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# Neurocognitive Determinants of Memory Enhancement

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for the degree of Doctor of Philosophy in Psychology

by

Niccolo Reggente

2018

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# ABSTRACT OF THE DISSERTATION

Neurocognitive Determinants of Memory Enhancement

by

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Doctor of Philosophy in Psychology

University of California, Los Angeles, 2018

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The identification of neurocognitive correlates supporting enhanced memory has far reaching implications, from improving education and productivity to mitigating ailments caused by memory disorders. The work presented within this dissertation leverages behavioral paradigms, Virtual reality (VR), and neuroimaging tools to unveil the neural processes responsible for enhanced memory. The methodological tools used throughout this dissertation were drafted in an attempt to create an ecologically valid medium with theoretical extensions into education and rehabilitation. Of particular focus is how the parallel recruitment of reward and/or spatial processing systems during the encoding of information can serve to upregulate mnemonic processing and enhance memory. Specifically, Chapter 1 examines how memory-retrieval can be modulated by reward and whether individual differences in anatomical connectivity within reward processing and elaborative semantic encoding circuits, as measured with diffusion tensor imaging (DTI), are associated with value-induced modulation of memory.

The remaining chapters focus on the use of VR to implement the Method of Loci (MoL), the world's most ancient and effective mnemonic. Behavioral and neuroimaging analyses were designed to test a hypothesized mechanism of action behind the MoL's efficacy: explicit binding of information to the spatial scaffolding of an environment recruits neural systems supporting the encoding of space, which bolsters recall breadth and strength. To test this hypothesis, the dissertation first reviews the literature and presents VR as a way to increase the ecological validity of fMRI memory research (Chapter 2). Chapter 3 then investigates how the MoL can be implemented within VR and reveals which facets of the technique are most responsible for its potent impact on human memory. Chapter 4 extends the work in Chapter 3 by evaluating virtual strategies for reusing the same environment when encoding multiple lists of information—a necessity when considering the time consuming nature of creating memorable virtual environments. Chapter 5 demonstrates how mental representations of virtual environments can be decoded using functional magnetic resonance imaging (fMRI), setting the stage for an investigation into whether virtual encoding environments can be decoded during recall (the work conducted in Chapter 6).

The dissertation of Niccolo Reggente is approved.

Martin M. Monti

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University of California, Los Angeles

2018

# DEDICATION

To all those who have selflessly labored to make known the unknown.

# TABLE OF CONTENTS

# LIST OF FIGURES

## CHAPTER 1

## CHAPTER 2

## CHAPTER 3

## CHAPTER 4

## CHAPTER 5

**CHAPTER 6**

# LIST OF TABLES

## CHAPTER 3

## CHAPTER 5

## CHAPTER 6

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The adage “stand on the shoulders of giants” means far more than leveraging and acknowledging the work of those who came before you. To me, it also includes all the contributions that allow you to arrive at such a vantage point in the first place. For that, I thank my parents who afforded me with the opportunity to find the solace of science. They saw a curious mind whose environment was not encouraging of such philosophies and guided it to a place where it could flourish. Simply put, this work would not exist without such early opportunities and endless encouragement. I also owe an enormous debt of gratitude to my advisor, Dr. Jesse Rissman, who took a chance on me and spent countless hours in the trenches with me as I “cut my teeth”. From grant applications to poster figures, Jesse’s mentorship has been all-encompassing, detailed, encouraging, and empowering. Dr. Nanthia Suthana was also one of my first sources of inspiration for a majority of the work contained within this dissertation and her mentorship has been invaluable throughout my doctoral career. Both Dr. Martin Monti and Dr. Alexander (Sasha) Bystritsky have been crucial in helping me to identify a career path that appropriately leverages my skillsets. My wife and collaborator, (Amy) Zhong Sheng Zheng is a goddess; her ability to accentuate strengths, identify weaknesses, and instill confidence is unparalleled. I couldn’t do anything half as well if not for her. A special thanks is also owed to my collaborator Joey Essoe for her invaluable assistance in the design and implementation of the virtual paradigms utilized throughout this work. Forde “JubJub” Davidson also deserves a world of credit for his detailed work on developing the virtual suite of software and environments. Finally, to all those who have engaged with me on philosophical discussions, the insights were not

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> NR, MC and JR had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. MC, AC, BK, NR and JR: study concept and design. NR, MC, ZSZ, AC, BK and JR: acquisition, analysis, or interpretation of data; administrative, technical and assessment support. NR and JR: drafting of the manuscript; statistical analysis. BK, MC, JR, and AC: obtained funding.

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NR, JE, ZM, AT, JM, NS, JR conducted the literature review and wrote the manuscript. AT, NR, JR generated figures.

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## Featured Publications

**Reggente, N**., Essoe, J. K. Y., Aghajan, Z. M., Tavakoli, A. V., McGuire, J. F., Suthana, N. A., & Rissman, J. (2018). Enhancing the ecological validity of fMRI memory research using virtual reality. *Frontiers in Neuroscience*, 12, 408.

**Reggente, N.,** Cohen, M. S., Castel, A., Knowlton, B. J., & Rissman, J. (2018). Memory recall for high reward value items correlates with individual differences in white matter pathways associated with reward processing and fronto-temporal communication. *Frontiers in Human Neuroscience*, 12, 241.

**Reggente, N.**, Moody, T. D., Morfini, F., Sheen, C., Rissman, J., O'Neill, J., & Feusner, J. D. (2018). Multivariate resting-state functional connectivity predicts response to cognitive behavioral therapy in obsessive–compulsive disorder. *Proceedings of the National Academy of Sciences*, 201716686.

Zheng, Z. S., **Reggente, N.,** Lutkenhoff, E., Owen, A. M., & Monti, M. M. (2017). Disentangling disorders of consciousness: Insights from diffusion tensor imaging and machine learning. *Human brain mapping*, *38*(1), 431-443.

## General Introduction

The late physicist Stephen Hawking suggested that humans are on the brink of a new phase of evolutionary progress: “self-designed evolution”, where technological progress has outpaced the effects of genetic modifications that could confer adaptive advantage. This notion suggests that the seemingly eternal battle against entropy, which was historically waged at the molecular level, is now in the hands of consciousness. At such a horizon, the understanding of one’s self is paramount; it is only through elucidation of the cause-effect chain of cognition that one can gain confidence in reducing uncertainty and instantiating order amidst the universe’s gravitation to the contrary. In this light, nature’s greatest accomplishment is that of memory; no other tool has so fundamentally altered one’s ability to predict the future than the one used to model the past. By understanding memory, we afford ourselves with a toolkit to alter our own consciousness in a way that robustly prepares it for future events-- increasing the likelihood of preserving our existence and, as a result, satisfying the intent of evolution. As such, research towards understanding memory and identifying the scenarios that permit it to be enhanced is imperative.

The work presented throughout this dissertation examines memory encoding phenomena that result in reliable alterations in memory strength during recall. Two such scenarios are investigated: 1) preferential recall of information that is associated with behavioral salience; 2) enhanced mnemonic capacity when information is encoded within the scaffolding of spatial environments. Investigations into both scenarios are framed by their evolutionary significance and reveal insights important for both brain-mapping and technological development.

In regards to the first scenario: A need for preferential recall presents itself quit regularly; daily life bombards us with an insurmountable amount of information, only some of which may be important to remember. By understanding the mechanisms supporting the selective filtering of what we remember, we stand to increase / decrease its breadth for our conscious benefit. Chapter 1 of this dissertation investigates how reward can modulate one's prioritization of to-be-remembered information. Specifically, in a value-directed-remembering task where series of words were presented alongside a point value, participants were asked to maximize their point score when later recalling the information. Diffusion tensor imaging (DTI) analyses were conducted to unveil which anatomical pathways in the brain correlated with the individual differences observed in a) the number of high-value words recalled and b) the degree to which a participant was sensitive to point-value—as quantified by their preferential recall of words associated with a high value.

The second scenario, where spatially augmented information yields enhanced retrieval, is most prominently seen in the popular mnemonic technique known as Method of Loci (MoL). In order to implement the MoL, one is typically instructed to conjure up a familiar structure (e.g., a childhood home) that will serve as their "memory palace". While mentally navigating through this environment, one can imagine "placing" a series of to-be-remembered items in different locations. When later attempting to retrieve this list of items, one can mentally reconstruct the environment and "observe" each of the objects along the route. If characterized and operationalized, the contributing factors to the

MoL's historical and empirically validated enhancement of memory could be distilled and leveraged to augment and enhance memory throughout nearly every aspect of daily life. Pre-existing evidence of our affinity to augment space with our cognition is all around us: calendars organize our time in a spatial format, fretboards and piano keys bring clarity to music theory using spatial arrangements, professionals litter their desks with stickie-notes, infants count on their fingers, and Italians talk with their hands. Indeed, evidence is appearing which demonstrates that the neural mechanisms supporting spatial processing are also recruited for accomplishing other impressive feats of human cognition: grid cells fire in response to appropriate transversions through abstract, conceptual spaces (Constantinescu et al., 2016) and the same regions supporting navigation are leveraged when one navigates their digital file system (Benn et al., 2015). The neural systems supporting space and navigation seem to reflect something profound about the nature of reality; artificial agents naturally emerge grid cells in their computation code as they learn to move about space in a goal-directed manner (Banino et al., 2018).

This dissertation seeks to confirm the critical contribution of spatial encoding mechanisms to the success of the MoL from both a behavioral and neuroscientific standpoint. The narrative throughout this dissertation rests on the assumption that if space is emboldening the encoding processes, then a distinct neural signature indicative of such a process should be evident during recall. That is, a contextual reinstatement of encoding environment should be present when a participant is engaged in recalling information that was learned in that environment. To accomplish this feat, the work in this dissertation relies on Virtual reality (VR) to provide an investigational medium that permits a collection of quantifiable spatial metrics—a method whose ecological validity, specific to fMRI investigations of memory, is argued in Chapter 2. In Chapter 3, VR is utilized to create a virtual rendition of the MoL. Traditionally implemented within the confines of one's mental imagery (an inherently elusive medium), the translation of the MoL into a virtual realm permits for a novel ability to selectively permit , isolate, and record actions. Specifically, Chapter 3 investigates whether a removal of features which allow information to be explicitly bound to the spatial context affects the efficacy of the MoL. Chapter 4 makes important extensions to the VR-MoL developed in Chapter 3 by evaluating strategies for reusing virtual environments for the encoding of multiple lists of information. In order to ascertain the ability to test a hypothesis of contextual reinstatement underlying the MoL's effectiveness, the work in Chapter 5 was conducted to confirm that the decoding of environmental context within one's mental imagery using fMRI is feasible. Finally, Chapter 6 leveraged the same VR-MoL technology developed in Chapter 3 and searched for evidence during recall, conducted during an fMRI scan, that was informative of which environment the participant encoded the information in—a direct test of this dissertation's contextual reinstatement hypothesis.

In summary, the work contained within this dissertation seeks the elucidate the neurocognitive determinants underlying enhanced memory with specific attention paid to value-directed-remembering and spatially-augmented-learning. Through the use of VR, neuroimaging, and machine learning, this dissertation presents novel findings that contribute meaningfully to the discussion of ecologically valid memory enhancement.

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## Background

### Neuroimaging Methods

Often referred to as brain imaging, neuroimaging is broadly defined as the use of various techniques to either directly or indirectly image the structure and function of the nervous system. This dissertation and its associated publications will reference neuroimaging data collected from magnetic resonance (MR) machines. MR machines elegantly utilize strong magnetic fields to align Hydrogen protons within the to-be-measured body part of interest, radio frequency pulses to offset that alignment, and radio receivers to measure the emittance of electromagnetic energy given off by the Hydrogen protons as they realign (Bloembergen et al., 1948). The relative amounts of energy given off varies as a function of tissue type and such differences can be plotted so as to produce inferential "images". By way of intersecting planes of magnetic field gradients, these images have a 3D resolution whose smallest unit is known as a "voxel". Depending on the imaging modality used, voxels contain pertinent information as to either the static structure or temporally dynamic function of the matter. The proceeding sections will illustrate two such MRI modalities, Diffusion Weighted Imaging (DWI) and functional Magnetic Resonance Imaging (fMRI) that will be used in this dissertation.

### Diffusion Weighted Imaging (DWI)

The spread of a fluid across a space is known as diffusion. Particles suspended in a fluid will diffuse randomly when agitated with any amount of thermal energy-- resulting from an ensemble of collisions amongst atoms, molecules, and other particles. Known as Brownian motion, this random state can be used as a diffusivity baseline against which deviations can permit contrast inferences (Pierpaoli et al., 1996).

Imagine a glass cube of water. The movement of water in that cube is completely random, limited only by the boundaries of the cube. If a researcher were to look at the water in the center of the cube from any angle, it would exhibit a Gaussian diffusion from whichever angle researcher was looking from (Hagmann et al., 2006). A sampling of all points along a sphere focused on the center of the cube should result in random mean diffusion (i.e. zero, Brownian). However, diffusion of water along the outer border of the cube is subject to micrometric hindrance with the cube’s surface. Deviations from the random ground state of Brownian motion would only be seen at the limits made by the cube; the water is not free to keep moving through the walls of the cube and thus it must move elsewhere—a non-random event. Additionally, when diffused along directions parallel to one of the cube’s borders water will move faster than in directions perpendicular to the cube’s borders. This hindrance phenomenon is what allows for researchers to compare relative rates of water diffusion at different regions of space.

A combination of magnetic gradient and radio frequency pulses used in MR machines can perturb hydrogen protons in water so as to influence the phase of their spins – a calculable phenomenon since spins in the presence of a heterogeneous magnetic field lead to a decrease in signal intensity (Torrey, 1956). With MR gradients, water in the brain can be exposed to different magnetic field strengths depending on its position along the gradient axis – providing a spatial contrast (Hagmann et al., 2006). Thus, if a hydrogen proton in the water changes its phase in non-Brownian way, that would suggest the present of physical deviations such as the aforementioned cube’s boundaries. A region of space (i.e. a voxel) that has random brownian motion is said to be “isotropic”. If a voxel has non-random motion, it has a scalar value between zero and one that describes the degree of anisotropy of the diffusion process, birthing the common DWI term fractional anisotropy (FA).

Such an observation allows for the inference that water molecules are being restricted by the presence of molecular barrier (e.g. cell membranes, myelin, etc.) within a particular voxel of tissue (Pierpaoli et al., 1996). Since DWI can be measured from multiple angles, a 360 degree sampling of the same section of space (i.e. a voxel) can reveal the preferred directionality of diffusion and, subsequently, the directionality of the barrier (Bammer, 2003). Thereby, DWI measures the preferred directionality of water diffusion within a voxel and allows researchers to make inferences regarding the underlying structural makeup of that voxel. The method of combining many such DWI sampling angles of the same section of space is known as Diffusion Tensor Imaging (Mori et al., 1999).

By examining the inter-voxel relationships of preferred directionality, one can assess each voxel’s structural connectivity with every other voxel in the brain – a procedure known as tractography (Ciccarelli et al., 2003). That is, by determining the preferred diffusion direction within one voxel, one can identify whether or not that direction continues into neighboring voxels, allowing for the inference to be made that the same barrier is spanning across multiple voxels. This ability affords researchers with the potential ability to inferentially trace axonal fiber bundles, which would span many thousands of voxels.

The abundance of myelin on axonal fibers can have a significant impact on the magnitude of the preferred directionality of water's diffusion (Hodaie et al., 2012). As such, researchers have been able to insinuate that regions that are more readily linked by tractography algorithms are actually more structurally connected. Probabilistic tractography methods, and, as a proxy, DWI itself, was validated in vitro with invasive tracers (Dyrby et al., 2007).

## Functional Magnetic Resonance Imaging (fMRI)

The same MR principles discussed above, whereby an image of the brain can be created by measuring the emittance of electromagnetic energy given off by the realignment of Hydrogen protons within a magnetic field, can be used to track fluctuations in the brain across time. Such a feat is possible given the serendipitous nature of neural activity and it's downstream electromagnetic influence. The metabolic requirements to support neuronal firing create a neurochemical signaling cascade that locally recruits oxygen. Oxygen is transported throughout the bloodstream by hemoglobin. Hemoglobin, when oxygen is attached to it, is a diamagnetic substance, meaning it will tend to take a position at right angles to the lines of the magnetic force—a property that diminishes the MR signal, which is relying on the alignment of all protons with the magnetic field induced by the machine (Poldrack et al., 2011).

However, neurons and neuroglia will pull the oxygen off of the hemoglobin for use in cellular respiration. This "deoxygenated Hemoglobin" is paramagnetic, meaning it will take a position parallel and proportional to the intensity of the magnetizing field. Thus, the MR signal will be more detectable, and thereby stronger, where there is a concentration of deoxygenated hemoglobin. This paramagnetic property of deoxygenated hemoglobin becomes a naturally occurring contrast agent for MRI that is known as the blood oxygen level dependent (BOLD) signal (Ogawa et al., 1990). Essentially, researchers are deducing that if there is a great deal of deoxygenated hemoglobin (as detected by an increase in BOLD signal) isolated in a particular area, then a population of neurons must have needed respiration in that region.

If a researcher were to time-lock perceptual inputs and/or cognitive processing to such BOLD-response contrast images, they could spatially specify which regions of the brain support that particular task/event. Belliveau et al. (1991) successfully showed that one could accomplish such a feat by demonstrating a functional mapping of the human visual cortex in response to visual stimuli. In modern fMRI experiments, a BOLD contrast image is collected once every one or two seconds. By comparing images collected at different time points, researchers can examine, at the voxel level, how different regions are recruiting blood as a function of task.

Since researchers leveraging MRIs are able to collect a sampling north of a million voxel at each timepoint, it makes it possible to also examine the degree of temporal synchrony across multiple voxels. Functional connectivity measures the correlation of any two voxels’ (or groups of voxels, known as a region of interest [ROI]) BOLD signal across time (Biswal et al., 1995). Such a measurement allows researcher to infer which disparate regions of the brain are working in unison to process the many facets of conscious experience.

## Machine Learning

Machine learning is broadly defined as a set of statistical procedures and basic learning axioms that gives “computers the ability to learn without being explicitly programmed” (Munoz, 2014). Regardless of the underlying content, machine learning algorithms can examine the features of something, compare it to the features of another thing and classify the two as either the same or different. For the analyses mentioned in this dissertation, the machine learning algorithms used will be confined to the domain of supervised learning – a branch that deals with attempting to find patterns in sets of data by informing the algorithm of different classes that break up the data. Essentially, supervised machine learning involves finding exemplars with a category of objects, quantifying them into some set of features, and informing the algorithm that those examples are all the “same” in that they represent the category.

For example, a researcher could create a “feature set” that is made up of RGB pixel intensities (e.g. a digital photo) and “teach” the algorithm that some of photos are of houses and that others are of faces. The algorithm will plot the features of each photo (i.e. which pixels at which RGB intensities) in a higher dimensional feature space that has as many dimensions as features such that each “example” will become a single point in that space. By labeling these points with which category they fit in (e.g. houses and faces), a pattern should emerge whereby the cluster of points that represent pictures of faces emerges is unique and distinguishable from the cluster of points that represent pictures of houses. The algorithm can then draw a “decision boundary” that most efficiently separates the two cluster sets. With such a decision boundary, one could project new points into that feature space and “guess”, depending on which side of the decision boundary it lies, whether or not the features that created that point belong to a picture of a face or a human. Whether or not the algorithm is able to correctly label the point is known as classification accuracy.

Just as with RGB values from pixels in a digital photo, a feature set can be made up of BOLD values from different voxels. Instead of labels reflecting the content of a digital picture, they can also associate BOLD voxel values with what an individual is seeing or thinking while that BOLD “picture” was taken. The work contained within this dissertation will utilize voxel-specific BOLD images (or second order derivatives of those images) as features and cognitive states as categorical labels of those features. A cross-validation methodology has been employed with all analyses throughout this dissertation. Cross-validation, as it pertains to the domain of fMRI, is a procedure where a researcher will index *n* BOLD images that they know were taken while the subject was looking at a picture of, say, a face and *n* more taken when the subject was looking at a house. They will then train their machine learning algorithm on *(n-l)*k* images, where *l* is a number greater than the number of class labels (*k*). The algorithm can then create a set of points that positions each exemplar’s feature set in an n-voxel feature space. After demarcating a decision boundary, the algorithm will guess the category of the *l* left-out BOLD images (i.e. answering the question: was this BOLD image collected when someone was looking at houses or faces?). The number of correct guesses the classifier makes will be recorded and the process will be repeated again where a different *l* BOLD images are “left out”, until each of *n* BOLD images are left out at least once. The average accuracy of each iteration (named a fold) of the cross-validation is taken to be the algorithm’s overall accuracy.

Naturally, feature sets that contain some information pertaining to the classification at hand will yield a greater classification accuracy. Much in the same way that the name of the first person to buy a house doesn't tell you much about its sale price, the BOLD activity in someone's skull shouldn't tell you anything about whether or not they were looking at a house or a face at any given time (i.e. its classification accuracy would be at random-chance). This insight is what has driven the field of information-based functional brain mapping. The analyses mentioned in this dissertation will make particular use of the searchlight-brain-mapping technique developed by Kriegeskorte and colleagues (2006). This approach involves creating a sphere around a voxel and using that voxel, along with those captured in the surrounding spherical geometry, to be the feature set for a classification. The accuracy outcome from using that feature set across a cross-validation is then assigned to the voxel upon which the spherical ROI was centered. Repeating this process for each voxel in the brain results in an image where each voxel is representative of how informative the multivariate patterns of BOLD activity in those voxels are in regards to the classification at hand. Regions with higher classification accuracy are reasonably thought to be more involved with the detailed processing surrounding the cognitive activity at hand. For example, if a region can contribute information towards a successful classification of faces and houses, it could be interpreted that that region cares about houses, faces, or both especially when compared to other non-informative brain regions.

A slimmed-down approach that looks at the correlation across multiple voxels across different examples of the same stimulus category as opposed to across examples of a different stimulus category is known as representational similarity analysis (Kriegeskorte et al., 2008). The assumption is that ensembles of voxels (whether spatially disparate or contiguous) that exhibit similar, consistent, and coherent patterns of responses to one cognitive task and different patterns to others are more involved in that cognitive task that other ensembles of voxels that do not exhibit as much within-category vs. across-category dissimilarity. If the response was different each time, one could insinuate that there is no predictable response in those areas of the brain to that particular stimulus and, thus, perhaps has little involvement as to the processing of that task. This RSA approach can also be utilized within a searchlight brain mapping procedure.

## Virtual Reality (VR)

Virtual reality, in the loosest sense, is the use of computers to render virtual environments in which human users can control and navigate an “avatar” or use virtual machinery. Today, many users leverage headsets, capable of tracking head motion, body gestures, and spatial displacement (e.g. HTC Vive, Oculus Rift) in order to achieve an immersive virtual reality experience that intentionally mirrors reality. VR has been posited as a method that stands to increase the ecological validity of memory experiments leveraging fMRI (Chapter 2; Reggente et al., 2018). The experiments mentioned in this prospectus will use a combination of large open source virtual reality software and custom coding that renders a virtual environment onto a 2D computer monitor whereby a user can interact with the environment and presented material using their mouse and keyboard.

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## Chapter 1: Memory recall for high reward value items correlates with individual differences in white matter pathways associated with reward processing and fronto-temporal communication

### Abstract

When given a long list of items to remember, people typically prioritize the memorization of the most valuable items. Prior neuroimaging studies have found that cues denoting the presence of high value items can lead to increased activation of the mesolimbic dopamingeric reward circuit, including the nucleus accumbens (NAcc) and ventral tegmental area (VTA), which in turn results in up-regulation of medial temporal lobe encoding processes and better memory for the high value items. Value cues may also trigger the use of elaborative semantic encoding strategies which depend on interactions between frontal and temporal lobe structures. We used diffusion tensor imaging (DTI) to examine whether individual differences in anatomical connectivity within these circuits are associated with value-induced modulation of memory. DTI data were collected from 19 adults who also participated in an fMRI study involving a value-directed memory task. In this task, subjects encoded words with arbitrarily assigned point values and completed free recall tests after each list, showing improved recall performance for high value items. Motivated by our prior fMRI finding of increased recruitment of left-lateralized semantic network regions during the encoding of high value words (Cohen et al., 2014), we predicted that the robustness of the white matter pathways connecting the ventrolateral prefrontal cortex with the temporal lobe might be a determinant of recall performance for high value items. We found that the mean fractional anisotropy of each subject's left uncinate fasciculus, a fronto-temporal fiber bundle thought to play a critical role in semantic processing, correlated with the mean number of high value, but not low value, words that subjects recalled. Given prior findings on reward-induced modulation of memory, we also used probabilistic tractography to examine the white matter pathway that links the NAcc to the VTA. We found that the number of fibers projecting from left NAcc to VTA was reliably correlated with subjects' selectivity index, a behavioral measure reflecting the degree to which recall performance was impacted by item value. Together, these findings help to elucidate the neuroanatomical pathways that support verbal memory encoding and its modulation by value.

## Introduction

As we go about our day-to-day lives, we often find ourselves bombarded with new information, only some of which may be important to remember. A growing body of research has begun to characterize the cognitive and neural mechanisms that support our ability to prioritize the encoding of those items that we believe will be most valuable to later recall (for reviews, see Castel, 2008; Shohamy and Adcock, 2010; Miendlarzewska et al., 2016). In an experimental setting, the relative importance of individual items is typically conveyed to participants by cues indicating the point value or reward magnitude that could be earned if that item is correctly remembered on an ensuing test. Functional magnetic resonance imaging (fMRI) studies have found that cues denoting the presence of high reward value items can lead to increased activation of the mesolimbic reward circuit, including the nucleus accumbens (NAcc) region of the ventral striatum and the ventral tegmental area (VTA) of the midbrain (Adcock et al., 2006; Cohen et al., 2014). The NAcc, which receives inputs from the ventromedial prefrontal cortex conveying information about motivational salience, is thought to represent the magnitude of anticipated reward (Delgado et al., 2000; Knutson et al., 2001). Its projections to dopamine-producing neurons of the VTA can trigger the release of dopamine into the hippocampus, promoting synaptic plasticity via long-term potentiation, which serves to strengthen one's memory for information encountered in close temporal proximity to the value cue (Lisman and Grace, 2005). While the engagement of these mechanisms may be automatically triggered in response to value cues, such cues may also serve to promote memory encoding by encouraging the individual to allocate increased attention to high value information and employ cognitive strategies to process that information in a more effective manner (Cohen et al., 2017; Middlebrooks et al., 2017). One particularly effective strategy is the engagement of elaborative encoding processes, in which an item's semantic attributes are processed in a deep manner (Craik and Tulving, 1975; Castel, 2008). This often entails the effortful generation of visual images, associations, or stories in an effort to make the item's representation more memorable. Recent evidence from fMRI studies indicates that engagement of the brain's so-called "semantic network" (Binder and Desai, 2011) which includes regions of the left ventrolateral prefrontal cortex (VLPFC) and lateral temporal cortex, is markedly increased during the encoding of high value items (Cohen et al., 2014; 2016). Although functional neuroimaging studies like these have contributed to our understanding of these two putative mechanisms of reward value-induced memory enhancement—one tied to the brain's dopaminergic reward circuitry and one tied to strategic engagement of the semantic network—these studies have also highlighted substantial individual differences in the degree to which people engage these mechanisms (Adcock et al., 2006; Cohen et al., 2014; 2016).

In the present study, we sought to examine whether individual differences in the degree to which item reward value impacts memory encoding might be at least partially explained by individual differences in the structural integrity of key anatomical pathways within the brain's reward system and semantic control system. To accomplish this, we used diffusion tensor imaging (DTI) data to measure the structural characteristics of several white matter pathways that we hypothesized might have relevance to reward value-incentivized remembering. One such pathway of interest was the uncinate fasciculus (UF), a fiber tract that connects portions of the inferior prefrontal cortex (PFC) with the anterior temporal lobe (Schmahmann et al., 2007; Von Der Heide et al., 2013; Leng et al., 2016; Hau et al., 2017). Prior DTI studies have strongly implicated the UF in both semantic processing (Matsuo et al., 2008; McDonald et al., 2008; Acosta-Cabronero et al., 2011; de Zubicaray et al., 2011; Galantucci et al., 2011; Agosta et al., 2012) and aspects of episodic memory (Diehl et al., 2008; Lockhart et al., 2012; Thomas et al., 2015; Wendelken et al., 2015; Alm et al., 2016).

Although our primary candidate for a white matter pathway involved in controlled semantic processing and verbal memory was the UF, we also examined the putative role of another major pathway—the inferior frontal occipital fasciculus (IFOF). This pathway connects ventrolateral PFC regions with more posterior areas of the temporal cortex, as well as with some occipital regions (Catani and Thiebaut de Schotten, 2008). Individual differences in the integrity of this pathway have also been linked to behavioral performance on tests of semantic memory (de Zubicaray et al., 2011) and semantic control (Nugiel et al., 2016), and damage to this pathway can lead to semantic paraphasias (Mandonnet et al., 2007).

Finally, with respect to the brain's reward circuitry, our analysis focused on examining whether the robustness of the connection between the NAcc and VTA (Morales and Margolis, 2017) would be predictive of individual differences in reward value-based modulation of memory. Prior DTI work has associated increased NAcc-VTA connectivity with better reward learning performance (Samanez-Larkin et al., 2012). Furthermore, fMRI-based measurements of functional connectivity have reported strong coupling between NAcc and VTA during the intrinsic resting state (Kahn and Shohamy, 2013), as well as heightened coupling between these regions during novelty-induced reward anticipation (Krebs et al., 2011).

For each of these candidate pathways we derived metrics of white matter integrity from the DTI data of individual participants, who also performed a value-directed remembering task (Cohen et al., 2014). The task was designed to incentivize selective encoding of valuable information (Castel, 2008). Specifically, on each trial, participants were presented with a high or low value cue that preceded the display of a unique word and indicated the number of points they would earn if they subsequently recalled that word. Given the relatively large number of words on each list, participants were unlikely to remember them all, and thus it was advantageous for them to prioritize the memorization of words associated with a high value in their attempt to maximize their point total. It is important to note that although the points accumulated by participants in this task had no tangible reward value (i.e., they could not be converted to a monetary payout), the motivational salience of these point values was reflected in both participants' memory behavior and in the value-modulated engagement of reward-related regions in the midbrain and ventral striatum (Cohen et al., 2014). We quantified a participant’s success on this value-directed remembering task using three metrics: the average number of high and low value words recalled per list (Mean High Recall and Mean Low Recall) and “Selectivity Index,” a putative trait variable that indexes the degree to which each participant prioritized the memorization of high value items over low value items (Castel et al., 2002). To the extent that successful recall of high value words depends on the engagement of deep semantic processing during encoding (Cohen et al., 2014; Cohen et al., 2017), we hypothesized that participants’ ability to remember high value items would correlate with individual differences in the structural integrity of the UF and/or IFOF pathways that have been implicated in semantic control, and potentially also with the NAcc-VTA pathway associated with reward processing. We furthermore hypothesized that individual differences in the robustness of the NAcc-VTA pathway might correlate with variability in reward-related modulation of learning, as captured by their Selectivity Index measure.

## Methods

### *Participants*

Twenty-two adults were enrolled in this study. Data from three participants were excluded from analysis: one for being a non-native English speaker and two for whom we were unable to acquire diffusion-weighted MRI data (one participant’s scanning session was discontinued due to discomfort and the other due to time constraints). The remaining 19 participants (10 female; mean age = 21.8 ± 3.7 years) were all right-handed, native English speakers who reported no current psychoactive medications or severe psychiatric or neurological disorders. All participants either had normal or corrected-to-normal vision. Participants were recruited via flyers placed around the

UCLA campus and were remunerated for their participation. Written informed consent was obtained from each participant, and all procedures were approved by UCLA's Medical Institutional Review Board (IRB #11-002443).

### *Behavioral procedure*

A value-directed memory task, adapted from an experimental paradigm developed by Castel and colleagues (2002; Castel, 2008), was administered in the MRI scanner as participants underwent functional imaging. Extensive details about the protocol have been previously reported (Cohen et al., 2014; 2016), and key elements are summarized below. Participants performed five study-test cycles, each consisting of the study of a list of 24 unique words followed by a free recall test; in addition, two study-test cycles were completed as practice prior to the scanning session. The words were 4-8 letter concrete nouns, and each was assigned a point value indicating how many points could be earned if that word was later recalled. Half of the words were arbitrarily assigned a high value (10, 11, or 12 points) and the other half were assigned a low value (1, 2, or 3 points); value assignment was counterbalanced across participants. During each study list, the presentation of 12 high value and 12 low value words was intermixed in a pseudorandomized fashion. Each trial began with a numeric value cue presented inside of a gold coin symbol (2 s), followed by a fixation cross (3 – 6.75 s). Then, the to-be-remembered word was presented (3.5 s) followed by another fixation (1.5 s). During the inter-trial interval (3.75-8.75 s), participants performed a simple vowel/consonant judgment task designed to prevent continued rehearsal of the words. Upon the conclusion of each 24-word list, fMRI scanning momentarily ceased and participants were given 90 s to recall as many words as possible from the preceding list, with an emphasis to maximize their total point score. Immediately after recall was complete, participants were given feedback on the points earned for that list.

In order to index the degree to which each participant selectively prioritized the memorization of high value items, while taking into account the overall memory ability of that participant, we computed a measure known as *Selectivity Index* (Castel et al., 2002) using the formula: (actual score – chance score) / (ideal score – chance score), where "actual score" indicates the total number of points earned, "chance score" indicates the point total that the participant would have earned had the point values been randomly assigned (i.e., mean point value multiplied by number of words recalled), and "ideal score" indicates the point total that would have been earned if the *N* words that the participant recalled were only those with the highest *N* point values. As an illustrative example, if a participant recalled only four words on a given list, and the points associated with these words were 12, 10, 11, and 12, then the participant's Selectivity Index would be very high. The ideal score for four words would be 48 (since there are four 12-point words on each list); the participant's actual score would be 45; the chance score would be 26, since the average point value across all list items was 6.5 points; thus, the Selectivity Index in this case would be: (45 – 26)/(48 – 26) = 0.86. In this way, we calculated the Selectivity Index for each list, and then averaged across lists to yield a single score.

### *MRI scanning procedure*

MRI data were acquired on a 3.0T Siemens Tim Trio Scanner at the UCLA Staglin IMHRO Center for Cognitive Neuroscience equipped with a 12-channel receive-only phased array head coil. A high-resolution T1-weighted anatomical image was obtained using a 3D MPRAGE sequence (TR = 1900 ms, TE = 3.26 ms, flip angle = 9°, FoV = 250 mm, voxel size = 0.98 x 0.98 x 1.0 mm). Diffusion weighted imaging data were obtained using a multi-directional diffusion weighting (MDDW) spin-echo echoplanar imaging (EPI) sequence (64 non-collinear directions, b-value = 1000 s/mm$^2$, TR = 9000 ms, TE = 93 ms, echo spacing = 0.69 ms, 60 axial slices, FoV = 190 mm, voxel size = 2.0 x 2.0 x 2.0 mm) with a non-diffusion weighted reference volume (b=0 s/mm$^2$). Prior to the acquisition of these structural scans, functional EPI data were obtained as participants performed the value-directed memory task; results from analysis of those data have been previously reported (Cohen et al., 2014). Stimuli were presented using E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA), and images were shown via either a custom-built MR-compatible rear projection system, or via MR-compatible goggles (Resonance Technology, Inc.).

### *Diffusion tensor imaging data processing*

Diffusion MR data were preprocessed using the FMRIB's Diffusion Toolbox (FMRIB Software Library, FSL version 5.0.6; http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL). All diffusion-weighted images were corrected for eddy currents and aligned to the b0 reference volume. A brain-tissue-only mask was created for each subject using Brain Extraction Tool (BET) and applied to all images. Tensor models were fit to the diffusion data from each voxel using DTIFIT to produce whole-brain fractional anisotropy (FA) maps for each subject.

All analyses were conducted in subject-specific diffusion space in an effort to minimize resampling of the diffusion data. Because our principal analyses involved several regions-of-interest (ROIs) that were defined in standard Montreal Neurological Institute

(MNI) template space, these ROIs were reverse normalized to the space of each subject's diffusion data according to the following workflow: Each subject's anatomical image (MPRAGE) was normalized to a standard T1-weighted template in MNI space using a symmetric diffeomorphic image registration procedure implemented in the Advanced Normalization Tools (ANTS) Toolbox (Avants et al., 2008). The inverse of this transformation was then applied to all standard space ROIs, bringing each ROI into subject-specific MPRAGE space. Next, each subject's non-diffusion-weighted b0 reference volume was aligned to their MPRAGE using 12-parameter linear-affine registration using FMRIB's Linear Image Registration Tool (FLIRT), and the inverse transform of this registration was applied to the ROIs, bringing each ROI into subject-specific diffusion space.

ROI masks for tracts of interest were defined based on the Johns Hopkins University (JHU) white matter tractography atlas (Mori et al., 2005; http://cmrm.med.jhmi.edu). For each fiber tract, we calculated mean FA values for each individual within separate left hemisphere and right hemisphere ROIs. Our primary fronto-temporal tract of interest were the left and right UF (Figure 1A), following previous work demonstrating the relationship between UF integrity and semantic control (Harvey et al., 2013). We also examined the mean FA of each subject's left and right IFOF (Figure 1B), as studies have linked this pathway to semantic processing/control (de Zubicaray et al., 2011; Nugiel et al., 2016). As a control analysis, designed to rule out the possibility that generalized differences in white matter tract integrity would correlate with our behavioral measures, we extracted the mean FA of each subject's left and right corticospinal tract—a tract with no prior association with either reward or memory that has been used as a control pathway in prior studies examining DTI correlations with memory behavior (Winston et al., 2013; Schlichting and Preston, 2016). For all JHU-defined masks, we applied a 10% probability threshold to ensure sufficient coverage of the entire pathway, while avoiding excessive sparsity/shrinkage (that would result if higher thresholds were applied). Since the IFOF and UF masks had considerable anatomical overlap in the JHU atlas, with the UF essentially existing as a subset of the IFOF, we conducted additional analyses in which we excluded all UF voxels from the IFOF mask and only examined the portions of the IFOF that did not show any anatomical overlap with the UF.

For our analysis of anatomical connectivity between the NAcc and VTA, we implemented a probabilistic tractography approach, as no pre-defined atlas was available for this pathway. A left and right NAcc ROI were anatomically defined for each subject using their MPRAGE scan (Figure 1C); this was accomplished using FreeSurfer's automatic subcortical segmentation routine (http://freesurfer.net/fswiki/SubcorticalSegmentation). Given the challenge of demarcating the anatomical boundaries of the VTA in T1-weighted MR images of individual subjects, we defined a VTA ROI using a probabilistic atlas of human VTA (Murty et al., 2014; http://web.duke.edu/adcocklab) with a 50% probability threshold (Figure 1D).

Using FSL's PROBTRACKX, in conjunction with BEDPOSTX (Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques), each subject's diffusion image underwent a Bayesian estimation of diffusion parameters at each voxel using a Markov-chain Monte Carlo sampling techniques while modeling and accounting for crossing fibers (Behrens et al., 2003; Behrens et al., 2007). Using 5000 samples of the distribution of diffusion parameters, 5000 streamlines from each seed voxel were created and this distribution of streamlines was used to create a likely tract location. By taking many such samples, the probabilistic tractography algorithms build up a posterior distribution on the streamline location or the connectivity distribution of each seed ROI to each target ROI.

Our primary measure of interest was the total number of samples from the seed ROI that reached the target mask. To normalize the results and ensure our results would not be driven by variance in the seed ROI size, we divided the total streamline count by the total number of samples sent out from the seed mask (i.e., 5000 * number of voxels in the seed ROI) (Johansen-Berg et al., 2005). This tract strength value was then correlated with our behavioral measures of interest. To ensure that our results were not being driven by the size of the target ROI, we computed a partial correlation controlling for the size of the target ROI (note that although the same VTA ROI was used as the target ROI for all subjects, its size varied across participants based on the transformations needed to reverse normalize this ROI from MNI space to the native anatomical space of each subject). Tract strength measures, as indexed by DTI tractography, have been shown to correlate strongly with actual neuroanatomical connectivity as revealed by retrograde tracer injections (Donahue et al., 2016). Because we had a priori reason to believe that higher FA values (which reflect increased directional structure of white matter tissue) and higher tract strength values would be an indicator of more robust anatomical connectivity and thus associated with improved task performance, we assessed the significance of the brain-behavior correlations using one-tailed tests. We controlled our false discovery rate (FDR; i.e., Type I error rate) by correcting the observed p-values in accordance with the expected proportion of false discoveries amongst the rejected hypotheses for all brain-behavior correlations (Benjamini and Hochberg, 1995). As such, all reported brain-behavior p-values have been FDR-corrected, and results that achieve $p < 0.05$ (corrected) are reported as significant. Direct comparisons of a given region's correlation with two behavioral measures (e.g., high value recall vs. low value recall) were assessed using a two-tailed test for the difference between two dependent correlations with one variable in common (Steiger, 1980) using an online utility (http://quantpsy.org/corrtest/corrtest2.htm; Lee, 2013).

## Results

### *Behavioral performance*

Our analyses focused on three behavioral measures of interest: (1) High Value Recall (the mean number of high value words recalled per list, averaged across the 5 lists), (2) Low Value Recall (the mean number of low value words recalled per list, averaged across the 5 lists), and (3) Selectivity Index. Across participants, the average High Value Recall score was 8.65 (SD = 1.87), which was significantly greater than the average Low Value recall score of 3.18 (SD = 2.72), $t_{18} = 9.27$, $p = 2.84 \times 10^{-8}$. The average Selectivity Index score was 0.605, which was significantly greater than zero (i.e., value-insensitive recall), $t_{18} = 11.48$, $p = 1.03 \times 10^{-9}$.

### *Brain-behavior correlations: fractional anisotropy (FA)*

We first examined whether individual differences in the mean FA of our primary fronto-temporal pathway of interest, the uncinate fasciculus (UF), were correlated with each of our three behavioral measures **(**Figure 2). For the left UF, we found that mean FA showed a strong positive correlation with High Value Recall ($r = 0.746$, $p = 0.0025$) but not with Low Value Recall ($r = 0.219$, $p > 0.2$), and this difference in correlation magnitude was significant ($z = 2.606$, $p = 0.0046$). For the right UF, we found that mean FA also showed a positive correlation with High Value Recall ($r = 0.551$, $p = 0.0378$) but not with Low Value Recall ($r = 0.177$, $p > 0.3$). However, this difference in correlation magnitude only trended towards significance ($z = 1.582$, $p = 0.057$). A direct comparison between the effects in left and right UF revealed a significantly stronger relationship with High Value Recall performance in the left hemisphere ($z = 2.099$, $p = 0.018$). When correlating mean FA with Selectivity Index, we did not observe a significant effect in either left UF ($r = 0.177$, $p > 0.3$) or right UF ($r = 0.123$, $p > 0.3$).

Mean FA along the inferior frontal occipital fasciculus (IFOF) pathway also showed a positive correlation with High Value Recall for both the left ($r = 0.631$, $p = 0.015$) and right ($r = 0.624$, $p =0.015$) hemisphere ROIs. There was no difference in correlation magnitude as a function of hemisphere ($z = 0.047$, $p > 0.9$). Mean FA in the IFOF did not significantly correlate with Low Value Recall on the left ($r = 0.308$, $p > 0.2$) or right ($r = 0.336$, $p > 0.1$) hemisphere. Despite the finding of significant correlations with High Value Recall and non-significant correlations with Low Value Recall, a direct test of the difference in correlation coefficients failed to yield significant effects in either the left IFOF ($z = 1.47$, $p = 0.142$) or right IFOF ($z = 1.309$, $p = 0.191$). Selectivity Index also showed no relationship with FA in left IFOF ($r = -0.050$, $p > 0.4$) or right IFOF ($r = 0.047$, $p > 0.3$).

Given the strength of our UF findings and the spatial overlap of our atlas-defined UF and IFOF ROIs, we next assessed whether the significant relationship between High Value Recall and FA along the IFOF could potentially be driven by the FA values that were also included in our analyses of the UF. In order to test this hypothesis, we conducted a follow-up analysis where only portions of the left and right IFOF masks that were non-overlapping with the left and right UF masks were analyzed (we refer to resulting ROI as $\text{IFOF}_{\text{exclusive}}$). We found that mean FA did not significantly correlate with High Value Recall in the left $\text{IFOF}_{\text{exclusive}}$ ($r = 0.363$, $p > 0.1$) nor Low Value Recall ($r = 0.177$, $p > 0.2$). A similar observation was seen for the right $\text{IFOF}_{\text{exclusive}}$; mean FA did not significantly correlate with High Value Recall ($r = 0.417$, $p > 0.1$) nor Low Value Recall ($r = 0.070$, $p > 0.4$). When correlating mean FA with Selectivity Index, we did not observe a significant effect in either left $\text{IFOF}_{\text{exclusive}}$ ($r = -0.030$, $p > 0.4$) or right $\text{IFOF}_{\text{exclusive}}$ ($r = 0.170$, $p > 0.2$). These results suggest that the value effects documented above for the entire IFOF ROIs were actually driven heavily by FA levels within the anterior portion of these ROIs that overlapped with the UF.

As a control analysis to rule out generic effects of white matter health/integrity and task performance, we examined the mean FA of the corticospinal tract. Mean FA within the left corticospinal tract did not correlate with High Value Recall, Low Value Recall, or Selectivity Index (all r’s < 0.238, all p’s > 0.1). The same was the case for the right corticospinal tract (all r’s < 0.289, all p’s > 0.1).

