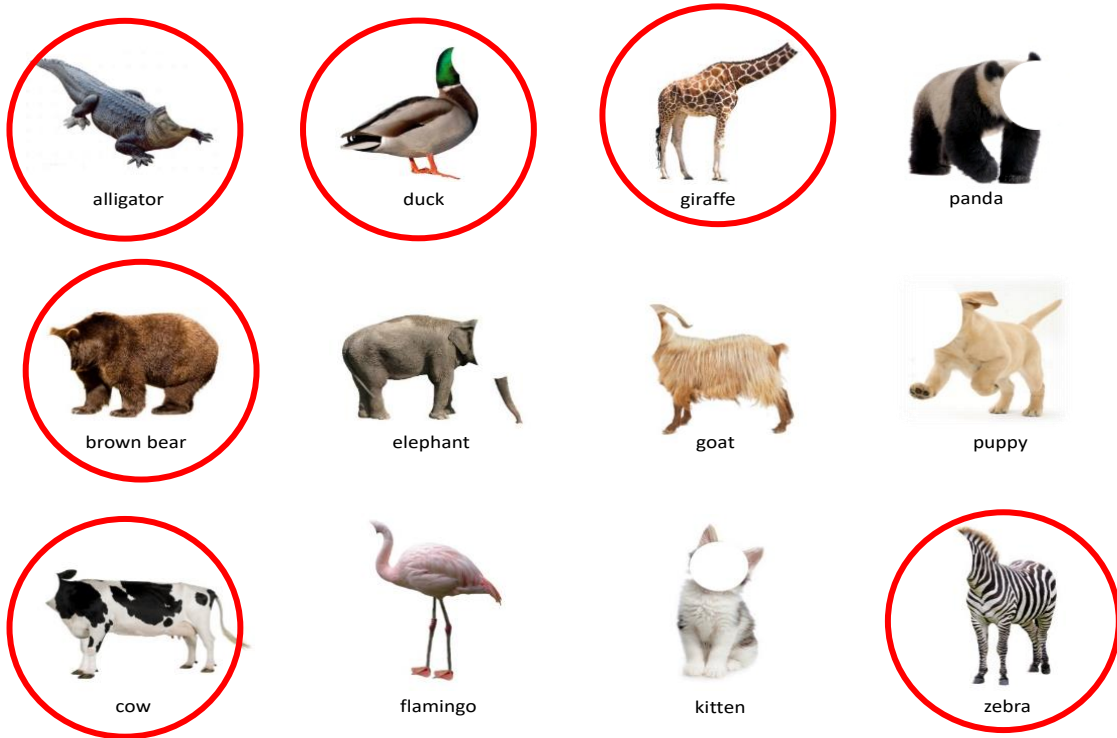


Figure 21 | "Animal" target items (circled in RED) and lures

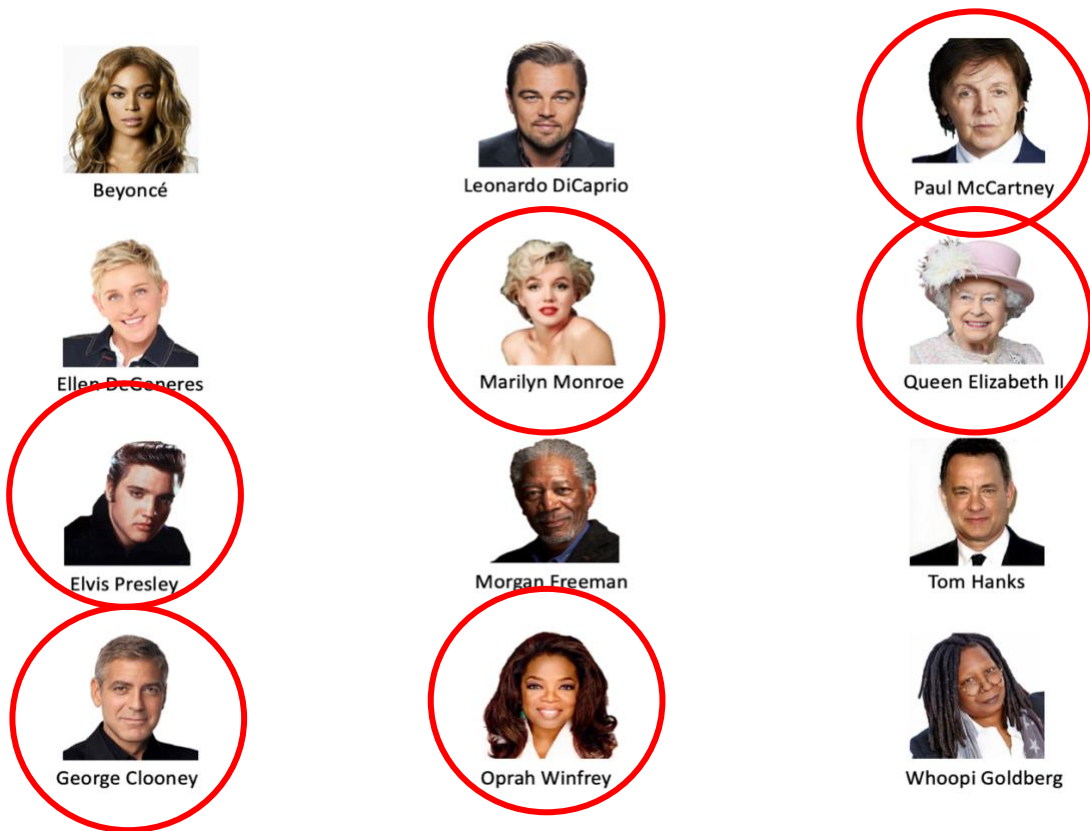


Figure 22 | "Face" target items (circled in **RED**) and lures



Figure 23 | "Other" target items (circled in RED) and lures

## APPENDIX E

### Questionnaire on Spatial Representation (QSR)

*(Pazzaglia et al., 2000)*

1. Do you think you have a good sense of direction?

1 (not at all) 2 3 4 5 (very good)

2. Are you considered by your family or friends to have a good sense of direction?

1 (not at all) 2 3 4 5 (very much)

3. Think about the way you orient yourself in different environments around you. Would you describe yourself as a person:

a. who orients him/herself by remembering routes connecting one place to another?

1 (not at all) 2 3 4 5 (very much)

b. who orients him/herself by looking for well-known landmarks?

1 (not at all) 2 3 4 5 (very much)

c. who tries to create a mental map of the environment?

1 (not at all) 2 3 4 5 (very much)

4. Think of an unfamiliar city. Write the name . . . . . Now try to classify your representation of the city:

a. survey representation, that is a map-like representation

1 (not at all) 2 3 4 5 (very much)

b. route representation, based on memorising routes

1 (not at all) 2 3 4 5 (very much)

c. landmark-centred representation, based on memorising single salient landmarks (such as monuments, buildings, crossroads, etc.)

1 (not at all) 2 3 4 5 (very much)

5. When you are in a natural, open environment (mountains, seaside, country) do you naturally individuate cardinal points, that is where north, south, east, and west are?

1 (not at all) 2 3 4 5 (very much)

6. When you are in your city do you naturally individuate cardinal points, that is do you find easily where north, south, east, and west are?

1 (not at all) 2 3 4 5 (very much)

7. Someone is describing for you the route to reach an unfamiliar place. Do you prefer:

a. to make an image of the route?

1 (not at all) 2 3 4 5 (very much)

b. to remember the description verbally?

1 (not at all) 2 3 4 5 (very much)

8. In a complex building (store, museum) do you think spontaneously and easily about your direction in relation to the general structure of the building and the external environment?

1 (not at all) 2 3 4 5 (very much)

9. When you are inside a building can you easily visualize what there is outside the building in the direction you are looking?

1 (not at all) 2 3 4 5 (very much)

10. When you are in an open space and you are required to indicate a compass direction (north-south-east-west), do you:

a. point immediately?

b. need to think before pointing?

c. have difficulty?

11. You are in a complex building (many doors, stairs, corridors) and you have to indicate where the entrance is, do you:

a. point immediately?

b. need to think before pointing?

c. have difficulty?