### *Brain-behavior correlations: tract strength*

Our primary reward circuit pathway of interest was the connection between the NAcc and VTA. Given that our probabilistic VTA ROI was bilateral by nature, we elected to combine the left and right NAcc ROI into a single bilateral NAcc ROI, and we then assessed the relationship between the mean tract strength of the NAcc-VTA pathway and each of our three behavioral performance measures. This was done using partial correlations that controlled for the size of the VTA target ROI, and thus the associated scatterplots **(**Figure 3) depict the standardized residuals of each variable rather than the raw values. Individual differences in the tract strength of the NAcc-VTA pathway correlated significantly with High Value Recall ($r = 0.509$, $p = 0.0455$) but not with Low Value Recall ($r = -0.167$, $p > 0.3$), and this difference in correlation magnitude was significant ($z = 2.780$, $p = 0.0054$). Furthermore, this pathway's tract strength correlated significantly with individual differences in Selectivity Index ($r = 0.533$, $p = 0.0394$).

## Discussion

In this study, we used diffusion weighted imaging to assess the relationship between microstructural integrity of white matter pathways and individual differences in value-directed remembering. Our analyses revealed a significant positive correlation between participants' ability to recall high reward value words and the structural integrity of two white matter pathways of interest:  the UF and the tract connecting the NAcc and the VTA. No such correlation was found between these pathways and participants' ability to recall low reward value words. Furthermore, the strength of the NAcc→VTA connection was strongly correlated with individual differences in Selectivity Index, suggesting that this mesolimbic pathway may constitute one key determinant of reward-driven modulation of memory encoding behavior.

Prior research using the value-directed remembering paradigm has yielded evidence that participants preferentially engage in deep semantic encoding of high reward value items relative to low reward value items (Castel, 2008; Cohen et al., 2017), and that this is associated with value-related differences in neural activity within lateral prefrontal and temporal lobe regions thought to be key components of the brain's semantic network (Cohen et al., 2014). Cohen et al. (2016) also found a positive correlation between Selectivity Index and activity in these brain regions during encoding of high reward value items, with no such effect apparent during encoding of low reward value items, suggesting that selectivity in young adults is driven primarily by enhanced semantic encoding of high reward value words.

Motivated by these findings, our DTI analyses focused heavily on exploring whether individual differences in the anatomical robustness of the UF pathway, which connects the ventral PFC with the anterior temporal lobe, might be one factor that predicts memory for high value items. As is common in the DTI literature, we indexed the microstructural integrity of white matter pathways by measuring their mean FA. This measure denotes the degree of restriction that water molecules encounter when diffusing within a given voxel, and as such is increased whenever that voxel's underlying tissue is rich with coherently oriented myelinated axons. Our finding that the mean FA of participants' UF predicted their ability to recall high value words, but not low value words, suggests that having a robust UF may be conducive to deploying effective semantic encoding strategies to ensure retention of valuable information. Although this correlation with high value recall was observed in both hemispheres, only in the left UF was the correlation significantly greater with high value recall than low value recall, suggesting that the key behavioral phenomenon in our task—enhanced memory for high value words—may be more strongly associated with fronto-temporal connections within the left hemisphere. This is consistent with our interpretation of this effect as being attributable to the prioritized engagement of semantic processing. We also examined the putative contributions of another major white matter pathway connecting ventrolateral PFC regions with posterior sensory cortices—the IFOF—but found that after excluding the anterior portion of this pathway that overlapped with the UF, its mean FA was uncorrelated with behavioral performance on our task.

In our task paradigm, participants' ability to remember high value words (i.e., their Mean High Recall score) likely reflects the efficacy with which they can engage in encoding strategies to promote the retention of information they hope to be able to later remember. Early "depth of processing" research demonstrated that elaborative encoding, the process of associating meaning with to-be-remembered information, results in greater retention relative to encoding the information at a superficial level via rote rehearsal (Woodward et al., 1973; Craik and Tulving, 1975; Bradshaw and Anderson, 1982). When tasked with encoding words, those who employ an elaborative encoding strategy are effectively linking the meaning of a word with related concepts – binding its representation into a broader semantic network and creating more potential retrieval routes that could later facilitate successful recall. In this experiment, because some words are deemed to be more valuable to remember than others in regards to the task at hand, it is likely that engagement of elaborative semantic encoding is roughly proportional to the point value assigned each word.

A number of prior studies have linked the UF pathway to aspects of semantic and/or associative encoding. Although our study examines structure-function relationships by capitalizing on individual differences in white matter integrity and behavioral performance in cognitive healthy adults, many valuable insights have been derived from studies of clinical populations or older adults. For instance, in a study of aphasic patients with varying degrees of comprehension deficits, Harvey and colleagues (2013) found that individual differences in the structural integrity of the left UF were predictive of patients' performance on tasks requiring semantic control. Specifically, patients with lower UF integrity as indexed by mean FA, showed a diminished ability to ignore semantically related distractors and identify associative relationships when understanding a word. These findings were taken as evidence that the UF plays an important role in semantic control, by virtue of its ability to connect cognitive control regions of the anterior ventrolateral PFC with anterior temporal lobe regions thought to be critical for storing word meanings (Visser et al., 2010). Abnormal FA values in the UF have also been correlated with deficits in confrontational naming and semantic memory in patients with temporal lobe epilepsy (McDonald et al., 2008). In further support of the role of UF in semantic processing, studies of semantic dementia patients have frequently reported decreases in FA (or decreases of a related measure known as radial diffusivity) in the UF, particularly in the left hemisphere but occasionally bilaterally (Matsuo et al., 2008; Acosta-Cabronero et al., 2011; Galantucci et al., 2011; Agosta et al., 2012). Individual differences in left UF integrity also correlate with performance on tests of semantic memory in healthy older adults (de Zubicaray et al., 2011). The left UF has also been associated with performance on episodic memory tasks, including the learning of paired associations between visual images (Thomas et al., 2015; Alm et al., 2016) and a task requiring mnemonic control to prioritize the encoding of relative images and ignore distractors (Wendelken et al., 2015). Damage to this pathway is correlated with deficits in immediate and delayed verbal memory (Diehl et al., 2008; McDonald et al., 2008) and visual associative memory (Lockhart et al., 2012).

It is worth noting that not all studies that have examined structural correlates of semantic control have found a reliable correlation with UF integrity. For instance, Nugiel and colleagues (2016) conducted a verb generation study in which subjects were presented with a noun and asked to generate a related verb. The authors assessed the semantic relatedness between the noun and the provided verb using latent semantic analysis (LSA) and found that individual differences in LSA score (their proxy for semantic control) were not related to FA in the UF, but rather correlated with FA in the left IFOF, and also showed an unanticipated correlation with FA in the inferior longitudinal fasciculus (ILF), a pathway typically associated with high-level vision. While their findings diverge from those of the present study, there were several major methodological differences that may have contributed to this discrepancy. Our atlas-based UF and IFOF ROIs had considerable anatomical overlap in the anterior portion, requiring us to exclusively mask out overlapping voxels to isolate effects that were uniquely attributable to IFOF. As such, our procedure may underestimate the potential contribution of anterior IFOF fibers extending into prefrontal cortex, whereas Nugiel and colleagues’ use of ROI-to-ROI deterministic tractography may have been more sensitive to these fibers. Furthermore, the tasks used in our respective studies were markedly different, raising the possibility that IFOF integrity is more consequential for the type of semantic control needed to rapidly retrieve word associations, whereas UF integrity may be more important for the type of control needed to facilitate elaborative semantic encoding of words. Future studies will be necessary to better characterize the roles of the UF and IFOF pathways in semantic control and verbal memory.

There is also reason to believe that the UF pathway could more generally play a role in reward-incentivized behavior. For instance, studies in monkeys have shown that the UF is critical for tasks like conditional rule learning where they must associate a particular object with a particular choice location that is rewarded (Parker and Gaffan, 1998; Bussey et al., 2002). In DTI work with human subjects, Camara and colleagues (2010) found that FA values in a region within the UF correlated with the difference in BOLD activity in the ventral striatum when a participant earned a loss versus a gain in a gambling task (i.e., was more sensitive to punishments). This finding suggests that the structural integrity of the UF is predictive of an individual’s reward processing behavior. UF FA has also been shown to predict a participant’s ability to delay gratification in a sample of children and adolescents (Olson et al., 2009). These reward-related findings may be attributable to the fact that the UF is a critical pathway connecting parts of the limbic system with the orbitofrontal cortex. Reward contingencies, like those leveraged in our study, have been shown to be encoded in the orbitofrontal cortex (Fellows, 2011), and to depend critically on the integrity of white matter projections from this region (Rudebeck et al., 2013). Given the role of the OFC in maintaining reward representation, it is reasonable to presume that that the OFC would be responsible for relaying that reward information to semantic processing regions within temporal lobe by way of the UF (Olson et al., 2015).

Despite the putative involvement of the UF pathway in reward-driven behavior, we did not find a significant correlation between UF integrity and Selectivity Index—our primary behavioral measure of the degree to which a participant's encoding efforts were optimized to maximize their accumulation of reward points given the total number of items they were able to recall. To the extent that Selectivity Index can be thought of as a marker of participants' reward sensitivity, the fact that this measure did not correlate with UF FA suggests that its role in our task paradigm was probably more related to enhancing the encoding of high value items via elaborative semantic encoding rather than adaptively regulating one's motivation to learn in accordance with item value. That said, individual differences in the Selectivity Index measure did show a significant correlation with the tract strength of a mesolimbic white matter pathway connecting a critical reward-related region of the ventral striatum (NAcc) with a dopamine-producing midbrain region (VTA). In other words, participants with a more robust NAcc-VTA pathway tended to be those individuals who were more selective in their encoding efforts. Selectivity Index increases across lists as participants experience limits in the amount of information that can be recalled on each list (Castel, 2008; Ariel and Castel, 2014). Those participants with stronger anatomical connections in this reward pathway may be more sensitive to feedback on recall performance across lists. These participants may prioritize the encoding of the highest value words given the number of words that can be recalled per list based on task experience—what they learned from performance on prior lists and awareness of their own memory capacity. In this way, mesolimbic reward circuitry may play a key role in the metacognitive ability of adjusting encoding strategy based on experienced recall ability.

Our finding that NAcc-VTA connectivity predicted participants’ selectivity on a value-directed remembering task accords well with prior research linking motivationally significant information to dopaminergic projections from tegmental areas to ventral striatal areas (Camara et al., 2009). Such processes allow for cognitive resources to be geared toward relevant information during memory encoding, as dictated by potential reward (Wittmann et al., 2005; Wittmann et al., 2008; for review, see Shohamy and Adcock, 2010).  In the current study, words preceded by a high value cue are much more indicative of a subsequent reward (i.e., accumulation of points) than their low value counterparts. In our analysis of fMRI data collected from these same participants (Cohen et al., 2014), we found significantly increased activity in both the NAcc and VTA during the encoding of high value versus low value items. Such engagement of the brain’s core reward circuitry supports the notion that point values, although not linked to monetary gain in our paradigm, were nonetheless processed as salient reward cues and used to modulate behavior (akin to the intrinsic reward value of point accumulation in many video games). The present DTI findings expand upon this result by showing that the robustness of the white matter pathway connecting these two regions is likely one important determinant of both how well, and how selectively, individuals will encode the high value words based on feedback across lists.

Taken together, our results suggest that when presented with a reward value-indicating cue, communication between the NAcc and VTA may act as a gating mechanism to determine if elaborative encoding processes, as facilitated by the UF, will be upregulated to preferentially bolster the encoding of the proceeding word. The UF may fulfill the additional role of facilitating information transmission across the OFC and temporal/limbic regions to continually update the association of a reward value with a word. The integrity of both of these circuits appears to be a critical determinant of behavioral performance in this task paradigm. Although we have been attributing the structural correlates of value-related memory modulation to effects that exert their influence during encoding, it is important to note the possibility that item reward values could impact retrieval dynamics as well. For example, Castel and colleagues (2013) found that people tend to recall higher value items first, which could be due to the fact that these items were most strongly encoded, but also could be a strategic operation to prevent the buildup of output interference from diminishing the accessibility of high value items. That said, we have reason to believe that the value effects in our study are predominantly indicative of processes engaged at the time of encoding. Post-experiment questionnaires revealed that all participants reported the use of verbal strategies during encoding to help them remember the words (Cohen et al., 2014). Moreover, a series of behavioral experiments using variants of this paradigm found evidence that providing participants feedback on their point totals at the conclusion of each study-test cycle (as was done in the present study) serves to guide learners' use of metacognitive control to more selectively employ encoding strategies that will promote later recollection of high reward value items (Cohen et al., 2017). Finally, fMRI measurement of brain activity levels during word encoding revealed strong effects of reward value and correlations with Selectivity Index across a number of regions associated with semantic and reward processing (Cohen et al., 2014).

Our findings should be interpreted with some caution given the relatively small size of our sample. Future studies with larger samples would be useful to both assess the replicability of our effects, as well as to explore the putative contributions of additional white matter pathways. Given our limited experimental power, we chose to focus our brain-behavior correlation analyses on a small number of pathways for which the literature provided a priori rationale to expect value-related effects. It would also be advantageous for future work to examine the degree to which individual differences in UF and NAcc-VTA integrity predict performance on a wider range of reward-incentive memory tasks. For instance, it is possible that the role of left UF is particularly pronounced for paradigms involving verbal stimuli, for which the use of elaborative semantic encoding strategies is most effective; paradigms using visual stimuli may not show such a structure-function relationship for this region. Finally, it will be interesting to explore whether the white matter pathways implicated in our study as predicting value-based memory effects in a sample of younger adults will show similar effects in older adults. Functional neuroimaging work comparing younger and older adults on this paradigm revealed that while both populations show elevated recruitment of the left-lateralized semantic network during the encoding of high value words, younger adults engage these regions—along with reward-related regions—more proactively than older adults (Cohen et al., 2016). Diffusion imaging could offer additional insights into the nature of age-related changes in value-directed remembering and individual differences that predict preserved memory selectivity.

## Figure Captions

**Figure 1.** Regions of interest. **A)** Left Uncinate Fasciculus (UF) overlaid on a standard T1-weighted template in MNI space. The UF was defined using a probabilistic white matter tractography atlas (Johns Hopkins University [JHU]; Mori et al., 2005). **B)** Left

inferior frontal occipital fasciculus (IFOF) ROI defined using the same procedure. **C)** Nucleus accumbens (NAcc) ROI, aligned to and overlaid on a representative subject's MPRAGE. The NAcc was defined using FreeSurfer's automatic subcortical segmentation routine on the T1-weighted structural image. **D)** Ventral tegmental area (VTA) ROI, aligned to and overlaid on a representative subject's MPRAGE. The VTA was defined using a probabilistic atlas of the human VTA (Murty et al., 2014) at a 50% threshold.

**Figure 2.** Scatter plots depicting the brain-behavior correlations focused on individual differences in mean fractional anisotropy (FA) within the uncinate fasciculus (UF) and metrics of memory recall performance. Correlations are plotted for the relationship of mean FA in **A)** L UF and **B)** R UF with mean number of high value words recalled. **C & D)** Same as A & B, but with mean recall for low value words. **E & F)** Same as A & B, but with each subject's mean Selectivity Index. * $p < 0.05$ (corrected) comparing the *r*-value to a one-tailed Student's *t*-distribution.

**Figure 3.** Correlation between NAcc-VTA tract strength and behavioral measures. The tract strength values represent the number of samples that reached the target ROI (VTA) when emanating from a seed ROI (NAcc), using a probabilistic tractography approach and normalizing for the number of samples sent out. The values shown here are standardized residuals controlling for ROI size in each subject. Correlations are plotted for the relationship of NAcc-VTA tract strength and **A)** the mean number of high value words recalled, **B)** mean number of low value words recalled, and **C)** Selectivity Index. * $p < 0.05$ (corrected) comparing the *r*-value to a one-tailed Student's *t*-distribution.

# Figures

**Figure 1. Regions of interest.**

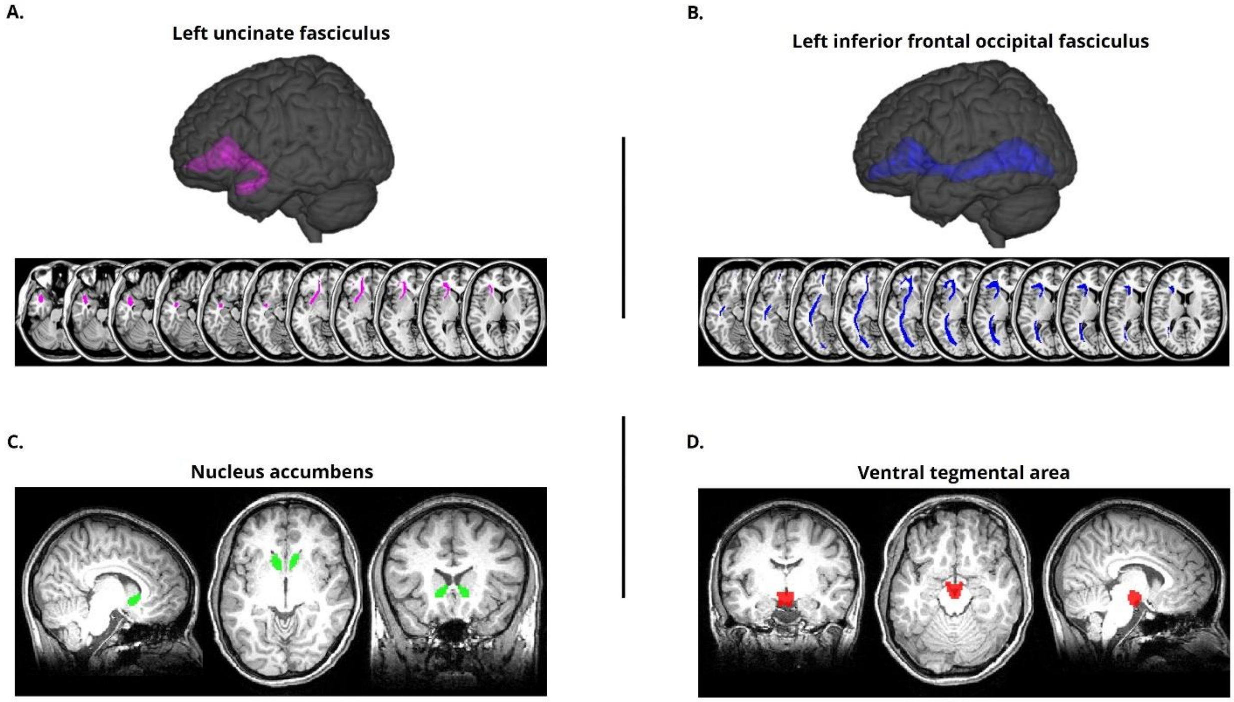


**Figure 2. Scatter plots depicting the brain-behavior correlations focused on individual differences in mean fractional anisotropy (FA) within the uncinate fasciculus (UF) and metrics of memory recall performance.**

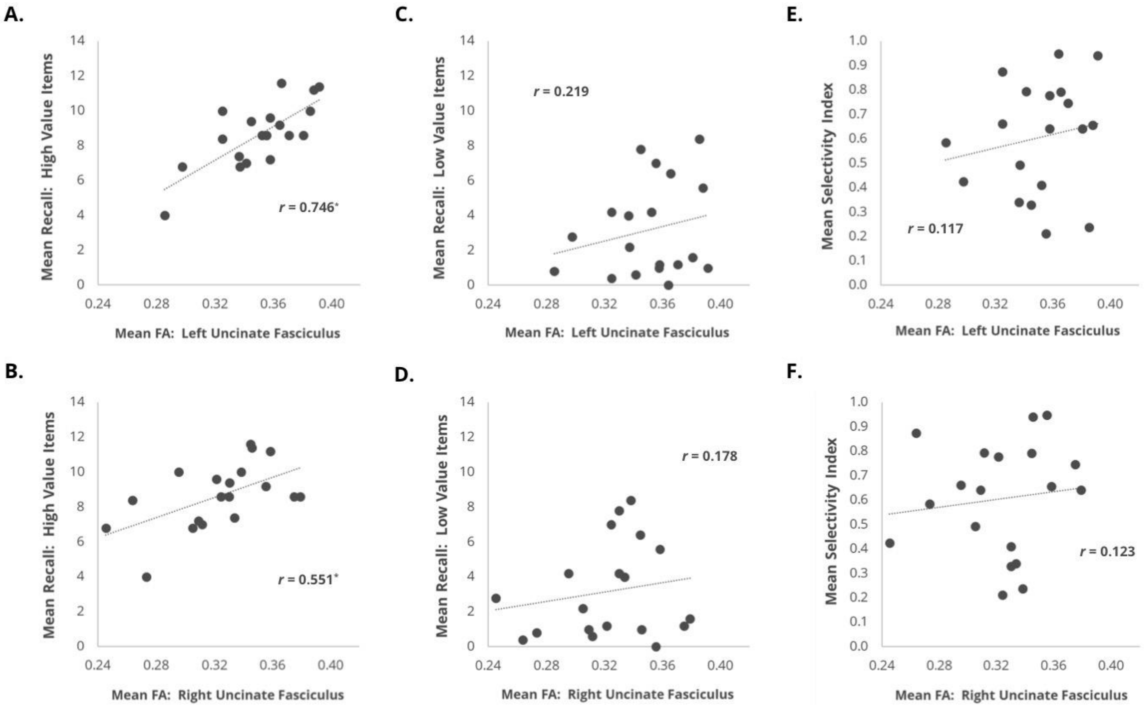
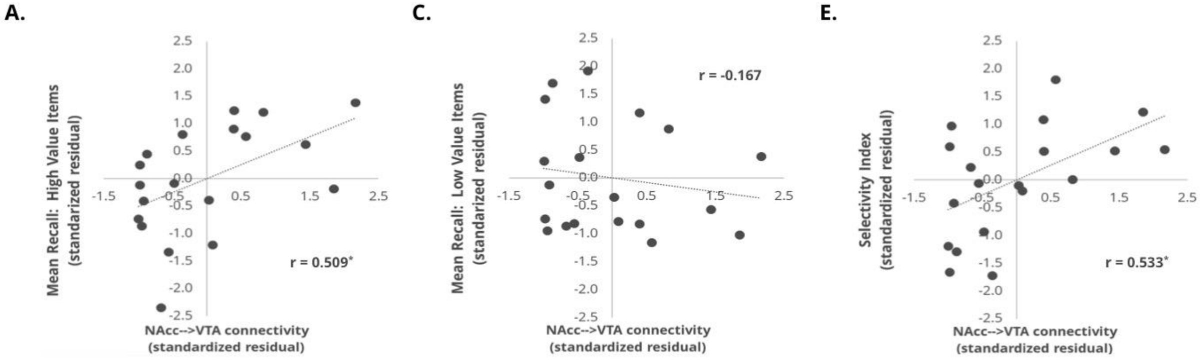


**Figure 3. Correlation between NAcc-VTA tract strength and behavioral measures.**



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# Chapter 2: Enhancing the ecological validity of fMRI memory research using virtual reality

## Abstract

Functional magnetic resonance imaging (fMRI) is a powerful research tool to understand the neural underpinnings of human memory. However, as memory is known to be context-dependent, differences in contexts between naturalistic settings and the MRI scanner environment may potentially confound neuroimaging findings. Virtual reality (VR) provides a unique opportunity to mitigate this issue by allowing memories to be formed and/or retrieved within immersive, navigable, multisensory contexts. This can enhance the ecological validity of task paradigms, while still ensuring that researchers maintain experimental control over critical aspects of the learning and testing experience. This mini-review surveys the growing body of fMRI studies that have incorporated VR to address critical questions about human memory. These studies have adopted a variety of approaches, including presenting research participants with VR experiences in the scanner, asking participants to retrieve information that they had previously acquired in a VR environment, or identifying neural correlates of behavioral metrics obtained through VR-based tasks performed outside the scanner. Although most such studies to date have focused on spatial or navigational memory, we also discuss the promise of VR in aiding other areas of memory research and facilitating research into clinical disorders.

## Introduction

Virtual reality (VR) is a term used to encompass any computer-generated experience that induces a sense of presence—the feeling of being transported to and inhabiting a place different from one's immediate surroundings (McCreery et al., 2013; Steuer, 1992). Given the intimate relationship between context and memory (Godden and Baddeley, 1975; Smith, 1988), VR provides a powerful means to enhance the ecological validity of memory research by providing realistic virtual environments (VEs) in which participants can learn information and/or draw upon past memories to guide their behavior. These VEs can be highly customized to meet the needs of a wide variety of tasks and offer experimental control over the learning experience. Given these characteristics, along with the recent surge in VR technological development and accessibility (Figure 1a), it is unsurprising that cognitive neuroscientists interested in the brain mechanisms of memory have increasingly found ways to incorporate VR into their fMRI studies.

Experimental designs employing VR and fMRI to study memory predominantly fall into three categories: 1) having participants actively engage in VR experiences in the scanner while functional neuroimaging data are acquired, 2) scanning participants as they are prompted to retrieve information previously acquired in a VE, and 3) identifying structural or functional correlates of behavioral metrics obtained through the use of VR (Figure 2). One virtue of VR as an experimental tool is its ability to enable the translation of research paradigms that have been used extensively in animal research, which may not otherwise translate readily to human participants for ethical or technical reasons. For example, a direct human analog of the Morris water maze—dropping a participant into a pool of cloudy water in the search of an invisible platform—would likely raise the ethical eyebrows of any Institutional Review Board, yet such a task paradigm can be implemented in VR. Likewise, VR empowers neuroscientists to create experiments that would either be impossible or impractical without the use of VR (e.g., imposing invisible boundaries, altering/morphing environmental features, or teleporting a participant between contexts).

Given the field’s increasing appreciation that different brain activation profiles tend to be evoked by the retrieval of memories for laboratory-encoded stimuli versus real-world events (Chen et al., 2017; Chow et al., 2018; Roediger and McDermott, 2013), researchers sometimes go to great lengths to increase the ecological validity of their tasks. For instance, wearable cameras can be used to capture photographs of participants’ real-world experiences so that memories for these events can later be probed in the scanner (Chow and Rissman, 2017). A related approach involves having participants engage in real-world navigation tasks. In one such study, Schinazi and Epstein (2010) created a 3km outdoor walking course for participants to traverse. Later, fMRI data were collected while participants were tested on their recollection for buildings encountered on the route. While the fMRI results revealed interesting effects within visuospatial processing regions such as the retrosplenial cortex, reflecting the interplay between landmark-identification and route direction at navigationally pertinent decision points, the authors acknowledged that their behavioral results were largely consistent with those of a similarly designed VR study by Janzen and Weststeijn (2007). A subsequent fMRI study then showed that comparable neuroimaging findings could be obtained used a VR-based route navigation task (Wegman and Janzen, 2011).

Although real-world task paradigms will continue to have value in memory research, VR paradigms have the potential to provide a less labor-intensive and more highly controlled investigational medium that sacrifices relatively little in terms of neural processing and experimental outcome.

While VR allows for precise control over stimuli and contexts, providing greater consistency across participants than can typically be attained in real-world designs, it is not without its caveats. Recently, there has been debate as to whether VR-based navigation should be considered true navigation (Minderer et al., 2016; Taube et al., 2013). One of the most crucial arguments against the fusion of VR and fMRI is that when lying in a scanner, vestibular self-motion (idiothetic) cues cannot match external landmark-based (allothetic) cues since otolith organs will persistently relay a signal that the individual is supine. Decoupling of cues can cause a reorientation (Wang and Spelke, 2002) and force one system into domination (Dolins and Mitchell, 2010; Golledge, 1998). Further adding to these complications, visual cues alone have proven insufficient to elicit accurate distance measurements (Witmer and Kline, 1998) and turn responses (Riecke et al., 2012), which can lead to impaired navigation. Meanwhile, on a neuronal level, the activity pattern of cells implicated in spatial representation, such as place cells, grid cells and head-direction cells (Buzsáki and Moser, 2013) have been shown to differ between real-world environments and VEs (Aghajan et al., 2015; Chen et al., 2013; Ravassard et al., 2013)

Nevertheless, the neural responses of spatially selective cells in VR resemble those observed in real navigation under certain circumstances (Aronov and Tank, 2014; Domnisoru et al., 2013; Killian and Buffalo, 2018). Additionally, VR navigation has been shown to maintain hippocampal theta rhythms (Ekstrom et al., 2005), albeit with some differences from real-world navigation (Aghajan et al., 2017; Bohbot et al., 2017; Jacobs, 2014). Various VR accessories, including head-mounted displays (HMD) can be used to increase participants' immersion (Figure 1a; Dede, 2009) and, subsequently, spatial understanding (Bowman and McMahan, 2007; Ruddle et al., 1997). Importantly, Ganesh et al. (2012) found that increasing participants' self-identification with an avatar resulted in increased engagement of left inferior parietal lobe regions associated with self-identification and improved recognition memory for traits associated with their avatar. Furthermore, brain activity patterns expressed during recall remain similar despite encoding in real-world vs. fictional environments (Spiers and Maguire, 2006). Even navigation through digital folders (Benn et al., 2015) and abstract conceptual space (Constantinescu et al., 2016) recruits similar brain structures and processes.

Given that the overarching goal of cognitive neuroscience research is to understand the brain mechanisms that give rise to our thoughts and behaviors, VR affords researchers with the ability to execute task paradigms that more closely mimic the way we use our cognition as we dynamically engage with our environment. This mini-review surveys the burgeoning neuroimaging literature on VR applications to memory research. In so doing, we hope to illustrate some creative ways in which researchers have leveraged VR to increase the ecological validity of memory experiments and conduct studies that would be relatively infeasible without the use of VR.

## Harnessing the Affordances of VR to Aid Memory Research

Although neural recordings from freely moving rodents have provided crucial insights into spatial memory functioning, ethical and physical limitations have prevented a direct replication of these studies in human participants. However, VR offers researchers boundless, safe, and controllable environments to conduct analogs of foundational experimental paradigms like the Morris water maze (MWM; Morris, 1984), radial arm maze (RAM; Olton et al., 1977), and random foraging tasks. Indeed, when combined with fMRI, VR has afforded researchers with the ability to quickly iterate manipulations of different MWM task features (e.g., distal vs. no cues; visible vs. invisible platforms) to determine hippocampal dependence (Kolarik et al., 2016; Shipman and Astur, 2008), identify compensatory mechanisms following scopolamine injection (Antonova et al., 2011), examine functional connectivity changes (Woolley et al., 2015), and investigate the different neural patterns recruited when using egocentric vs. allocentric navigation strategies (Rodriguez, 2010a). A research group even recently replicated their rodent body-behavior findings in humans using a VR version of the MWM (Müller et al., 2018).

Virtual variations of the RAM have equipped researchers to study working memory and decision-making in both win-shift (Demanuele et al., 2015) and win-stay (Cyr et al., 2016) paradigms. VR also allows for real-time changes to RAM and similar tasks. For instance, shuffling distal cues and providing visual navigational guidance (e.g., following arrows on the ground) has made it possible to disentangle cognitive decision-making from other processes of interest (Marsh et al., 2010). The ability to “teleport”, restrict access to certain areas with virtual “walls”, and track the precise location of the subject within the VE permit researchers to tease apart place-based and sequence-based strategies (Igloi et al., 2015). VR versions of the RAM were also used to assess the integrity of the hippocampus—predicting risk or severity in a variety of psychiatric disorders (Astur et al., 2005; Wilkins et al., 2017). Such insights are in line with the growing trend of using VR to provide objective diagnostic metrics (Cogné et al., 2017; van Bennekom et al., 2017). For instance, Migo et al. (2016) identified behavioral and neural correlates of completing the RAM task in patients with amnestic mild cognitive impairment (MCI), which extends upon the work of King et al. (2002) who showed that when changing virtual viewpoints, MCI patients could not recall the positions of objects. Similar spatial memory tests have been conducted on athletes following mild traumatic brain injury (Slobounov et al., 2010).

Given the expanse of possibilities afforded by VR, experimental paradigms can move beyond the replication of rodent studies. By familiarizing participants with a VE, experimenters can probe a participant's spatial memory by asking them to navigate from one location to another—a general paradigm that also can be used to test orientation, route-learning, and viewpoint-dependence (Brown et al., 2014; Dimsdale-Zucker et al., 2018; Stokes et al., 2015). Indeed, many such studies have used VEs to examine the neural correlates supporting navigation under different manipulations such as: using one landmark vs. many (Wegman et al., 2014), finding one's way vs. following a visible path (Hartley et al., 2003), relying on coarse vs. global strategies (Evensmoen et al., 2013), leveraging survey vs. route knowledge (Gillner and Mallot, 1998; Wolbers et al., 2004), tracking paths and distances (Chrastil et al., 2015; Wolbers et al., 2007), varying head directions (Shine et al., 2016), egocentric and/or allocentric related manipulations (Suthana et al., 2009; Wolbers et al., 2008), and navigating towards a goal in healthy (Brown et al., 2016; Rodriguez, 2010b) and clinical populations (Thomas et al., 2001). Embedding several such manipulations within a single VR study, Dhindsa and colleagues (2014) utilized fMRI to measure signal fluctuations as participants oriented themselves towards a learned location in a VE that lost critical features one-by-one. Their results provided empirical evidence in support of the Byrne et al. (2007) model of orientation and navigation, which emphasizes the translation of egocentric representations in parietal cortex to allocentric representations in the hippocampus. Furthermore, virtual renditions of familiarized real-world environments can allow researchers to probe memory for real-world objects using virtual cues—a technique previously used to examine the neural correlates of egocentric representations for objects outside of one's visual field (Schindler and Bartels, 2013).

The use of concurrent fMRI and VR also begets an opportunity to examine neural underpinnings of spatial information that is being encoded incidentally. For example, following periods of egocentric navigation, researchers can provide participants with a spatial memory test using a bird's eye view of the environment (Figure 1B)—a metric of allocentric memory that has been used to explain differences in navigational ability (Pine et al., 2002). Other examples come from fMRI studies looking for evidence of pattern separation and pattern completion processes (Yassa and Stark, 2011). By having participants complete the same relative distance task across different, but visually similar, environments, Kyle et al. (2015) found that the more distinguishable a neural representation is of an environment (i.e. successful pattern separation), the less the interference of competing memories will hinder performance. Relatedly, a human analog of the attractor dynamic model of mnemonic processing (Leutgeb et al., 2007) was demonstrated by Steemers et al. (2016): hippocampal responses to VEs that were constructed by linearly morphing two previously-known VEs exhibited nonlinear (sigmoid-like) response properties indicative of pattern completion, despite participants' behavioral reports that they consciously perceived linear morphs. By leveraging multivoxel pattern analysis in the hippocampus to decode a participant's location within a virtual environment, Hassabis et al. (2009) corroborated the classic function of hippocampal place cells (O'Keefe and Dostrovsky, 1971), albeit at a far less granular level. VR-based random foraging tasks have also been used to identify population-based grid-cell-like activity patterns in human entorhinal cortex (Doeller et al., 2010)—a measurement whose consistency over time could be prognostic of Alzheimer's Disease risk (Kunz et al., 2015)—and 3D place coding representations in human hippocampus (Kim et al., 2017).

VEs can also be utilized to systematically, and quantitatively, investigate processes that rely on imagined navigation. For example, Legge et al. (2012) familiarized participants with a VE that they were later instructed to use as a "memory palace" while they implemented the Method of Loci mnemonic strategy of mentally 'placing' a set to-be-remembered items along a route within an imagined environment. In this way, the authors matched the size, detail, and exposure time to the environment—properties that are often confounded in traditional implementations of this mnemonic technique (Yates, 1966). Further, the use of imagined virtual navigation has revealed fMRI signals that exhibit grid-cell-like properties (Bellmund et al., 2016; Horner et al., 2016) and activity patterns associated with location and facing direction (Marchette et al., 2014). Equalizing environments used for imagination tasks is particularly relevant in the domain of prospective memory (the ability to maintain a representation of intended tasks and execute them at the appropriate time and place). For instance, VR has recently been used in conjunction with high-resolution fMRI to index the degree to which specific goal and sub-goal locations are represented within hippocampal activity patterns during route planning, reflecting prospective coding of navigational intentions (Brown et al., 2016). Additionally, Kalpouzos and Eriksson (2013) familiarized participants to a VE and subsequently collected fMRI data while they mentally executed intended tasks within the imagined VE—a design that reduced variability in neural representation for environment.

Given that a time-course of fMRI activity can be collected during virtual navigation, it is possible to examine the different temporal phases of navigation behavior (Demanuele et al., 2015). Previous work has examined: planning vs. execution (Xu et al., 2010), encoding versus retrieval (Suthana et al., 2011), periods of object manipulation (Baumann et al., 2003a), and active vs. guided periods (Baumann et al., 2003b). Persson et al., (2013) measured hippocampal activity as participants navigated through a virtual maze and found that males and females show dissociable recruitment of left and right hippocampus during active navigation relative to orientation judgements made at maze end-points. Additionally, events that occur within VR (e.g., encountering another avatar who dispenses objects) can be dissociated from their visual scene context by using different approach routes (Burgess et al., 2001). Even metrics like memory for heading direction (Baumann and Mattingley, 2010) and environmental size/complexity (Baumann and Mattingley, 2013) can be investigated by examining fMRI activity levels at relevant task time points (e.g., when the participant is facing North; Figure 2A), without explicitly probing the participant.

In addition to navigation studies, VEs can be employed to study object-place associative memory. VR can be used to efficiently change the constellation of objects and their identities, with respect to locations within the VEs (e.g., shuffling object identities (Wong et al., 2014), modulating their saliency (Buchy et al., 2014), or altering the environment boundaries (Lee et al., 2016)). Object-place memory tasks have also shown that emotion is bound to places by examining how the co-occurrence of task-irrelevant emotional events alongside encoding can heighten subsequent retrieval activity (Chan et al., 2014)—extending findings that show place cells remapping once an environment becomes associated with fear (Moita et al., 2004). VR allows for object-place experiments to be conducted with high precision, immersion, and repeatability—a set of capabilities that make it particularly useful for obtaining diagnostic metrics in clinical populations (e.g., schizophrenia patients; Hawco et al., 2015).

Performance on VR-based tasks can also serve as a useful measuring instrument for examining factors outside of the learning experience that may affect behavior. For instance, Rauchs et al. (2008) investigated the neurocognitive effects of sleep deprivation on a series of virtual navigation tests. Researchers can also examine how fMRI signals measured in one setting (e.g., during resting fixation) might predict individual differences in performance on VR-based tasks performed outside the scanner. For example, Wong et al. (2014) identified patterns of resting-state activity and functional connectivity that correlated with participants' memory for objects that had been learned in a room-scale VE the day before. In another study, Wegman and Janzen (2011) scanned participants while passively viewing a route through a VE to identify brain regions associated with navigation-based decision points, later using the functional connectivity profile of those regions during resting-state to account for individual differences in spatial memory.

## Discussion

While fMRI has served as a powerful tool in human memory research, it requires participants to be placed in a context that is far from naturalistic—a potential confound for many memory studies. The inclusion of VR in fMRI memory investigations allows researchers to utilize immersive and navigable contexts for stimulus presentation both inside and outside the scanner (Figure 1a). Moreover, it affords researchers a medium in which to conduct experiments that is both replicable and controllable.

Facets unique to VR position it as an indispensable toolkit for specific types of investigations. For instance, creating invisible walls that restrict movement, but retain the visibility of distal cues would not be possible outside of a VE (Lee et al., 2016). Work by Bergouignan et al. (2014), which used VR to induce out-of-body experiences in the scanner while examining the role of perceiving the world from the perspective of one's own body for successful episodic encoding of real-life events, would not have been possible without the use of VR. The same concept applies to VR's ability to "blend" VEs (Steemers et al., 2016) or shift participants' perspective within the same VE (Sulpizio et al., 2016). Additionally, VR has the capacity to even the playing field in experiments that hinge on the use of imagination (e.g., Legge et al., 2012): it provides a common virtual space instead of relying on familiar real-world environments that could vary across individuals as a function of their pre-experimental exposure to the environment.

VR technologies can also bolster the ecological validity of fMRI for researchers and clinicians to obtain objective diagnostic metrics for patient populations (Cogné et al., 2017; King et al., 2002; Plancher et al., 2012; van Bennekom et al., 2017). With HMDs, cross-institutional collaboration can be facilitated as participants immersed in VR will not be cognizant of the real-world environmental cues. Such attributes are particularly advantageous for the examination of disorders that are highly context-dependent (e.g., post-traumatic stress disorder). For instance, researchers have utilized VR to induce context-specific fear-conditioning (Ewald et al., 2014; Huff et al., 2011; Tröger et al., 2012) and fear extinction (Ahs et al., 2015; Dunsmoor et al., 2014)—dramatically extending current treatment methods which often require therapy to occur in a context that is dissimilar from where the fear was acquired (for review see Bohil et al., 2011; Maples-Keller et al., 2017). Furthermore, compared to many real-world tasks, VR-based experimental techniques can be replicated in shorter time spans.

The utilization of VR in fMRI studies need not be daunting nor expensive; open-source software such as OpenSim (http://opensimulator.org) and equipment found in most scanner suites (Figure 1a), such as MR-compatible stereoscopic goggles and joysticks/joypads, make it increasingly accessible. Nonetheless, VR research is still in its infancy and not without limitations. Given the visual-vestibular disconnect of most setups, some participants may experience nausea and be unable to complete the study (Sharples et al., 2008). However, advances in HMD display technology are already helping to alleviate motion-sickness concerns. Devices that increase immersion through haptic feedback (e.g., Tesla Suit) and stationary locomotion (e.g., Omni Treadmill) or setups that create room-scale environments (e.g., cave automatic virtual environment; Figure 1a) afford researchers with the ability to employ encoding paradigms that increasingly resemble “real life” circumstances, making the neural correlates associated with the formation and recall of such memories more likely to generalize to real-world behaviors.

## Figure Captions

**Figure 1.** A) A limited showcase of currently available VR technologies. Devices are sorted as a function of their ability to provide the participant with a sense that they are "in" a virtual environment (immersiveness; y-axis) and the system's affordability (x-axis). "Window on World" refers to a traditional desktop and monitor setup. CAVE=cave automatic virtual environment—a real world room that leverages projectors, HMDs, and motion capture to create room-size virtual experiences. B) Examples of common perspectives presented to participants while actively navigating VEs or during spatial memory tests. Both first- and third-person viewpoints provide an egocentric perspective whereas a bird's eye view provides an allocentric one.

**Figure 2.** Examples of VR-fMRI experimental paradigms.

A) MR-compatible joysticks/gamepads and 3D stereoscopic goggles allow for participants to enter a VE while laying supine in the scanner. By time-locking events of interest (e.g., a participant's heading direction while traversing the world) to the corresponding fMRI signals, researchers can identify neural correlates associated with specific task conditions or behaviors. In this example, entorhinal cortex activity is associated with the grid-cell-like property of hexagonal symmetry during navigation. Figures adapted with permission from Doeller et al. (2010).

B) Participants can perform VR-based learning tasks outside of the scanner, and their memory for information encoded within a VE can later be tested in the scanner using traditional fMRI task paradigms. In this example, trials can be coded based on each object's properties within the VE (e.g., whether or not the object was located at a pertinent decision-point) to reveal incidental neural differences during retrieval as a function of the encoding experience. Figures adapted with permission from Janzen and Weststeijn (2007).

C) Just as questionnaires and computer tasks reveal individual differences in a host of behavioral metrics, VR can serve as an instrument to gather unique behavioral data points (e.g., number of times a participant revisited a particular location). Researchers can then examine whether these performance metrics can account for variance in brain activity or connectivity measured in a completely different context (e.g., while participants are simply resting in the scanner). Figures adapted with permission from Wong et al. (2014).

# Figures

Figure 1. VR systems as a function of Affordability and Immersiveness.

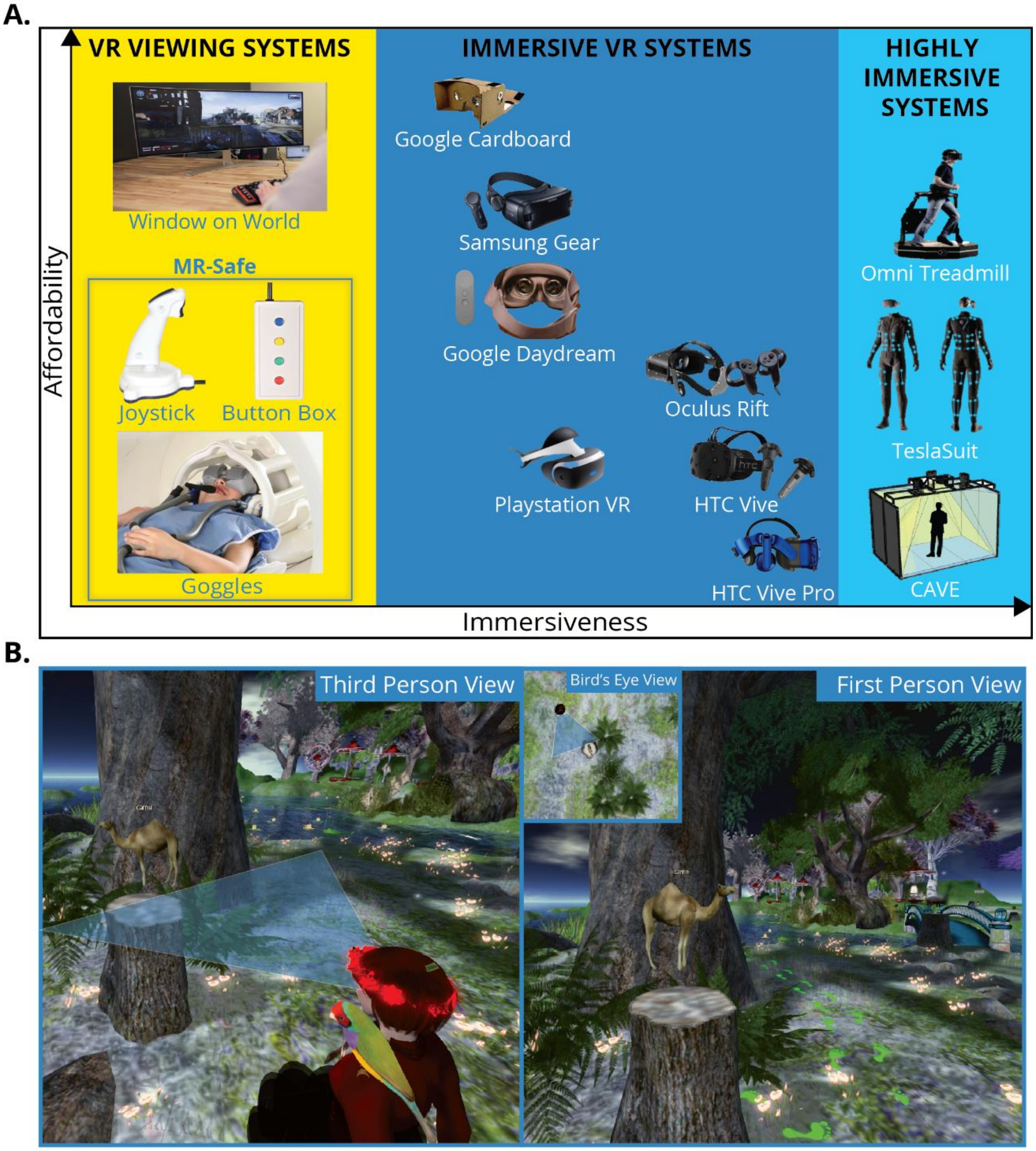
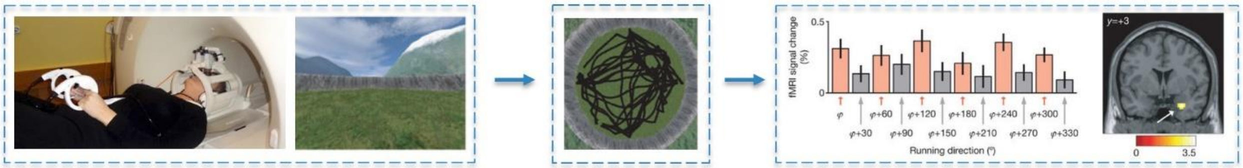


**Figure 2. Examples of VR-fMRI experimental paradigms.**

**A) Presenting participants with VR experiences in the scanner**

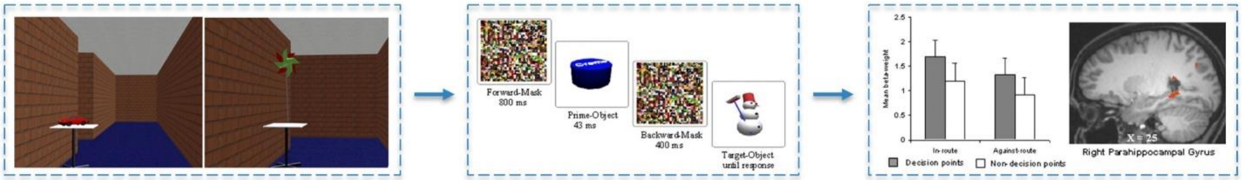


Participant navigates a VE and performs task using MR-compatible joypads and display

Behavior in the VE can be used to define timepoints of interest

Analyses reveal neural correlates supporting processes of interest

**B) Prompting participants to retrieve information previously acquired in a VE**



Prior to scanning, participants learn the location of objects within a VE

Participants perform an object recognition task in the scanner

Analyses unveil brain regions showing differential object recognition responses as a function of their location within the VE

**C) Identifying functional correlates of behavioral metrics obtained through VR**

Participant navigates a room-scale VE

Collect resting-state fMRI data from the participant

Analyses identify functionally connected nodes at rest that account for individual differences in VR-behavior

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# Chapter 3: The Method of Loci in virtual reality: Explicit binding of objects to spatial contexts enhances memory

## Abstract

The present study leverages novel virtual reality software to create a highly controllable rendition of the Method of Loci (MoL) technique. Specifically, we created three virtual environments where participants (n=60) could encode three lists of 15 objects, iteratively displayed for 20s as 3D renderings in front of their avatar. Our experimental group was given the additional functionality to click on the objects and “freeze” them—a phenomenon we argue explicitly binds the to-be-encoded object to the spatial scaffolding of the surrounding environment. We found that despite matched engagement, exposure, and performance expectations in the control group, participants in the experimental group recalled 25% more objects. We also observed a strong relationship between spatial memory for objects and landmarks in the environment with verbal recall strength—a finding that spanned across groups. These results provide evidence for spatially mediated processes underlying the effectiveness of the MoL and contributes to theoretical models of memory that emphasize spatial encoding as the primary currency of mnemonic function.

## Introduction

The Method of Loci (MoL), also commonly referred to as the Memory Palace technique, has long been appreciated as a highly effective and easily implementable mnemonic (Yates, 1966), with most users reporting it to be helpful and engaging (Qureshi et al., 2014). Indeed, empirical studies spanning several decades have reliably substantiated the centuries of anecdotal praise for the MoL’s effectiveness in bolstering mnemonic recall (Bower, 1970; Briggs et al., 1970; Crovitz, 1971; Dalgleish et al., 2013; McCabe, 2015; Roediger, 1980; Ross and Lawrence, 1968), with one observing a seven-fold increase in ordered recall over a rote rehearsal method (Bower, 1970). In light of such consistent efficacy, one would predict that the MoL is a complicated, time-consuming mnemonic. Conversely, the MoL is relatively simple to implement. Instructions are typically given as some minor deviation of the following:

> *Close your eyes and imagine yourself walking through a familiar location (e.g. your childhood home). Imagine an object that you'd like to remember and place it somewhere (e.g. on the front doorknob). Walk, in your mind's eye, to a new location and a place another to-be-remembered object in another location. When you want to remember the list of objects, simply retrace your path and observe the items in their placed locations.*

According to *De Oratore* by Marcus Cicero, the MoL was first formalized in 55 B.C.E by the Greek poet and orator Simonides de Ceos (Cicero and Wilkins, 1963). As the story goes, Simonides survived a tragic building collapse that killed all the members of a dinner party he was attending. While assisting the surviving family members who were trying to reclaim the unrecognizable bodies of their loved ones, Simonides was surprised by his incredibly accurate recall for the spatial arrangement of guests around the table. Simonides was regularly faced with the need to memorize long speeches. As such, he was motivated to understand the mechanisms behind his marked improvement in recall capacity. His conclusion was that since the information he was trying to recall was ordered along a spatial border (the table), it was easier to recall-- a notion perhaps best encapsulated by the following passage:

> *Noting that it was through his memory of the places at which the guests had been sitting that he had been able to identify the bodies, he realized that orderly arrangement is essential for good memory.* (Yates, 1966)

The MoL has recently witnessed a modern resurgence, initiated perhaps by the work of Joshua Foer— a freelance journalist who, while chronicling memory championships, discovered the MoL and used it, along with other mnemonic techniques, to win the 2006 U.S.A Memory Championship (Foer, 2011). Additionally, the crime drama television series, Sherlock, with over 12 million viewers, has also directly alluded to the method by way of the protagonist's creation of a "Mind Palace" (Hurran, 2014). Despite this historic and growing popularity, little is known about which aspects of the Method of Loci are most potent in providing its users with enhanced mnemonic recall. There has been no direct empirical evidence confirming Simonides' original theory.

In fact, there are several facets embedded in the MoL that could be responsible for its effectiveness in increasing recall. Since the traditional implementation of the MoL takes place within one's mental imagery, it stands to reason that the mnemonic could enhance memory by using the same mechanisms as pictorial strategies; text illustrations generally enhance learner's performance on a variety of cognitive outcomes (Levin, 1983). Some may argue that the technique is effective due predominantly to the parallel recruitment of neural processes supporting mental representation (Paivio, 1990 as in McCabe, 2015). Since implementers traditionally choose a familiar location to place objects, their memory increase could be due to their insertion of personal meaning into the information, a phenomenon known as the self-reference effect (Rogers et al., 1977). Additionally, the chosen environments could be embedded with personally relevant emotional contexts, which could heighten arousal and modulate memory consolidation (for review, see: Hamann, 2001). Furthermore, learning information from a first-person perspective could theoretically recruit autobiographical encoding processes. Given that autobiographical memory has a stark neurocognitive differences compared to memory for recently learned non-life related events (Chen et al., 2017), it could be that the MoL benefits from a parallel recruitment of such networks and upregulates encoding processes. Such translation to episodic memory would also explain the memory enhancement for lists detected when using mnemonics that leverage narratives (Herrmann et al., 1973) and the observation that narratives presented with a consistent point of view results in better comprehension and memory (Black et al., 1979).

In light of traditional psychological investigations on recall, it also stands to reason that the MoL could be creating a desirable difficulty (Bjork, 1994), which has been reliably shown to increase test performance (Pyc and Rawson, 2009). The "textbook" explanation seems to suggest that the effectiveness of the MoL could be due to the way it a) mandates an increase in effortful attention to the material and b) elaborates on the encoded information, increasing the stability of and increasing the breadth of the memory's engram (Bellezza, 1996). Yet another factor could be an increase of rumination time, which allows for to-be-remembered information to propagate throughout Long-Term Working Memory (developed by Ericsson and Kintsch, 1995). Case-studies of world-class memory champions (Hu et al., 2009) seem to corroborate this claim (Hu and Ericsson, 2012). However, a more recent case-study looked at the verbal reports of an individual who can recall 300 digits presented at 1 digit/s. Analysis revealed that the champion’s trick was to create associations between physical locations and the to-be-remembered information, allowing that information to be rapidly stored in Long Term Memory (Ericsson et al., 2017).

This latter most finding by Ericsson and colleagues (2017), that associations between information and a physical location were underlying a memory champion’s enhanced recall abilities, provides a particularly attractive explanatory variable for what makes the MoL so effective: the placement of information within a spatial environment. An emphasis on the spatial component within the MoL would certainly be true to form for Simonides’s original observation and the naming of the MoL; loci, plural of locus, are defined as particular positions—an object’s (or abstraction’s) location. This notion is empirically supported by a neuroimaging study by Kondo et al. (2005) which showed that brain areas traditionally involved in the processing of spatial information (e.g. parahippocamal gyrus and retrosplenial cortex) were recruited during recall after participants encoded information using the MoL. Additionally, functional neuroimaging has also revealed that memory champions, who most often report use a spatially based encoding strategy, recruit brain regions that support spatial memory (Maguire et al., 2003).

A framing of memory in terms of spatial processing in is line with evolutionary theories which posit that the creation of a mind was to engage in purposeful movement (Dennett, 1993; Llinás, 2001; Llinas and Ribary, 2001; Wolpert and Ghahramani, 2000) and the observation that the medial pallium, whose allocortex forms the hippocampal formation, evolved alongside hominid navigation into novel terrain (Jacobs, 2003). As such, the hippocampus, whose involvement in episodic recall is well documented (Rissman and

Wagner, 2012; Scoville and Milner, 1957; Squire, 1992; Squire and Zola, 1996; Tulving and Markowitsch, 1998; Vargha-Khadem et al., 1997), appears to have been originally intended for generating a cognitive map that allowed for purposeful movement (e.g. acquire resources, avoid danger) by providing a memory for one's own location and their relation to environmental stimuli (O'Keefe and Nadel, 1978). This notion is at least partially supported by the evolutionary timeline of the modern human's cortex. Hominids have utilized the encoding of verbal information to increase their fitness for, at maximum, 400,000 years (Aiello and Dunbar, 1993). Compared to archaeological evidence suggesting that bipedal locomotion over long distance in hominids began 3.6 million years ago (Stern Jr. Jack T. and Susman Randall L., 2005), it stands to reason that human memory for space, and the neural architecture that supports it (i.e. the medial temporal lobe), has an evolutionary prowess above that for all other forms and facets of memory.

Indeed, theoretical interpretations of empirical research on spatial navigation and memory emphasize the primacy of space for the encoding of information (for review see (Robin et al., 2018). Much like Scene Construction Theory (Hassabis and Maguire, 2007, 2009; Maguire and Mullally, 2013; Mullally and Maguire, 2014), this notion positions scenes as the primary currency of the hippocampus. In fact, the definition of autobiographical memory is always situated within a specific spatiotemporal context (Moscovitch et al., 2016; Tulving, 2002). This is perhaps most eloquently characterized by the finding that spatial information is recalled earlier in the retrieval process (Hebscher et al., 2017). Adding important evidence to the notion that spatial processes are inherently and subconsciously recruited for the encoding of information, Constantinescu et al. (2016)  unveiled that the manipulation of abstract information (i.e. creating conceptual relationships) elicits the same activity patterns exhibited by grid-cells, which are fundamental to purposeful navigation (Hafting et al., 2005). Relatedly, navigation through digital folders has been shown to recruit the same areas involved in real-world spatial navigation (Benn et al., 2015). While a full investigation into the fused function of the medial temporal lobe for the encoding of both spatial and episodic memory is beyond the scope of this article, it is important to note that, at minimum, spatial context has a dominant neural signature in the coding of events (Eichenbaum and Cohen, 2014) and that spatial cues lead to quicker and more detailed memories (Hebscher et al., 2017; Horner et al., 2016; Merriman et al., 2016; Robin et al., 2016).

Disentangling the inherently co-contributing factors of the MoL to determine which are most fundamental for the technique’s success would be immensely difficult if researchers instructed participants to rely on their mental imagery to implement the strategy. Not only are there notable individual differences in mental imagery ability (Cui et al., 2007; Kosslyn et al., 1984), but the amount of time physically spent in an environment, the aura of emotion those environments subconsciously carry, and the size and uniqueness of those environments all vary, in sometimes unquantifiable ways, across participants. As such, a controllable and operationalized investigation requires an experimental approach that does not mandate the use of mental imagery for encoding. Indeed, previous investigations have strategized to counteract individual differences by providing participants with standardized images or familiar nearby locations to use (Bower and Reitman, 1972; Kliegl et al., 1990; McCabe, 2015; Moè and

De Beni, 2005). While creative, such paradigms could theoretically eliminate some of the contributing variables of interest (e.g. volitional navigation).

In addition to the inability to ascribe an underlying cause behind the MoL using mental imagery, the use of effective mnemonic strategies is low (McCabe et al., 2013). Despite the well-intentioned endorsement of mnemonic improvement techniques being incorporated into curriculums (Balch, 2005; Carney and Levin, 1998; Shimamura, 1984), such instructions may end in vein; undergraduates often don’t implement the strategies they are academically familiar with (Susser and McCabe, 2013). This apparent mental barrier is quite noteworthy; even research subjects who receive explicit instructions to use the MoL have troubles complying (Legge et al., 2012). As if to even further de-motivate its adoption, most MoL studies report a need to have long training periods before the technique becomes effective (e.g. 4 to 6 hours of training in the study by (Brooks et al., 1993).

The present study positioned itself to simultaneously a) test the hypothesis that the binding of information to a spatial scaffolding underlies the effectiveness of the MoL and b) provide proof-of-concept for a user-friendly technology that mandates compliance in use of the MoL. The current investigation leverages Virtual reality (VR) to implement an operationalized rendition of the MoL. VR serves as a particularly viable medium for increasing the ecological validity of memory experiments in general (Chapter 2; Reggente et al., 2018) and allows for the control and capture of experimental details (e.g. exposure time and place of each seen object). Furthermore, by providing a novel and common set of environments for participants, this VR paradigm mitigates the concerns regarding individual differences in mental imagery, environmental size, complexity, and exposure time discussed above. Previous VR-based investigations by Legge et al. (2012) serve as the foundation for utilizing virtual environments for both implementing the MoL and increasing participant compliance.

Participants (n=60) in the current study viewed three lists of 15 objects, displayed iteratively for 20s as 3D objects in front of their avatar. Each object remained floating in front of the avatar until it was replaced by the subsequent object on the list. All participants freely navigated about an environment for the duration of that list's encoding before moving to the next environment and list. Participants were randomly assigned to one of two groups. The control group was briefed on a fictitious strategy dubbed "Walk and Learn" (WaL) that they were told enhanced memory by being active while encoding information in order to counteract any potential effects of anticipated task demands (Rummel and Meiser, 2013) or performance (Bandura, 1993; Martell and Willis, 1993). The experimental group was briefed on the traditional implementation of the MoL and told that this virtual rendition could serve to enhance their memory. If spatial representations are fundamental to episodic memory, altering the explicitness with which encoded information is bound to an encompassing spatial scaffold should alter recall strength. In order to test this notion, and simultaneously provide evidence that recruitment of spatial processes is the contributing factor to the effectiveness of the MoL, we sought to isolate, as much a possible, the spatial aspect of the MoL. To accomplish this, the MoL group was granted the additional functionality to click on an object and "freeze" it—a phenomenon that more explicitly binds the to-be-encoded object to the spatial scaffolding of the surrounding environment. In order to prevent an experimenter-driven direct association between objects and the environment during recall, subjects were told that each of the three lists were items that belonged to a fictional individual; during recall, participants were cued to recall the items belonging to each of the fictional individuals. In additional to verbal recall, participant's spatial memory for objects and landmarks within each environment was also tested and analysis examined the correlates of various spatial metrics with aspects of verbal recall performance.

## Methods

### *Participants*

67 participants were recruited for this study by way of posted flyers throughout the UCLA campus and listings on UCLA's online participant pool. Seven participants were unable to finish the study in its entirety due to technical issues (e.g. objects did not appear or did not render completely). As such, a total of 60 participants, aged 18-27 (M=21, SD=2.25; 30 females) participated in this study for either university credit or cash-payment (N=17).

Participants were required to be right-handed, have normal or corrected-to-normal vision and hearing, have a mastery of the English language, and report no diagnosed learning disabilities, substance dependencies, nor prescriptions for psychotropic medications. Additionally, to prevent unequal exposure to the experimental apparatus, applicants were not permitted to participate if they had more than five hours of previous experience with the VR software used in this experiment (Second Life [http://secondlife.com] or its open-source virtual simulator OpenSimulator [http://opensimulator.org]). Eligibility screening was conducted prior to the participant's enrollment in the study using the Research Electronic Data Capture (REDCap) online survey systems (Harris et al., 2009).

Participants were automatically assigned to one of two groups (MoL or WaL) based on gender and the order in which they were recruited for the study to ensure an even sampling of males and females within each group. The Institutional Review Board at UCLA approved all recruitment and testing procedures.

### *Materials*

All tasks were presented on a 27” LG Monitor (1600 x 900 (32bit)(60Hz) display) connected to a custom-built computer running a 64-bit Windows 7 Professional Operating System on an Intel® Core™ i7-3770K Central Processing Unit (CPU) @ 3.50 GHz (8 CPUs) with 32GB of Random Access Memory (RAM) and an AMD® Radeon Graphics Processor with 4GB of RAM.

All virtual environments were created using OpenSimulator (http://opensimulator.org; Release 0.9.0.0)—an open-source virtual simulator of Second Life (http://secondlife.com/) and viewed using the Firestorm Viewer (The Phoenix Firestorm Project, Inc; http://www.firestormviewer.org/; Release x64 5.0.7.52912). Screen recordings of participant activity were captured using FRAPS real-time video capture and benchmarking (Beepa Pty Ltd; https://www.fraps.com; v3.5.99) A total of five distinct virtual environments (VEs) were created for this study (“Toon World”, Ruin World”, “Lagoon World”, “Moon World”, and “Avatar Island”; Figure 1a). Despite being designed specifically to maximize distinctiveness, each VE that was used during encoding and encoding practice (all worlds except for Avatar Island) was created with the exact same dimensions (a 64 x 64 grid of accessible space) and was populated with eight distinct landmarks at the cardinal perimeter points (i.e. North, Northeast, East, etc.; Figure 1b).

Custom-coded software was created and “worn” by the participant’s avatar by way of two digital Heads Up Displays (HUDs). The first HUD rendered a count of collected and total tokens (Figure 2a) on the participant’s screen. A total of 20 tokens were available for participants to collect in each VE: coins in Toon World, rings in Ruin World, and seashells in Lagoon World (Figure 2a). All tokens were matched for color and size and scattered about each environment to ensure even exploration of the VEs. The release of these tokens was triggered by the experimenter via control desks located above the environments (Figure 2b). The control desk recorded the total time taken by the participant to collect all tokens in the environment.

The second HUD rendered a 3D object 1m in front of the participant’s avatar (Figure 3a), updating its position with each change in location and orientation until a participant clicked on the object-- at which point the object would freeze in place unless clicked again. The object’s name appeared above each object in small white text. The experimenter used a separate control desk to control which objects would render in which order and for how long during each encoding. This control desk recorded the precise location of each item in the environment (x,y coordinates) with a temporal resolution of 1s. A total pool of 60 3D open-source objects was gathered for this study from TurboSquid (https://www.turbosquid.com) and modified using Blender (https://www.blender.org). Objects were randomly sampled, without replacement, from this pool when creating the list of objects used for participant encoding. See

Supplemental Information Appendix 1 for a visual list of the objects used in this experiment.

Verbal recall tests were digitally recorded with participant permission and cued conversationally by experimenters. Spatial recall tests (Figure 4.) were conducted and analyzed using custom MATLAB (The Mathworks, Inc., 2012b) code and Psychophysics Toolbox (Version 3; Brainard, 1997), which allowed participant's to view a bird's eye view of the VEs and pinpoint their cursor to the cued location of landmarks, tokens, and objects they encountered. Finally, all statistical tests were conducted using custom R (R Core Team, 2013; http://www.R-PRoject.org/) and MATLAB code.

### *Procedure*

All participants were familiarized with our VR software by first visiting "Avatar Island" and practicing their use of a keyboard and mouse to navigate about and change their perspective in the VE. The experimenter allotted a maximum of five minutes for the participant to showcase their ability to execute directed action with their avatar (e.g. move forward, turn around). Participants remained in first-person view during this orientation and throughout the duration of the experiment.

Following orientation, participants were teleported in a random order to the Southern-most region of each VE used for encoding (Toon World, Lagoon World, Ruin World). Participants were instructed to navigate about each VE and "walk through" each token until all 20 were collected. Participants were given five minutes to collect the tokens and encouraged to explore the environment with any remaining time, taking care to note any landmarks. After visiting each of the three VEs once, participants were teleported back, again in a random order, to the same starting locations. This time, participants were instructed to collect the tokens as quickly as possible and given a maximum of three minutes to do so.

After completing the second-round of token collection, participants were given group-specific encoding instructions. Participants in both groups were informed that a series of 15 objects would iteratively render in front of their avatar for 30s each before disappearing. Prior to viewing each list of objects, participants were told that the objects they were about to see belonged to one of three fictional-individuals (Otto, Pike, or Viola) and that they would later be asked to recall the list of items belonging to that individual, in the order in which they were originally presented. Which objects were on each list, which fictional-individual was associated with that list, and the environment in which the list was encoded was randomized for each participant. All participants were encouraged to walk about the environment while viewing the objects; the objects would remain in front of the avatar regardless of movement and view. Participants assigned to the WaL group were fictitiously informed that they were employing a virtual rendition of "active learning"— presented as a well-documented memory enhancement procedure. Conversely, participants in the MoL group were briefed on the classic implementation and effectiveness of the MoL technique and told they would be employing the strategy using a suite of VR tools. Critically, MoL participants were given the additional instruction to click on the object and "freeze" it in a location of their choosing, allowing the participant the freedom to navigate away from the stationary object until its disappearance. Once clicked, the participant was given the freedom to click the object again and reactive its previous behavior of following the avatar's movements. For a complete transcript of each group’s instructions, see Supplemental Information Appendix 2.

After receiving instructions, but prior to encoding the lists of objects, participants were teleported to Moon World where they practiced the viewing and placement (for MoL participants) of three geometrical objects (sphere, cube, pyramid). Subsequently, participants encoded a total of three lists of 15 objects across the three encoding environments. Following this encoding period, participants viewed screen recordings of their movements about the environment for a total of 22.5minutes. These recordings served as rehearsal periods and presentation order was randomized for each participant. Immediately after rehearsal, participants were cued with a fictional-individual’s name and asked to verbally recall the appropriate list of objects in the order in which they were originally presented. Participants were given a maximum of two minutes and encouraged to recite as many objects as they could in the case that they could no longer retain a temporal order to their recall.  Following each recall attempt, the participant was asked to recall the same list of items, but in the reverse order—starting with the last item on the fictional-individual’s list and ending with the first. As with forward-recall, participants were allotted two minutes for reverse-recall and were informed they could recall items out of order if need be. Recall list order was randomized across participants.

As a final test, participants were submitted to a spatial memory task (Figure 4.) where they indicated the last seen (WaL) or placed (MoL) locations of each object. Specifically, participants used the computer mouse to direct a rectangular cursor and indicate the location of a cued object on a bird’s eye view of the encoding environment. Each object and its name was shown on a prompt screen before showing the full-screen map. After providing responses for each object encoded within a given environment, participants were asked to indicate the location of each landmark and then each token before moving on to the next environment. During the landmark portion of this spatial memory task, the map was stripped of its landmarks. During the token portion, participants were asked to indicate the location of each of the 20 tokens and shown the locations of each of their preceding choices. The presentation order of objects, landmarks, and environments for spatial tasks was randomized across participants. See Figure 5 for a visualization of the experimental procedure.

### *Behavioral Scoring*

Subjects' verbal recall was transcribed and scored by two separate experimenters and discrepancies were resolved by a third. All recall metrics are reported as the total words recalled across the three lists (45 total words). Recall strength was assessed using three metrics: number of words recalled ($\text{Recall}_{\text{total}}$ or $\text{Reverse-Recall}_{\text{total}}$), number of words recalled in the correct order (Clustering or Reverse-Clustering), and the number of words a subject recalled before making an error ($\text{Recall}_{\text{error}}$ or $\text{Reverse-Recall}_{\text{error}}$). $\text{Recall}_{\text{total}}$ was defined by the total number of words recalled before the time-limit by a participant—only counting words that actually belonged to the cued fictional individual. Clustering was calculated using a serial clustering metric, adjusted for chance, developed by (Stricker et al., 2002) and given by:

$$\text{Serial Clustering} = X - (r - 1)/N$$

where X is the total number of observed pairs of adjacent words in the recalled list that were also beside each other in the original presentation list, r is the total number of correct words recalled in the trial, and N is the total number of words presented in a list (N=15 in all calculations). The amount of serial clustering expected by chance during verbal recall is a fraction less than one, suggesting that serial clustering is not highly expected by chance. This serial clustering metric is reported as $\text{Clustering}_{\text{serial}}$. We also report a metric of clustering that is not corrected for chance and is calculated as the total number of correct pairs of adjacent words in the recalled list, referred to hereafter as $\text{Clustering}_{\text{simple}}$. Finally, $\text{Recall}_{\text{error}}$ was defined as the number of words recalled before an error was made where error is defines as either the recall of a word that was not on the list or the recall of a word that was on the list, but did not immediately follow the preceding recalled word.

Behavioral metrics from the spatial memory task were calculated as the average Euclidean distance between the coordinate vectors (x,y) for an object's actual placed (MoL) or last-seen (WaL) location in the environment and that indicated by the subject. A metric denoting the average proximity of objects to landmarks within an environment was calculated as the Euclidean distance between an object and its nearest landmark. Finally, a "base metric" for each participant's spatial memory was calculated as the difference in time taken to collect all the tokens throughout each environment from the first and second attempts. Given that token-collection was conducted before groups received encoding instructions, this measure should reflect an individual's baseline spatial memory.

### *Presence*

A six-question survey, developed by Slater and colleagues over the course of several investigations (Appendix 3; Slater, McCarthy, & Maringelli, 1998; Slater, Usoh, & Steed, 1994; Slater, Usoh, & Chrysanthou, 1995; Slater, Usoh, & Steed, 1995) was used as a measure of presence. A metric was calculated for each participant as the number of responses that were rated to be $\geq 6$ and is referred to hereafter as $\text{Presence}_{\text{Slater}}$. A separate ten-item, five-point scale questionnaire that was derived from multiple sources and was intended to quantify a participant's level of presence was also used (Appendix 4; Fox, Bailenson, & Binney, 2009). A metric was calculated for each participant as the average score across all ten items and is referred to in this manuscript as $\text{Presence}_{\text{Fox}}$. Both measures of presence were collected during a post experimental questionnaire using REDCAP (Harris et al., 2009). Finally, to assess the potential impact of environment on presence, subjects were asked to provide a ten-point scaling in response to the following question form for each world: "To what degree did you feel you were 'in' (Toon/Lagoon/Ruin) World as you moved around?"

### *Statistical Analyses*

Analyses were conducted using a one-way analysis of variance (ANOVA) whenever comparing means of two or more independent groups of data and the F-statistic is reported as well as its associated p-value. Significant p-values ($p<0.05$) were submitted to a follow-up test using a one-sample t-test and reported with a t-statistic and associated p-value. The strength and direction of associations between two continuous variables were conducted by computing Pearson's linear correlation coefficient (r) and p-values are reported from a t-test comparing that coefficient to the null hypothesis of no-relationship (i.e. 0). Direct comparisons between two correlations were conducted in the presence of a significant correlation within any group to determine if a) the groups differed as a function of their relationship to the metric of interest or b) one group was driving the effect observed across all participants. Significance of correlation comparisons was assessed using a two-tailed test for the difference between either two independent correlation coefficients (e.g. MoL free recall and MoL object-placement memory vs. WaL free recall and WaL object-placement memory) (Cohen and Cohen, 2003) or two dependent correlations with one variable in common (e.g. MoL free recall and MoL object-placement memory vs. MoL free recall and MoL coin collection time difference) (Steiger, 1980) using an online utility (http://quantpsy.org/corrtest/; (Lee and Preacher, K. J, 2013; Preacher, 2002). For analyses where multiple metrics were collected for each group (e.g. landmark-object proximity across worlds), a multivariate analysis of variance (MANOVA) was conducted and the F-statistic and Wilk's Λ are reported.

Finally, a stepwise linear regression was implemented to examine the impacts of additional variables on a linear model of group on recall metrics. Independent variables of interest were those that were either a) previously revealed a group difference(e.g. spatial memory) or b) of general interest due to supporting literature (e.g. gender). An analysis of deviance was conducted on the nested models to determine the most parsimonious model; F-statistics and associate p-values are reported and beta-coefficients were analyzed with a t-test.

## Results

### *Verbal Recall*

Participants assigned to the MoL group had an average $\text{Recall}_{\text{total}}$ score of 10.487 words compared to the $\text{Recall}_{\text{total}}$ of 8.2 words for participants in the WaL group; this difference was significant [F(1,58)=6.2, p=0.016]. The effect was stronger during Reverse-$\text{Recall}_{\text{total}}$ for participants assigned to MoL group recalled an average of 10.59 words compared to 7.923 by the WaL group [F(1,58)=7.35, p=0.009]. There was no effect of the three encoding environments on $\text{Recall}_{\text{total}}$ in the MoL group [F(2,89)=.13, p=.876] or WaL group [F(2,89)=.01, p=0.988]. The same was true for Reverse-$\text{Recall}_{\text{total}}$ in the MoL [F(2,89)=.02, p=.979] and WaL [F(2,89)=.04, p=0.959] groups. There was no group effect of $\text{Clustering}_{\text{serial}}$ [F(1,58)=1.04, p=.311] or $\text{Clustering}_{\text{simple}}$ [F(1,58)=1.62, p=.207] even though MoL participants had $\text{Clustering}_{\text{serial}}$ and $\text{Clustering}_{\text{simple}}$ scores of 4.57 and 5.323, respectively, compared to 3.7 and 4.133 for the WaL group. The same was true for Reverse-$\text{Clustering}_{\text{serial}}$ (MoL=14.5; WaL=15.43) [F(1,58)=1.04, p=.311] and $\text{Clustering}_{\text{simple}}$ (MoL=16.8; WaL=12.67) [F(1,58)=2.23, p=.14]. There was also no difference between groups in $\text{Recall}_{\text{error}}$ (MoL=3.522; WaL=3.477) [F(1,58)=0.0029, p=0.957] and Reverse-$\text{Recall}_{\text{error}}$ (MoL=1.944; WaL=1.623) [F(1,58)=0.23, p=0.633].

*Spatial Memory*

Participants took significantly less time to collect tokens on their second attempt in each world ($\text{Ruin}_{\text{run1}}$=121s, $\text{Ruin}_{\text{improvement}}$=32.697s, t(118)=-8.438, p<.001; $\text{Toon}_{\text{run1}}$=188.35s, $\text{Toon}_{\text{improvement}}$=55.183s, t(118)=-6.535, p<.001; $\text{Lagoon}_{\text{run1}}$=231.083s, $\text{Lagoon}_{\text{improvement}}$=77.066s, t(118)=-6.924, p<.001). There was a significant difference in improvement as a function of world [F(2,89)=8.57, p<0.001], driven by a significant difference between token-collection improvement in Lagoon and Ruin World (t(58)=-4.077, p<0.001). There was no effect of group in token-collection improvement in either

Ruin World (MoL=31.693s; WaL=33.7s)[F(1,59)=0.09, p=0.767], Toon World (MoL=66.767s ; WaL=43.6s)[F(1,58)=2.26, p=0.138], or Lagoon World (MoL=81.4s ; WaL=72.733s)[F(1,58)=0.18, p=0.67]—confirming that neither group had an inherently advantageous baseline spatial memory prior to encoding.

Participants assigned to the MoL group had a significantly lower average Euclidean distance between the locations they indicated they had placed an object vs. their actual locations (i.e. better spatial memory) compared to the WaL group, who indicated where they had last-seen each object (MoL= 13.596; WaL=23.176) [F(1,58)=26.15, p<0.001]. There was no group difference in spatial memory for Landmarks (MoL=20.32; WaL=24.05)[F(1,58)=1.88, p=0.176] or coins (MoL=3.782; WaL=3.82)[F(1,58)=.06, p=0.804].

Adding a participant's average object-placement error score to a linear model of group on $\text{Recall}_{\text{total}}$ significantly increased the model's explanatory power [F(56,2)=9.826, p<0.001]. The same effect was seen when Reverse-$\text{Recall}_{\text{total}}$ was used as the dependent variable [F(56,2)=11.697, p<0.001]. Object-placement error also increased the model's explanatory power when $\text{Clustering}_{\text{simple}}$ [F(56,2)=9.538,p<0.001], Reverse-$\text{Clustering}_{\text{simple}}$ [F(56,2)=7.73,p=0.001], $\text{Clustering}_{\text{serial}}$ [F(56,2)=7.591,p<0.001], Reverse-$\text{Clustering}_{\text{serial}}$ [F(56,2)=7.879,p<0.001], $\text{Recall}_{\text{error}}$ [F(56,2)=4.513,p=0.015], and Reverse-$\text{Recall}_{\text{error}}$ [F(56,2)=3.255,p=0.046] were used as the dependent variable.

### *Forward Verbal Recall vs. Spatial Memory*

There was a significant, negative correlation between $\text{Recall}_{\text{total}}$ and error on the object-placement task (r=-0.57, p<0.001). $\text{Recall}_{\text{total}}$ score was also significantly correlated with average Euclidean distance on the landmark-placement task (r=-0.566, p<0.001). The same relationship was seen between $\text{Recall}_{\text{total}}$ and coin-placement task performance (r=-.383, p=0.003). Participant performance on the object-placement task also had a strong relationship with $\text{Clustering}_{\text{serial}}$ (r=-0.453, p<0.001), $\text{Clustering}_{\text{simple}}$ (r=-0.486, p<0.001), and $\text{Recall}_{\text{error}}$ (r=-0.295, p=0.022). Clustering was also related to participant performance on the landmark-placement task ($\text{Clustering}_{\text{serial}}$: r=-0.393, p=0.002; $\text{Clustering}_{\text{simple}}$: r=-0.427, p<0.001), but not the coin-placement task ($\text{Clustering}_{\text{serial}}$: r=-0.178, p=0.173; $\text{Clustering}_{\text{simple}}$: r=-0.207, p=0.112). $\text{Recall}_{\text{error}}$ was also related to performance on the landmark-placement task (r=-0.27, p=0.037), but not the coin-placement task (r=-0.223, p=0.087). A participant's baseline spatial memory (difference in token-collection times across attempts) showed no relationship with $\text{Recall}_{\text{total}}$ (r=0.081, p=0.537), $\text{Clustering}_{\text{serial}}$ (r=0.084, p=0.525) or $\text{Clustering}_{\text{simple}}$ (r=0.082, p=0.536), or $\text{Recall}_{\text{error}}$ (r=0.061, p=0.642).

### *Forward Verbal Recall vs. Spatial Memory (Within Group)*

Participants assigned to the MoL group showed a strong relationship between $\text{Recall}_{\text{total}}$ and error on the object-placement task (r=-0.572, p<0.001); this relationship was not any stronger than that observed across all participants (z=0.013,p=0.989). Participants assigned to the WaL group also showed a significant negative correlation between $\text{Recall}_{\text{total}}$ and error on the object-placement task (r=-0.449, p=0.013) that did not differ from the correlation using all subjects (z=-0.715, p=0.475) or the correlation using only MoL subjects (z=-.614, p=.54). Within MoL participants only, the relationship between $\text{Recall}_{\text{total}}$ and spatial error on the landmark-placement task was stronger (r=-0.655, p<.001), but not significantly, compared to the correlation using all subjects (z=-0.609, p=.542). WaL participants also showed a significant relationship between $\text{Recall}_{\text{total}}$ and landmark-placement performance (r=-0.452, p=0.012), but no difference from the correlation using all subjects (z=0.661, p=.508). The difference in correlations between MoL and WaL participants was not significant (z=-1.09, p=.275). Performance on the coin-placement task was significant in its relation to $\text{Recall}_{\text{total}}$ by the MoL group (r=-.437, p=0.016), but not the WaL group (r=-0.353, p=.056). However, the difference in these correlations was not significant (z=-0.366, p=0.714) and the correlation calculated using all subjects was no different than when relying only on MoL (z=-0.278, p=0.781) or WaL (z=0.149, p=0.882) participants.

MoL group participants' performance on the object-placement task correlated strongly with their $\text{Clustering}_{\text{serial}}$ (r=-0.618, p<0.001) and $\text{Clustering}_{\text{simple}}$ (r=-0.639, p<.001), but not more than that observed across all subjects (serial z=0.999, p=0.318; simple z=1.147, p=0.251). Within the WaL group, there was no relationship between the object-placement task and $\text{Clustering}_{\text{serial}}$ (r=-0.34, p=0.066) or $\text{Clustering}_{\text{simple}}$ (r=-0.36, p=0.05). Despite this difference, the WaL group's relationship between Clustering and object-placement scores did not differ significantly from that of the entire group ($\text{Clustering}_{\text{serial}}$: z=-0.575, p=0.562; $\text{Clustering}_{\text{simple}}$: z=-0.478, p=0.633); nor with that of the MoL group ($\text{Clustering}_{\text{serial}}$: z=-1.55, p=0.13; $\text{Clustering}_{\text{simple}}$: z=-0.867, p=0.386). Performance on the landmark-placement task was related to $\text{Clustering}_{\text{serial}}$ in the MoL group (r=-0.403, p=0.027) and the WaL group (r=-0.369, p=0.045) as well as $\text{Clustering}_{\text{simple}}$ (MoL: r=-0.454, p=0.012; WaL: r=-0.373, p=0.043). This difference in groups was not significant ($\text{Clustering}_{\text{serial}}$: z=-0.147, p=0.883; $\text{Clustering}_{\text{simple}}$: z=-0.359, p=0.719) and neither group differed from the correlation using all participants

(Clustering$_{serial}$: MoL: z=-0.051 p=0.959; WaL: z=0.12, p=0.904; Clustering$_{simple}$: MoL: z=-0.143, p=0.886; WaL: z=0.275, p=0.783). Performance on the coin-placement task was not significant in its relationship to Clustering (Clustering$_{serial}$: MoL: r=-0.084, p=0.661; WaL: r=-0.2578, p=0.169; Clustering$_{simple}$: MoL: r=-0.136, p=0.475; WaL: r=-0.266, p=0.155).

There was no relationship between performance on the object-placement task and Recall$_{error}$ in the WaL group(r=-0.236, p=0.21), but a significant relationship did exist for the MoL group (r=-0.521, p=0.003). However, this difference in correlations was not significant (z=-1.239, p=0.215), nor did each group differ from the observation when using all participants (MoL: z=-1.71, p=0.241; WaL: z=0.272, p=0.786). Participant's performance on the landmark-placement task showed no relationship to Recall$_{error}$ in neither the MoL (r=-0.291, p=0.119) nor WaL (r=-0.26, p=0.165) groups. Performance on coin-placement task had no relationship with Recall$_{error}$ in neither the MoL(-0.16, p=0.399) nor WaL (r=-0.274, p=0.142) groups.

There was also no significant relationship between MoL participants' baseline spatial memory and Recall$_{total}$ (r=0.106, p=0.578), Clustering (Clustering$_{serial}$: r=0.01, p=0.961; Clustering$_{simple}$: r=0.019, p=0.922), and Recall$_{error}$ (r=-0.06, p=0.754). The same pattern was observed in WaL participants: Recall$_{total}$ (r=0.183, p=0.334), Clustering (Clustering$_{serial}$: r=0.232, p=0.218; Clustering$_{simple}$: r=0.228, p=0.227), and Recall$_{error}$ (r=0.203, p=0.283).

### *Reverse Verbal Recall vs. Spatial Memory*

Reverse-Recall$_{total}$ showed a highly significant relationship with performance on the object-placement (r=-0.61, p<.001), landmark-placement (r=-0.592, p<.001), and coin-placement (r=-0.337, p=0.009), but not baseline spatial memory (r=0.075, p=0.571). Reverse-Clustering$_{serial}$ showed a significant relationship with performance on the object-placement (r=-0.35, p=0.007) and landmark-placement (r=-0.41, p=0.001) tasks, but not with coin-placement (r=-0.187, p=0.153) or baseline spatial memory (r=0.084, p=0.525). Reverse-Clustering$_{simple}$ had a relationship with performance on the object-placement (r=-0.463, p<0.001) and landmark-placement (r=-0.425, p<0.001) tasks, but not with the coin-placement task (r=-0.172, p=0.19) or baseline spatial memory (r=0.007, p=0.959). Reverse-Recall$_{error}$ was significantly related to a participant's performance on the object-placement (r=-0.3, p=0.02) and landmark-placement (r=-0.338, p=0.008) tasks, but not with the coin-placement task (r=-0.17, p=0.193) or baseline spatial memory (r=0.058, p=-.658).

### *Reverse Verbal Recall vs. Spatial Memory (Within Group)*

Reverse-Recall$_{total}$ had a significant relationship with performance on the object-placement task for participants assigned to the MoL (r=-0.576, p<0.001) and WaL (r=-0.516, p=0.004), with no difference in strength across groups (z=-0.314, p=0.753) or compared to the relationship across all participants (MoL: z=0.225, p=0.822; WaL: z=0.591, p=0.555). Reverse- Recall$_{total}$ also had a relationship with performance on the landmark-placement task for participants in the MoL group (r=-0.721, p<.001) and the WaL group (r=-0.456, p=0.011), but despite this difference in correlations was not significant (z=-1.53, p=0.125) and neither group's correlation differed from the correlation observed when using all participants (MoL: z=-0.98, p=0.327; WaL: z=0.807, p=0.42). Reverse- Recall$_{\text{total}}$ did not share a significant relationship with performance on the coin-placement task for participants in the MoL group (r=-0.292, p=0.119), but did show one for the WaL group (r=-0.395, p=0.031); the difference in correlations was not significant across groups (z=0.43, p=0.667) or compared to the relationship identified when using all participants (MoL: z=0.214, p=0.831; WaL: z=-0.287, p=0.774).

Reverse-Clustering$_{\text{serial}}$ was related to performance on the object-placement task for participants in the MoL (r=-0.552, p=0.002) and WaL (r=-0.37, p=0.045) groups; these relationships were not significantly different (z=-0.855, p=0.392) and did not differ from the result observed when using all participants (MoL: z=1.095, p=0.274; WaL: z=0.098, p=0.922). The finding was slightly different when comparing Reverse-Clustering$_{\text{simple}}$ to object-placement performance: participants assigned to the MoL group showed a relationship (r=-0.571, p<0.001), but one was not observed in the WaL group (r=-0.326, p=0.079). However, this difference in correlations was not significant (z=1.141, p=0.254) and neither differed from the statistic observed when using all participants (MoL: z=0.633, p=0.527; WaL: z=-0.697, p=0.486). Performance on the landmark-task was significantly correlated with Reverse-Clustering for MoL participants (Reverse-Clustering$_{\text{serial}}$: r=-0.55, p=0.002; Reverse-Clustering$_{\text{simple}}$: r=-0.578, p<0.001), but not WaL participants (Reverse-Clustering$_{\text{serial}}$:: r=-0.303, p=0.103; Reverse-Clustering$_{\text{simple}}$: r=-0.245, p=0.193); this difference in correlations was not significant (Reverse-Clustering$_{\text{serial}}$: z=1.123, p=0.262; Reverse-Clustering$_{\text{simple}}$: z=1.504, p=0.133) and neither group statistic was different than that observed when relying on all participants (Reverse-Clustering$_{\text{serial}}$: MoL: z=0.782, p=0.434; WaL: z=-0.526, p=0.599; Reverse-Clustering$_{\text{simple}}$: MoL: z=0.88, p=0.379; WaL: z=-0.872, p=0.383). There was no significant relationship between performance on the coin-placement task and Reverse-Clustering in either group (Reverse-Clustering$_{serial}$: MoL: r=-0.213, p=0.258; WaL: -0.165, p=0.385; Reverse-Clustering$_{simple}$: MoL: r=-0.243, p=0.196; WaL: -0.095, p=0.617).

Reverse-Recall$_{error}$ was not significantly related to performance on the object-placement task for participants assigned to the MoL (r=-0.318, p=0.086) or WaL (r=-0.325, p=0.08) groups. Performance on the landmark-placement task was significantly related to Reverse-Recall$_{error}$ for MoL participants (r=-0.527, p=0.003), but not WaL participants (r=-0.215, p=0.254). Despite this difference, the correlations did not vary significantly (z=1.351, p=0.177), nor did either differ from the statistic observed when relying on all participants (MoL: z=1.002, p=0.316 ; WaL: z=-0.571, p=0.568). Performance on the coin-placement task did not correlate with Reverse-Recall$_{error}$ in either the MoL (r=-0.017, p=0.929) or WaL (r=-0.277, p=0.139) group.