## APPENDIX F

### Pearson's Correlations Computed in JASP

**Table 2 | Assigned – Assigned: Forward FD & Within-town RSA**

Variable		Avg_F_FD	BA11_FxB_avg	BA25_FxB_avg	HPL_FxB_avg	HPR_FxB_avg
1. Avg_F_FD	Pearson's r	—				
	p-value	—				
2. BA11_FxB_avg	Pearson's r	-0.276	—			
	p-value	0.253	—			
3. BA25_FxB_avg	Pearson's r	0.347	0.170	—		
	p-value	0.145	0.487	—		
4. HPL_FxB_avg	Pearson's r	0.280	-0.244	0.408	—	
	p-value	0.246	0.314	0.083	—	
5. HPR_FxB_avg	Pearson's r	0.260	0.132	0.027	0.192	—
	p-value	0.283	0.589	0.913	0.432	—

**Table 3 | Assigned – Assigned: Backward FD & Within-town RSA**

Variable		Avg_B_FD	BA11_FxB_avg	BA25_FxB_avg	HPL_FxB_avg	HPR_FxB_avg
1. Avg_B_FD	Pearson's r	—				
	p-value	—				
2. BA11_FxB_avg	Pearson's r	0.519	—			
	p-value	0.023	—			
3. BA25_FxB_avg	Pearson's r	-0.092	0.170	—		
	p-value	0.709	0.487	—		
4. HPL_FxB_avg	Pearson's r	-0.180	-0.244	0.408	—	
	p-value	0.460	0.314	0.083	—	
5. HPR_FxB_avg	Pearson's r	-0.035	0.132	0.027	0.192	—
	p-value	0.888	0.589	0.913	0.432	—

**Table 4 | Midroute – Midroute: Forward FD & Within-town RSA**

Variable		Avg_F_FD	BA11_FxB_avg	BA25_FxB_avg	HPL_FxB_avg	HPR_FxB_avg
1. Avg_F_FD	Pearson's r	—				
	p-value	—				
2. BA11_FxB_avg	Pearson's r	-0.642	—			
	p-value	0.003	—			
3. BA25_FxB_avg	Pearson's r	0.084	-0.328	—		
	p-value	0.734	0.170	—		
4. HPL_FxB_avg	Pearson's r	0.188	-0.075	0.130	—	
	p-value	0.441	0.762	0.596	—	
5. HPR_FxB_avg	Pearson's r	0.293	-0.331	-0.292	0.036	—
	p-value	0.223	0.166	0.226	0.883	—

**Table 5 | Midroute – Midroute: Backward FD & Within-town RSA**

Variable		Avg_B_FD	BA11_FxB_avg	BA25_FxB_avg	HPL_FxB_avg	HPR_FxB_avg
1. Avg_B_FD	Pearson's r	—				
	p-value	—				
2. BA11_FxB_avg	Pearson's r	-0.230	—			
	p-value	0.343	—			
3. BA25_FxB_avg	Pearson's r	0.538	-0.328	—		
	p-value	0.018	0.170	—		
4. HPL_FxB_avg	Pearson's r	-0.111	-0.075	0.130	—	
	p-value	0.651	0.762	0.596	—	
5. HPR_FxB_avg	Pearson's r	-0.099	-0.331	-0.292	0.036	—
	p-value	0.686	0.166	0.226	0.883	—

**Table 6 | Assigned – Midroute: Forward FD & Forward RSA**

Variable		Avg_F_FD	BA11_F_avg	BA25_F_avg	HippoL_F_avg	HippoR_F_avg
1. Avg_F_FD	Pearson's r	—				
	p-value	—				
2. BA11_F_avg	Pearson's r	-0.384	—			
	p-value	0.105	—			
3. BA25_F_avg	Pearson's r	-0.022	0.309	—		
	p-value	0.929	0.198	—		
4. HippoL_F_avg	Pearson's r	-0.121	0.300	0.122	—	
	p-value	0.623	0.212	0.620	—	
5. HippoR_F_avg	Pearson's r	0.437	0.314	0.322	0.355	—
	p-value	0.062	0.190	0.179	0.136	—

**Table 7 | Assigned – Midroute: Backward FD & Backward RSA**

Variable		Avg_B_FD	BA11_B_avg	BA25_B_avg	HippoL_B_avg	HippoR_B_avg
1. Avg_B_FD	Pearson's r	—				
	p-value	—				
2. BA11_B_avg	Pearson's r	0.064	—			
	p-value	0.794	—			
3. BA25_B_avg	Pearson's r	-0.220	-0.356	—		
	p-value	0.365	0.134	—		
4. HippoL_B_avg	Pearson's r	0.208	-0.017	0.285	—	
	p-value	0.392	0.945	0.237	—	
5. HippoR_B_avg	Pearson's r	-0.262	0.341	-0.101	-0.269	—
	p-value	0.278	0.153	0.682	0.266	—

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