Baseline spatial memory was not related to Reverse-Recall$_{total}$ for either MoL (r=0.085, p=0.657) or WaL (r=0.204, p=0.28) participants. There was also no relationship between Reverse-Clustering and baseline spatial memory (Reverse-Clustering$_{serial}$: MoL: r=-0.024, p=0.9; WaL: r=0.142, p=0.453; Reverse-Clustering$_{simple}$: MoL: r=-0.011, p=0.953; WaL: r=0.106, p=0.579). Reverse-Recall$_{error}$ had no relationship with baseline spatial memory (MoL: r=0.078, p=0.681; WaL: r=0.068, p=0.72).

### *Object-Landmark Proximity*

MoL participants placed objects closer to landmarks depending on encoding environment [F(2,89)=44.91, p<0.001]. This observation was driven by a marked average decrease in an object's Euclidean distance to the nearest landmark in Ruin (7.923) compared to Toon (15.454; t(58)=7.53, p<0.001) and Lagoon (12.389; t(58)=4.467, p<0.001); the difference between Toon and Lagoon was also significant (t(58)=3.065, p<0.001). WaL participants also varied in the proximity of where they had last seen objects to the nearest landmark [F(2,89)=66.42, p<0.001]. Again, the effect was due to a closer proximity of objects to landmarks in Ruin (8.52) compared to Toon (15.188; t(58)=6.668, p<0.001) and Lagoon(12.085; t(58)=3.566, p<0.001); the difference between Toon and Lagoon was also significant (t(58)=3.103, p<0.001). A MANOVA revealed no difference in proximity of objects to landmarks between the MoL and WaL groups [F(2,57) = 13.74, p=0.436; Wilk's Λ = 0.971].

MoL participants' $\text{Recall}_{\text{total}}$ showed no relationship to object-landmark proximity (r=-0.01, p=0.958). Neither did WaL subjects, although a trend was observed (r=0.359, p=0.051). The same was true for $\text{Reverse-Recall}_{\text{total}}$ (MoL: r=-0.088, p=0.645; WaL: r=0.3, p=0.107). No relationship with object-landmark proximity was seen in $\text{Clustering}_{\text{simple}}$ (MoL: r=-0.071, p=0.71; WaL: r=0.346, p=0.061), $\text{Clustering}_{\text{serial}}$ (MoL: r=-0.063, p=0.742; WaL: r=0.337, p=0.069), $\text{Reverse-Clustering}_{\text{simple}}$ (MoL: r=-0.153, p=0.421; WaL: r=0.165, p=0.384), or $\text{Reverse-Clustering}_{\text{serial}}$ (MoL: r=-0.152, p=0.423; WaL: r=0.169, p=0.373). While MoL participants showed no relationship between object-landmark proximity and $\text{Recall}_{\text{error}}$ (MoL: r=-0.066, p=0.727), WaL subject did (r=0.388, p=0.034); however, neither group showed an object-landmark correlation with $\text{Reverse-Recall}_{\text{error}}$ (MoL: r=-0.226, p=0.229; WaL: r=0.216, p=0.252).

### *Effect of Gender*

Adding a participant's gender to a linear model of group and object-placement spatial memory on $\text{Recall}_{\text{total}}$ significantly increased the model's explanatory power [F(52,4)=4.292, p=0.005]. Upon further examination, the interaction term representing object-placement spatial memory and gender was the only significant coefficient [t(58) = -2.486, p = 0.016]. When $\text{Reverse-Recall}_{\text{total}}$ was the dependent variable, the same increase in explanatory power due to gender was observed [F(52,4)=4.969, p=0.002]. In this case, both object-placement spatial memory and its interaction with gender had significant coefficients [object-placement: t(58)=2.037, p=0.047: placement x gender interaction: t(58)=-2.444, p=0.018]. No other recall metrics, when used as the dependent variable, had their variance explained further by the inclusion of gender in the model: $\text{Clustering}_{\text{simple}}$ [F(52,4)=1.347,p=0.265]; $\text{Reverse-Clustering}_{\text{simple}}$ [F(52,4)=1.216,p=0.315]; $\text{Clustering}_{\text{serial}}$ [F(52,4)=1.678,p=0.336]; $\text{Reverse-Clustering}_{\text{serial}}$ [F(52,4)=1.034,p=0.399]; $\text{Recall}_{\text{error}}$ [F(52,4)=0.763,p=0.554]; $\text{Reverse-Recall}_{\text{error}}$ [F(52,4)=0.842,p=0.505].

*Effect of Presence*

A participant's $\text{Presence}_{\text{Slater}}$ showed no relationship to $\text{Recall}_{\text{total}}$ (r=0.127, p=0.335) and a participant's group assignment played no role in their score [F(1,58)=1.24, p=0.27]. $\text{Presence}_{\text{Fox}}$ also showed no relationship with $\text{Recall}_{\text{total}}$ (r=0.092, p=0.487) and no effect of group [F(1,58)=0.03, p=0.864]. In response to the questions "To what degree did you feel you were 'in' (Toon/Lagoon/Ruin) World as you moved around?", participants indicated equal immersion across all encoding environments [F(2,177)=0.82, p=0.441]; there was no effect of group.

*Post-Experimental Questionnaire*

When asked how confident they were regarding their performance on a fictional ordered recall test the following day, participants in the MoL group had higher confidence compared to WaL participants [F(1,54)=5.12,p=0.028]. This group effect went away when subjects were asked about their confidence in a fictional recall test one week later [F(1,58)=3.12, p=0.082] or one month later [F(1,57)=1.05, p=0.309].

Participants indicated whether or not they had heard of the Method of Loci / Memory palace technique before taking part in this study. Previous exposure to the technique played no role in determining participant's $\text{Recall}_{\text{total}}$ [F(2,57)=0.14, p=0.871].

## Discussion

### *Study summary*

This study presents the first utilization of VR software to implement the MoL. Similar to Legge et al. (2012), participants were able to leverage standardized virtual environments as their "memory palaces", eliminating the confounding and unquantifiability aspect of relying on mental imagery to execute the mnemonic. Additionally, the current paradigm provided participants with functionality to actually encode lists within the virtual environments by continually rendering 3D objects in front of their avatar as they navigated about the virtual environments. Importantly, this technology all but enforced compliance in implanting the intended technique—an issue that has plagued previous studies (Legge et al., 2012).

With the precise experimental control afforded by the technology employed, this study sought to disentangle the various facets that could theoretically contribute to the efficacy of the MoL. Specifically, it was tested whether or not the explicit binding of objects to the spatial environment was a major contributing factor to the MoL's ability to reliably increase memory strength. To accomplish this, participants were assigned to one of two groups: WaLand MoL. Participants across both groups were matched for exposure duration, encoding environments, and gender balance. The authors fictitiously informed participants assigned to the WaL group that they were utilizing a proven memory enhancement to counteract any potential effects of anticipated task demands (Rummel and Meiser, 2013) or performance (Bandura, 1993; Martell and Willis, 1993) that could be interpreted as the success of MoL participants who were briefed on the efficacy of the MoL. Apart from these instructions, the only difference between the groups was that MoL participants were given the ability to click on an object at any point during their navigation about the environment. This click would "freeze" the object in place until the exposure duration was completed and a new object appeared in front of their avatar. To avoid explicit reactivation of the encoding context during recall, the experimenter cued the participant with the name of a fictional-individual to whom the objects were purported to belong. Finally, all participants were subjected to additional testing of their spatial memory to acquire metrics of baseline and encoding-specific egocentric and allocentric memory to examine the relationship across individual differences to list-recall strength.

### *Summary of findings*

Despite encoding information in a pictorial, contextually rich, and active fashion, participants in the WaL group recalled 27.8% less objects than their MoL counterparts who more explicitly bound the to-be-encoded information to the spatial scaffolding of the virtual environments. It is worth noting that MoL participants had the possibility to view the item for a decreased period of time given that they were permitted to face the other direction from the object or walk away from it entirely after placement—a possibility not extended to the WaL group. The finding of a significant effect in light of such a potential occurrence strengthens confidence in this observed effect, as does the observation that the effect of recall was even stronger when participants were cued to recall in the reverse order. Participants in the MoL group also showed better spatial memory for the location of objects within the environments. However, the relationship between individual differences in recall and the object-placement task within the MoL group was no stronger than that observed in the WaL group, suggesting that the effect of remembering where an object was in the environment is intimately related to the memory of the object itself, independent of group. This interpretation is strengthened by our finding that adding a participant's object-placement score to a linear model group on recall significantly improved its explanatory power.

Since the MoL has traditionally been applauded for its ability to increase ordered recall, it is initially surprising that despite quantifiable increases in ordered recall for MoL participants, there was no significant effect of ordered recall from the start of recall ($\text{Recall}_{\text{error}}$) or throughout any phase of recall ($\text{Clustering}_{\text{simple}}$ and $\text{Clustering}_{\text{serial}}$). Typically, a high serial clustering score is indicative of above-average rote recall (Fisher and Deluca, 1997; Harnadek and Rourke, 1994), due mostly to the forging of associated between words during an imagery or directed-association strategy. It could stand to reason that the remaining factors that were shared across both groups (e.g. 3D objects, effortful attention) contributed to the effectiveness in serial recall across both groups so much so that there wasn't enough room for improvement. However, the observation that significant portions of the variance in serial recall was correlated with a participant's spatial memory for where they had last-seen (WaL) or placed (MoL) an object provides for an alternative explanation. Importantly, a significant relationship between performance on the object-placement task and serial recall ($\text{Clustering}_{\text{simple}}$ , $\text{Clustering}_{\text{serial}}$ , and $\text{Recall}_{\text{error}}$) was exclusive to participants in the MoL group, suggesting that memory for object locations could assist participants with following a path from object to object—a phenomenon that is more easily instilled when the objects are more explicitly associated with the spatial environment. However, no comparisons of correlations across groups were found to be significant, even when MoL was significant and WaL was not. A lack of differences across groups in correlations between spatial memory and metrics of recall insinuate that spatial memory and verbal recall have an intimate relationship, regardless of encoding instructions.

Crucially, it was not the case that participants with greater baseline spatial memory performed better on the task. Specifically, groups did not differ in their improvement between token-collection attempts nor on the token-placement tasks. Interestingly enough, performance on the landmark-placement task was related to participant's recall in all metrics. This could be reflective of the degree to which a participant was encoding the spatial arrangement of the environment in which they were encoding. To address the potential that participants were benefiting from an elaborative encoding of specific objects to landmarks in the environment, we analyzed for relationships between recall and the average proximity of objects to their nearest landmark. Only a relationship between $\text{Recall}_{\text{error}}$ and object-landmark proximity was found for WaL groups only, which could imply that even participants that did not bind objects to the environment experiences a slightly similar effect by viewing their early objects near landmarks.

Gender increased the explanatory model of group and object-placement on recall. This effect was so potent that the only significant coefficient in the model was the interaction between gender and object-placement performance. This finding was specific to the primary variable of interest ($\text{Recall}_{\text{total}}$) and no other metrics of recall. There was no observed impact of either presence in the virtual environment or previous exposure to the MoL on any measured recall metric.

Taken together, these findings add important empirical evidence to the conversation surrounding the primacy of spatial contexts in encoding (for review see Robin et al., 2018). Specifically, our findings that non-baseline assessments of spatial memory strength were predictive of every recall metric, independent of encoding instructions, suggests that if one can forge a memory for an object within a loci, there is a greater likelihood of that object being remembered. Given that the MoL enforces exactly this behavior during encoding, it should come as no surprise that MoL has been so historically effective and that removing this integral feature of the technique (i.e. no explicit placement / binding of the object to the environment) practically eliminates its effectiveness.

### *Limitations*

A limitation of this current study is that recall was only tested immediately after a rehearsal period. Further investigations are needed to elucidate the impacts of this strategy on long-term memory; it could be the case that the recall metrics which yielded insignificant differences across groups would be significant as a function of time. Additionally, a version of the experiment that does not include a recall period could exacerbate the differences across groups; the MoL group may have been able to encode more information in less time, if the total time was limited across groups.

### *Future Directions*

With the need for humans to remember lists of objects rapidly declining (digital text and voice memos are rapidly accessible and permit near infinite storage), a strategy that increases your ability to recall more items seems more effort than it’s worth; why create a memory palace for today’s list of groceries when it is probably easier, more reliable, and less time consuming to create a checklist on one’s smartphone or notepad? In fact, despite the widespread knowledge of the technique’s effectiveness, most learners admit to never using the technique – even when explicitly instructed to do so in an experiment (Legge et al., 2012). Undergraduates even report their lack of use of mnemonic strategies, despite their knowledge of its effectiveness (Susser and McCabe, 2013); the most common strategy amongst undergraduates for studying is still rote repetition (Karpicke et al., 2009).

The once revered “art of memory” seems to now only be reserved for a small niche of memory enthusiasts who practice mnemonic techniques for relatively useless, but impressive, personal goals (e.g. Memorizing Pi to the nth decimal place) or understandably motivating competitive reasons (e.g. the World Memory Championship carries a $30,000 prize; Foer, 2011). There is simply no longer a need for modern humans to leverage their cortex to encode long lists of objects; technology has outpaced human evolution and can simply not be surpassed in regards to storage capacity.

However, the reliable effectiveness of the MoL, and the evolutionary prowess that it leverages, need not be limited to increasing the recall of simple concrete nouns. While further research will be needed to verify the possibility of extending the technique out of the list-learning domain, one can certainly speculate on the ability for spatial strategies to bolster recall for procedural, conceptual, and episodic memory—all aspects of human cognition that currently require a human consciousness and cannot necessarily be offloaded to a computer. While it has been suggested that mnemonics are limited in applicability and don’t conform to theory or structure of general memory, emerging concepts which emphasize the primacy of spatial constructs for the encoding of events (Mullally and Maguire, 2014; Robin et al., 2018) permit for novel and creative ways to utilize space to both operate on and retain information—perhaps most poetically visualized as a child learning a sequence of numbers using their fingers.

Such operations could even take advantage of the incidental learning that occurs as one navigates about a space and, subsequently, apply rule sets to specific facets of the environment that represent complex operations. For instance, a learner could navigate about a virtual room that contains only a large elephant and then move through a doorway into another room where a monkey is opening the passenger door of a car that has 2 balloons tied to it. The learner could later be instructed to mentally traverse this memorable path and write down the first letter of each object they encounter, with the simple instructions to insert an equal sign whenever they pass through a door and exponents whenever they see balloons. By simply recalling this scene, the learner could incidentally unveil a “memory” for E=MC$^2$. Similar, seemingly non-tangible concepts (e.g. fractions) also stand to benefit from spatially based incidental encoding tricks (e.g. floors separating numerators and denominators). Extending the MoL in ways where it can permit for the encoding of information beyond just that of simple objects is of high importance when considering the broader educational impacts of such a technology.

Additionally, the MoL has even been utilized for therapeutic purposes: Researchers have increased the recall of self-affirming memories and coping protocols for individuals with depression (Dalgleish et al., 2013; Werner-Seidler and Dalgleish, 2016) and provided an aid for both aging (Rapp et al., 2002; Verhaeghen et al., 1992; West, 1995; Yesavage, 1983) and memory-impaired populations (Richardson, 1995; Tate, 1997). Our paradigm significantly decreases the reported extensive training necessary to train users to implement the MoL (between 2 and 24 hours; (Bower and Reitman, 1972; Brehmer et al., 2008; Brooks et al., 1993; Kliegl et al., 1990; Moè and De Beni, 2005). Such ease of use could position virtual renditions of the MoL to more rapidly benefit populations with memory ailments.

Perhaps in the future, researchers could even use spatial environments to identify solutions that are particularly unsolvable using only computer memory and processing. As an example, researchers have been able to crowd source solutions to various protein folding problems by translating the problem into a visuospatial online video game (http://fold.it; Cooper et al., 2010). At the very minimum, exposing learners to the MoL and potential ways to leverage it for encoding useful information provide them with ecologically valid learning tools; McCabe (2015) found that students who were given an MoL exercise at the start of the semester used it as study technique-- an effect the author attributes to the fact that the students were able to metacognitively observe the improvement in their memory. Virtual memory software, like that leveraged in this study, stands to revitalize the ability of memory enhancement techniques to impact learners in an entertaining and effective fashion.

## Behavioral Piloting Summary

Prior to landing on the current experimental design, three behavioral pilot experiments were conducted to optimize a) the number of items per list, b) the number of worlds / lists, and c) differences in encoding / recall instructions as a function of group. Methodological details and subsequent experimental results are briefly described below. Only variations from the methods described above are mentioned; all other experimental designs and apparatus remained the same.

### *Behavioral Pilot 1 (n=23; MoL=11)*

This version of the experiment featured only two lists, each containing 15 items encoded in either Toon World or Ruin World. See Appendix 5 for a full transcript of encoding and recall instructions. This experimental paradigm unveiled a significant increase in recall strength across all measures of mnemonic recall for MoL subjects as compared to WaL subjects. MoL subjects recalled an average of 14.45 words per list compared to 11.2 for control subjects. MoL subjects were almost at ceiling (15). MoL subjects recalled 11.6 words in the right sequence, where controls recalled 6.45. Additionally, MoL subjects recalled 9.95 words before making an error compared to the 4.95 words in control subjects. See Figure 10 for results.

### *Behavioral Pilot 2 (n=11)*

This version of the experiment was exactly the same as Behavioral Pilot 1, except there were a total of three lists of 15 items each in an attempt to combat the observation that MoL subjects were at ceiling when only 2 lists were used. Lagoon World was the third world used to encode the objects. The effect observed in Behavioral Pilot 1 remained when adding a third list of 15 items encoded in a third virtual environment, although the effects were slightly weaker – due mostly to the small n. MoL subjects recalled significantly greater recall strength across all metrics. MoL subjects recalled an average of 12.83 words per list compared to 10.2 for control subjects. MoL subjects recalled 7.45 words in the right sequence, where controls recalled 5.27. Additionally, MoL subjects recalled 6.33 words before making an error compared to the 4.26 words in control subjects. See Figure 11 for results.

### *Behavioral Pilot 3 (n=27)*

In this version of the experiment, each list of objects was given a name; subjects were told that the items on each list belonged to one of three people (Otto, Viola, or Pike). This was included so as to prepare for an fMRI version of the experiment where our hypotheses mandated that we did not explicitly bring to mind the encoding environment prior to recall.  When subjects were asked to recall the list of items encoded in each world, they were told to recall the items from a cued person's list (e.g. Otto's list of items). We also dramatically altered the instructions for the WaL group so as to try and equate everything across the groups aside from the placement of the objects. Finally, all subjects were additionally requested to recall the items in reverse order, starting with the last item on the list and making their way to the first. See Appendix 6 for a full transcript of encoding and recall instructions. All effects were abolished in this version of the experiment. See Figure 12 for results. Upon further review of the video recordings, it was determined that WaL participants were acting, effectively, as MoL participants; the instructions emphasized the location of an object during retrieval and many WaL participants were seen stopping at specific locations to continue encoding objects, effectively “freezing” the object in that place.

## Figure Captions

**Figure 1.** Virtual Environments and Landmarks

A) The five Virtual Environments (VEs) created for this study using OpenSim Software. Toon World, Ruin World, and Lagoon World were used for encoding. Viewpoints within encoding environments reveal the participant’s starting location in the southmost area of the world, facing North. Avatar Island was used to familiarize subjects with navigation within our VEs and Moon World was used to exposure participants to the object-placement technology. All environments rested within a 64 x 64 grid region border. B) The 24 landmarks placed in the eight cardinal locations (N,S,W,E,NW,NE,SW,SE) along the perimeter of each of the three encoding VEs. The figure’s arrangement of each landmark reflects their placement in each environment. Landmark names are as follows, starting with the landmark in the upper left corner (i.e. NW) and moving clockwise for each environment: Toon (slide, penguin pool, mushrooms, lollipop tree, Tetris blocks, water pipes, flamingo pool, doghouse), Ruin (fish fountain, treasure chests, giant telescope, armillary sphere, large bell, red flags, sun plaque, bubbling cauldron), Lagoon (fern statue, horse saddle, giant cactus, kayak, two curvy chairs, surfboard, fireplace, ridged planters).

**Figure 2.** Token Collection Task and Software

A) Tokens collected by participants upon their first entries into each VE. Tokens varied as a function of world: coins in Toon World, rings in Ruin World, and shells in Lagoon World. Each world contained 20 tokens and a Heads Up Display (HUD) indicated a participant's progress as they collected each of the tokens. B) Experimenter token-control platforms, located on a platform floating above each environment. Experimenters were able to leverage these control platforms to clear tokens, initiate the collection phase, and collect metrics concerning a participant's token collections.

**Figure 3.** Object Encoding Task and Software

A) Objects continually rendered in front of participants as they navigated about each encoding environment. A Heads Up Display (HUD) rendered the objects and provided a light (green shown here) indicating whether participant was currently in the encoding phase. Objects were visible for a period of 20s before disappearing and a new object appearing in its place. Participants were able to view the object from all angles of its pitch and yaw axes by rotating about the object. Participants assigned to the MoL group were given the additional instructions to "click" on the object and "freeze" it in a location of their choosing. Shown here is a beer in Toon World, trophy in Ruin World, and a pumpkin in Lagoon World. B) Experimenter object-control platform, located on a platform floating above each environment. Experimenters were able to leverage these control platforms to load in participant/environment specific lists of objects, send objects to the participant's HUD, and collect metrics concerning each object's location within the environment at a temporal resolution of 1s.

**Figure 4.** Object/Landmark/Token Placement Task

Participants were shown an allocentric, “bird’s eye” view of each environment (Toon World used here) that contained landmarks (A) for object-placement and token-placement tasks and one that was stripped of its eight landmarks (B) for landmark-placement tasks. C) The instruction screen immediately preceding each placement trial. Participants were provided with a 2-D image of an object they encoded and instructions to click on the map location where they placed (MoL) or last saw (WaL) the object. D) The mouse cursor participants used to select the location of the cued object/landmark/token. E) A grid overlay delineating the 4,096 (64 x 64) cells available for participant selection via their cursor. This grid was not visible to participants, but could be inferred given the cursor’s inability to be placed outside of each cell—the cursor would “snap” to fit into the nearest, overlapping grid cell.

**Figure 5.** Experimental Paradigm

All participants underwent a familiarization phase that first included a general orientation in Avatar Island, followed by five minutes of token-collection in each of the three encoding environments and then a three-minute period of token collection that was preceded with an emphasis on collection speed. If participants completed token-collection before the time limit was up, they were encouraged to explore the environments until time expired. Afterwards, participants were read group-specific instructions and teleported to Moon World to practice encoding (viewing and walking for WaL and viewing, walking, and placement for MoL). All subjects then encoded a list of 15 objects in each of the three environments. After the third encoding session, participants were shown screen recordings of their activity within each environment. Following these rehearsal periods, subjects were cued to verbally recall the list of items in forward and, immediately after, reverse encoding order. After forward and reverse-recall sessions for each of the three lists, subjects were submitted to spatial recall tests for object, landmarks, and tokens encountered in each environment. For any phase of the experiment that required a cycling through the three VEs, visitation/testing order was randomized.

**Figure 6.** Average Free Recall Scores

Average number of words recalled (y-axis) across the three VEs in regards to each behavioral measure of interest (x-axis), as a function of group (MoL vs. WaL). *p<0.05, **p<0.01

**Figure 7.** Spatial Memory Scores

A) Participant performance on the object-placement, landmark-placement, and token-placement tasks, as a function of group. Error was defined as the average Euclidean distance between where a participant indicated they had placed (MoL) or last seen (WaL) a cued object vs. the actual location of that object in the corresponding VE. The same analysis was used to probe participant memory for an environment’s static features: landmarks and coins. Lower average Euclidean distance (error) is seen as higher spatial memory. B) Average improvement on the token collection from Run 1 to Run 2, as a function of group. Reduction in time (y-axis) is reported in seconds as (Run 2 time from start to last-token collected) – (Run 1 time from start to last-token collected). C) Time to completion, defined as Time from start to last-token collected, as a function of Run, collapsed across groups. ***p<0.001

**Figure 8.** Individual Differences In Free Recall vs. Allocentric Memory Performance

A) Scatter plot depicting a participant's average number of words recalled across the three VEs (x-axis) vs. their average performance on the object-placement task. B) Scatter plot depicting a participant's average number of words recalled across the three VEs (x-axis) vs. their average performance on the landmark-placement task. Individual points are color coded to reflect group membership. Trend lines indicate the linear trend across all participants, irrespective of group, and are accompanied by r-values and p-values.

**Figure 9.** Object-Landmark Proximity

Heat map indicating the total number of objects placed by a group's participants within each cell of the 64x64 environmental grid, overlaid on a bird's-eye view of each VE. B) Average proximity of an object to the nearest environmental landmark (defined by Euclidean distance) as a function of encoding environment and group. ***p<0.001

**Figure 10.** Results From Behavioral Pilot 1

This version of the experiment utilized only two worlds, each displaying a list of 15 items for 30s each followed by a video-playback rehearsal period. Total = average number of objects recalled across the two worlds. Correct Sequence = average number of objects that were recalled in the correct order across the two worlds. Before Error = average number of objects recalled before the subject made an error. See Appendix 5 for encoding and retrieval instructions.

**Figure 11.** Results From Behavioral Pilot 2

This version of the experiment utilized all three worlds, each displaying a list of 15 items for 30s each followed by a video-playback rehearsal period. Total = average number of objects recalled across the two worlds. Correct Sequence = average number of objects that were recalled in the correct order across the two worlds. Before Error = average number of objects recalled before the subject made an error. See Appendix 5 for encoding and retrieval instructions.

**Figure 12.** Results From Behavioral Pilot 3

This version of the experiment utilized all three worlds, each displaying a list of 15 items for 30s each followed by a video-playback rehearsal period. However, subjects received different instructions as compared to Behavioral Pilot 2 so as to further equate the two groups. Total = average number of objects recalled across the two worlds. Correct Sequence = average number of objects that were recalled in the correct order across the two worlds. Before Error = average number of objects recalled before the subject made an error. See Appendix 6 for more detailed encoding and retrieval instructions.

## Table Captions

**Table 1.** Relationship between free-recall and spatial memory

R-statistics denoting the relationship between a participant’s average free recall memory and average performance on placement tasks (object, landmark, and coin) and their baseline spatial-memory (reduction in time between first and second coin collection attempts). Analyses were conducted separately for forward and reverse recall attempts. Rows in bold denote the relationship when relying on all participants in the study (n=60), and the accompanying rows beneath indicate results observed when relying exclusively on participants assigned to the WaL (n=30) or MoL (n=30) groups.

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, † Significantly different from other group ($p<0.05$),

‡ Significantly different from effect observed using all participants ($p<0.05$).

## Figures

### Figure 1. Virtual Environments and Landmarks

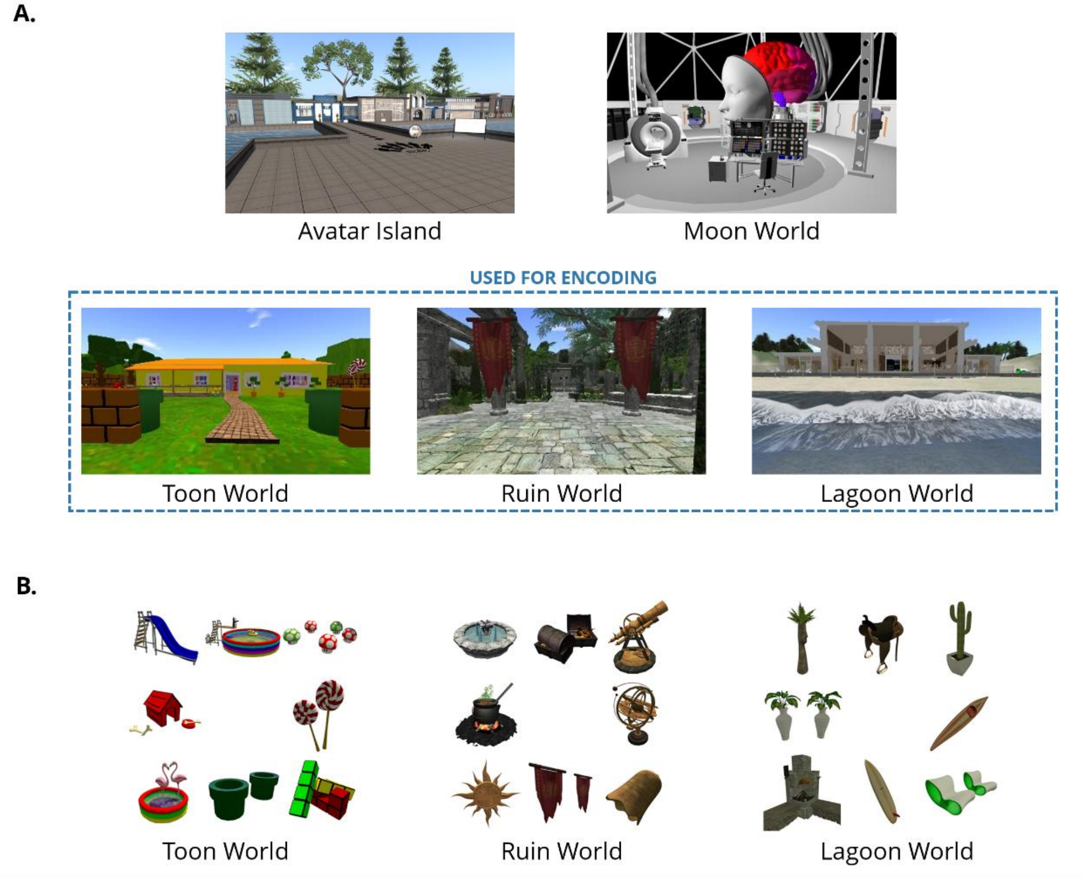
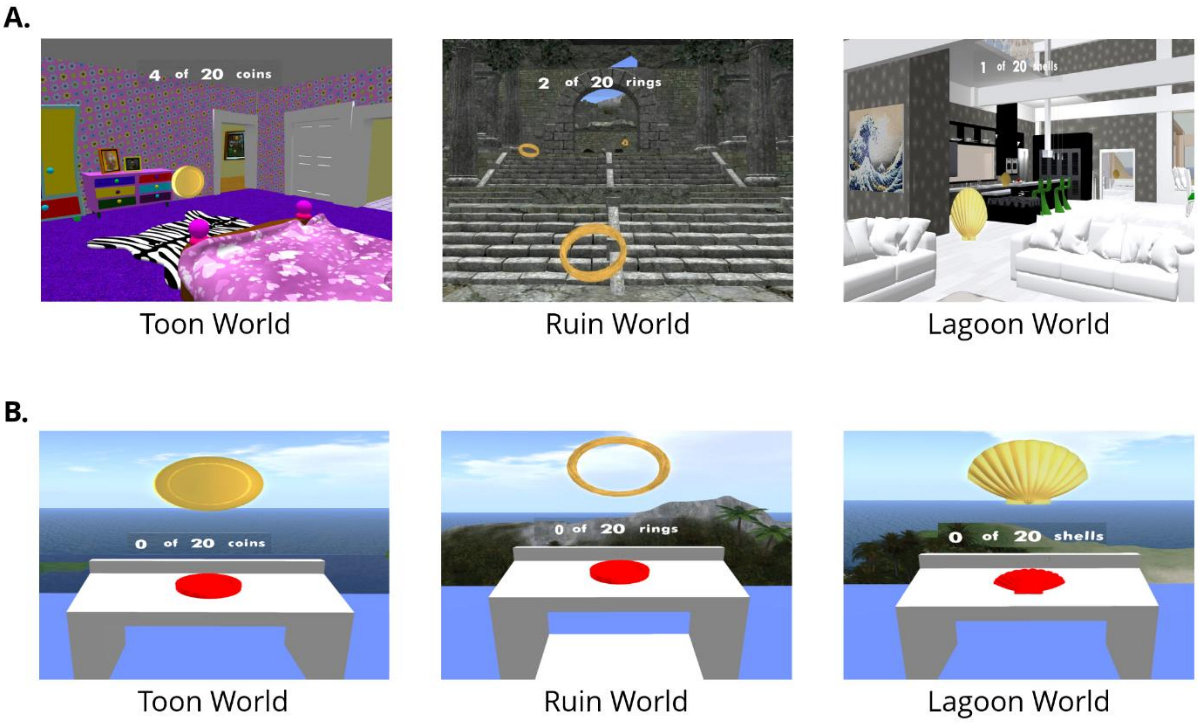


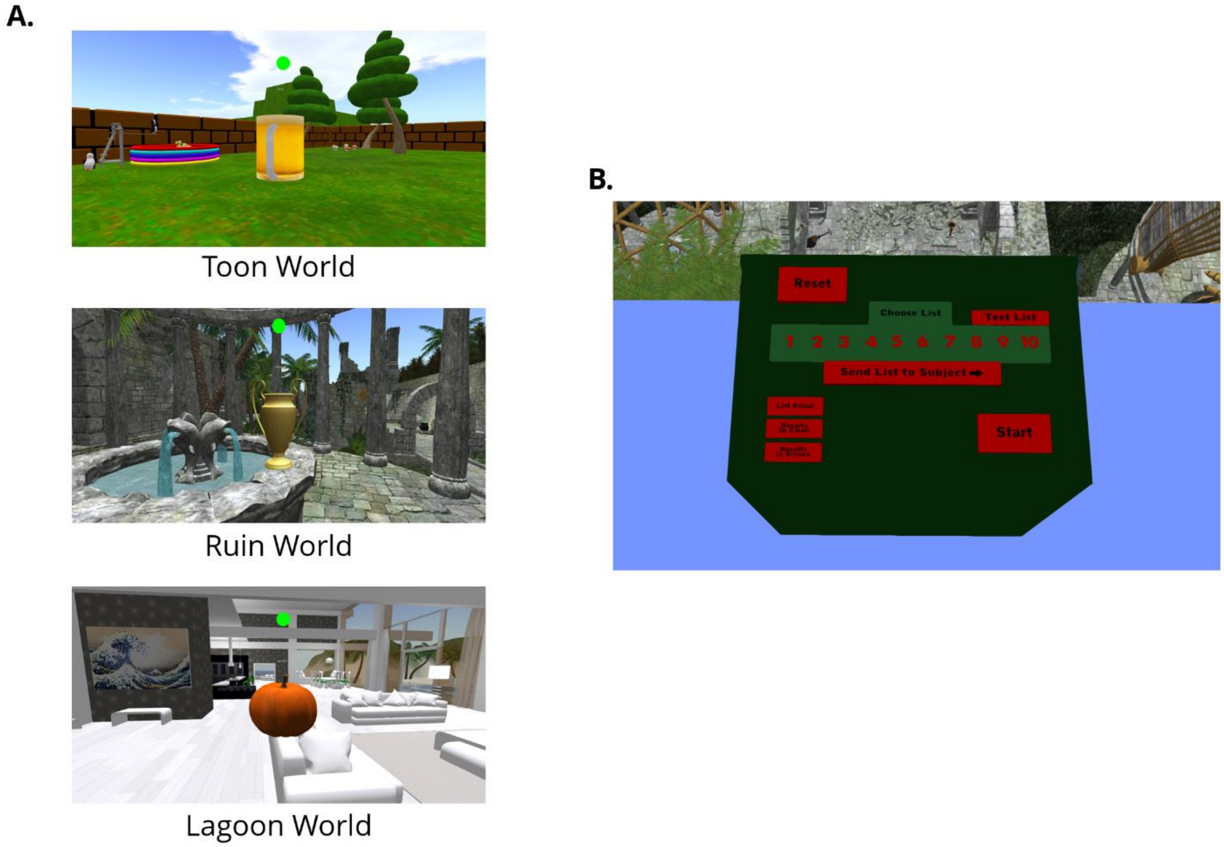
**Figure 2. Token Collection Task and Software**



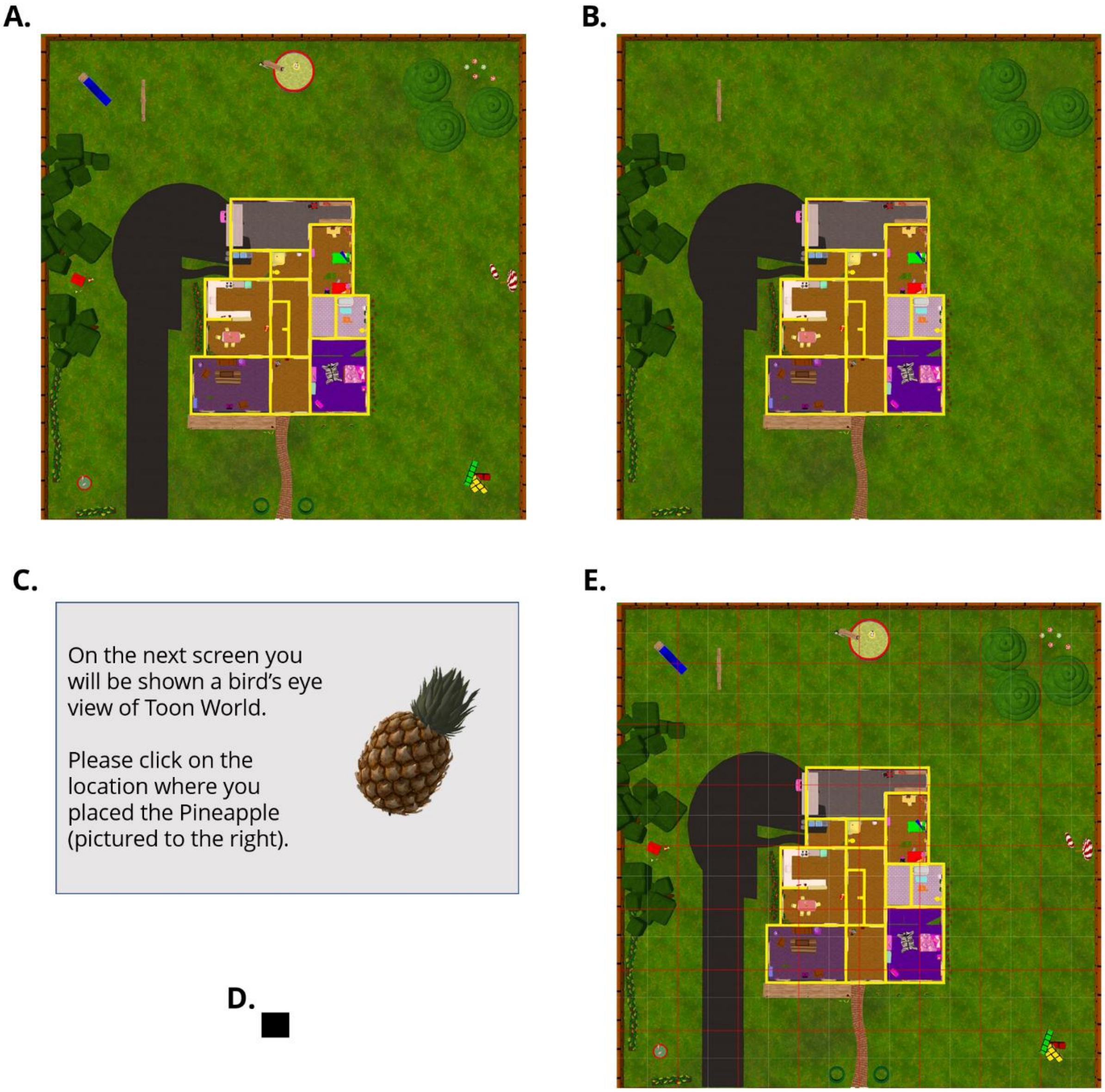
Toon World Ruin World Lagoon World

Toon World Ruin World Lagoon World

## Figure 3. Object Encoding Task and Software



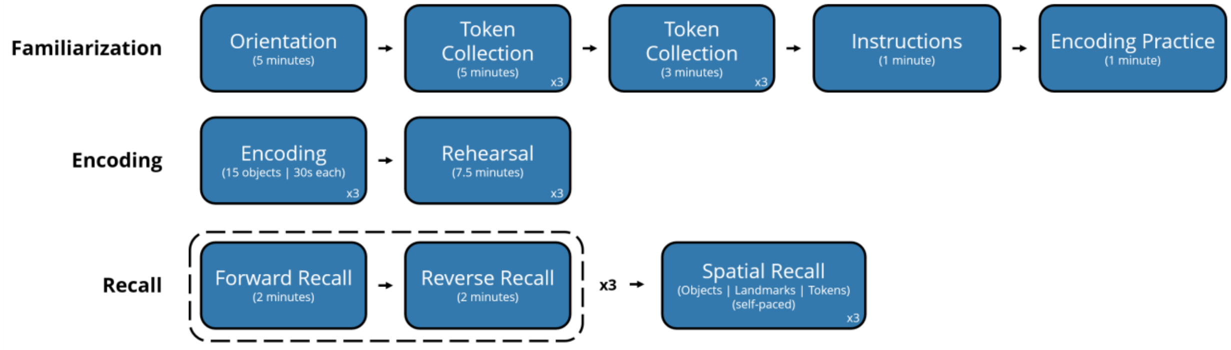
## Figure 4. Object/Landmark/Token Placement Task



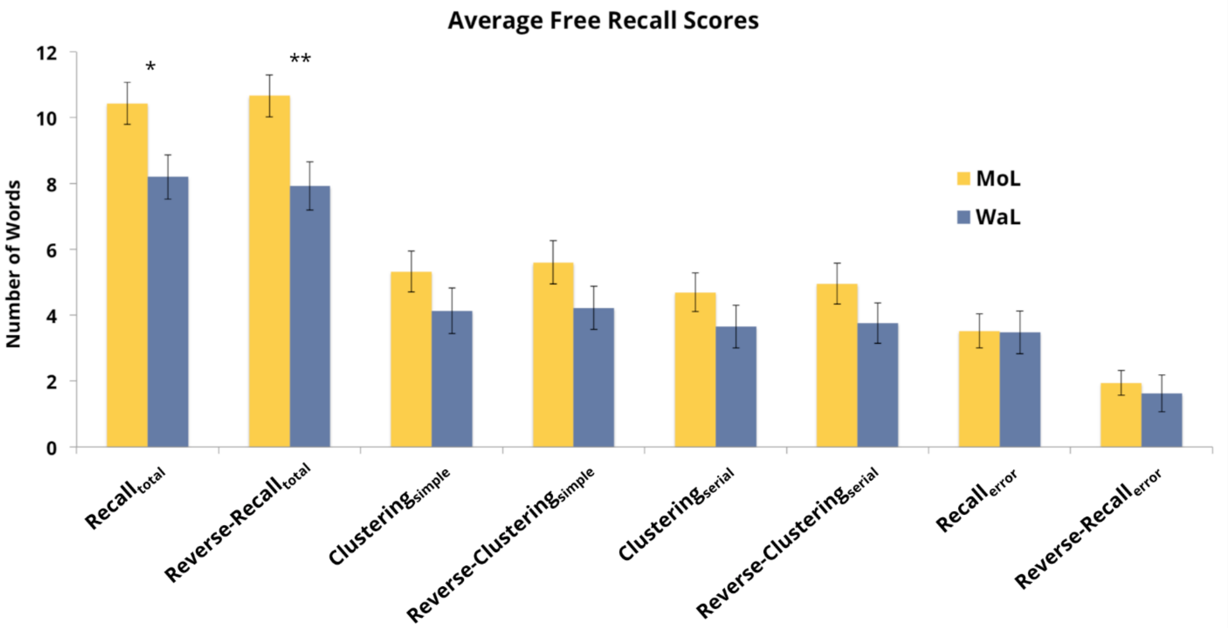
On the next screen you will be shown a bird’s eye view of Toon World.

Please click on the location where you placed the Pineapple (pictured to the right).

**Figure 5. Experimental Paradigm**



## Figure 6. Average Free Recall Scores



# Figure 7. Spatial Memory Scores

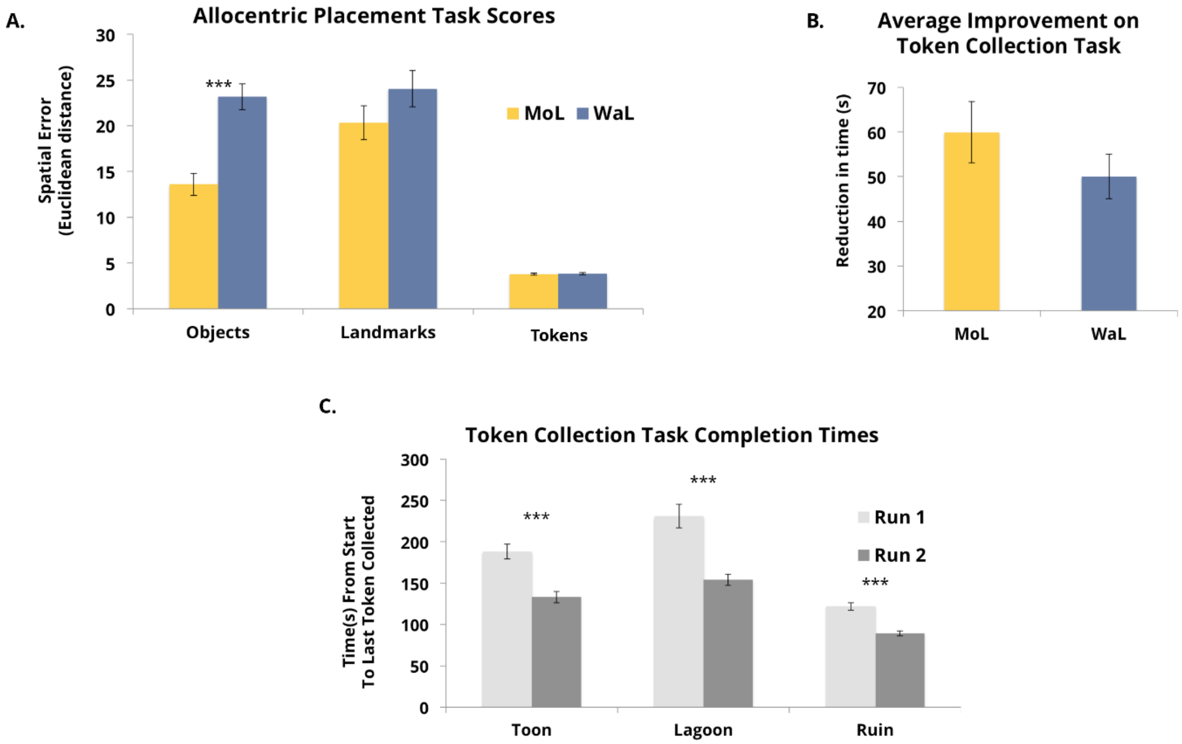


**Figure 8. Individual Differences In Free Recall vs. Allocentric Memory Performance**

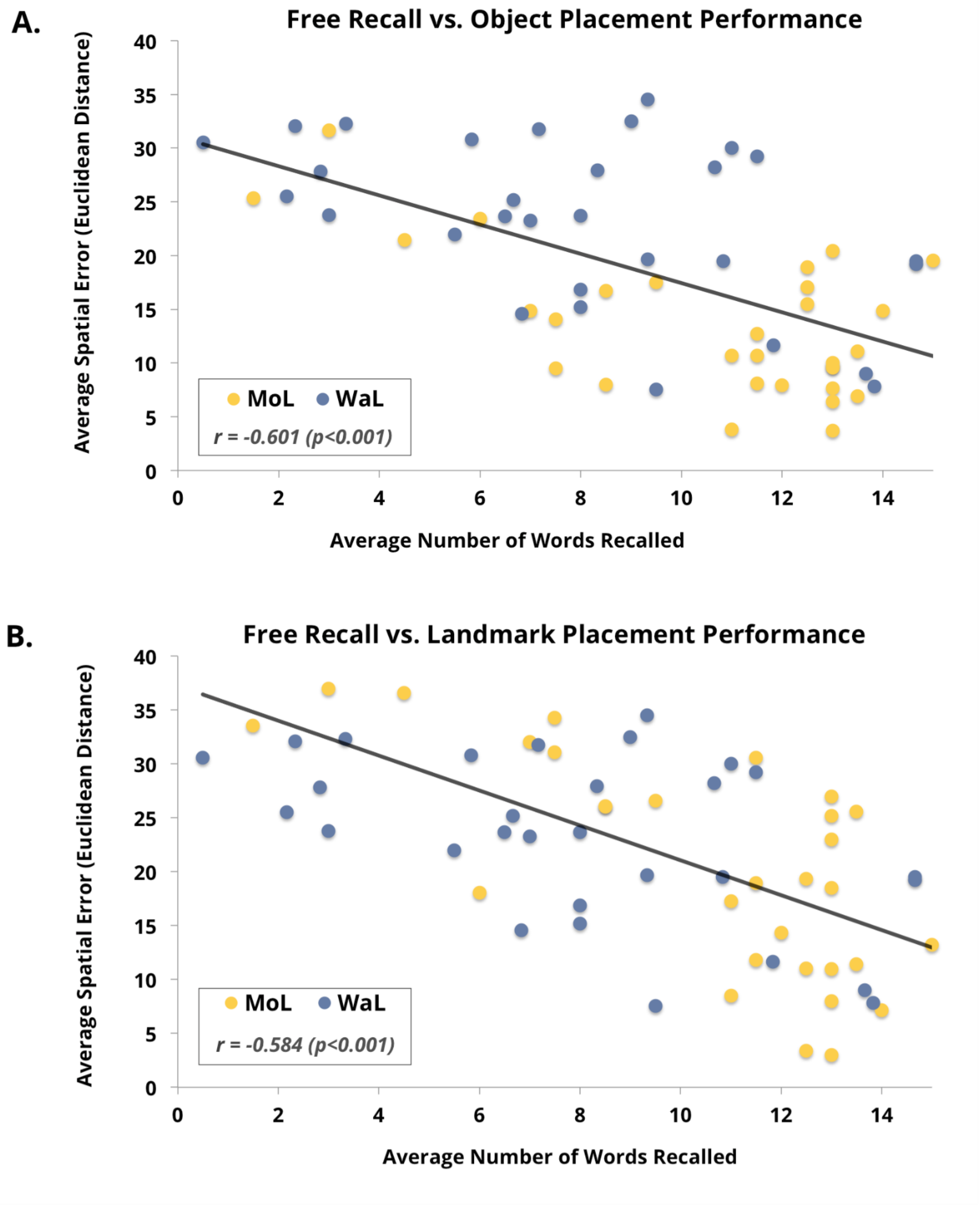


**Figure 9. Object-Landmark Proximity**

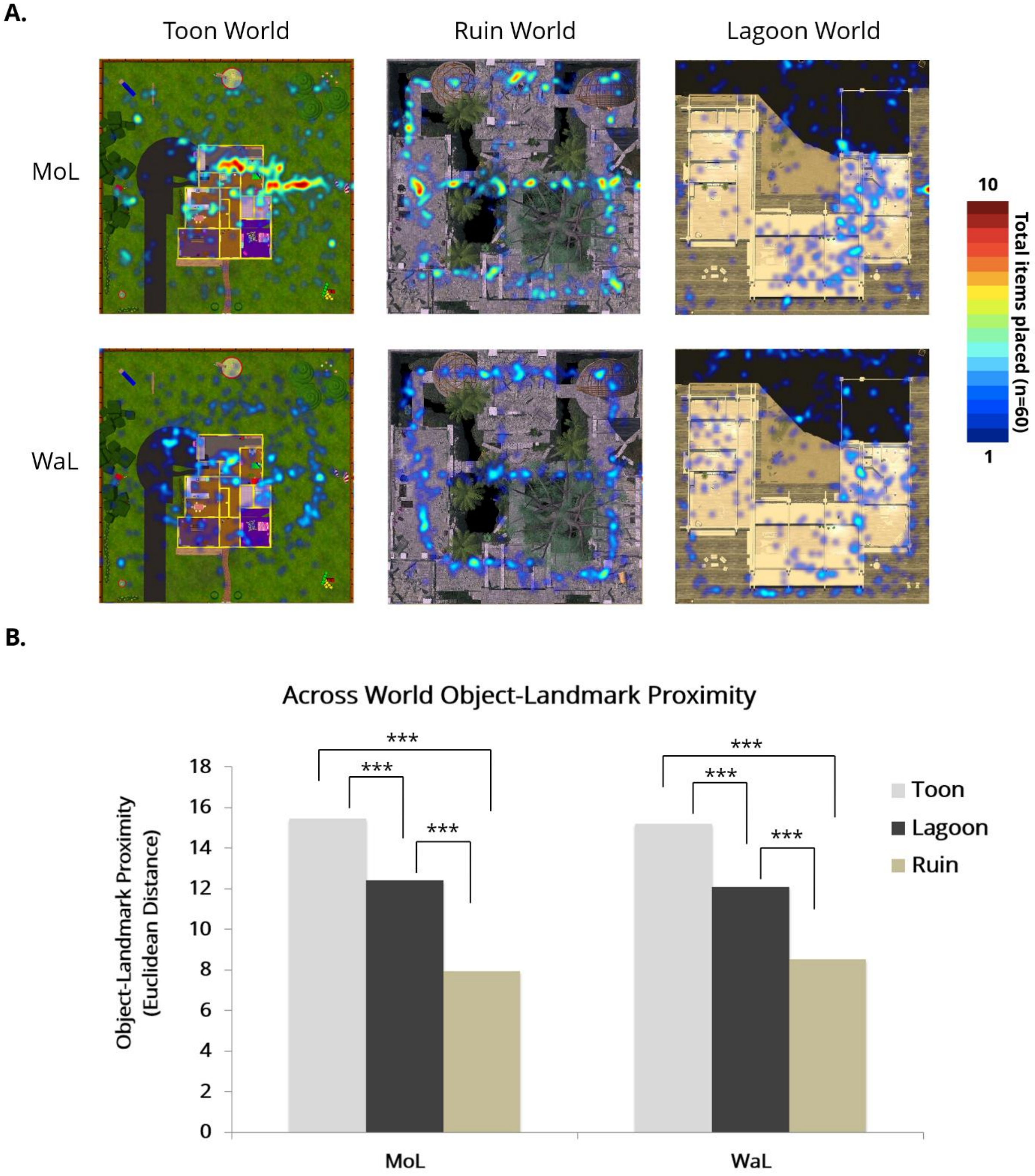


**Figure 10. Results From Behavioral Pilot 1**

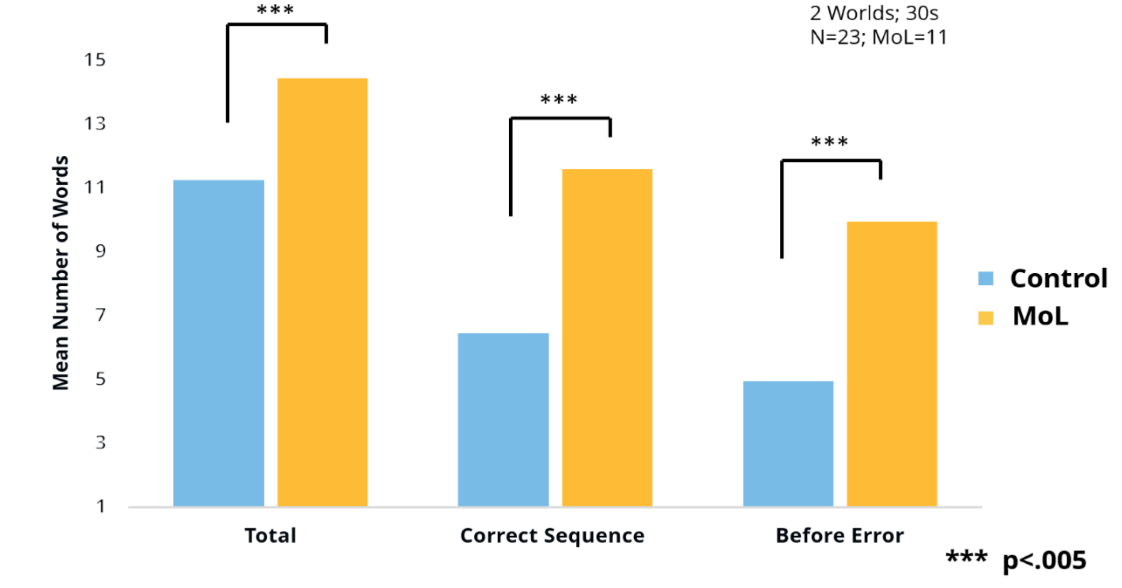
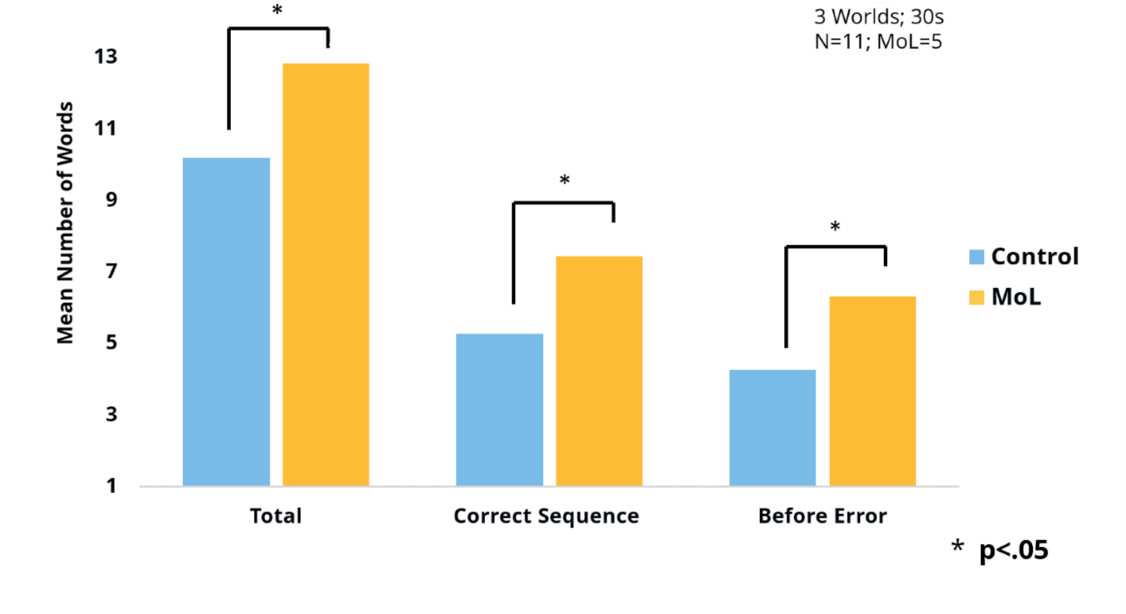
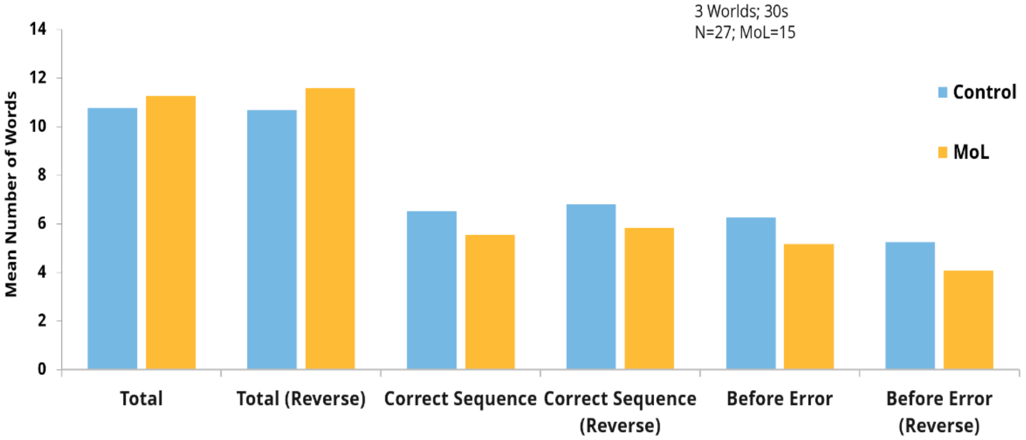


**Figure 11. Results From Behavioral Pilot 2**



## Figure 12. Results From Behavioral Pilot 3



## Tables

### Table 1. Relationship between free-recall and spatial memory

| | | Object-Placement | Landmark-Placement | Coin-Placement | Baseline Spatial Memory |
|---|---|---|---|---|---|
| Forward Recall | **Recall$_{total}$** | -0.57*** | -0.566*** | -0.383** | 0.081 |
| | MoL | -0.572*** | -0.655*** | -0.437* | 0.106 |
| | WaL | -0.449* | -0.452* | -0.353 | 0.183 |
| | **Clustering$_{serial}$** | -0.453** | -0.393** | -0.178 | 0.084 |
| | MoL | -0.618*** | -0.403* | -0.084 | 0.01 |
| | WaL | -0.34 | -0.369* | -0.258 | 0.232 |
| | **Clustering$_{simple}$** | -0.486*** | -0.427*** | -0.207 | 0.082 |
| | MoL | -0.639*** | -0.454* | -0.1356 | 0.019 |
| | WaL | -0.36 | -0.373* | -0.266 | 0.228 |
| | **Recall$_{error}$** | -0.295* | -0.27* | -0.223 | 0.061 |
| | MoL | -0.521** | -0.291 | -0.16 | -0.06 |
| | WaL | -0.236 | -0.26 | -0.274 | 0.203 |
| Reverse Recall | **Recall$_{total}$** | -0.61*** | -0.592*** | -0.337** | 0.075 |
| | MoL | -0.576*** | -0.721*** | -0.292 | 0.085 |
| | WaL | -0.516** | -0.456* | -0.395 | 0.204 |
| | **Clustering$_{serial}$** | -0.35** | -0.41** | -0.187 | 0.053 |
| | MoL | -0.552** | -0.55** | -0.213 | -0.024 |
| | WaL | -0.37* | -0.303 | -0.165 | 0.142 |
| | **Clustering$_{simple}$** | -0.463*** | -0.425*** | -0.172 | 0.007 |
| | MoL | -0.571*** | -0.578*** | -0.243 | -0.011 |
| | WaL | -0.326 | -0.245 | -0.095 | 0.106 |
| | **Recall$_{error}$** | -0.3* | -0.338** | -0.17 | 0.058 |
| | MoL | -0.318 | -0.527** | -0.017 | 0.078 |
| | WaL | -0.325 | -0.215 | -0.277 | 0.068 |

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# Appendix

**Appendix 1** – Pool of objects from which lists were randomly sampled.

ball, balloon, basket, beer, bicycle, briefcase, camel, car, cat, cherry, cigar, cow, dog, frog, guitar, hammer, handbag, hat, helmet, horse, key, leaf, lemon, net, orange, pineapple, pot, pumpkin, record, rocket, rooster, rope, sandal, ship, snail, snake, sunglasses, telephone, tooth, trophy, umbrella, watch, watermelon, whale, whistle

**Appendix 2** – Experimental Instructions

*MoL Encoding*

People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the "Memory Palace" strategy that can be used to aid your memorization of a list of items. Conceived in Ancient Greece, this strategy takes advantage of the fact that information is more easily remembered when it is associated with a spatial location. In its classic implementation, the Memory Palace strategy involves imagining yourself navigating a familiar environment (e.g., your home) and mentally "placing" each of a list of objects at a specific memorable location along your path. For example, if you had to remember bananas, eggs, and peppers, in that order, you could imagine yourself walking up to the door of your home, where you find a banana on the doorknob; after entering the door, you see eggs hanging on strings from the ceiling in the entryway; after moving through them, you see peppers all over the floor in the living room. When it is later time to retrieve the list of objects, you would simply re-imagine yourself walking along the original path you traversed and observing each item on the list -- right in the place that you left it.

While this memorization strategy typically involves placing a list of to-be-remembered items using only one’s imagination, we have created a platform for you to implement this strategy by placing items as you navigate along a path through a virtual reality environment. We are now going to teleport you to an area where you can practice using the technique I just described to you. Please teleport to Moon now by scrolling out of first person view.

In this world, a series of three 3D objects will appear in front of you, one at a time. Please move about the environment and find a memorable location to place each object. When you click on the shape, it will be placed in that location. Be sure to try and place the items along a path that you would be able to recreate later, as this will help you when you are later asked to recall the objects in order. Each item will be available for you to view for 20 seconds before a new one appears.

We are now going to teleport back to each of the virtual environments you explored when you collected tokens. These environments will be your “virtual memory palaces”. While you are in each environment, a series of 15 items will appear in front of you, one-at-a-time, just like during the practice. You will be able to view each item and walk around the environment with it for up to 20 seconds before a new item appears. Within that 20-second time frame, you will be able to “place” each item in a location of your choosing by clicking on the item itself. We encourage you to place the items so that you can make the most out of the environment and what you see around you, especially the landmarks. Be sure to try and place the items along a path that you would be able to recreate later, as this will help you when you are later asked to recall the objects in order. Please do not take longer than 20 seconds for any given item; otherwise you would miss the opportunity to place that item.

“You will be in [WORLD NAME]. Your task is to remember these items in the order they were presented. These objects belong to [Name]. We will ask you to tell us the items belong to [NAME], so be sure to remember that you learned [NAME]’s List in [WORLD NAME]. Teleport to the [WORLD NAME] so you can see the items belonging to [NAME]. Right now you are at the southern part of the map. So straight ahead is North, to your left is West, and to your right is East.”

*WaL Encoding*

People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the “Walk and Learn” strategy that can be used to aid your memorization of a list of items. Motivated by decades of cognitive psychological research, this strategy takes advantage of the active nature of learning. Although people often attempt to memorize information while staying in one place (e.g., sitting at a desk), this strategy encourages the learner to walk around during learning. The changing scenery serves to stimulate the brain’s memory system and makes the information you encounter more memorable. After all, humans did not evolve to learn information while sitting at desk, but rather our brains are exquisitely adapted to acquire new information as we actively move about our environment.

This strategy can be implemented by going on an actual walk, or even imagining oneself on a walk, and studying the to-be-remembered information along the way. We have created a platform for you to implement this strategy by studying a set of items as you walk through a virtual reality environment. We are now going to teleport you to an area where you can practice using the technique I just described to you. Please teleport to Moon now by scrolling out of first person view. In this world, a series of three 3D objects will appear in front of you. Please walk around and explore this world as you view each of these items. Each item will be available for you to view for 20 seconds before a new one appears. (Give me a moment to load these items)”

We are now going to teleport back to each of the virtual environments you explored while collecting tokens. While you are in each environment this time, a series of 15 items will appear in front of you, one at a time, just like during the practice. You will be able to view each item and walk around the environment with it for up to 20 seconds before a new item appears. Your goal is to memorize each set of 15 items, and later you will be asked to recall the items you encountered in each environment in the order in which they were presented.

You will be in [WORLD NAME]. Your task is to remember these items in the order they were presented. These objects belong to [LIST NAME]. We will ask you to tell us the items belong to [LIST NAME], in order, so be sure to remember that you learned [LIST NAME] in [WORLD NAME]. Teleport to the [WORLD NAME] so you can see the items belonging to [LIST NAME].

### *MoL Forward Recall*

I would now like you to tell me, in the order in which they appeared, the list of 15 objects you saw that belong to [Name]. Please close your eyes and imagine yourself walking through the environment where you originally saw [Name]’s List so you can view each item where you placed it. Try and mentally recreate the same exact path you originally travelled when you placed the items so you can remember the order of the items. Just say each item aloud as you come across it or remember it. Imagining each item in relation to context of the environment, such as a nearby landmark, may help as well. As you are trying to recall the items in order, if you cannot remember one of the items, feel free to skip over that item and continue recalling the remainder of the list in order (skipping additional items if need be). If you reach a point where you can no longer remember the items in order, just try and remember as many items as you can from [Name]'s List.

*MoL Reverse Recall*

We are now going to do some more verbal recall, but this time it will be slightly different. This time, I'd like for you to start with the last item you saw on [Name's] List and tell me each item in the list in reverse order until you get to the first item you saw on from [Name's] List. As you are trying to recall the items in reverse order, if you cannot remember one of the items, feel free to skip over that item and continue recalling the remainder of the list in reverse order (skipping additional items if need be). If you reach a point where you can no longer remember the items in reverse order, just try and remember as many items as you can from [Name]'s List.

Please close your eyes and imagine yourself walking through the environment where you originally saw [Name]'s List so you can view each item where you placed it. Try and recreate the same exact path you originally travelled when you placed the items, but mentally walk along this path in reverse so you can remember the reverse order of the items. Just say each item aloud as you come across it or remember it. Imagining each item in relation to context of the environment, such as nearby landmark, may help as well. If you reach a point where you can no longer remember the items in reverse order, just try and remember as many items as you can from [Name]’s List

*WaL Forward Recall*

I would now like you to tell me, in order, the list of objects you saw that belong to [NAME]. As you are trying to recall the items in order, if you cannot remember one of the items, feel free to skip over that item and continue recalling the remainder of the list in order (skipping additional items if need be). If you reach a point where you can no longer remember the items in order, just try and remember as many items as you can from [Name]’s List.  When you begin, please close your eyes and try to imagine yourself walking through the environment where you originally saw [Name]'s List. Are you ready to begin? Start.

*WaL Reverse Recall*

We are now going to do some more verbal recall, but this time it will be slightly different. This time, I’d like for you to start with the last item you saw on [Name’s] List and tell me each item in the list in reverse order until you get to the first item you saw on from [Name’s] List. As you are trying to recall the items in reverse order, if you cannot remember one of the items, feel free to skip over that item and continue recalling the remainder of the list in reverse order (skipping additional items if need be). If you reach a point where you can no longer remember the items in reverse order, just try and remember as many items as you can from [Name]’s List. When you begin, please close your eyes and try to imagine yourself walking through the environment where you originally saw [Name]'s List.

**Appendix 3** – Presence Survey (Slater)

1) Please rate your sense of being there in the virtual reality.

2) To what extent were there times during the experience when the virtual reality became the 'reality' for you, and you almost forgot about the 'real world' of the laboratory in which the whole experience was really taking place?

3) When you think back about your experience, do you think of the virtual reality more as images that you saw, or more as somewhere that you visited?

4) During the course of the experience, which was strongest on the whole, your sense of being in the virtual reality, or of being in the real world of the laboratory?

5) When you think about the virtual reality, to what extent is the way that you are thinking about this similar to the way that you are thinking about the various places that you've been today?

6) During the course of the virtual reality experience, did you often think to yourself that you were actually just sitting in a laboratory wearing a helmet, or did the virtual reality overwhelm you?

**Appendix 4** – Presence Survey (Fox)

1) To what extent do you feel the avatar is an extension of yourself?

2) To what extent do you feel that if something happens to the avatar, it feels like it is happening to you?

3) To what extent do you feel you were in the same room with the avatar?

4) To what extent do you feel you embodied the avatar?

5) To what extent did the avatar seem real?

6) To what extent were you involved with the virtual world?

7) To what extent did you feel surrounded by the virtual world?

8) To what extent did you feel like you were inside the virtual world?

9) To what extent did it feel like you visited another place?

10) How much did the virtual world seem like the real world?

**Appendix 5** – Behavioral Pilot 1 Experimental Instructions

*MoL Encoding*

People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the "Memory Palace" strategy that can be used to aid your memorization of a list of items. Conceived in Ancient Greece, this strategy involves mentally 'placing' each piece of information you wish to remember in a specific location within an imagined environment. For instance, if you had a list of 15 items to remember, you could conjure up a memory of a familiar environment (like your childhood home) and mentally walk through this environment, placing each item on the list in a memorable place within the environment. When it is later time to retrieve the information, you would simply re-imagine yourself walking along that same route and hopefully each item on the list would be right there where you left it. Today, we'd like you to teach you this memorization technique using virtual reality.

We are now going teleport back to each of the virtual environments you just explored. These environments will be your “virtual memory palaces”. While you are there this time, a series of objects will appear in front of you, one-at-a-time. You will be able to view each object and walk around the environment with it for up to 30 seconds before a new item appears. Within that 30 second time frame, you will be able to “place” each item in a location of your choosing by clicking on the object itself (not the location). Please do not take longer than 30 seconds, otherwise you would miss the opportunity to place that item. Your task is to remember these objects in the order they were presented. We will test your memory on these at the end of the experiment.

### *WaL Encoding*

People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the “Walk and Learn” strategy that can be used to aid your memorization of a list of items. This strategy is designed to take advantage of the active nature of learning. We are now going teleport back to each of the virtual environments you just explored. While you are there this time, a series of objects will appear in front of you, one-at-a-time. You will be able to view each object and walk around the environment with it for up to 30 seconds before a new item appears. Your task is to remember these objects in the order they were presented. We will test your memory on these at the end of the experiment.

### *MoL Recall*

We’d like for you to now recite to us, in order, the list of objects you saw in [WORLD]. If you’d like, feel free to close your eyes and imagine yourself walking through the environment and viewing each item in the location in which you placed it. Imagining it in relation to context of the environment, such as nearby landmarks may help as well. To capture the order of the items, it might be a good idea to recreate the same exact path you originally travelled. Just say each item aloud as you come across it or remember it. If you cannot remember them in order, that's alright; try and just remember as many items as you can from that environment.

*WaL Recall*

We'd like for you to now recite to us, in order, the list of objects you saw in [WORLD]. If you'd like, feel free to close your eyes and imagine yourself walking through the environment and viewing each item as it was presented in the environment. To capture the order of the items, it might be a good idea to recreate the same exact path you originally travelled, if you remember. Just say each item aloud as you come across it or remember it. If you cannot remember them in order, that's alright; try and just remember as many items as you can from that environment.

**Appendix 6** – Behavioral Pilot 3 Experimental Instructions

*MoL Encoding*

"People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the "Memory Palace" strategy that can be used to aid your memorization of a list of items. Conceived in Ancient Greece, this strategy involves mentally "placing" each piece of information you wish to remember in a specific location within an imagined environment. For instance, if you had a list of 15 items to remember, you could conjure up a memory of a familiar environment (like your childhood home) and mentally walk through this environment, placing each item on the list in a memorable place within the environment. When it is later time to retrieve the information, you would simply re-imagine yourself walking along that same route and hopefully each item on the list would be right there where you left it.

We are now going to teleport you to an area where you can practice using the technique I just described to you. Please teleport to Moon now by scrolling out of first person view. In this world, a series of three 3D shapes will appear in front of you. Please move about the environment and place the shapes in locations of your choosing. For example, try placing them on a sofa or coffee table inside the Moon world. Each item will be available for you to view for 30 seconds before a new one appears.

We are now going to teleport back to each of the virtual environments you explored when you collected tokens. These environments will be your “virtual memory palaces”. While you are there this time, a series of items will appear in front of you, one-at-a-time, just like during the practice. You will be able to view each item and walk around the environment with it for up to 30 seconds before a new item appears. Within that 30-second time frame, you will be able to place” each item in a location of your choosing by clicking on the item itself. We encourage you to place the items so that you can make the most out of the environment and what you see around you, especially the landmarks. Please do not take longer than 30 seconds; otherwise you would miss the opportunity to place that item.

You will be in [WORLD NAME]. Your task is to remember these items in the order they were presented. These objects belong to [LIST NAME]. We will ask you to tell us the items belong to [LIST NAME], so be sure to remember that you learned [LIST NAME] in

[WORLD NAME]. Teleport to the [WORLD NAME] so you can see the items belonging to [LIST NAME]. Right now you are at the southern part of the map. So straight ahead is North, to your left is West, and to your right is East.

*WaL Encoding*

People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the “Walk and Learn” strategy that can be used to aid your memorization of a list of items. Conceived in Ancient Greece, this strategy involves mentally walking in an imagined environment with objects that you wish to remember. For instance, if you had a list of 15 items to remember, you could conjure up a memory of a familiar environment (like your childhood home) and mentally walk through the environment, mentalizing each object in the list – one after another. When it is later time to retrieve information, you simply re-imagine your walk along the same route and hopefully each item on the list would reappear in your memory as you walk.

We are now going to teleport you to an area where you can practice using the technique I just described to you. Please teleport to Moon now by scrolling out of first person view. In this world, a series of three 3D shapes will appear in front of you. Please walk around and explore this world as you view each of these items. Each item will be available for you to view for 30 seconds before a new one appears.

We are now going to teleport back to each of the virtual environments you explored while collecting tokens. While you are there this time, a series of items will appear in front of you, one at a time, just like during the practice. You will be able to view each item and walk around the environment with it for up to 30 seconds before a new item appears.

You will be in [WORLD NAME]. Your task is to remember these items in the order they were presented. These objects belong to [LIST NAME]. We will ask you to tell us the items belong to [LIST NAME], so be sure to remember that you learned [LIST NAME] in [WORLD NAME]. Teleport to the [WORLD NAME] so you can see the items belonging to [LIST NAME]. Right now you are at the southern part of the map. So straight ahead is North, to your left is West, and to your right is East.

### *MoL Forward Recall*

I would now like you to tell me, in order, the list of objects you saw in [LIST NAME]. If you would like, feel free to close your eyes and imagine yourself walking through the environment and viewing each item as it was presented in the environment. To capture the order of the items, it might be a good idea to recreate the same exact path you originally travelled, if you remember. Just say each item aloud as you come across it or remember it. Imagining each item in relation to context of the environment, such as nearby landmark, may help as well. If you cannot remember them in order, just say as many items as you can from that list.

### *MoL Reverse Recall*

We are now going to do some more verbal recall, but this time slightly different. I would like you to tell me, in order, the list of objects from [Name's] List. However, this time, I'd like for you to start with the last item you saw on [Name's] List and tell me each item in the list in reverse until you get to the first item you saw on from [Name's] List. If you would like, feel free to close your eyes and imagine yourself walking through the environment and viewing each item as it was presented in the environment. To capture the order of the items, it might be a good idea to recreate the same exact path you originally travelled, if you remember. Just say each item aloud as you come across it or remember it. Imagining each item in relation to context of the environment, such as nearby landmark, may help as well. If you cannot remember them in order, just say as many items as you can from that list.

### *WaL Forward Recall*

I would now like you to tell me, in order, the list of objects you saw in [LIST NAME]. If you would like, feel free to close your eyes and imagine yourself walking through the environment and viewing each item as it was presented in the environment. To capture the order of the items, it might be a good idea to recreate the same exact path you originally travelled, if you remember. Just say each item aloud as you come across it or remember it. Imagining each item in relation to context of the environment, such as nearby landmark, may help as well. If you cannot remember them in order, just say as many items as you can from that list.

### *WaL Reverse Recall*

We are now going to do some more verbal recall, but this time slightly different. I would like you to tell me, in order, the list of objects from [Name’s] List. However, this time, I’d like for you to start with the last item you saw on [Name’s] List and tell me each item in the list in reverse until you get to the first item you saw on from [Name’s] List. If you would like, feel free to close your eyes and imagine yourself walking through the environment and viewing each item as it was presented in the environment. To capture the order of the items, it might be a good idea to recreate the same exact path you originally travelled, if you remember. Just say each item aloud as you come across it or remember it. Imagining each item in relation to context of the environment, such as nearby landmark, may help as well. If you cannot remember them in order, just say as many items as you can from that list.

## Chapter 4: Reusing a Memory Palace: An evaluation of virtual strategies

### Abstract

The Method of Loci (MoL) has been widely regarded as an effective mnemonic technique for thousands of years (Yates, 1966). Such historic prowess remains relevant in the modern age; the MoL is, by and large, the most widely utilized technique amongst competitive memory athletes (Foer, 2011). Recent developments in Virtual reality (VR) have even enabled researchers to implement virtual versions of the MoL, whereby participants place lists of to-be-remembered objects within a series of virtual environments (VEs; Reggente et al., 2018). Given that varying context across lists promotes differentiation (Howard and Kahana, 1999), practitioners of the MoL will try to leverage different environments to encode separate bundles of information. However, this inserts an unnecessary limit on the MoL's potential as a function of the expanse of environments the user is familiar with. Instead, a large proportion of memory champions leveraging the MoL will implement strategies that allow for them to “reuse” the same memory palace to encode multiple lists of information. In the current study, we tested two such strategies, implemented between encoding two lists of 20 objects within a single VE to determine the most effective strategy: 1) a cleanout / reversal learning strategy whereby participants actively tried to forget the previously learned information by watching objects fade upon a revisit to their placed location 2) an elaborative encoding strategy that permitted participants to place new objects at the locations of previously placed objects –weaving together a visuospatial scene that associated items across multiple lists. Results indicate no advantage for either the cleanout or elaborative encoding strategy in regards to the total number of words recalled across the two lists.

Additionally, we observed a deficit in recall for the second list of items specific to participants leveraging an elaborative encoding strategy, compared to those using the cleanout method and a control group who simply took a break between encoding sessions. While forgetting was minimized in the elaborative encoding group across recall attempts for the same list of objects, intrusions were also increased. Taken together, our results suggest that sufficiently large VEs may be able to permit inter-environmental subsections that prevent intrusion when encoding multiple lists of information.

## Introduction

Previous research has shown that virtual reality can serve as a medium for the implementation of the Method of Loci (MoL) technique, offering a near 30% increase in memory strength for subjects that actively place objects about an environment as compared to a control group that walked with objects in virtual environments (VEs; Chapter 3). This research also implicated that one's spatial memory for a particular virtual environment was correlated with outcome memory strength—emphasizing the importance of spatial memory for list-learning in VEs and subsequently offering that it may be prudent to continually increase a subject's familiarity with established VEs.

If memory is to be characterized as a constellation of representations of co-occurring stimuli (Rumelhart and McClelland, 1988), then it stands to reason that the spatial context enveloping an event constitutes a significant portion of the engram dedicated to that event (see Tulving, 1993). As such, it appears that the phenomenon of contextual reinstatement (Bartlett, 1932; Tulving, 1993) is dominated by spatial environments—a notion that is theorized to underpin findings that position space as the primary currency of the brain's encoding mechanisms (Mullally and Maguire, 2014; Robin et al., 2016, 2018). This posit is particularly salient when considering that memory retrieval depends on both reactivating an engram (i.e. pattern completion) and dissociating it from other engrams despite an overlap in nodes that make up multiple such representations (i.e. pattern separation; Yassa and Stark, 2011).

Neural ensembles in the hippocampus are thought to accomplish this differentiation partially through the use of attractor networks (Hopfield, 1982). Linear changes in the layout of a spatial environment (e.g. morphing from a square to circular enclosure) elicit alterations in hippocampal coding for that space only after "enough" of a change has occurred; otherwise, the pattern continues to exhibit attractor dynamic properties by representing the "new" environment in the same way as the original environment (Leutgeb et al., 2005). The readout of such patterns determines behavior as well. The degree of sigmoidal hippocampal responses (i.e. attractor dynamics) to the linear morphing of familiar environments (e.g. pictorial overlay of 20% environment A, 80% environment B) predicts participant behavior on an object-place task whereby participants would have learned item A's location in both environments A and B and then tested on their object-place memory when inserted into novel, linear morphs of environments A and B; that is, if the hippocampus is representing an A/B morphed environment in more of an A-like fashion, the participant will provide a place-based response that is closer to the object's learned location in A than the analog in B (Steemers et al., 2016).

While the learning of information across multiple contexts is beneficial for certain types of memory like motor-skill acquisition (for review, see Magill and Hall, 1990), mnemonic strategies like the MoL, which depending on binding information to a spatial environment, benefit more so from the compartmentalization of certain lists of information within a single environment. It follows that if an environment that has previously been utilized for the encoding of visual objects, it is theoretically ripe for interference when one is looking to encode new information within that same environment. Several experiments have tangentially investigated contextual interference by having participants learn multiple lists of items and observing errors in list membership during recall. For example, Keppel and Zavortink (1969) showed that when using the peg words method (an effective mnemonic based on creating mental associations between items and numbers that have previously been associated with independent objects) for learning several lists in succession, there is a significant degree of retroactive interference whereby items from previous lists infiltrate subjects' recall attempts of subsequent lists. Additionally, Winograd (1968) showed that objects which fell into the same category suffered from poor list differentiation. That is, if an object belonged to a category that was shared by both lists, that object was more likely to cause retroactive interference than an object that belonged to a category that was unique to only one list. Additional evidence comes from the observation that changing context can assist with directed forgetting (Sahakyan and Kelley, 2002) and that context is the most potent predictor of the lag recency (see Raaijmakers and Shiffrin, 1981) and end-of-list recency effects (Howard and Kahana, 1999). The effect of object-category on retrieval processes is so potent that a to-be-recalled object's category can be decoded using functional magnetic resonance imaging (fMRI) several seconds before the recall of the object itself (Polyn et al., 2005). Such neural signatures have behavioral implications as well; if a subject's brain activity expresses patterns representative of list A's context while they encode list B, their subsequent recall will misattribute list B's items to list A (Gershman et al., 2013). With a small stretch of reasoning, replacing "categories" with environments that served as a contextual backdrop, the encoding of multiple lists of objects within the same environment could lead to poor list differentiation.

Taken together, it would appear that establishing a new, distinct environment for each list of to-be-remembered information would be most prudent in the aim of maximizing the retainment of information and reducing interference across lists, especially during strategies like the MoL, which explicitly depend on the spatial environment for its efficacy. However, seeing as the creation and learning of such virtual environments is a cost and time intensive process, it would be beneficial to keep the number of unique environments to a minimum. Thus, the development of a method that allows for one to implement the MoL for multiple lists of items within the same environment is imperative. The process of "cleaning out" one's memory palace, so as to reuse it for encoding of new information, is a common practice for memory champions that traditionally employ the MoL (Foer, 2011). This "clean out" process requires spending a prolonged period of time imagining the destruction or removal of objects that were previously placed in one's mental memory palace. Often times, implementers of the method will animate the destruction so as to make the process more vivid (e.g. using a broom to sweep away items or a grenade to blow them up).

This "cleanout" practice is an extension of what is known as "reversal learning" – a process that can be used to "forget" previously learned associations of material, including information bound to spatial environments (Schrijver et al., 2004). The process is thought to be a higher order executive function and is known to be mediated by the ventrolateral prefrontal cortex (Cools et al., 2002). Essentially, the goal of reversal learning / memory updating would be to maximize differentiation across multiple lists of items so as to decrease interference.  Underwood (1949) observed that the greatest number of intrusions across multiple lists of learned materials occur with low differentiation. Yates (1966) postulated a “wax-tablet” theory in which one’s mental imagery could house a mnemonic cue and, temporarily, a to-be-forgotten item that could be wiped out or erased, similar to the “unlearning hypothesis” (Melton and Irwin, 1940). Such a theory would seem to be supported by the effectiveness memory champions meet when “erasing” previously learned information from their mental memory palaces.

Early experiments have investigated humans’ ability to update their memory using mnemonic devices. Surprisingly, some studies yield relatively counterintuitive results that seem to de-emphasize the importance of “reversal learning” and instead encourage retaining the previously learned material and incorporating it into the learning of new material. For example, Bellezza (1982) found that when associative interference was maximized (e.g. learn A-B and then A-C to encourage learning B-C), only a limited disruption of updating was observed. Exemplifying the notion that forging items, in contrast to forgetting them, is a more potent strategy for reducing interference, Bower and Reitman (1972) developed a strategy that they dubbed “progressive elaboration” so as to combat retroactive interference when using the peg words method to encode successive lists of information. Their progressive elaboration involves a subject progressively adding new objects to a picture whereby each *n*th object on each list is associated alongside the *n*th object from the other lists. The authors use the following example to illustrate:

> *Suppose the third word in Lists 1, 2, 3 were swing, cigar, fish, respectively. With the peg word "3 is a tree," the scenes progressively elaborated during learning of the lists might be: for List 1, "a swing hanging from branches of a tree"; for List 2, "a cigar lying on the swing on the tree"; for List 3, "a fish smoking a cigar while swinging under a tree.*

Such a method appears to embrace the issue of contextual interference head on. In their experiment, Bower and Reitman (1972) compared subjects using this progressive elaboration to control subjects who were instructed to create entirely new imagined scenes for each list, specifically not calling to mind the words from previous lists associated to each peg word as it was used anew. The experiment also included a variant where participants used the MoL instead of the peg words technique; subjects were instructed to use the progressive elaboration technique and re-use the same loci (locations of their choosing along a path from their Stanford dorm to their Wednesday classes) for each *n*th object on a list, allowing the items to actively interact as illustrated above. The authors hypothesized that in the peg words method, subjects using the progressive elaboration strategy would show less retroactive interference across lists. However, they were cautious of extending this hypothesis to the MoL as they were weary that locations would birth fewer concrete relations than an object peg. However, participants in the progressive elaboration condition (in both the peg words and MoL groups) remembered more material at the end-of-session test and one-week-later test compared to the subjects who were instructed to use an entirely new association each time. Interestingly, they also observed that participants in the new-association group had a marked recency effect (lists learned later showed greater memory strength) in the end-of session test, where the other groups did not. However, the progressive elaboration participants in both the peg word and MoL groups showed a primacy effect (lists learned first showed great memory strength) after a week had passed. Finally, intrusions were significantly more present during end-of-sessions tests as compared to immediate tests, but did not vary as a function of subject group. These findings are extended by the observation that increasing the amount of nonredundant elaboration one inflicts on an object when employing the MoL (e.g. by rating each object on it's pleasantness) increases the accessibility of that visual image and the effectiveness of the mnemonic technique (Yesavage and Rose, 1984).

In summary, it appears as though two potential strategies exist for reducing contextual interference during the recall of independent lists of information: 1) a cleanout / reversal learning strategy whereby one actively tries to forget the previously learned information before encoding new lists and 2) an elaborative encoding strategy that involves weaving together a visuospatial scene that associates items across multiple lists. Leading theories of memory and anecdotal reports of memory champions supports the former, but the latter has significant empirical support, albeit limited. It is the aim of this proposed study to elucidate the most efficient method for one to reduce retroactive interference and maximize recall strength when encoding multiple lists of objects within the same virtual environments. Briefly, this current work leveraged virtual encoding software developed for Chapter 3 and allowed participants to encode a list of objects within a VE. Subsequently, participants were assigned to groups, whose instructions and afforded virtual functionality permitted for an evaluations of strategies in reducing contextual interference when learning a second list within the same VE: 1) elaborative encoding whereby the nth object on list 2 was encoded alongside the nth object of list 1, 2) cleanout whereby participants could see all previously placed objects “fade” before encoding list 2, and finally, as a control, 3) the passage of time between encoding visits to the VE.

## Methods

### *Participants*

135 participants were recruited for this study using UCLA’s psychology department online subject pool, which awards participants with class credit for participating in research studies. 33 participants could not finish the study due to either motion sickness (n=6) or technical issues (e.g. objects did not render or disappear appropriately). Thus, a total of 102 participants, aged 18-33 (M=20.74, SD=2.48, 52 females) completed this study.

Participants were required to be right-handed, have normal or corrected-to-normal vision and hearing, have a mastery of the English language, and report no diagnosed learning disabilities, substance dependencies, nor prescriptions for psychotropic medications. Additionally, to prevent unequal exposure to the experimental apparatus, applicants were not permitted to participate if they had more than five hours of previous experience with the VR software used in this experiment (Second Life [http://secondlife.com] or its open-source virtual simulator OpenSimulator [http://opensimulator.org]). Eligibility screening was conducted prior to the participant’s enrollment in the study using the Research Electronic Data Capture (REDCap) online survey systems (Harris et al., 2009).

### *Materials*

Extensive material description is reported in Chapter 3, but also briefly described below. All tasks were presented on a 27” Monitor connected to a custom-built computer running Windows 7 Professional Operating System. Virtual environments and software were developed using OpenSimulator (http://opensimulator.org; Release 0.9.0.0). Two distinct VEs were leveraged in this study: “Lagoon World” for participant orientation and “Toon World” for encoding (Figure 1A). Both VEs sat on a 64 x 64 grid (arbitrary virtual units) with eight distinct landmarks are the cardinal perimeter points (i.e. South, Southwest, West, etc.; Figure 1B).

Two digital Heads Up Displays (HUDs) were worn by the participant’s avatar during two different phases on the experiment. The first HUD presented an on-screen digital counter of the coins that the participant had collected throughout Toon World and was triggered by an experimental control desk located above the world, which also recorded the total time taken by the participant to collect all the coins (Figure 1C). The second HUD permitted for a list of 3D objects to render in front of the participant’s avatar with the functionality to click on the object and “freeze” it in place (Figure 1D); group-specific functionality (described below) was also afforded by this second HUD. An experimental control platform located above Toon World provided experimenters with the ability to control which list of objects were to be rendered, how long they were present for, and which group the participant was assigned to. The control platform also provided reports for the precise location of each item in the environment with a 1s time-scale resolution.

60 3D objects were rendered for this study using Blender (https://www.blender.org), relying partially on open-source objects acquired from TurboSquid (https://www.turbosquid.com). Objects were randomly sampled, without replacement, from this pool when creating the two lists of 20 objects each used for participant encoding.

With participant permission, verbal recall tests were digitally recorded and cued conversationally by experimenters. Spatial recall tests (Figure 3.) were conducted and analyzed using custom MATLAB (The Mathworks, Inc., 2012b) code and Psychophysics Toolbox (Version 3; Brainard, 1997), which showed participants (for the first time) a bird's eye view of Toon World and allowed them to pinpoint cursor to the cued location of landmarks, coins, and objects they encountered. Finally, all statistical tests were conducted using custom R (R Core Team, 2013; http://www.R-PRoject.org/) and MATLAB code.

*Procedure*

All participants were first placed in Lagoon World where they were instructed how to navigate using the mouse and keyboard. Experimenters confirmed all participants could move and adjust their looking direction comfortably before moving to the next phase. Subjects were then teleported to Toon World where they were told to collect 20 coins that were located about the environment, with explicit instructions to take note of the layout of the environment and its landmarks and to stay within the boundaries of the environment. Participants were given 5 minutes to collect all the coins and instructed to spend any remaining time exploring the environment of their own volition. Afterwards, participants took a short break while the experimenter prepared the next task. Upon returning, participants were briefed on the traditional implementation of the MoL and how the present VR software would allow for them to implement the technique, virtually (see Appendix 1 for a full transcript of the instructions). Afterwards, they were teleported to Lagoon World where they practiced the encoding process using a test list of 3D objects ("pyramid", "cube", and "sphere"). The objects appeared for 20s each and subjects learned to move about Lagoon World with the objects and how to click on them to trigger the freezing of the object in its current location (x, y, z).

What follows is a detailed description of each participant group's specific encoding and retrieval paradigm. Of note is that, in sum, all participants were exposed to each object on each list (40 total objects; 20 per list) for a total of 30s within Toon World by the end of the paradigm. All participants were informed that each list belonged to one of two fictional individuals ("Otto" or "Pike") and told that they would later be instructed to recall the list of items in their original presentation order as cued by the individual's name. Participants were also instructed to recall in the reverse order. In both recalls, participants were told to remember as many items as they could, even if they could not recall the order. Figure 4 provides a detailed schematic of the experiment for each group.

### *Cleanout Group*

Participants assigned to the cleanout group were given 20s to view and place each object on the first list of items. Afterwards, they were given a short 2-minute break. Following the break, they were given two minutes to verbal recall first in the original encoding order and, subsequently, in the reverse of the original encoding order. Afterwards, they were submitted to the spatial recall task to test their allocentric memory for where they placed the items on list. Participants were then informed of the traditional implementation of the cleanout technique (see Appendix 2 for full instruction transcript) and told that they would be trying to forget the information they just encoded by watching the objects “fade” in the locations they originally placed them. Next, participants were placed back into Toon World where a black sphere was located where they placed the first item on the first list (Figure 2A, left panel). Participants were instructed to navigate to the black sphere. Upon reaching the sphere, it would disappear, revealing the object they had previously placed at that location. Immediately after rendering, the object would begin to fade for a period of 10s until it disappeared completely (Figure 2A, right panel). After viewing each item on the list fade, participants were transported back to the southernmost region of Toon World and repeated the encoding and recall process for the second list. Following this second encoding / recall period, participants were given a surprise forward and reverse recall test for the items on list 1, cued by the fictional individual’s name. Following this third recall period, cleanout participants were submitted to a second spatial memory test for the location of objects on list 1, followed immediately by a spatial memory test for the location of the coins collected in the environment and objects located throughout the environment. Finally, they were submitted to the post-experimental questionnaire before being dismissed from the experiment.

### *Elaborative Encoding Group*

Elaborative encoding participants were also given 20s to view and place each object on the first list of items and were also subsequently submitted to a forward/reverse/spatial memory test after a 2-minute break. Following this break, participants were briefed on the traditional implementation of the elaborative encoding technique (see Appendix 3 for full instruction transcript) and told that they would be implementing the technique using our VR software. After instructions, participants were placed back into the southernmost portion of Toon World, where they were presented with the first object on list 2. At the same time as the first object appeared, a black sphere was rendered at the location where the participant placed the first object on list 2. The subject was instructed to walk with the object to the black sphere. Upon reaching the black sphere, but not before 20s had elapsed since the object from list 2 was rendered, the black sphere would disappear, revealing the first object on list 1 that was placed in that location. Participants had 10s to view both objects at the same time and place the object from list 2 on, below, or next to the object from list 1. After placing each nth object on list 2 with its counterpart nth object on list 2, all participants were tested on the forward/reverse/spatial recall for list 2's items. Like in the cleanout group, participants were then submitted to surprise forward/reverse/spatial recall tests for list 1's objects, followed by a spatial memory test for the landmarks and coins in Toon World, and finally a post-experimental questionnaire.

### *Control Group*

Participants in the control group were given 30s to view and place each object on the first list before taking a short two minute break and then being tested on their forward/reverse/spatial recall for list 1's objects. Following recall, control participants were given 10 minutes to take a break in which they were restricted from using their cell phone or computer. After this break, participants repeated the same encoding process as they did for list 1, but for the second list of objects. No mention of the previous objects or any strategy was mentioned between the encoding of the two lists. After encoding all objects on list 2, participants were tested for their forward/reverse/spatial recall for list 2's objects, followed by the same surprise forward/reverse/spatial recall prompt for list 1's objects, a spatial memory test for the landmarks and coins in Toon World, and finally the same post-experimental questionnaire.

### *Behavioral Scoring*

Participants' verbal recall recordings were transcribed by one of the five experimenters in charge of scheduling and testing participants. The primary recall metrics of interest were performance on the surprise recall test as a function of group and previous recall attempts, the total number of objects recalled across all sessions, and how individual differences in spatial memory for learned objects and their degree of presence in the environment played a mediating role. Performance on all recall tests was measured using three metrics: 1) the number of words correctly recalled within the 2-minute time-limit ($\text{Recall}_{\text{total}}$ / $\text{Reverse-Recall}_{\text{total}}$), 2) the number of adjacent word pairs that were representative of the original encoding order ($\text{Recall}_{\text{clustering}}$ / $\text{Reverse-Recall}_{\text{clustering}}$), and 3) the number of words recalled that were not on the cued list (Interference). Clustering was calculated using a serial clustering metric, adjusted for chance, developed by (Stricker et al., 2002) and given by:

$$\text{Recall}_{\text{clustering}} \text{ or } \text{Reverse-Recall}_{\text{clustering}} = X - (r - 1)/N$$

where X is the total number of observed pairs of adjacent words in the recalled list that were also beside each other in the original presentation list, r is the total number of correct words recalled in the trial, and N is the total number of words presented in a list

(N=20 in all calculations). Additional sets of second-order metrics were calculated as the difference in recall between recall 1 and recall 3 (both of which tested for memory of list 1's objects).

A participant's spatial memory for objects was calculated as the average Euclidean distance between the coordinate vectors (x,y) for where the participant actually placed the object vs. where they clicked on the bird's eye view of the map. The same metric was calculated for a participant's spatial memory for the landmarks. A third spatial metric was calculated to reflect a participant's memory for the location of coins within Toon World by calculating the average Euclidean distance between the selected location and the nearest coin, only allowing each coin to be considered the "nearest" exactly once. Finally, a metric denoting the average proximity of objects to landmarks within an environment was calculated as the average Euclidean distance between an object and its nearest landmark, within a list.

### *Presence*

Two independent measures of presence were collected via REDCAP (Harris et al., 2009) during the post-experimental questionnaire: 1) A six-question survey, developed and continually refined by another research group (Slater, McCarthy, & Maringelli, 1998; Slater, Usoh, & Steed, 1994; Slater, Usoh, & Chrysanthou, 1995; Slater, Usoh, & Steed, 1995), where the metric reported ($\text{Presence}_{\text{Slater}}$) is the number of responses rated as $\geq$ 6 and 2) A ten-question survey developed by Fox, Bailenson, and Binney (2009), where the reported metric ($\text{Presence}_{\text{Fox}}$) is the average score across all ten items. Participants were also given a simple 10-point scale question that asked: "To what degree did you feel you were ‘in’ Toon World as you moved around?” to acquire an environment-specific measure of presence.

### *Statistical Analyses*

Analyses comparing the various recall metrics across groups were conducted using a one-way analysis of variance (ANOVA); significant F-statistics ($p<0.05$) were submitted to a follow-up t-test of simple effects. If violations of normality were observed (kurtosis or skew > 1.96; (Gravetter and Wallnau, 2008) in the underlying dependent variable, a Kruskal-Wallis one-way analysis of variance test, which does not assume a normal distribution(Kruskal and Wallis, 1952), was used; the Chi-square and associated p-values are reported and a Mann-Whitney U test was conducted for follow-ups of simple effects. Examinations of individual differences across two continuous variables were calculated with a Pearson’s linear correlation coefficient; r-values are reported alongside p-values from a t-test comparing the r-value to a null hypothesis of no-relationship (i.e. $r=0$). In the presence of a significant correlation within any experimental group (or across all participants), a comparison of the correlation within the other groups was conducted using a two-tailed test for the difference between either two independent correlation coefficients (Cohen and Cohen, 2003) using an online utility (http://quantpsy.org/corrtest/; (Lee and Preacher, K. J, 2013; Preacher, 2002). For analyses where multiple metrics were collected for each group (e.g. landmark-object proximity across worlds), a multivariate analysis of variance (MANOVA) was conducted and the F-statistic and Wilk's Λ are reported.

To examine the impacts of additional variables on a linear model of experimental group on the various recall metrics, a stepwise linear regression was implemented for independent variables of interest. Examined variables included those that either a) previously revealed a group difference (e.g. spatial memory) or b) warranted investigation due to supporting literature (e.g. presence). An analysis of deviance was conducted on the nested models to determine if the model benefited from the inclusion of the additional variable (i.e. parsimonious); F-statistics and associate p-values are reported and beta-coefficients were analyzed with a t-test.

## Results

### *Forward Recall 1*

Despite both cleanout and elaborative encoding participants having seen List 1's objects for 10s less than participants in the control group at the time of Recall 1, there was no significant difference across groups in the total number of words recalled [H(2)=3.81, p=0.149]. There was a significant difference, however, in the number of words recalled in the correct order [H(2)=8.33, p=0.016], driven by participants recalling significantly less in the elaborative encoding group compared to cleanout (p=0.014) participants.

### *Forward Recall 2*

A significant effect of group on the total number of objects recalled was observed [H(2)=9.98, p=0.007], driven by the elaborative encoding group recalling significantly less than both the cleanout (p=0.012) and the control group (p=0.025). There was also a group effect on the number of objects recalled in the correct order [F(2,101)=5.77, p=0.004], driven by participants in the elaborative encoding condition recalling significantly less words in the correct order compared to control (p=0.007) and cleanout (p=0.019) participants. The number of intrusions was remarkably low across groups (Elaborative = 2 total intrusions; Cleanout = 2; Time = 0), and this minor difference was not significant.

*Forward Recall 3*

There was no significant difference across groups in the number of words recalled on the surprise recall test for List 1's objects [H(2)=5.36, p=0.068] nor for the number of words recalled in the correct order [F(2,101)=1.11, p=0.335]. There was also no effect of group on intrusion. The difference in recall attempts for List 1's object (i.e. recall 1 and surprise recall 3) was calculated as a measure of "forgetting". While participants in the control group had very little forgetting across recall attempts (M=0.618, SD=2.708), participants in the cleanout group actually recalled more objects on the surprise recall test (M= -1.06, SD=2.33), as did participants in the elaborative encoding group (M=-2.62, SD=3.31). This difference was significant [H(2)=16.04, p<0.001], due only to a significant difference between elaborative and control participants (p<0.001). Intrusions were low across groups (Elaborative= 8 total intrusions, Cleanout=2; Control=3), and this minor difference was not significant.

*Reverse Recall 1*

No difference in the number of words recalled was observed as a function of group [H(2)=2.71, p=0.258]. There was a significant difference in the number of words recalled in the correct reverse order, as a function of group [H(2)=8.44, p=0.015], driven by participants recalling significantly less in the elaborative encoding group compared to cleanout (p=0.014) participants.

### *Reverse Recall 2*

There was a significant effect of group on the total number of words recalled [H(2)=13.06, p=0.002]. Both cleanout (p=0.001) and control (p=0.034) participants recalled significantly more words than those in the elaborative encoding group. There was also a significant difference in the number of words recalled in the correct order [F(2,101)=7.28, p=0.001], driven by participants in the elaborative encoding condition recalling significantly less words in the correct order compared to control (p=0.012) and cleanout (p=0.002) participants. The total number of intrusions were low across groups (Elaborative = 7 total intrusions; Cleanout = 1; Control = 2), and no significant difference was observed.

### *Reverse Recall 3*

There was no significant difference across groups in the number of words recalled on the surprise recall test for List 1’s objects [H(2)=1.46, p=0.482] nor for the number of words recalled in the correct order [F(2,101)=1.87, p=0.159]. There was, however, a significant effect of intrusion [H(2)=10, p=0.007], with participants in the elaborative encoding group having significantly more intrusions than their control (p=0.043) and cleanout (p=0.008) counterparts. An effect of group was also observed on forgetting [H(2)=12.35, p=0.002], again driven by significantly less forgetting in the elaborative group compared to the control (p=0.002) group. The total number of intrusions were higher in this recall attempt and varied as a function of group (Elaborative = 40 total intrusions; Cleanout = 5; Control = 9) [H(2)=10, p=0.007], driven by elaborative encoding participants having more intrusions than cleanout (p=0.008) and control (p=0.043) participants.

*Recall Summary*

As a summary metric for each recall session, we also combined forward and reverse recall to yield a Total Recall for each retrieval attempt. Group had no effect on List 1's Total Recall for number of words [H(2)=3.43, p=0.18], but one was observed for correct order [H(2)=8.78, p=0.012], driven by less words recalled in the correct order by Elaborative participants, compared to cleanout participants (p=0.013). Total Recall on List 2 varied as a function of group on number of words recalled [H(2)=11.29, p=0.004], driven by elaborative participants recalling less than both cleanout (p=0.004) and control (p=0.03) participants, and the number of words recalled in the correct order [H(2)=12.19,p=0.002], driven by elaborative participants recalling less than both cleanout (p=0.005) and control (p=0.01) participants. There was no significant difference across groups in the number of words recalled on the surprise recall test for List 1's objects (Recall 3) [H(2)=2.84, p=0.242] nor for the number of words recalled in the correct order [F(2,101)=1.5, p=0.23]. See Figure 5 for recall results as a function of group and attempt.There was a strong effect for forgetting as a function of group [H(2)=16.8, p<.001], which was driven by elaborative participants forgetting far less material than both the cleanout (p=0.028) and control (p<0.001) groups (Figure 6). There was no effect of intrusions as a function of group during Recall 2, but one was observed during Recall 3 [H(2)=11.47, p=0.003], driven by participants in the elaborative encoding group having significantly more intrusions than both cleanout (p=0.005) and control (p=0.02) participants (Figure 7).

Collapsing across lists revealed no consistent effect in forward recall for the number of words recalled in total [H(2)=2.86, p=0.24] or in the correct order [H(2)=5.44, p=0.066].

The same was true for the number of words in total during reverse recall [H(2)=3.96, p=0.138]. However, there was a difference in group for the number of words recalled in the correct reverse order [H(2)=7.5, p=0.024], driven by elaborative encoding participants recalling significantly less than the cleanout group (p=0.018). Finally, collapsing across all lists and forward/reverse recall attempts revealed no difference in total number of words recalled [H(2)=3.46, p=0.177]. However, a small difference was found for the number of words recalled in the correct order [H(2)=6.61, p=0.037], but this was mainly driven by elaborative encoding participants recalling less than their cleanout counterparts (p=0.032).

### *Spatial Memory*

There was no effect of group on a participant’s spatial memory for the location of placed objects on the first [H(2)=1.84, p=0.399], second [H(2)=2.02, p=0.365], or third [H(2)=2.19, p=0.334] attempt. No effect of spatial forgetting (i.e. difference between spatial memory for Objects after Recall 1 vs. Recall 3) was observed as a function of group [ H(2)=0.46, p=0.796]. There was also no effect of spatial memory for the landmarks located about the environment, as recalled on the third spatial memory test [H(2)=1.35, p=0.51] nor a difference in groups on the coin-placement task [H(2)=0.04, p=0.979].

## Discussion

Previous research has shown that using MoL software within multiple VEs affords participants with enhanced mnemonic recall (Chapter 3). However, the creation of unique VEs is a time-consuming and effortful process, especially when attempting to induce a sense of fantasy—an environmental standard thought to increase the efficacy of the MoL (Bower, 1970). As such, the identification of a virtual strategy that would allow for the same VE to be used to encode multiple lists of information would increase the ecological validity of translating laboratory technology into consumer products. The current study sought to determine the best strategy with which to minimize interference and maximize encoding capacity when leveraging a single virtual environment (VE) to implement the Method of Loci (MoL).

We evaluated two such potential strategies: 1) A cleanout method, widely utilized by memory champions (Foer, 2011), where one revisits the locations where they placed to-be-remembered objects and actively engages in “destroying” the information in an act of directed-forgetting and 2) An elaborative encoding method, where one revisits the locations of previous objects on a list and places new objects on or around those objects to create a solitary dual-object representation. We created virtual software that allowed for participants assigned to the cleanout group to view and place a list of 20 objects and then return to the same environment to revisit the object locations and then watch the objects *fade* until disappearing before entering the environment for a third time to encode a new list of 20 objects. The software constructed for exclusive use by the elaborative encoding group allowed for participants to revisit the object locations where they previously placed to-be-remembered objects; however, upon re-rendering of the previous objects, participants were able to place a new object nearby—encouraging a representation of the two objects in simultaneity. A third participant group merely allowed participants to take a 10-minute break between the two encoding sessions and served as a control. Participants were evaluated based on the number of words they recalled in total, the number of words recalled in the correct order, the number of words forgotten (between recall attempts on the same list of objects), and number of intrusions (when the object recalled belonged to an incorrectly cued list).

Results from the current study indicate that neither the elaborative encoding nor cleanout strategy afforded participants with enhanced mnemonic recall compared to the control group, measured by the total number of words recalled and the number of words recalled in the correct order. The elaborative encoding group was actually at a disadvantage on these metrics, recalling significantly less words (and less in the correct order) than both the cleanout and control group during Recall 2. This finding suggests that when encoding a list of objects in an environment where such an encoding had recently occurred for a separate list, the elaborative encoding strategy devised for the current study is not preferable.

However, by the metric of forgetting, participants in the elaborative encoding paradigm had a clear advantage: participants recalled, on average, more words, compared to cleanout and control participants, during the second time recalling List 1’s items than they did the first time. This effect may have been observed due to the fact that participants in the elaborative control group had multiple independent exposures to the original encoding stimuli—an act that is known to bolster memory strength (Szpunar et al., 2004). While it is true that the Cleanout group also received an additional exposure to the original encoding stimuli between the first and second recall of List 1’s objects, this exposure did not have high fidelity to the first experience; the objects were fading and, thus, visually different at each time point compared to the entirety of the original experience. Additionally, cleanout participants were encouraged to actively forget the material they were reviewing—a process known as “reversal learning” which has been successfully used to “forget” previously learned associations of material, including information bound to spatial environments (Schrijver et al., 2004).

This advantage afforded to elaborative encoding participants was dismounted even further, by the observation that, in addition to recalling less words on the second list, the elaborative encoding group had significantly more intrusions during the second recall of List 1’s objects. This finding suggests that in their attempt to co-encode the two stimuli, participants in the elaborative encoding group confounded the two objects and reduced their independence, making it more likely to associate them together and, subsequently, recall them during the wrong cue.

Importantly, outside of the less-forgetting effect observed in elaborative encoding participants, neither of the experimental groups outperformed the control group, even when averaging across all recall attempts to obtain a Total Recall metric. As such, it appears that given the current study’s experimental stimuli, the most parsimonious approach to maximize recall, while minimizing interference, is to simply take a short break between encoding sessions. While one may be more likely to forget significantly less words from the first list after encoding a second list than if they had employed an elaborative encoding strategy, the cons of decreased recall for the second list and an overall increase in intrusions does not present an elaborative encoding strategy as a worthwhile pursuit.

While Bower and Reitman (1972) observed that elaborative encoding conducted within a single context, held in one’s mental imagery, was advantageous for recall over encoding across separate contexts, Karpicke and Smith (2012) found that repeated retrieval produced better long-term retention than repeated study with elaborative encoding. This lack of a replication, combined with the current study's results suggest that a successful elaborative encoding may depend on the experimental conditions and instructions. Indeed, it has been shown that integrated, highly elaborated memory traces are better recalled than either small unelaborated traces or large, poorly integrated traces (Bradshaw and Anderson, 1982). As such, encouraging behavior with concrete examples is prudent and it could perhaps be reasoned that the current study's virtual software does not allow for a highly elaborated memory trace since the functionality afforded to participants was a mere ability to place an object near a previously placed object. Specifically, no action was permissible in the current study's elaborative encoding scheme; participants could not have the two objects interact—a potentially critical component underlying the mnemonic's purported efficacy. Additional research will need to be conducted to assess the degree with which the elaborative encoding technique can be offloaded from mental imagery, where an infinite number of object and interaction combinations can be formed, and into a virtual reality software.

Given that the cleanout method is widely used amongst those who implement the MoL, especially competitive memory athletes (Foer, 2011), we were initially surprised to not see an advantage for participants afforded the ability to "forget" previous material before learning new material. Our previous work with this suite of custom VR software (Chapter 3) revealed the importance of binding objects with the scaffolding of a VE, and that one's spatial memory for where they placed an object was critically related to their recall of that object. Given the potency of those findings, it may be the case that intra-environment locations served as distinct enough loci that permitted for the encoding of multiple lists of information without the need to engage in forgetting. Much as a single university campus can be broken down into subsets of geo-fenced locales (e.g. Psychology Department Tower), the VE utilized in the current study could have been used by participants to differentiate the two lists (e.g. indoors vs. outdoors). Such a strategy would allow for participants to reap the benefits of spatially-directed encoding without  being subject to the interference effects often witnessed when doing so (Keppel and Zavortink, 1969). Recognizing this potential, there may not have been a need for a cleanout between encoding lists; there was enough space for both sets of objects to be encoded without overlap. Indeed, those who use the cleanout method are encoding orders of magnitude more objects than the 40 mandated by the current study. Future research would need to be conducted to determine a) if encouraging participants to use discrete sub-sections of the VE can prevent the need for a cleanout and b) what the maximal object : square foot ratio is for a single environment and, if when at ceiling, the cleanout method leveraged in the current study allows for a successful re-encoding within that environment.

## Figure Captions

**Figure 1.** Virtual Environment and Software

A) Left panel: “Toon World” where participants encoded both lists of information as seen from the southernmost region of the environment from a “first-person” egocentric viewpoint. Right panel: the eight landmarks situated in the cardinal positions around the perimeter of the environment, arranged respectively. B) Left panel: Example coin collected by a participant upon their first entries entry into Toon World. 20 coins were distributed across the environment and a Heads Up Display (HUD) indicated a participant’s progress as they collected each of the coins. Right panel: Experimenter token-control platform, located on a platform floating above Toon World. Experimenters were able to leverage this control platform to clear coins, initiate the collection phase, and collect metrics concerning a participant’s coin collection. C) Left Panel: Objects continually rendered in front of participants as they navigated Toon World. An HUD rendered the objects and provided a light (green shown here) indicating whether participant was currently in the encoding phase. Objects were visible for a period of 20s before disappearing and a new object appearing in its place. Participants were able to view the object from all angles of its pitch and yaw axes by rotating about the object. Participants were able to “click” on the object and “freeze” it in a location of their choosing. Shown here is a beer in Toon World. Right panel: Experimenter object-control platform, located on a platform floating above Toon World. Experimenters were able to leverage this control platform to load in participant specific lists of objects, delineate which group the participant was in, set the exposure time for objects, send objects to the participant’s HUD, and collect metrics concerning each object’s location within the environment at a temporal resolution of 1s.

**Figure 2.** Group-Specific Functionality

A) Functionality afforded exclusively to participants in the “Cleanout” group. Left panel: a participant initially sees a black sphere at the location where they previously placed an object. Right panel: Upon reaching the black sphere, the object appears and begins fading for 10s until it complete disappears and a new black sphere appears. B) Functionality afforded exclusively to participants in the “Elaborative Encoding” group. Left panel: a participant sees a black sphere in the location where they placed object n on list 1 while also being exposed to item n on list 2. Right panel: Upon reaching the black sphere, and allowing a minimum of 20s to pass since the participant was first shown object n on list 2, object n on list 1 appears for 10s and the participant is encouraged to place object n on list 2 on, about, or around object n on list 1.

**Figure 3.** Object/Landmark/Token Placement Task

Participants were shown an allocentric, “bird’s eye” view of Toon World that contained landmarks (A) for object-placement and token-placement tasks and one that was stripped of its eight landmarks (B) for a landmark-placement task. C) The instruction screen immediately preceding each placement trial. Participants were provided with a 2-D image of an object they encoded and instructions to click on the map location where they placed the object. D) The mouse cursor participants used to select the location of the cued object/landmark/token. E) A grid overlay delineating the 4,096 (64 x 64) cells available for participant selection via their cursor. This grid was not visible to participants, but could be inferred given the cursor’s inability to be placed outside of each cell—the cursor would “snap” to fit into the nearest, overlapping grid cell.

**Figure 4.** Experimental Paradigm

All participants underwent a familiarization phase that first included a general orientation in Avatar Island, followed by five minutes of token-collection. Afterwards, participants were read encoding instructions and teleported to Lagoon World to practice the placement of a set of test objects (cube, pyramid, sphere). All subjects then encoded a list of 20 objects in Toon World. Subjects in the elaborative and cleanout groups saw each objects for 20s; participants in the control group saw each object for 30s. Following the encoding of the list, participants were cued to verbally recall the list of items in forward and, immediately after, reverse encoding order. After this forward and reverse-recall session, participants were submitted to spatial recall tests for where they placed the objects (Figure 3.). Afterwards, participants in the control group took a 10 minute break and then repeated the same encoding process, but with a new list of items. During that same time, participants in the elaborative and cleanout group were placed back in the environment where a black sphere appears in the location of where they placed the first item on the first list. Participants in the cleanout group would navigate to the black sphere and, upon coming within a 3-meter radius of it, automatically trigger the placed item to reappear and begin fading for a period of 10s until it was completely invisible and a new black sphere appeared in the subsequent object's location. Participants in the elaborative encoding group were presented with objects on the second list as they made their way to the black sphere. The objects would appear for a minimum of 30s: the black sphere would not disappear until they had seen the object for 20s and then the previous object placed at that location would appear, allowing 10s for the participant to place the new object on, about, or around the previous object. After encoding both lists of information, all subjects were asked to recall the list of objects on List 2 in the forward and reverse order and were then subjected to the object-placement task for those objects. They then repeated this recall process for List 1 again. Finally, they were submitted to a landmark and coin-placement task where they indicated the location of the objects and coins previously seen in the environment. Finally, all subjects filled out the post-experimental questionnaire.

**Figure 5.** Recall Results

A) Number of words recalled at each recall attempt, collapsed across forward and reverse recall attempts (max=40; 20 objects per list, recalled twice). B) Total number of words recalled in the correct presentation order during both forward and reverse recall (where correct order was determined as the number of words recalled in the reverse of the original presentation order).

*p<0.05; **p<0.01; ***p<0.005

**Figure 6.** Forgetting Results

A) Difference in recall of list 1, which was cued during recall attempts 1 and 3. Negative numbers reflect an increase in recall from Recall 1 to Recall 3.

*p<0.05; **p<0.01; ***p<0.005

**Figure 7.** Intrusions Results

A) The average number of words recalled from the list of objects that was not cued for that particular recall attempt. Metrics are averaged across both forward and reverse recall attempts.

*p<0.05; **p<0.01; ***p<0.005

## Figures

Figure 1. Virtual Environment and Software

**Figure 2. Group-Specific Functionality**

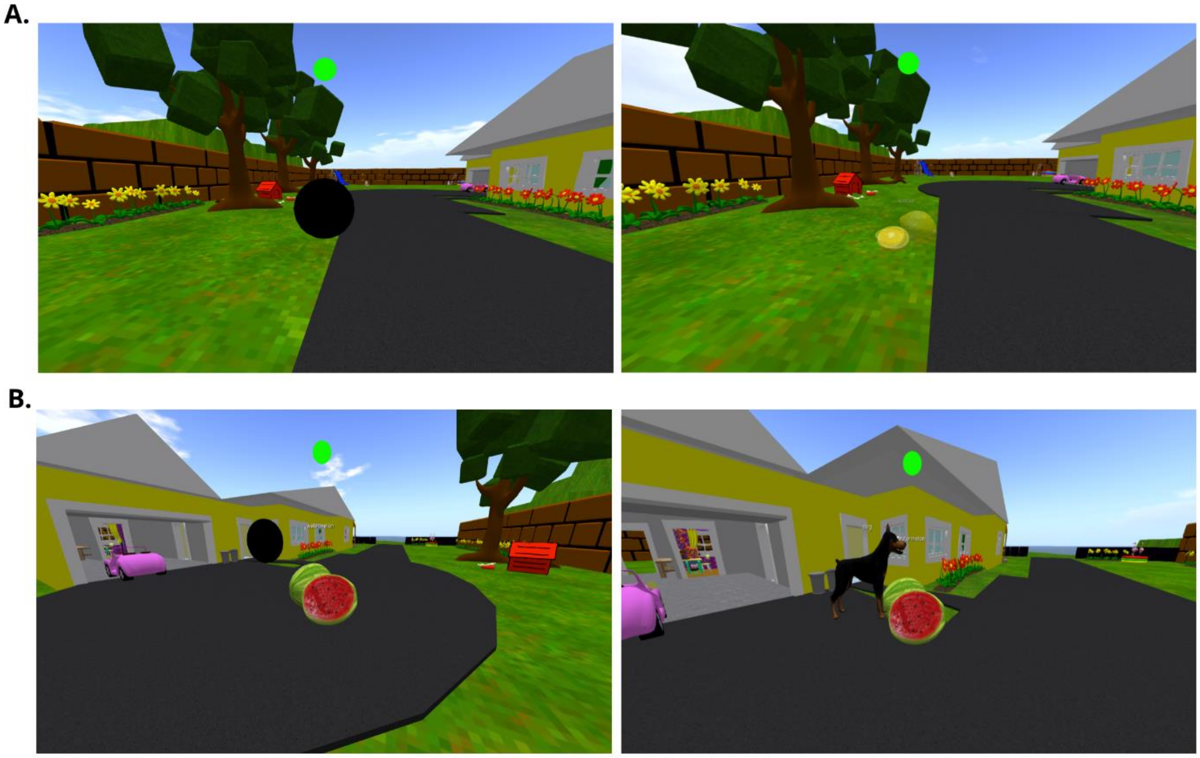
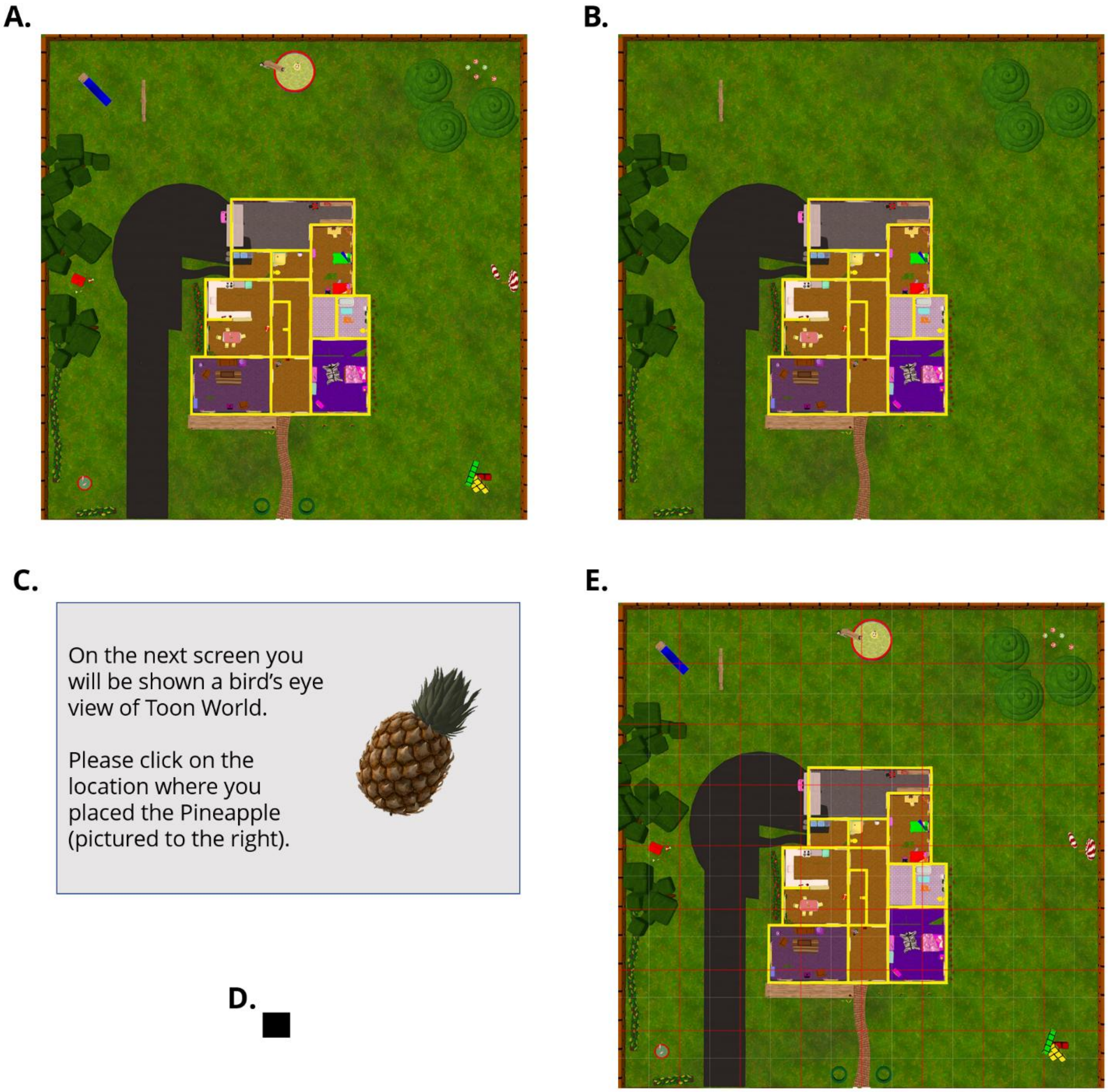


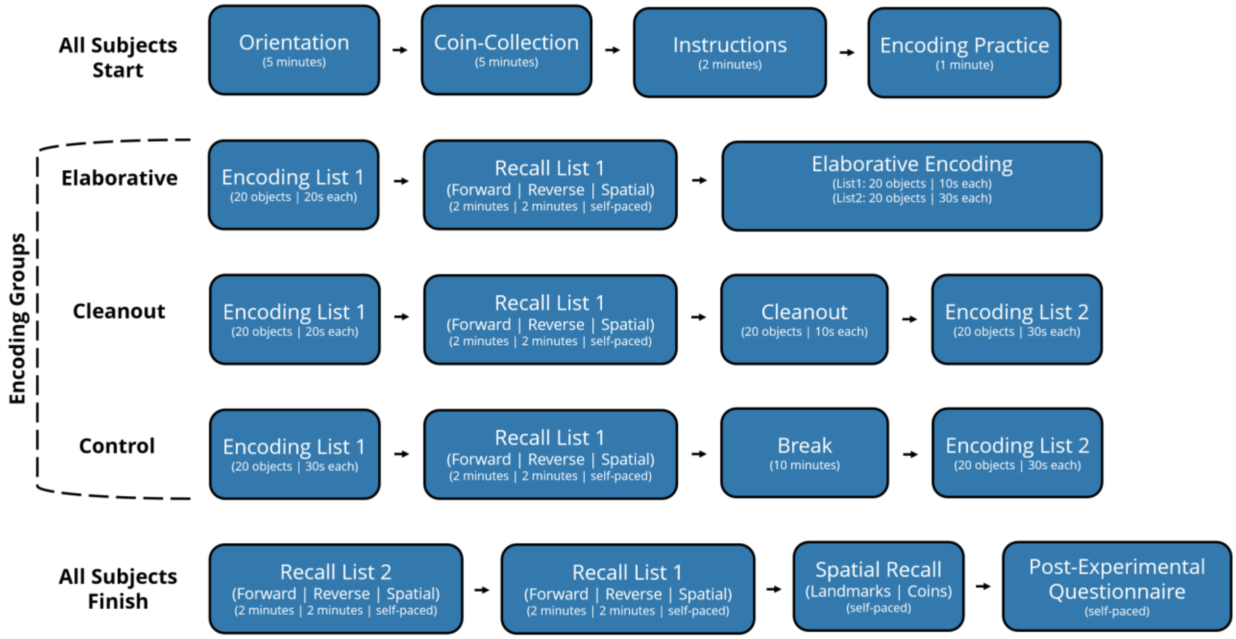
**Figure 3. Object/Landmark/Token Placement Task**



On the next screen you will be shown a bird's eye view of Toon World.

Please click on the location where you placed the Pineapple (pictured to the right).

Figure 4. Experimental Paradigm



## Figure 5. Recall Results

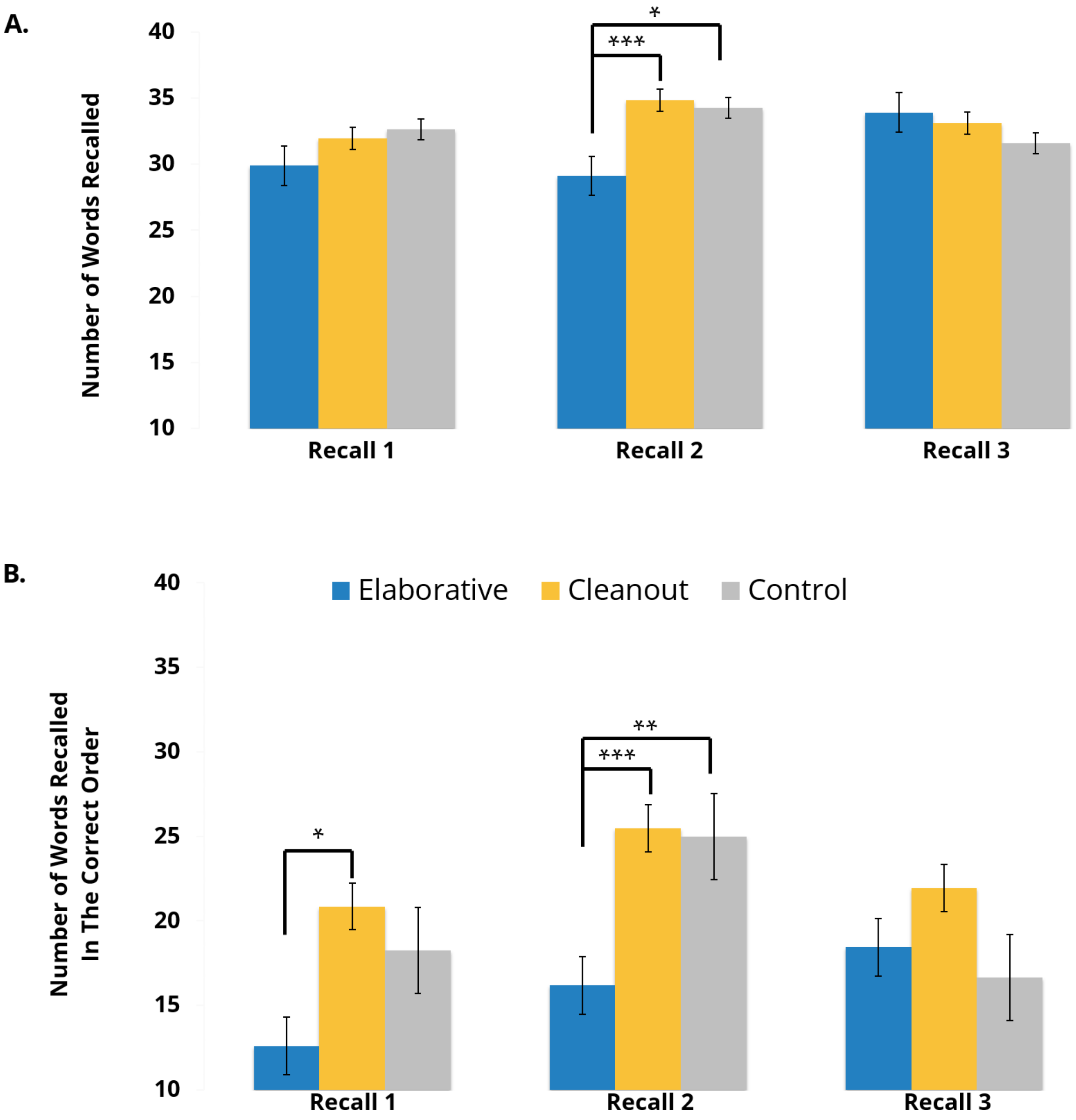


**Figure 6. Forgetting Results**

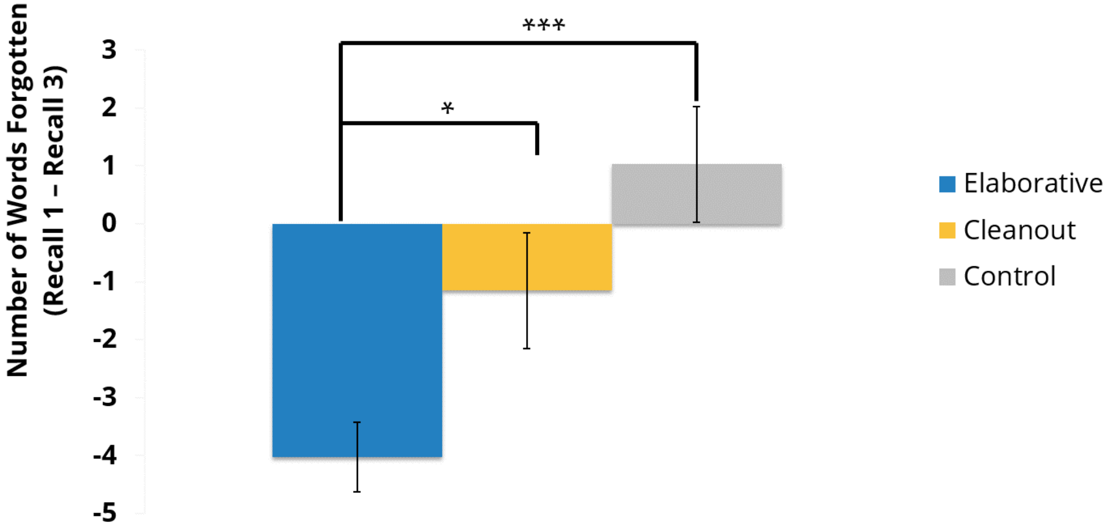
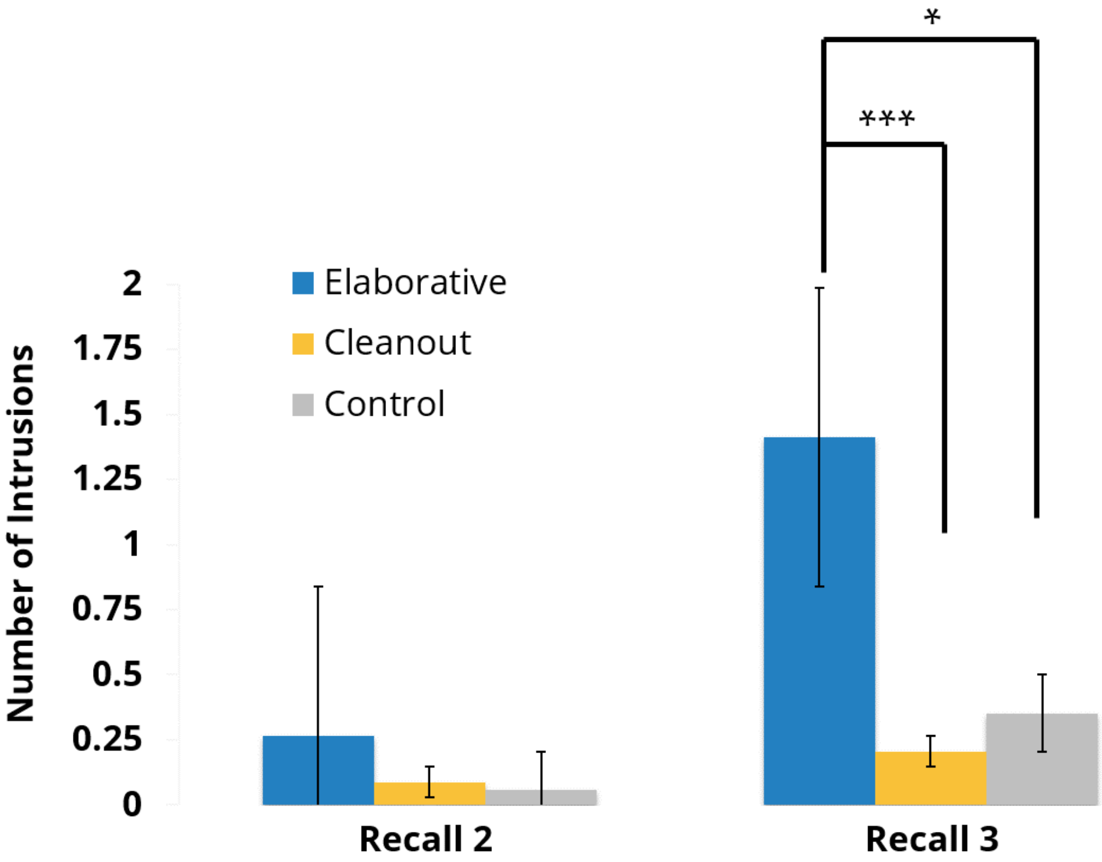


**Figure 7. Intrusions Results**



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## Appendix

### *Appendix 1 – MoL Encoding Instructions*

We are now ready to get started with the task. First, I'd like to explain a bit about this study.

People use a variety of strategies to memorize information. We would like to introduce you to one mnemonic technique known as the "Memory Palace" strategy that can be used to aid your memorization of a list of items.

Conceived in Ancient Greece, this strategy takes advantage of the fact that information is more easily remembered when it is associated with a spatial location. In its classic implementation, the Memory Palace strategy involves imagining yourself navigating a familiar environment (e.g., your home) and mentally "placing" each of a list of objects at a specific memorable location along your path.  For example, if you had to remember bananas, eggs, and peppers, in that order, you could imagine yourself walking up to the door of your home, where you find a banana on the doorknob; after entering the door, you see eggs hanging on strings from the ceiling in the entryway; after moving through them, you see peppers all over the floor in the living room. When it is later time to retrieve the list of objects, you would simply re-imagine yourself walking along the original path you traversed and observing each item on the list -- right in the place that you left it.

While this memorization strategy typically involves placing a list of to-be-remembered items using only one's imagination, we have created a platform for you to implement this strategy by placing items as you navigate along a path through a virtual reality environment.

We are now going to practice using the technique I just described to you.

In this world, a series of three 3D objects will appear in front of you, one at a time. Please move about the environment and find a memorable location to place each object. When you click on the shape, it will be placed in that location. Be sure to try and place the items along a path that you would be able to recreate later, as this will help you when you are later asked to recall the objects in order. Each item will be available for you to view for 20 seconds before a new one appears. (Please give me a moment to load these items)"

### ***Appendix 2 – Cleanout Instructions***

Great. We are now going to go back to Toon World. People who use the Memory Palace strategy we described to you often struggle with using the same environment to encode multiple lists of information. Experts typically employ a "clean out" strategy where they mentally imagine themselves going back into the environment, following their original path and, when coming across an object they placed in the environment, erasing it by imagining it fade away. The idea is that just like how we said earlier "information is more easily remembered when it is associated with a spatial location", removing that information from the spatial location helps you forget the objects.

While this clean out strategy typically involves using one's imagination, we have created a platform for you to implement this strategy by observing the items you previously placed fade away.

You are now going to go back to Toon World. Your task is to revisit the locations where you placed the objects from [First Name List]'s, in order, and watch them fade away as you try to forget that object and where it was in the environment. The task will go as follows: You will start at the South part of the environment and a black-sphere will appear where you placed the first item on the list. You will navigate to that black-sphere. Once you arrive, the object you placed there will appear and then fade. You should watch it fade as you try and forget that you learned that object and placed it in that location. After the fade is complete, a new black sphere will appear. You will visit each black sphere until you have watched all the objects you originally placed from [First Name List]'s List fade.

### *Appendix 3 – Elaborative Encoding Instructions*

Great. You are now going to go back to Toon World. People who use the Memory Palace strategy we described to you often struggle with using the same environment to encode multiple lists of information. Experts typically employ an "elaborative encoding strategy" to help them remember new lists. This works by revisiting the locations where you placed previous objects and placing new objects near them so that you remember both objects. It also helps to imagine those objects interacting with each other. For example, if you previously placed a banana and are now placing a frog, you could imagine a frog eating a banana.

While this elaborative encoding strategy typically involves using one's imagination, we have created a platform for you to implement this strategy by observing the items you previously placed re-appear so you can place new items above, below, or to the side of them.

Your task is to revisit the locations where you placed the objects from [First Name List]'s, in order, and place new items that belong to [Second Name List] alongside them. The task will go as follows: You will start at the South part of the environment and a new object, belonging to [Second Name List] will appear in front of your avatar. At the same time, a black-sphere will appear where you placed the first item on the list. You will navigate to that black-sphere, with the new object from [Second Name List]'s List in front of you. Once you arrive, the object you placed there from [First Name]'s List will appear. There may be a slight delay before the object appears. If so, just concentrate on remembering the item from [Second Name List]'s List.

# Chapter 5: Mapping neural representations of environmental context and path direction during imagined navigation of learned virtual environments

## Abstract

Constructing a rich egocentric representation of one's movement about an environment is a multi-faceted effort requiring a vast interplay across cortical areas responsible for visual processing, heading direction, and spatial coding. While electrophysiological recordings in rodents have identified robust neural correlates related to distinct aspects of navigation, experimental work with human participants offers the unique potential to elucidate the mechanisms of navigational mental imagery, a process we frequently engage in when planning a route or giving directions. In the present study, we first familiarized participants with navigational paths about three highly distinctive virtual environments. The next day, while undergoing functional magnetic resonance imaging (fMRI) scanning, participants viewed a series of first-person videos clips that indicated either clockwise or counter-clockwise movement around the perimeter of each environment. After several rounds of video viewing, participants performed a new task in which they were covertly cued to imagine themselves walking along each of these same routes. We leveraged support vector machines within a searchlight-mapping approach to identify brain regions whose local BOLD patterns coded for information pertaining to the participants' heading direction or environmental context. As expected, early visual areas along the dorsal stream were capable of decoding the environmental context during perception, with more downstream regions concerned with spatial navigation (e.g. parietal and retrosplenial cortices) supporting successful classification during imagery. We also identified regions implicated in working memory and retrieval (e.g. dorsolateral and medial prefrontal cortices) in supporting a contextual

reinstatement of perceptually derived activity patterns during imagery. Moreover, we also revealed regions that were informative of which direction (i.e. clockwise or counter-clockwise) during both perceived (e.g. V5 and Precuneus) and imagined (extrastriate cortex) navigation.

## Introduction

Navigating about one's environment is a multi-faceted effort requiring a faithful representation of the visuospatial layout and one's position and orientation within a space. A vast network of spatially tuned cells supporting different aspects have long been identified in rodent populations: place cells represent an organism's specific location within an environment (O'Keefe, 1979), grid cells provide a coordinate system for the calculation of trajectories between known places (Moser et al., 2014), head-direction cells indicate absolute compass direction (Taube et al., 1990a), boundary vector cells represent environmental edges and barriers (Lever et al., 2009), and a variety of cells provide a conjunctive representation of position, direction, and velocity (Sargolini et al., 2006). Analogous functionality has been observed in humans during directed and free navigation (see Spiers and Barry (2015) for a review).

A great deal of work has been conducted to decode the contents of visual consciousness using multi-voxel pattern analysis (MVPA; Harrison and Tong, 2009; Kamitani and Tong, 2005). These early studies leveraged relatively simple stimuli like oriented grating held in working memory to identify early visual regions sensitive to orthogonal orientations. Other studies leveraged more complex stimuli (like objects spanning several categories), combined with a searchlight-brain-mapping approach (Kriegeskorte et al., 2006), to unveil neural representations supporting the stimuli of interest (for review, see: Haxby et al., 2014). Developments in the field have now even permitted for the reconstruction of visual experiences based on brain activity evoked while participants view movies (Nishimoto et al., 2011). Despite an abundance of research dedicated towards unveiling the neural correlates supporting navigation (e.g. (Dhindsa et al., 2014; Hartley et al., 2014; Suthana et al., 2009), little work has been done to determine the possibility of decoding visual content while participants are engaged in more complex, visually-guided tasks, like navigation. In this current study, we sought to determine whether environmental context (i.e. which virtual environment (VE) a participant was viewing) was decodable from participants' blood oxygen level dependent (BOLD) signal as they were presented with egocentric first-person navigational pursuit videos that required visually-dependent feedback– a critical extension to research showing that still pictures of natural scene categories can be decoded using distributed patterns of activity in the brain (Walther et al., 2009). While the debate on whether or not navigation in Virtual reality (VR) is to be considered "true navigation" continues to evolve (Minderer et al., 2016; Taube et al., 2013a), experimental outcomes vary very little between virtual and real-world navigation and the ecological benefits of leveraging VR for fMRI research into memory outweighs its cons (for review see Reggente et al. (2018)).

Mental imagery is known to play a key role in successful navigation; whether planning out one's own route or providing directions to others, we must mentally simulate a trajectory through space and conjure up representations of pertinent contextual details. Research into decoding the contents of mental imagery has shown that it is possible to differentiate between categories of objects (Reddy et al., 2010) and where a participant believes they are in a virtual environment (Hassabis et al., 2009) without any explicit perceptual input. It has even been shown that it is possible to decode the contents of visual imagery during sleep (Horikawa et al., 2013). While neural correlates supporting distinct aspects of imagined navigation have been unveiled (e.g. (Ghaem et al., 1997; Ino et al., 2002; Rosenbaum et al., 2004), little work has been done to unveil whether context-relevant information is also embedded in such regions. As such, the current study also looked to replicate its visual decoding efforts within the imagery domain.

Previous research has suggested that regions in the human brain contain neural populations involved in the encoding and retrieval of allocentric heading information in humans (Baumann and Mattingley, 2010) and one study has shown that it is possible to decode heading direction in a 4-way classification of N, S,W,E (Rodriguez, 2010). Additionally, single-neuron recordings in the human entorhinal cortex while a participant navigates a VE have been shown to indicate whether they are taking a clockwise or counterclockwise path around a virtual road—a discovery that used the nomenclature of “path cells” to denote their function (Jacobs et al., 2010).

In the current study, participants were first familiarized with a series of three distinct VEs and the arrangement of landmarks about them. The next day, participants were placed into the scanner as they semi-passively watched a series of videos that showed first-person movement to and from landmarks within each VE. Importantly, the videos indicated either clockwise or counter-clockwise movement around the perimeter of each environment. Afterwards, they engaged in a directed mental navigation that was designed to implicitly recreate the same landmark-based, direction-specific routes within the confines of their mental imagery. MVPA analyses were utilized, within an information-based searchlight brain-mapping cross-validation framework, to reveal regions during perception and imagery that were maximally dissimilar enough across context to permit successful classification of unseen brain states. Additional analyses were conducted to decode the directionality of movement about the environment (i.e. clockwise vs. counterclockwise) during perceived and imagined navigation, irrespective of VE.

## Methods

### *Participants*

34 participants were recruited for this study by way of posted flyers throughout the UCLA campus and listings on UCLA's online participant pool. Two participants were unable to finish the study in its entirety due motion sickness encountered on Day 2. As such, a total of 32 participants, aged 18-23 (M=19, SD=1.1; 16 females), were analyzed in this study for either university credit or cash-payment (N=22).

Participants were required to be right-handed, have normal or corrected-to-normal vision and hearing, have a mastery of the English language, and report no diagnosed learning disabilities, substance dependencies, nor prescriptions for psychotropic medications. Participants were also asked about their motion sickness (e.g. do you get sick when reading in the back of a car), to avoid the enrollment of participants who were particularly prone. Additionally, to prevent unequal exposure to the experimental apparatus, applicants were not permitted to participate if they had more than five hours of previous experience with the VR software used in this experiment (Second Life [http://secondlife.com] or its open-source virtual simulator OpenSimulator [http://opensimulator.org]). Eligibility screening was conducted prior to the participant's enrollment in the study using the Research Electronic Data Capture (REDCap) online survey systems (Harris et al., 2009). The Institutional Review Board at UCLA approved all recruitment and testing procedures.

### *Materials*

A 27” LG Monitor (1600 x 900 (32bit)(60Hz) display) connected to a custom-built computer running a 64-bit Windows 7 Professional Operating System on an Intel® Core™ i7-3770K Central Processing Unit (CPU) @ 3.50 GHz (8 CPUs) with 32GB of Random Access Memory (RAM) and an AMD® Radeon Graphics Processor with 4GB of RAM was used to run the virtual software. The virtual environments were created using OpenSimulator (http://opensimulator.org; Release 0.9.0.0)—an open-source virtual simulator of Second Life (http://secondlife.com/) and viewed using the Firestorm Viewer (The Phoenix Firestorm Project, Inc; http://www.firestormviewer.org/; Release x64 5.0.7.52912). A total of four distinct virtual environments (VEs) were created for this study (“Toon World”, Ruin World”, “Lagoon World”, and “Avatar Island”; Figure 1A). Despite being designed specifically to maximize distinctiveness, each VE that was used during encoding and encoding practice (all worlds except for Avatar Island) was created with the exact same dimensions (a 64 x 64 grid of accessible space) and was populated with eight distinct landmarks at the cardinal perimeter points (i.e. West, North, Northwest, etc.; Figure 1B). A custom-coded Heads Up Display (HUD) was created for each participant and “attached” to their avatar. This HUD allowed for participants to see a “count” on their screen indicating the number of environment-specific tokens (coins in Toon World, seashells in Lagoon World, and rings in Ruin World) they had collected out of the total to-be-collected (20 tokens; Figure 1C).

All screen recordings used for the video-viewing portion of the fMRI task were captured using FRAPS Beepa Pty Ltd; https://www.fraps.com; v3.5.99) at 60fps and were generated using custom OpenSimulator scripts that controlled for the stability of the camera and perimeter lap time. Each video recording lasted exactly 30s and showed a "first-person" perspective, circumnavigating the environment (Figure 1D). To ensure that participants formed a robust encoding of each environment, each video started from one of the four landmarks at the cardinal perimeter points (N,S,W,E; Figure 1B) and provided a tour of the perimeter of the VE before returning back to the same landmark; presenting participants with a multitude of entrances to a VE ensures allocentric encoding (Suthana et al., 2009). For each starting landmark, two videos were presented to the participant throughout the experiment: one where the video moved in a "clockwise" direction (e.g. North towards Northwest) and another where it started moving in a "counterclockwise" direction (e.g. North towards Northeast). Each video consisted of an initial 2s of focus on the starting landmark, followed by circular movement about the perimeter of the environment, and finally ending with another 2s of focus on the starting landmark.

In-scanner stimuli were presented using E-Prime 2.0 software (Peirce, 2009) and images were shown via an MR-compatible rear projection system. Participants received auditory cues for mental navigation through MR-compatible headphones and responded using a 4 response button box (Appendix 1). All statistical tests were conducted using custom R (R Core Team, 2013; http://www.R-PRoject.org/) and MATLAB code.

### *Day 1 Behavioral Paradigm*

All participants were familiarized with navigating about a VE by first teleporting them to "Avatar Island" and then having the experimenter confirm that a participant could use the AWSD keys to move about the VE and utilize the computer mouse to adjust the pitch and yaw of their first-person perspective. After confirming their familiarization and demonstrating a general ability to execute directed actions with their avatar (e.g. move forward, turn around, etc.), participants were shown a slideshow that contained each of the landmarks they would find in each world. Each slide contained the name of the world and a landmark from that world. This served to assure that the participants knew exactly which objects in the world the experimenters were deeming to be named "landmarks".

Participants were then teleported to the southern-most region each of the encoding VEs in a random order. While in each VE, participants were instructed to navigate about the environment and "walk through" each token until all 20 were collected. Participants were given five minutes to collect the tokens and encouraged to explore the environment with any remaining time, taking care to make note of the landmarks they had previously seen in the slideshow.

After completing token-collection and subsequent free-exploration, participants were instructed by the experimenter to navigate to each of the Landmarks one-by-one (e.g. "Navigate to the Penguin Pool. Now navigate to the Lollipop Tree"). After visiting each landmark in an environment, participants were teleported to the next environment. Following this single-landmark guided-navigation task, participants were teleported, in a random order (ensuring no environment was visited twice in a row), back to the southern-most region of each VE to complete a dual-landmark guided-navigation task.

Specifically, participants were instructed to make sure they passed a separate landmark before reaching the final destination (e.g. “Navigate to the Water Pipes, making sure that you pass the Flamingo Pool along the way”). After completing the dual-landmark guided-navigation in each VE, participants were briefed on the instructions they would receive for Day 2. All participants were provided a handout that described the following day’s task demands and familiarized participants with the button-box-mapping (Appendix 1). They were also encouraged to refrain from illicit drug use, drink a normal amount of caffeine the following day, and aim for a minimum of seven hours of sleep.

### *Day 2 Behavioral Paradigm*

The next day, participants were teleported back into the southern-most region of each VE in a random order. While in each VE, participants were instructed by the experimenter to navigate to a landmark and then navigate around the perimeter of the environment, back to the same landmark, making sure that they pass a particular as the first landmark along the way (e.g. “Please head over to the Penguin Pool landmark. Now, please head in a circle around the perimeter of the map, back to the Penguin Pool. However, make sure that the first landmark you pass is the Mushrooms”).

As a final test, participants were submitted to a spatial memory task where they used the computer mouse to direct a rectangular cursor and indicate the location of a cued landmark on a bird’s eye view of the encoding environment that was stripped of its landmarks (Figure 2). Each landmark and its name was shown on a prompt screen before showing the full-screen map. After providing responses for each landmarks encoded within a given environment, participants were asked to indicate the location of each token before moving on to the next environment. The presentation order of landmarks and environments for spatial tasks was randomized across participants.

Afterwards, participants were placed in the scanner where they completed 4 runs of the video-viewing task (see Materials). Each run consisting of 6 videos presented in a pseudo-random fashion, ensuring that exactly two videos from each world were shown and no two videos from a world started from the same landmark. To ensure active attention, participants were instructed to make a button press each time the video passed a landmarks. Participants were explicitly instructed to pay close attention to the spatial layout of the environment, especially in regards to the location of landmarks, and the trajectory of each video (i.e. the order of landmarks that are passed). Between each video, participants completed an “active-baseline task” (6s) (Stark and Squire, 2001) that required them to make the appropriate button press in response to whether or not the product of a pair of numbers was odd or even.

After viewing all possible clockwise, counter-clockwise, landmark, and environment combinations (24 total trials), participants entered the “mental navigation” portion of the experiment. For each trial, participants were asked to close their eyes, construct a recreation of a particular environment and move about it in an instructed manner. Specifically, participants were cued via an instruction screen as to which environment they should imagine themselves in, which landmark to start at, and which landmark should be the first that they pass as they circumnavigate their way around the perimeter of the VE, back to the starting landmark (Figure 3). This was an implicit attempt to get participants to mentally recreate the content and directionality of the VE videos they watched previously. After on-screen instructions told them which environment, landmark, and first landmark to pass, participants were instructed to close their eyes and orient themselves at the landmark. Once oriented, they were instructed to make a button press, wait for a beep, and then begin navigating in the instructed direction, making a button press each time they passed a landmark until they arrived back at the starting landmark (upon which they could open their eyes). After each trial, participants were asked to rate (on a scale of 1-4) how vividly they were able to reconstruct the given path and environment. After visiting each landmark and navigating either clockwise or counterclockwise in each environment (24 trials; 4 runs; 6 trials per run), participants were removed from the scanner. Finally, participants were given a post-experiment questionnaire that gauged their free-placement of objects onto blank squares representing the layout of each map. This questionnaire also examined the vividness with which they were able to recreate each environment (Appendix 2).

### *fMRI Acquisition Parameters*

Magnetic Resonance Imaging (MRI) data were acquired with a 3.0T Siemens Trio Scanner at the UCLA Staglin Center for Cognitive Neuroscience using a 32-channel head coil. We acquired a high-resolution T2-weighted anatomical scan acquired by magnetization-prepared 180 degrees radio-frequency pulses and rapid gradient-echo (MPRAGE). TR/TE = 6670ms/62ms. Resolution = 0.8x0.8x3.0 mm$^3$. For the functional portion of our task we acquired a series of T2*weighted blood-oxygen level dependent (BOLD) images by Echo Planar Imaging (EPI) with a multiband acceleration factor of 3. TR/TE = 1500/33. Flip angle = 90°. Slice thickness = 2.25mm. In-plane resolution = 2.25x2.25x2.5 mm$^3$. 60 interleaved axial slices. In addition, we collected two matched-bandwidth structural scans to use as an intermediate step in registration.

### *fMRI Data Preprocessing*

fMRI data pre-processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied: motion correction parameters were estimated using MCFLIRT (Jenkinson et al., 2002); non-brain removal using BET (Smith, 2002); grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor; high pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma=50.0s). B0 field unwarping was run with FEAT’s FUGUE using an EPI dwell time of .69ms. Given our fast TR, we opted to not include a slice-timing correction. We used FLIRT to align each participant’s BOLD timecourse to MNI space, first aligning each participant’s middle-timepoint BOLD image from each run to their MPRAGE, followed by aligning their MPRAGE to a 2mm MNI template, and finally applying run-specific transformation matrices to each BOLD image in the run. Prior to each analysis, voxelwise time-courses for each run were filtered using a Savitsky-Golay digital filter (Chen et al., 2004; Çukur et al., 2013; Press and Teukolsky, 1990) with a polynomial order of 3 and then z-scored across the temporal dimension.

### *fMRI Methods*

We employed a support vector classifier with a linear kernel using libSVM (nu-SVC, c=1; Chang and Lin, 2011) and a searchlight brain mapping approach (radius= 5voxels; Kriegeskorte et al., 2006) to decode which regions in the brain contained information related to the differences across virtual environments and path directionality (i.e. clockwise or counter-clockwise) both when the participant was viewing videos and when they were engaged in mental imagery. Category labels were assigned based on environmental context and path-directionality (i.e. clockwise vs. counterclockwise). Importantly, path-directionality labels were assigned to all trials, irrespective of which world the video or mental imagery was constructed in. For both video-viewing and imagery based classifications, we leveraged a cross-validation approach whereby the classifier was trained on n-1 runs worth of valid trials and tested on the trials from the left-out run. For analyses of contextual reinstatement, the classifier was trained on all valid video-viewing trials and then tested on all valid mental-imagery trials. For all classifications, we prevented a bias in the classifier by balancing exemplars within each classification category. Specifically, we randomly sampled from the over-represented category to match the number of trials in the category with the least representations. To maximize the likelihood that each trial was used for training, we repeated each cross-validation over 50 iterations, averaging the across-iterations classification results.

For each BOLD time series collected during a mental imagery trial, we identified the middle third of the time course (relative to each participant’s total time taken to complete the mental navigation task)  and averaged the images contained therein—creating an average BOLD pattern of activity. We elected to only include trials where the participant completed the mental navigation task in no less than 10.5s (7 TRs) and subsequently rated their vividness with at least a 3 or 4. We acknowledged that while completion of the mental navigation could be appreciably quicker than that of the video-viewing length of the same route (30s), a participant completing the task in less than one third of the time could be indicative of a rushed performance and, subsequently, a less high-fidelity BOLD signal. The “middle-third” of each time course for the video-viewing portion was the same across all trials and participants; the middle 10s of video-viewing was averaged and used as the BOLD pattern of activity.

To assess significance at the group-level, we created a null-distribution using the binomial inverse of the cumulative distribution function. The center of the distribution was the expected chance accuracy (33% for environmental context; 50% for path-directionality) and the number of trials was given as the total number of classifications conducted across all participants. We set a significance cutoff to be the top 1% of the distribution ($p<0.01$), Bonferroni corrected for the total number of searchlight masks (36% for "which-world" and 53% for "which-direction" analyses). Finally, we report regions where 50 contiguous voxels were assigned significant accuracy values.

## Results

Our main results focus on regions capable of decoding which world the participant was viewing/imagining (i.e. environmental context) and decoding which direction, irrespective of world, they were viewing/imagining. We also present results indicating the involvement of select regions in perceptual reinstatement during mental imagery (i.e. results from when the classifier was trained on data collected during perceptual trials and tested on imagery trials. Regions containing informative patterns of activity towards a successful classification were revealed by thresholding whole-brain searchlight maps (Kriegeskorte et al., 2006) at a significant classification accuracy and imposing a reliable contiguous-voxel cluster size (see Methods). All results are featured in Tables 1 and 2 and Figures 3-8.

### *Decoding During Perception*

### *Environmental Context*

The classifier was able to successfully decode environmental context (i.e. Which World) the participant was viewing videos from. While peak accuracy (59%; chance=33%) was found in R. V1, almost the entirety of the bilateral dorsal visual steam yielded significant classification results. Bilateral Frontal Eye Field areas were also significant for decoding the contents of visual consciousness, albeit at a much lower accuracy (37% peak). See Table 1 for peak activation clusters and Figure 3 for whole brain searchlight accuracy maps.

### *Path-Directionality*

The classifier was also able to decode which direction (i.e. clockwise vs. counterclockwise) with which the video was displaying a circumnavigation of the environment. Specifically, classification results were irrespective of environment—all available clockwise vs. counterclockwise trials were utilized in the cross-validation. Peak accuracies (55%; chance = 50%) were found in significant clusters throughout the Precuneus, Lingual gyrus, Orbitofrontal cortex, and V5. Intriguingly all results were left lateralized. See Table 2 for peak activation clusters and Figure 4 for whole brain searchlight accuracy maps.

### *Decoding During Mental Navigation*

### *Environmental Context*

Although we observed a depreciated peak accuracy (39%; chance=33%), there was a widespread set of regions that were able to significantly decode environmental context while the participant was mentally navigating about the three different environments.

Clusters were observed in the L. Superior Parietal Lobule (SPL), L. Intraparietal Lobule (IPL), R. Parietal Cortex, R. Retrosplenial cortex, and R. Premotor and sensorimotor regions. See Table 1 for peak activation clusters and Figure 5 for whole brain searchlight accuracy maps.

### *Path-Directionality*

Only one cluster in the R. Extrastriate area yielded significant decoding accuracy (55%; chance=50%) when determining which direction (i.e. clockwise vs. counterclockwise) the participant was heading during the mental navigation task, irrespective of environmental context. See Table 2 for peak activation clusters and Figure 6 for whole brain searchlight accuracy maps.

### *Contextual Reinstatement*

### *Environmental Context*

When the classifier was trained to dissociate environmental context during perception (i.e. video-viewing) and tested on imagery data (i.e. mental navigation), it was able to identify a broad set of regions whose pattern of BOLD activity during imagery contributed to a significant classification. Peak accuracy clusters (39%; chance=33%) were found in the L. Medial Prefrontal Cortex (MPFC), L. Anterior Thalamus, R. Temporo-Parietal Junction (TPJ), R. Superior Temporal Gyrus (STG), R. Orbitofrontal cortex, and Right Dorsolateral Prefrontal Cortex (DLPFC). See Table 1 for peak activation clusters and Figure 7 for whole brain searchlight accuracy maps.

### *Path-Directionality*

When the classifier was trained on all available direction trials during perception (i.e. viewing clockwise vs. counterclockwise videos, irrespective of environmental context) and tested on imagery data, it identified several significant peak accuracy (55%; chance=50%) clusters in Bilateral IPS, and R. TPJ.

## Discussion

The current study reveals a wide set of cortical regions whose pattern of BOLD activity was dissociable enough to permit significant classification of environmental context ("Which World") and path-directionality ("Which Direction") during video-viewing (perception) and directed mental-navigation (imagery). The employed decoding scheme also permitted for the unveiling of regions whose activity during perception for representing environmental context and heading direction was self-similar during imagery—a proxy for contextual reinstatement.

Given the stark perceptual differences across the three VEs and previous work on decoding visual consciousness/working memory from human brain signals (Harrison and Tong, 2009; Haynes, 2009), we expected our classifier to perform well when decoding which world a participant was viewing. In line with previous research, the classifier relied on early visual (with peak accuracy in R. V1) and dorsal stream regions in order to decode the contents of visual perception (for a review of similar efforts, see Haynes and Rees, 2006). The ability for the FEFs to decode environmental context may have emerged based on our task design, which encouraged participants to be on the lookout for environmental landmarks and to button-press when the video was passing one. Importantly, the FEFs are thought to be involved in converting the outcome of visual processing into motor commands (Thompson and Bichot, 2005). In primates, neurons in the FEFs have been shown to respond to the behavioral significance of stimuli within specific contexts (landmarks against a VE backdrop in the current study), even though they aren't sensitive to specific features of visual stimuli (Thompson and Bichot, 2005). Additionally, the FEFs have been shown to modulate their responses based on instruction cues (Colby et al., 1996) and preparation for motor-decision processes based on context and previous experience (Bichot et al., 1996). Additionally, the FEF has been implicated in visual awareness (Grosbras and Paus, 2003) and transcranial magnetic stimulations (TMS) to the region shifts visual attention (Grosbras and Paus, 2002). Although visual consciousness and attention are not to be conflated (Lamme, 2004), the recurrent processing exchange between V1 (visual consciousness) and FEF (visual attention) could allow for information to be relayed back-and-forth between the two regions. Taken together, our FEF results could indicate context-specific visual attention that is concerned with motor-planning in familiar environments. Future research will be needed to discover if familiar virtual environmental context can be decoded within the FEFs without a motor task.

Research into decoding the contents of mental imagery has shown that it is possible to differentiate between categories of objects (Reddy et al., 2010) and where a participant believes they are in a virtual environment (Hassabis et al., 2009) without any explicit perceptual input. It has even been shown that it is possible to decode the contents of visual imagery during sleep (Horikawa et al., 2013). A number of research groups have unveiled a common neural signature supporting both perceptual and imagined content. For instance, Albers et al. (2013) found that mental images can be decoded from activity patterns in early visual cortex— a finding they posit provides evidence for visual cortex in creating a “blackboard” (Bullier, 2001) that is used during both bottom-up stimulus processing and top-down internal generation of mental content. Indeed, it also has been shown that imagination of objects, scenes, body parts, and faces in a particular part of the visual field all recruit regions that highly overlap with the perception of those categories during visual presentation to left and right visual fields (Cichy et al., 2012). Ganis et al., (2004) also showed that visual imagery and visual perception recruit the same neural processing regions. However, they note that the overlap was neither complete nor uniform across their two task sets, with perception recruiting more early visual regions and imagery eliciting activation in more extrastriate regions. In line with these results, we saw that decoding environmental context during mental imagery relied on the more downstream visual association area. We also observed the recruitment of nearby dorsal stream regions like the parietal cortex, which were also observed at the anterior tail of the large cluster whose peak accuracy was in V1 during perceptual decoding efforts. Ishai et al. (2000) showed that decoding perceptual images was driven by activity in right-lateralized visual areas, whereas the decoding of visual imagery was more left-dominant—a finding that supports ours: R. V1 contained voxels with peak accuracy in differentiating environmental context during video viewing whereas the L. Visual Association area was the most accurate visual area for decoding which world a participant was completing the mental navigation task.

While the above referenced research illustrates that a great deal of work has been done to decode the contents of one’s mental imagery (see Kamitani and Tong (2005) for the first such example), those studies were more concerned with visual orientations and object categories—a substantially different endeavor compared to decoding which virtual environment a participant was completing a mental navigation task. Decoding mental imagery of places has also been shown to activate corresponding stimulus-specific brain regions (O'Craven and Kanwisher, 2000). However, the authors note that their efforts were dependent on the content of the visual image. The task demands of the current study are more multi-faceted compared to the mere visualization of a single object; participants were to orient themselves within a familiar VE and then navigate about the VE in a goal-directed manner, keeping a constant mental tally of both their current position and nearby landmarks. As was seen in our results, other spatial mental imagery tasks also see a lack of primary visual area recruitment (Mellet et al., 1996). Importantly, early visual cortex re-activation during mental imagery is indeed selective and varies as a function of task design an aspects of perceptual anticipation theory (see Kosslyn and Thompson (2003) for review) As such, it remains sensible that the only overlap in visual regions that was observed for decoding environmental context from perception and imagery was the L. Visual Association Area.

In support of this reasoning is the current study's identification of regions typically implicated in spatial processing as being informative for decoding environmental context during mental imagery. The largest cluster observed was in the SPL—a region that has been implicated in spatial attention (Corbetta et al., 1995) and shown to be visually dependent in preparation for movement (Caminiti et al., 1996), even when conducting spatial scanning through mental imagery (Schicke et al., 2006)—extending its role in visual imagery (Pelgrims et al., 2009). The SPL has also been shown to have a preference for searching for files in digital folders as opposed to searching within a control task (Benn et al., 2015)—emphasizing the recruitment of this region, even in abstract conditions like the current study's VEs. Another robust finding was in the IPL—a region concerned with egocentric spatial representations (Lenggenhager et al., 2006) and maintaining attention to spatial locations over time (Malhotra et al., 2009). Facets of route information (e.g. global vs. local) are also present within the IPL (Evensmoen et al., 2013), with a particular emphasis on egocentric-based judgements of relative distance (Parkinson et al., 2014). IPL also shows a preference for navigating about recently learned environments (like the VEs the participants were exposed to for the first time the previous day) over more familiar environments (like the UCLA campus; see Spiers and Barry (2015) for review). Yamazaki et al. (2009) also suggest a role for IPL as the level of abstraction increases, which may explain the selective presence of this region in imagery over perceptual findings. Activity in IPL has also been informative in decoding the location of an object within a virtual arena (Rodriguez, 2010). Finally, IPL has shown to have a pre-stimulus activity profile that is consistent with a putative role in "listening for recollection"—an internally directed attentional state posited to promote recollection of event details and bias mnemonic decision making toward the reliance on recollected details over perceived familiarity (Quamme et al., 2010). Taken together, the environmental-context information contained within SPL and IPL during imagery may reflect a context-specific egocentric spatial attention that supports navigation about recently learned environments and making judgments that are dependent on previously recollected details (i.e. videos shown prior to mental navigation that participants were encouraged to reproduce), even when the space is more "abstract", like with VEs.

Analysis also unveiled environment-context-specific recruitment of R. parietal cortex. The parietal cortex has been widely implicated in spatial attention (Burgess et al., 1999;

Colby and Goldberg, 1999; Husain and Nachev, 2007; Mesulam, 1999; Schotten et al., 2005; Yantis et al., 2002), as well as encoding spatial location (Andersen et al., 1985), creating motor commands for operations in extra-personal space (Mountcastle et al., 1975), and updating representations of visual space (Colby and Goldberg, 1992), especially from an egocentric (first-person) perspective (Vogeley and Fink, 2003). The R. parietal cortex has also been shown to selectively respond to mental imagery tasks (Farah, 1989; Harris et al., 2000), especially during motor imagery (Jeannerod, 1995). Given this purported set of roles, and our right-lateralized finding, it is reasonable to infer that the R. parietal cortex operates on environmental-context information available within one's mental imagery to navigate about a VE—a task that requires consistent spatial attention and, in our task, preparation for motor commands that are executed as a function of spatial location. Further in support of our posit that the current study's mental imagery task was less dependent on early visual regions due to its specific emphasis on spatial navigation is the revelation of informative patterns within retrosplenial cortex for decoding environmental context. retrosplenial cortex has been shown to be crucial when finding one's way, particularly without the use of visual cues (Cooper et al., 2001). Damage to the retrosplenial cortex has also been shown to create difficulty in route-finding (Maguire, 2001; Suzuki et al., 1998)—a condition called Heading Disorientation (Aguirre and D'Esposito, 1999).

The reliably differentiable patterns of BOLD activity expressed in the premotor and sensorimotor regions as a function of environmental context during mental imagery may again reflect the nature of our task design (as reasoned above regarding recruitment of FEF during visual perception). Single-cell recordings from motor regions in primates have revealed that when asked to complete a sequence of button presses without visual input (akin to our mental navigation task where participants had to button press when passing an object), neuronal firing is substantially hire than compared to when visual input is provided (Mushiake et al., 1991). Additionally, these neurons were found to be sequence-specific during mental imagery, suggesting that task-relevant information is embedded in motor regions. Indeed, task-related neurons in premotor areas modulate their firing frequency in relation to motor tasks which require visual information, even before movement was initiated (Godschalk et al., 1985). Such context-dependence was also shown to be independent of actual finger muscle activity (Hepp-Reymond et al., 1999)—a confound that was controlled for in the current study since all environments had the same number of landmarks, evenly paced about the environment (i.e. same number of button presses / pacing of those button presses were equated across VEs). Furthermore, when human participants are cued by abstract visual stimuli, activity in premotor regions is significantly increased compared to freely selected movements (Moisa et al., 2012). Taken together, our premotor and sensorimotor regions may contain internally generated, context-specific information that guides appropriate sequences of motor responses, much like the evidence for context sensitivity for intended grasps in premotor cortices (Marangon et al., 2011).

The methodological procedures employed by the current study measured “contextual-reinstatement” and produced a metric of how well the multi-dimensional decision boundaries created by the classifier during perception were useful in discriminating environmental context during imagery. That is, regions yielding a significant contextual-reinstatement classification accuracy must have expressed a BOLD pattern of activity during mental navigation that was maximally similar enough to that observed during perception. The opportunity remains likely that regions revealed during the contextual reinstatement analysis need not also be informative for context-decoding efforts isolated to perceptual or imagery-based navigation; the decision boundary formed by the classifier as its trained on perceptual data may not be informative of environmental context, but patterns of activity expressed during imagery may conform to such higher-order delineations. As such, interpretations of contextual reinstatement results should be framed as regions whose processing during mental imagery varies as a function of environmental-context in the same way as during perception.

The largest cluster that showed significant decoding accuracy for contextual-reinstatement of environmental context was observed in the MPFC—a region whose activity, in relevance to this current study, has been collectively suggested to support learning associations between context, locations, events, and corresponding adaptive responses (for review, see Euston et al., 2012). Additionally, activity in the MPFC has been implicated in assigning first-person-perspectives (Vogeley and Fink, 2003) and used to decode the location of an object in a virtual arena during a navigation task (Rodriguez, 2010). The current study’s task-demands almost perfectly reflect a situation that would mandate recruitment of MPFC processing: participants took a first-person perspective as they recalled the associations between objects (landmarks) and specific locations in the environment. As such, MPFC activity could be reinstating place-object associations (i.e. where a landmark is) in a first-person perspective that is specific to encoding environment. Given that this functionality is shared across all environments, there was no dissociable pattern of activity in MPFC that was robust enough to permit a successful perceptual or imagery-based classification; a decision boundary could have been formed that did not allow new exemplars to be predicted with high enough accuracy in our within-domain cross-validation to be considered significant in accordance with our thresholding. Ganis et al. (2004) postulated that cognitive control processes function comparably in both imagery and perception, whereas sensory processes may be engaged differently by visual imagery and perception. As such, the act of recall may have accentuated the representation of imagery exemplars, making MPFC activity specific to memory retrieval and not perception nor imagery.

The anterior thalamus has also been implicated in supporting memory retrieval (Hamani et al., 2011; Wolff et al., 2006), especially spatial memory/navigation by way of a hippocampal-anterior thalamic axis (Aggleton et al., 2010; Aggleton and Brown, 1999; O'Mara, 2013; Warburton et al., 2000). The anterior thalamus' indistinguishable involvement across environmental contexts in both video-viewing and mental navigation (inferred by an inability to classify using those data-sets) follows the same line of reasoning as the MPFC's memory-specific functionality. The logic also extends to a role of accentuated contextual reinstatement in the both the DLPFC, a region consistently implicated in working memory (Curtis and D'Esposito, 2003; Fregni et al., 2005), and TPJ, which is also involved in working memory (Anticevic et al., 2010) and functionally connected with the hippocampus during memory retrieval, but not during encoding (Huijbers et al., 2011). Finally, the orbitofrontal cortex's role in memory, especially for abstract visual information (Frey and Petrides, 2002), crossmodal associations (Lipton et al., 1999; Tsukiura and Cabeza, 2008), and directed attention towards overcoming interference (Stuss et al., 1982), could also explain our contextual-reinstatement-specific observation.

Taken as a whole, decoding environmental context in the perceptual and imagery domains revealed regions traditionally associated with visual consciousness and spatial navigation / motor planning, respectively. Additionally, measures of contextual reinstatement revealed regions predominantly concerned with working memory and retrieval. These results suggest that information supporting environmental context is also embedded in regions traditionally concerned with supporting spatial processing in general.

Our investigations into decoding path-directionality about a VE were more exploratory. Previous research has suggested that regions in the human brain contain neural populations involved in the encoding and retrieval of allocentric heading information in humans (Baumann and Mattingley, 2010) and one study has shown that it is possible to decode heading direction in a 4-way classification of N, S,W,E (Rodriguez, 2010). However, this study’s task design, much like in the Hassabis et al. study (2009), had participants first visually navigate about a space to a goal location and then used the post-trial fMRI data for classification. Our study is unique in that the guidance for navigation was given only by showing pictures of landmarks where participants should orient and navigate towards. Thus, the BOLD data used to successfully decode which environment the participant was navigating about was reflective of their natural, volitional navigational pursuits.

Despite a rich literature on the function of head-direction cells in rodents, little research has been conducted to decode directionality during human navigation. Given that head-direction cells fire in an absolute compass manner—only firing when the animal is moving in a particular compass direction within the environment (Taube et al., 1990b)—it is not practical to assume that our successful decoding efforts relied on neural information relayed by head-direction cells. The decoding of “direction” in this current study was conducted to reveal regions that could differentiate “clockwise” vs. “counter-clockwise” during imagined navigation. Indeed, our heading-direction classification results did not rely on any of the brain regions containing head-direction cells (retrosplenial cortex (Chen et al., 1994), medial entorhinal cortex (Giocomo et al., 2014), anterior thalamus (Taube, 1995), lateral mammillary nucleus (Stackman and Taube, 1998), or dorsal tegmental nucleus (Sharp et al., 2001)). Instead, a more likely contributor to the signal that was detected by our classifier would be the purported function of so called “path cells”. Single-neuron recordings in the human entorhinal cortex while a participant navigates a virtual environment have been shown to indicate whether they are taking a clockwise or counterclockwise path around a virtual road (Jacobs et al., 2010). Path cells are thought to continuously encode direction across the environment and can be selective to encode clockwise, counterclockwise, or both (but with different patterns of activity) movement about an environment. While, path cells are mostly found in the entorhinal cortex, they have also been observed in the hippocampus, parahippocampus, and orbitofrontal regions (Jacobs et al., 2010).

Partially in line with these previous findings, we observed that differential activations in orbitofrontal cortex to viewing videos were reliable enough to significantly decode whether the video was indicating movement in a clockwise vs. counterclockwise direction. While our searchlight-mapping procedure did not also reveal entorhinal, hippocampal, and parahippocampal regions, it is worth noting that previous research into path-cells have all utilized an active navigation scheme (Frank et al., 2000; Jacobs et al., 2010), as opposed to our relatively passive video-viewing paradigm where participants merely made a button press whenever passing a landmark. While inferred motion (e.g. an experimenter picking up a rat and facing them in specific directions) elicits the same firing pattern for head-direction cells (Taube et al., 1990a), it is unclear whether the same inference would be sufficient for path-cells; place cell preferential firing to discrete locations in an environment is abolished if animals are moved passively through the environment (Foster et al., 1989), so it could be the case for path-cells as well. At the very least, virtual navigation, which has sparked a debate as to whether or not it is to be considered true navigation (Minderer et al., 2016; Taube et al., 2013a), does seem to elicit path-cell activity (Jacobs et al., 2010). As such, it could be the case that the other regions revealed by the searchlight (Precuneus, Lingual Gyrus, and V5) are capable of computing the perceptual, passive analog function of path cells that subconsciously keep the representation of path-direction “online” and, if needed to compute a trajectory, recruit entorhinal and hippocampal processes to compute on a direction-specific cognitive map (Markus et al., 1995).

Indeed, the precuneus and its neighboring parieto-occipital sulcus has been implicated in abstract representations of facing direction (Vass and Epstein, 2013) and reports of precuneus activation shows its sensitivity to the direction of movements (Bonda et al., 1995; Parsons et al., 1995) and internal representation of locations, especially in regards to distal cues (Shipman and Astur, 2008), while walking through virtual environments (Malouin et al., 2003) and navigating computer file systems (Benn et al., 2015). Additionally, events that were made up of people, places, and objects were more easily distinguished when labeled by places and relying on activity in the Precuneus (see Robin et al., 2018). Generally, the Precuneus is also involved in visuo-spatial processing and first-person processing operations (for review see Cavanna and Trimble (2006) and Spiers and Barry (2015)). Also, the lingual gyrus has been implicated in the recollection of places (Burgess et al., 2001)  and navigation, be it through novel environments (see Spiers and Barry, 2015), digital folders (Benn et al., 2015), or when using the method of loci (Kondo et al., 2005). Additionally, V5 (also known as Middle Temporal Area (MT)) has classically been recognized as motion-sensitive (Dupont et al., 1994; Tootell et al., 1995) and known to contain axis-of-motion sets of selective columnar structures (Albright et al., 1984; Dubner and Zeki, 1971), so its sensitivity to directionality during video viewing was somewhat expected: the dominate leftward motion experienced at each turning point along the perimeter during counter-clockwise video-viewing is equal and opposite to that perceived during the clockwise video recordings. V5 is also selectively activated during motion imagery, compared to static imagery control (Goebel et al., 1998)—a finding the current study was unable to replicate, perhaps due to the nature of the VE stimuli we used, as opposed to oscillating Gabor patches.

Given the Precuneus' role in directionality, especially during mental imagery of motor movements (Gerardin et al., 2000; Stephan et al., 1995), and its scaled response to vividness of remembered events (Fletcher et al., 1995; Gilboa et al., 2004; Richter et al., 2016), it was surprising to not identify BOLD patterns of activation that were reliable to decode clockwise vs. counterclockwise mental movement. However, the differentiating signal encoded by the Precuneus may be more granular during mental imagery at each timepoint and hence washed out by our feature-set creation, which averaged the entire middle-chunk of the mental navigation trials. Instead, the classifier relied solely on the R. Extrastriate area to decode directionality during mental imagery, which is roughly 20mm dorsal to our V5 finding on the contralateral side during perception. TMS disruption to the extrastriate region has implicated it in direction discrimination (Hotson et al., 1994), with focal electrical stimulation to the region resulting in akinetopsia (motion blindness). Given that the extrastriate body area responds to the performance of motor actions (Astafiev et al., 2004), our findings could reflect a role for extrastriate in producing a feeling of movement in a particular direction during mental navigation.

In regards to contextual reinstatement of direction sensitivity, results focused on R. TPJ and bilateral IPS. Again, the TPJ's involvement in working memory (Anticevic et al., 2010) and functional connectivity with the hippocampus during memory retrieval, but not during encoding (Huijbers et al., 2011) could represent a path-directional sensitivity that is accentuated during retrieval. Since the R. TPJ, specifically, has been identified as a flexible hub that couples with the Default Mode Network to promote internally directed cognition as well as the Dorsal Attention Network for externally guided cognition (Corbetta et al., 2008; Spreng et al., 2010), it is sensible to assume a common role across perception and imagery. Additionally, TPJ activity has been implicated in linear combinations of movements through abstract spaces (Constantinescu et al., 2016) and shows a robust, common cortical metric for distance (Parkinson et al., 2014), which contains an embedded directional component (distance is often directional: e.g. the apple is five feet to the left of the pear). The IPS has been suggested to serve as an interface between perceptive and motor systems for controlling movements in space (for review see Grefkes and Fink, 2005), providing an action-oriented spatial reference frame (Colby, 1998) that has a visual topography (Swisher et al., 2007) and encoding spatial direction (Materna et al., 2008). As such, a distinguishable response within IPS to path-directionality may have been observed during perceptual based decoding, but not at significant thresholds due to the more passive nature of the task. Once there was a need for goal-directed action that was dependent on action (button presses as, the IPS may have re-expressed, and heightened, the activity patterns observed during the video-viewing trials.

In summary, this current work revealed a vast set of cortical regions that support the decoding of environmental context and path-directionality as participants viewed videos from and mentally navigated within a series of three virtual environments. Results revealed cortical regions concerned with the contents of visual consciousness and motion sensitivity during perception and those concerned with spatial navigation and orientation during mental imagery, suggesting the inclusion of content-specific information within regions that support basic navigational functioning. Interestingly, there was minimal overlap in cortical regions supporting both perceptual and mental distinctions. Regions more classically associated with mnemonic retrieval were unveiled during contextual-reinstatement analyses, which we postulate could reflect a memory-enhanced processing signal that more closely reflects the original encoding brain-state. Future work will be needed to more directly address the potential memory-induced upregulation of imagined navigation to match perceptual processes. Apart from the contribution to pursuits of human brain mapping, this work marks and important “proof-of-concept” that the decoding of environmental context and path-directionality during mental imagery can be accomplished. With this work, and substantial future research, brain-computer interfaces could theoretically allow for real-time spatial navigation by thought alone—a feat that has already seen impressive progress by way of researchers successfully allowing participants to navigate about a 2D maze while using real-time fMRI data (Yoo et al., 2004).

## Figure Captions

**Figure 1.** Virtual Environments and In-World Stimuli

A) The five Virtual Environments (VEs) created for this study using OpenSim Software. Toon World, Ruin World, and Lagoon World were used for encoding. Viewpoints within encoding environments reveal the participant’s starting location in the southmost area of the world, facing North. Avatar Island was used to familiarize subjects with navigation within our VEs and Moon World was used to exposure participants to the object-placement technology. All environments rested within a 64 x 64 grid region border. B) The 24 landmarks placed in the eight cardinal locations (N,S,W,E,NW,NE,SW,SE) along the perimeter of each of the three encoding VEs. The figure’s arrangement of each landmark reflects their placement in each environment. Landmark names are as follows, starting with the landmark in the upper left corner (i.e. NW) and moving clockwise for each environment: Toon (slide, penguin pool, mushrooms, lollipop tree, Tetris blocks, water pipes, flamingo pool, doghouse), Ruin (fish fountain, treasure chests, giant telescope, armillary sphere, large bell, red flags, sun plaque, bubbling cauldron), Lagoon (fern statue, horse saddle, giant cactus, kayak, two curvy chairs, surfboard, fireplace, ridged planters). C) A) Tokens collected by participants upon their first entries into each VE. Tokens varied as a function of world: coins in Toon World, rings in Ruin World, and shells in Lagoon World. Each world contained 20 tokens and a Heads Up Display (HUD) indicated a participant's progress as they collected each of the tokens**.** D) Starting viewpoints of 8 (of 24 total) 30s video clips that participants viewed in the scanner. Each clip from each world started at a cardinal location (North, South, West, or East) and moved in either a clockwise (as indicated by the top row) or counter-clockwise direction (bottom row) about the environment until it ended at the original starting location.

**Figure 2.** Landmark / Token Placement Task

Participants were first shown a picture of a landmark, along with its name (A) and, on the next-screen, were shown an allocentric, "bird's eye" view of each environment (Lagoon World used here) that was stripped of its landmarks (B). C) The mouse cursor participants used to select the location of the cued landmark/token. D) A grid overlay delineating the 4,096 (64 x 64) cells available for participant selection via their cursor. This grid was not visible to participants, but could be inferred given the cursor's inability to be placed outside of each cell—the cursor would "snap" to fit into the nearest, overlapping grid cell.

**Figure 3.** Mental navigation instruction screen

An example of stimuli that participants viewed in the scanner before they engaged in a mental imagery trial. Participants were briefed before the scanning session that this instruction page would inform them as to which world they should imagine themselves in, which landmark they should first orient themselves at, and which landmark should be the first that they pass as they mentally circumnavigate the world. Participants made a button press when they had finished reading this instruction prompt indicating they were ready to begin.

**Figure 4.** Whole brain searchlight accuracy maps from when the classifier was both trained and tested on perceptual video-viewing data to predict environmental context (i.e. decoding “Which World” the participant was viewing).

Significant accuracies surviving a 50-contiguous-voxel cluster threshold here are shown. Chance decoding accuracy was 33% (3 Worlds).

**Figure 5.** Whole brain searchlight accuracy maps from when the classifier was both trained and tested on perceptual video-viewing data to predict heading direction (i.e. decoding “Which Direction” the participant was viewing).

Significant accuracies surviving a 50-contiguous-voxel cluster threshold here are shown. Chance decoding accuracy was 50% (Clockwise vs. Counterclockwise).

**Figure 6.** Whole brain searchlight accuracy maps from when the classifier was both trained and tested on imagery data to predict environmental context (i.e. decoding “Which World” the participant was mentally navigating).

Significant accuracies surviving a 50-contiguous-voxel cluster threshold here are shown. Chance decoding accuracy was 33% (3 Worlds).

**Figure 7.** Whole brain searchlight accuracy maps from when the classifier was both trained and tested on imagery data to predict heading direction (i.e. decoding “Which Direction” the participant was imagining).

Significant accuracies surviving a 50-contiguous-voxel cluster threshold here are shown. Chance decoding accuracy was 50% (Clockwise vs. Counterclockwise). Results were limited to the posterior, right hemisphere.

**Figure 8.** Whole brain searchlight accuracy maps from when the classifier was trained on perceptual video-viewing data and tested on imagery data to predict environmental context (i.e. decoding “Which World” the participant was mentally navigating based on the pattern of response shown during perception of the same world).

Significant accuracies surviving a 50-contiguous-voxel cluster threshold here are shown. Chance decoding accuracy was 33% (3 Worlds).

**Figure 9.** Whole brain searchlight accuracy maps from when the classifier was trained on perceptual video-viewing data and tested on imagery data to predict heading direction (i.e. decoding “Which Direction” the participant was imagining).

Significant accuracies surviving a 50-contiguous-voxel cluster threshold here are shown. Chance decoding accuracy was 50% (Clockwise vs. Counterclockwise).

## Table Captions

**Table 1.** Significant searchlight results for decoding environmental context as a function of perception, imagery, and reinstatement.

**Table 2.** Significant searchlight results for decoding environmental context as a function of perception, imagery, and reinstatement.

## Figures

**Figure 1. Virtual Environments and In-World Stimuli**

## Figure 2. Landmark / Token Placement Task

## Figure 3. Mental navigation instruction screen

**Figure 4. Whole brain searchlight accuracy maps from when the classifier was both trained and tested on perceptual video-viewing data to predict environmental context (i.e. decoding "Which World" the participant was viewing).**

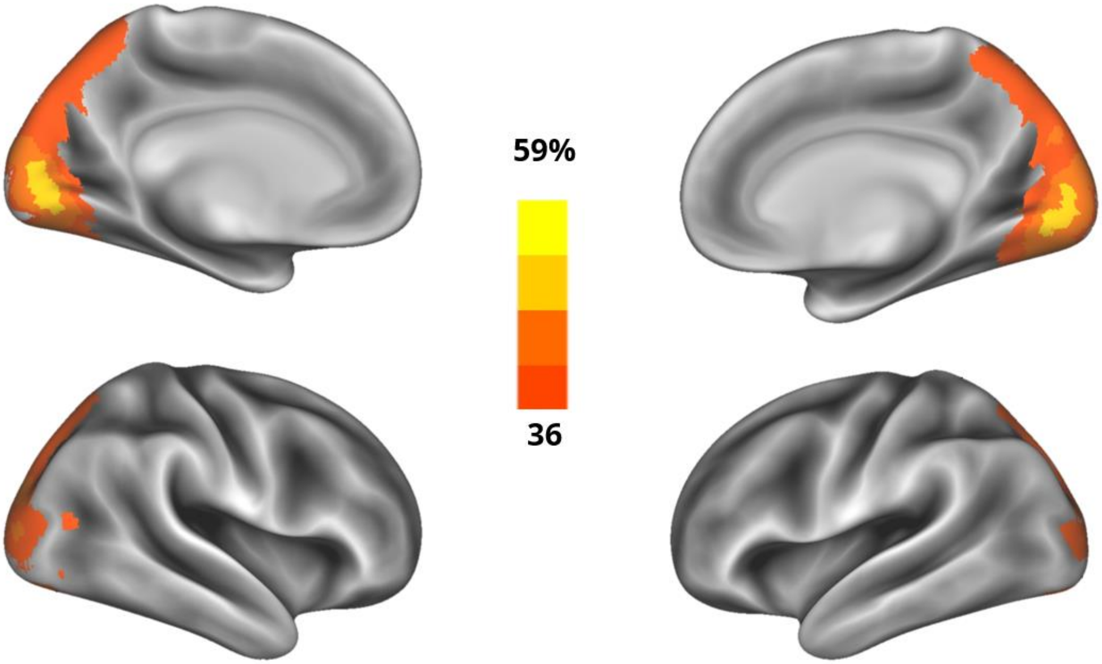


**Figure 5. Whole brain searchlight accuracy maps from when the classifier was both trained and tested on perceptual video-viewing data to predict heading direction (i.e. decoding "Which Direction" the participant was viewing).**

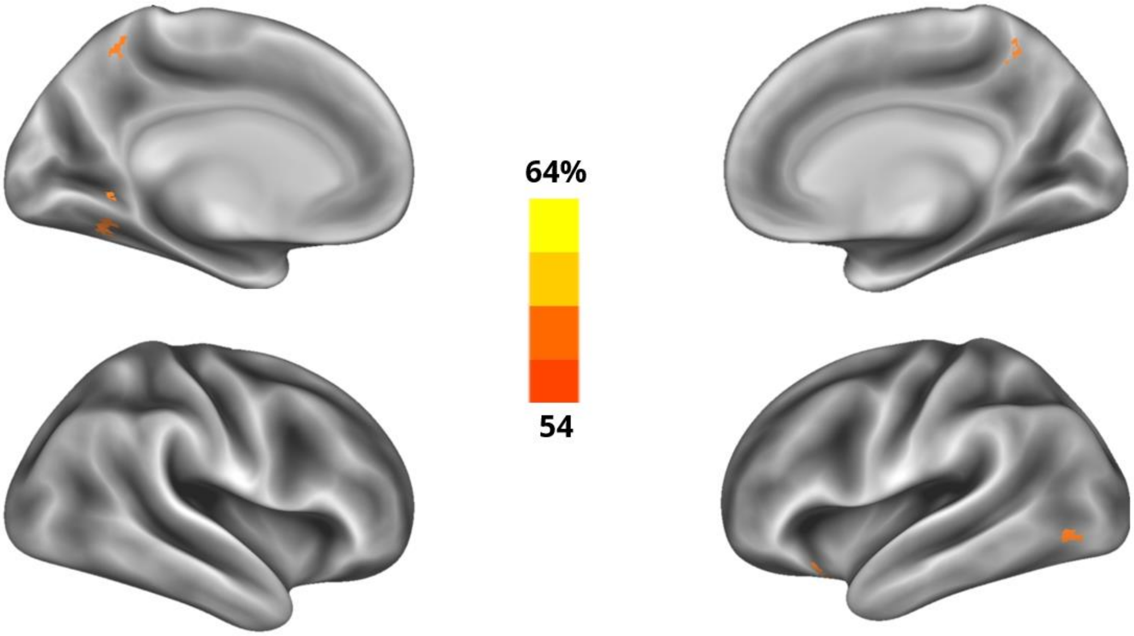


**Figure 6. Whole brain searchlight accuracy maps from when the classifier was both trained and tested on imagery data to predict environmental context (i.e. decoding "Which World" the participant was mentally navigating).**

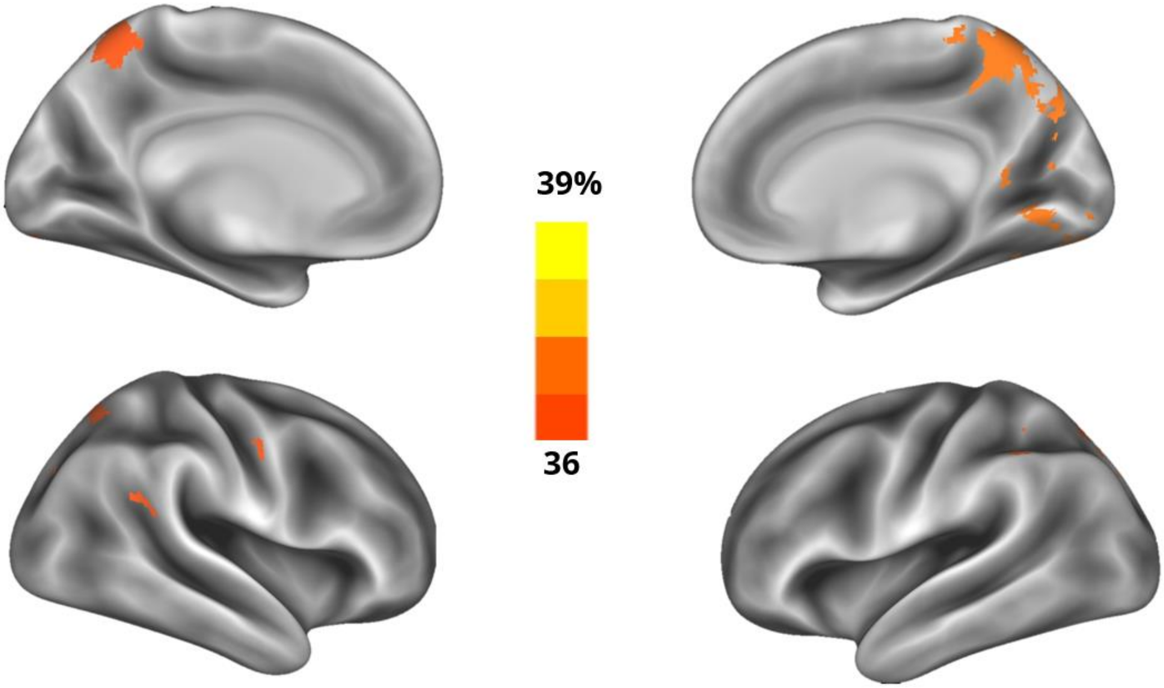


**Figure 7. Whole brain searchlight accuracy maps from when the classifier was both trained and tested on imagery data to predict heading direction (i.e. decoding "Which Direction" the participant was imagining).**

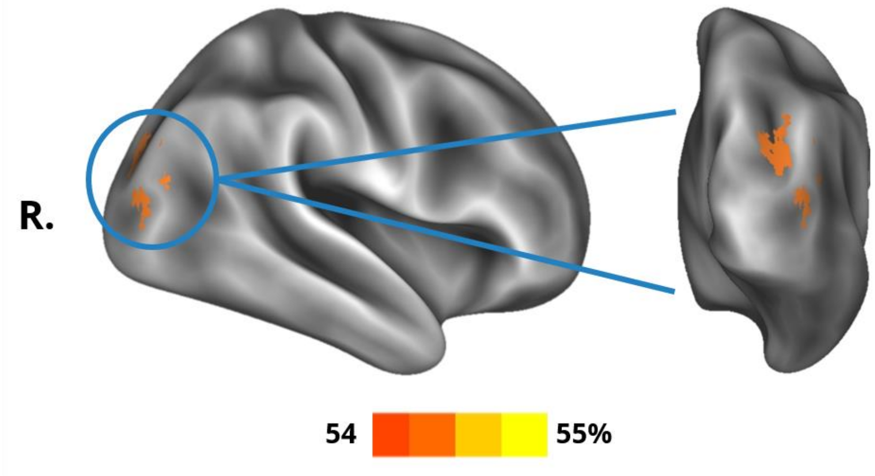


**Figure 8. Whole brain searchlight accuracy maps from when the classifier was trained on perceptual video-viewing data and tested on imagery data to predict environmental context (i.e. decoding "Which World" the participant was mentally navigating based on the pattern of response shown during perception of the same world).**

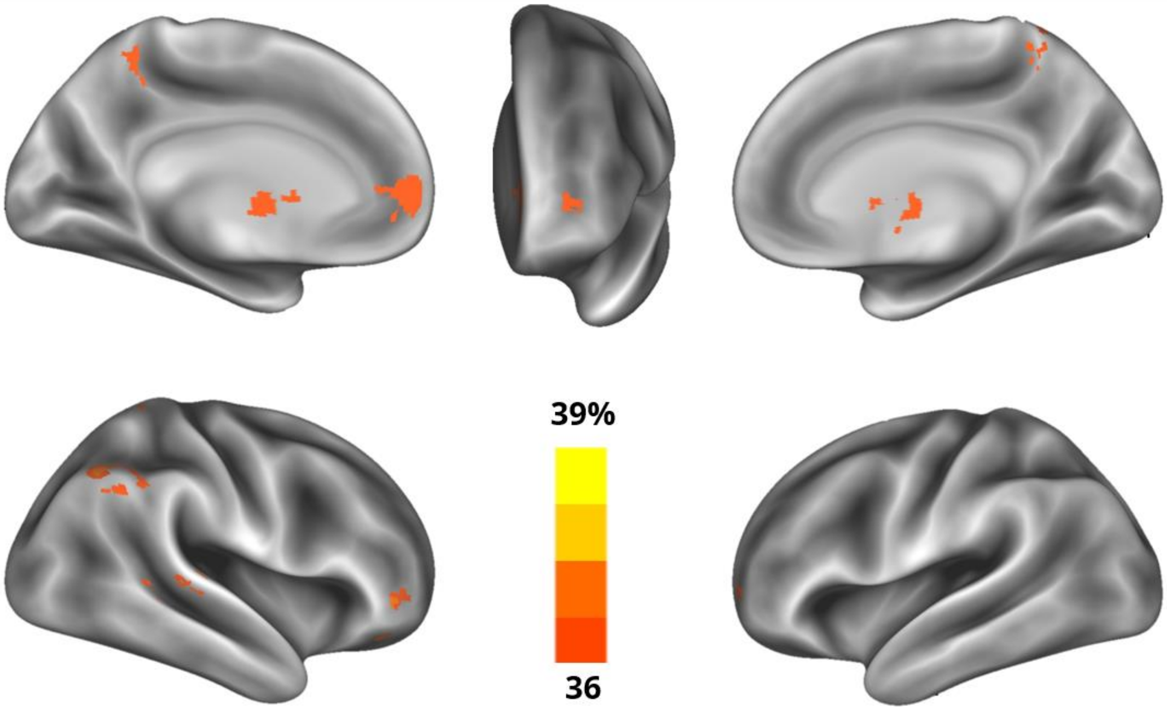
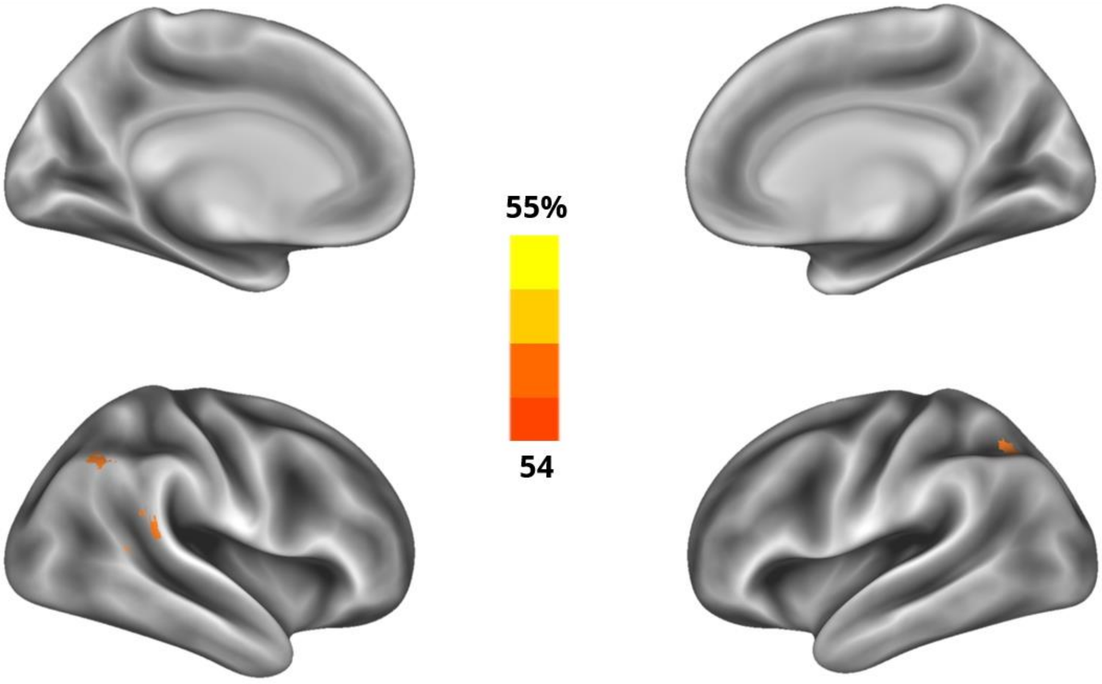
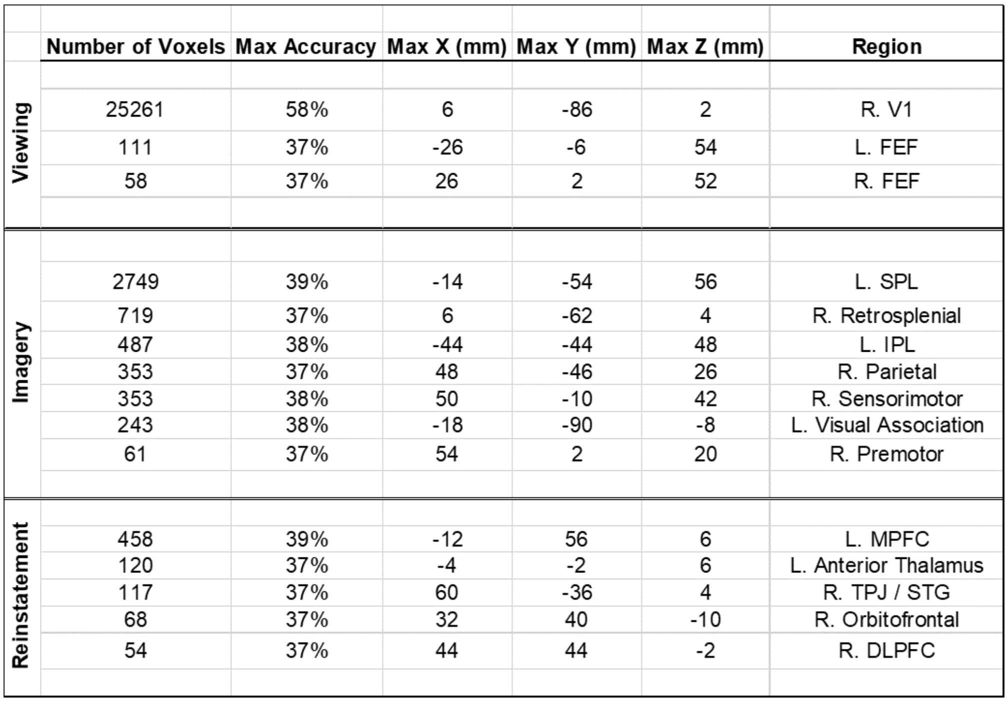


**Figure 9. Whole brain searchlight accuracy maps from when the classifier was trained on perceptual video-viewing data and tested on imagery data to predict heading direction (i.e. decoding "Which Direction" the participant was imagining).**



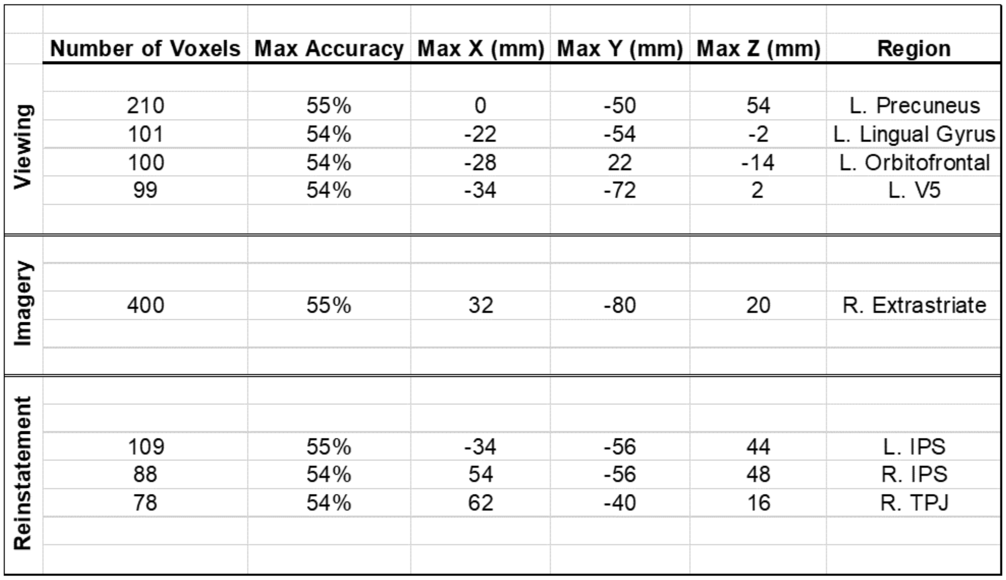
## Tables

### Table 1. Significant searchlight results for decoding environmental context as a function of perception, imagery, and reinstatement.



| | Number of Voxels | Max Accuracy | Max X (mm) | Max Y (mm) | Max Z (mm) | Region |
|---|---|---|---|---|---|---|
| **Viewing** | 25261 | 58% | 6 | -86 | 2 | R. V1 |
| | 111 | 37% | -26 | -6 | 54 | L. FEF |
| | 58 | 37% | 26 | 2 | 52 | R. FEF |
| **Imagery** | 2749 | 39% | -14 | -54 | 56 | L. SPL |
| | 719 | 37% | 6 | -62 | 4 | R. Retrosplenial |
| | 487 | 38% | -44 | -44 | 48 | L. IPL |
| | 353 | 37% | 48 | -46 | 26 | R. Parietal |
| | 353 | 38% | 50 | -10 | 42 | R. Sensorimotor |
| | 243 | 38% | -18 | -90 | -8 | L. Visual Association |
| | 61 | 37% | 54 | 2 | 20 | R. Premotor |
| **Reinstatement** | 458 | 39% | -12 | 56 | 6 | L. MPFC |
| | 120 | 37% | -4 | -2 | 6 | L. Anterior Thalamus |
| | 117 | 37% | 60 | -36 | 4 | R. TPJ / STG |
| | 68 | 37% | 32 | 40 | -10 | R. Orbitofrontal |
| | 54 | 37% | 44 | 44 | -2 | R. DLPFC |

### Table 2. Significant searchlight results for decoding environmental context as a function of perception, imagery, and reinstatement.



| | Number of Voxels | Max Accuracy | Max X (mm) | Max Y (mm) | Max Z (mm) | Region |
|---|---|---|---|---|---|---|
| **Viewing** | 210 | 55% | 0 | -50 | 54 | L. Precuneus |
| | 101 | 54% | -22 | -54 | -2 | L. Lingual Gyrus |
| | 100 | 54% | -28 | 22 | -14 | L. Orbitofrontal |
| | 99 | 54% | -34 | -72 | 2 | L. V5 |
| **Imagery** | 400 | 55% | 32 | -80 | 20 | R. Extrastriate |
| **Reinstatement** | 109 | 55% | -34 | -56 | 44 | L. IPS |
| | 88 | 54% | 54 | -56 | 48 | R. IPS |
| | 78 | 54% | 62 | -40 | 16 | R. TPJ |

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## Appendix

### *Appendix 1 – Participant Day 2 Instructions Handout (Provided on Day 1)*

Hello ____________________________!

Thanks for committing to coming back for the second day!

Remember that we need you to come to Franz Hall Room 8457 at the following date and time:

____________________________________

For this second day of the experiment we are going to have you complete a task in the lab before we walk over to the scanner and have you do several task while we scan your brain.

**IN LAB**

---

**Spatial Memory Task**

Remember those virtual environments you explored yesterday? We want to see how well you remember the location of the (8) Landmarks that were inside each of the three virtual environments. We would also like to see how well you remember the (20) coins that you collected in each environment.

You will be shown a “bird’s eye view” of each virtual environment and asked to click on the location of each landmark. You will be instructed as to which landmark to click on. You will also be asked to click on the 20 locations in which you found each coin within each environment.

---

**IN SCANNER**

You will be completing three tasks in the scanner. The number task (described below) will be interleaved within each of the other tasks. For example, you will do the Video Viewing Task (described below), then the number task, then the video viewing task, then the number task, etc. This will continue until you do the Mental Navigation Task (described below), which will also be interleaved with the number task.

All of the tasks will make use of a button box.  You will control this button box while you are in the scanner with your right hand. Your index finger will be on button 1; middle on 2; ring on 3; pinky on 4. Please remember these button assignments, as we will refer to them by number for the instructions.

---

## Number Judgment Task

After seeing a prompt that says “Get ready for number task” two numbers will appear on the screen.

It is your task to multiply the two numbers and decide if their product is Odd or Even.

If the product is ***Odd***, then you will push ***Button 1***.

If the product is ***Even***, then you will push ***Button 2***.

For Example, if you see the numbers 3 and 7 on the screen, then you would push Button 1, because their product (21) is Odd.

## Video Viewing Task

In this portion of the experiment, you will see videos taken from each of the virtual environments that you explored. You will see one video at a time before going back to the number judgment task.

Each video will start from one of the eight “landmarks” and provide a circular tour of the perimeter of the virtual environment before returning back to the same landmark.

It is your task to pay close attention to the videos. You will later, during the Mental Navigation Task (described later), imagine yourself navigating throughout the environment in a way similar to the videos. In order to successfully complete that task, you need to pay attention to the order of the landmarks that you pass in this task.

While viewing the videos, we want you to button press whenever you pass a landmark.

When the video passes the **first landmark** (which will appear on the screen for two seconds before the video starts playing) you will push **Button 2**.

For each of the **subsequent landmarks** that the video passes (there will be 7 of them), you will push **Button 3**

When the video arrives back at the **first landmark again**, you will push **Button 4**.

| Button | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |
|---|---|---|---|---|---|---|---|---|---|
| Landmark | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 1 |

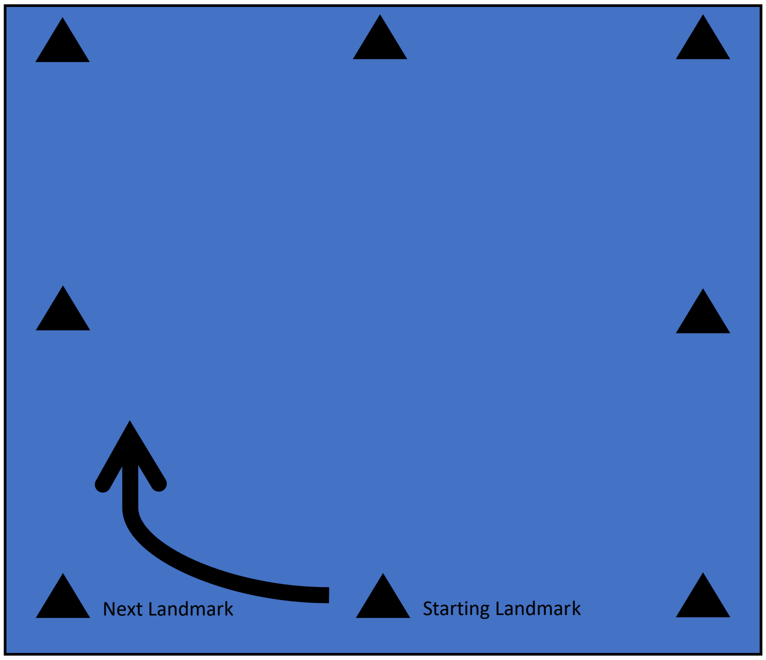
You will see one video at a time, making the appropriate responses, before going back to the number judgment task.

### Mental Navigation Task

In order to successfully complete this task, you will have needed to pay close attention to the videos presented during the Video Viewing Task. The purpose of this task will be to mentally imagine yourself in the virtual environment we ask and imagine yourself moving about the environment in a specific manner.

It is very important that you allow yourself to concentrate fully on forming a vivid and detailed image of the environment in your mind. It is also important to try and actually "see" each landmark as you move around the environment.

It is your task to mentally imagine yourself in the environment and navigate around it in a full circle, just like how you saw in the videos. We will prompt you with a screen that will tell you which world you need to imagine yourself in and which landmark to mentally "place" yourself in front of. We will also tell you which landmark is the "next" landmark. This "next" landmark informs you as to which direction you should head as you start to mentally imagine yourself navigating in a circle around the environment. The figure below shows an example.



Since this mental navigation task requires you to vividly imagine yourself in the environment, we will need you to close your eyes as you mentally navigate about the environment. The instructions for this task involve specific times for you to let us know when you have “oriented” yourself in the desired virtual environment and are ready to begin navigating. You will let us know that you have successfully oriented yourself in the environment by a button press. You will also let us know where you are in the environment by making a series of a button presses: one as you pass each landmark. Lastly, you will let us know when you are finished by making a button press when you have completely. Since you will have your eyes closed during this, please remember the following order of button presses and tasks.

1) Instruction Screen [Tells you which environment, which starting landmark, which next landmark]

a. You will **Button Press 1** when you are ready to **begin**.

2) Close Your Eyes

3) Imagine Yourself in the environment at the Starting Landmark

a. Once you feel as though you have vividly oriented yourself at the **Starting Landmark**, **Button Press 2**

4) Begin Navigating towards the Next Landmark

a. As you pass the **Next Landmark**, **Button Press 3**

5) Continue navigating in a circle around the virtual environment in the same direction.

a. As you pass **Each Landmark, Button Press 3**

6) Continue navigating until you get back to the Starting Landmark

a. When you have reached the **Starting Landmark Again, Button Press 4**

7) Open your eyes

After each of these mental traversion tasks, you will do a Number Judgment Task again.

---

Remember to get a good night’s sleep!

Remember to not drink or partake in illicit substance abuse the night before the scan!

Remember to wear comfortable clothing!

Thank you for taking the time to participate!

## ***Appendix 2 – Post Experimental Questionnaire***

Thank you for participating in this experiment! Your honest and detailed answers below will really help us with the analysis of this experiment. We greatly appreciate it!

**How vividly were you able to recreate Toon World?**

1 2 3 4 5 6 7 8 9 10

**How vividly were you able to recreate Ruin World?**

1 2 3 4 5 6 7 8 9 10

**How vividly were you able to recreate Lagoon World?**

1 2 3 4 5 6 7 8 9 10

**When you were mentally reimagining routes throughout the environments, did you feel like your speed was** faster / about the same / slower **than the videos you saw?**

**When you were mentally reimagining routes throughout the environment, did you feel like you were:** watching a movie clip / re-experiencing the environment

**When you were mentally reimagining routes throughout the environment, did you "jump" form landmark to landmark?**

Yes / No, I walked smoothly like in the video /

Other:__________________________________________

**When you were mentally reimagining routes throughout the environment, did you** actually see the landmarks / button press at the right interval spacing

**Did you feel dizzy at all at any point during this 2-Day experiment?**

Yes / No

**Which of the environments do you feel like was the most vivid and/or unique?**

Toon World / Ruin World / Lagoon World / All were equally vivid and/or unique

**Using the squares below, please write the name of each landmark in its appropriate location for each world.**

## Toon World

## Ruin World

# Lagoon World

# Chapter 6: Contextual reinstatement of virtual encoding environments during recall

## Abstract

Despite a rich history of anecdotal and empirical success in enhancing human memory, the Method of Loci (MoL) remains an understudied mnemonic device. While previous research has shown that explicit binding of items to the spatial scaffolding of an environment is crucial, above and beyond pictorial representations of information (Chapter 3) and that the environmental context can be decoded from mental imagery (Chapter 5), no studies have shown a neural pattern indicative of encoding environment when participants recall information learned using the MoL. To obtain a quantifiable metric of contextual reinstatement of encoding environment during recall, the current study tasked participants with learning lists of objects within a virtual implementation of the MoL that they were later asked to recall in the scanner. We trained a support vector machine classifier on blood oxygen level dependent patterns of activity expressed while participants viewed videos of the distinct encoding environments used for encoding and searched for regions whose recall activity (closed-eye verbal recall) conformed to the perceptual-derived decision boundary. Results suggest that brain regions involved in spatial processing and navigation (e.g. Insula, Superior Temporal Gyrus, Retrosplenial cortex), memory (bilateral hippocampus), contextual integration (Rostrolateral prefrontal cortex) and visual imagery (e.g. visual association area, V5) carry a signature of the encoding environment within the neural processes supporting different aspects of domain-invariant cognitive function, consistent with a role for contextual reinstatement in successful implementation of the MoL.

## Introduction

The Method of Loci (MoL), whose roots can be traced back to the ancient Greeks (Cicero and Wilkins, 1963), is designed to exploit the remarkable vividness of our visuospatial memories by using spatial environments as scaffolding for memorizing non-spatial content (Chapter 3). In order to implement the MoL, one is typically instructed to conjure up a familiar structure (e.g., a childhood home) that will serve as their “memory palace”. While mentally navigating through this environment, one can imagine “placing” a series of to-be-remembered items in different locations. When later attempting to retrieve this list of items, one can mentally reconstruct the environment and “observe” each of the objects along the route. Despite its widely acknowledged efficacy (Bower, 1970; Dalgleish et al., 2013; McCabe, 2015; Yates, 1966), little is known about the consequences of MoL-based learning on the neural correlates of later retrieval.

A previous functional magnetic resonance imaging (fMRI) study revealed a set of brain regions specific to recall after encoding using the MoL (Kondo et al., 2005).While informative, these findings essentially identify regions whose activity was greater during periods of enhanced mnemonic recall over that of less impressive recall—a finding in line with literature showing that enhanced BOLD activity in cortical regions (Canli et al., 2000), even at rest (Wig et al., 2008), and increases in functional connectivity (Wang et al., 2010; Wing et al., 2013) can serve as a correlate of memory enhancement. While univariate findings can elucidate the recruitment of episodic encoding brain networks during retrieval using the MoL, such insights do not provide granularity in regards to which mechanisms of the techniques are most potent in contributing to the reliable mnemonic enhancement witness by its practitioners.

This lack of clarity stems from the inherently elusive nature of the technique; the MoL is traditionally conducted within the confines of one’s mental imagery with no way of obtaining quantifiable metrics indicative of individual differences in execution, especially when considering the notable individual differences in mental imagery ability (Cui et al., 2007; Kosslyn et al., 1984). Furthering the confusion and inability to obtain objective metrics within participants is that each participant is typically instructed to use a familiar environment as their “memory palace”. This presents several issues: the amount of time an individual has physically spent in an environment, the aura of emotion those environments subconsciously carry, and the size and uniqueness of those environments all vary across participants. As such, a controllable and operationalized investigation requires an experimental approach that does not mandate the use of mental imagery for encoding.

Advancements in Virtual reality (VR) offer a unique opportunity to equalize exposure to virtual environments (VEs) since experimenters can design fantastical environments that are equally novel to all participants. While it has been debated whether or not navigation (a critical component in the MoL) in VR is to be considered “true navigation” (Minderer et al., 2016; Taube et al., 2013), there exists reasoning to believe that VR can increase the ecological validity of fMRI investigations of human memory (Reggente et al., 2018). Indeed, previous research has successfully exposed participants to VEs that were either subsequently used to execute the MoL within mental imagery (Legge et al., 2012) or served as the actual encoding environment, allowing participants to place to-be-remembered objects throughout the VE (Chapter 3).

In the current study, we sought to use VR and fMRI to test our hypothesis that the effectiveness of the MoL is driven by an explicit binding of objects to their spatial environment, recruiting neural architecture dedicated to the representation of and navigation about space—a set of cognitive processes that is arguably at the root of human cognition, especially memory (Robin et al., 2018). If memory is to be characterized as a constellation of representations of co-occurring stimuli (Rumelhart and McClelland, 1988), then it stands to reason that the spatial context enveloping an event constitutes a significant portion of the engram dedicated to that event (see Tulving, 1993). As such, it appears that the phenomenon of contextual reinstatement (Bartlett, 1932; Tulving, 1993) is dominated by spatial environments—a notion that is theorized to underpin findings that position space as the primary currency of the brain's encoding mechanisms (Mullally and Maguire, 2014; Robin et al., 2016, 2018). This posit is particularly salient when considering that memory retrieval depends on both reactivating an engram (i.e. pattern completion) and dissociating it from other engrams despite an overlap in nodes that make up multiple such representations (i.e. pattern separation; Yassa and Stark, 2011).

If a participant were to encode a set of information within a VE using the MoL, then, in accordance with our hypothesis, there should exist a neural signature of that VE during the recall of that information (i.e. environmental contextual reinstatement). To obtain such a metric, we designed a simple paradigm where participants used VR to implement a virtual rendition of the MoL and encode three lists of 15 objects across three distinct VEs, later recalling those lists of objects while in the scanner. Importantly, participants were told that each list of objects belonged to a fictional individual and were cued with that individuals name during recall so as to prevent any explicit reactivation of the original encoding environment. Following recall, participants watched a series of videos showcasing a tour of the VEs from an egocentric perspective. BOLD data collected during this video-viewing period was used to train a classifier model to differentiate the neural representations of the three distinct VEs, which allowed for us to index their reactivation during individual memory retrieval trials.

## Methods

### *Participants*

7 participants were recruited for this study by way of posted flyers throughout the UCLA campus. 6 participants were unable to finish the study due to a request to be removed from the scanner, which yielded insufficient data to conduct our analyses of interest. As a result, 1 participant (Male, 28) was analyzed. Participants were required to be right-handed, have normal or corrected-to-normal vision and hearing, have a mastery of the English language, and report no diagnosed learning disabilities, substance dependencies, nor prescriptions for psychotropic medications. Additionally, to prevent unequal exposure to the experimental apparatus, applicants were not permitted to participate if they had more than five hours of previous experience with the VR software used in this experiment (Second Life [http://secondlife.com] or its open-source virtual simulator OpenSimulator [http://opensimulator.org]). Eligibility screening was conducted prior to the participant’s enrollment in the study using the Research Electronic Data Capture (REDCap) online survey systems (Harris et al., 2009).

### *Materials*

The experimental materials leveraged in this current study are described extensively elsewhere (Chapter 3), but described briefly here. A total of three distinct virtual environments (VEs) were created for this study (“Toon World”, Ruin World”, “Lagoon World”; Figure 1A). Despite being designed specifically to maximize distinctiveness, each VE was created with the exact same dimensions (a 64 x 64 grid of accessible space) and was populated with eight distinct landmarks at the cardinal perimeter points (i.e. North, Northeast, East, etc.; Figure 1B). Heads Up Displays (HUDs) were alternately worn by participants as they collected tokens about the environment (Figure 1C) and viewed/placed objects (Figure 1D). Visual stimuli were presented in the scanner using MR-safe goggles (Resonance Technology, Inc.) and subject responses were collected using an MR-safe 1x4 button box (Current Designs). Verbal recall tests were digitally recorded with participant permission in the scanner using the Optoactive II noise-cancelling microphone and headphone system (http://www.optoacoustics.com/medical/optoactive-ii). All presentation materials were rendered using MATLAB (The Mathworks, Inc., 2012b) code and Psychophysics Toolbox (Version 3; Brainard, 1997). All statistical tests were conducted using custom R (R Core Team, 2013; http://www.R-PRoject.org/) and MATLAB code.

### *Procedure*

The experimental paradigm in this current study is identical to that described elsewhere (Chapter 3), except that all participants received the same encoding instructions and verbal recall and additional memory tests were conducted in the scanner.  Briefly, participants visited each VE in a random order and completed a series of token collection task that ensured even exploration of the VE across all participants.

Afterwards, participants were briefed on the classic implementation of the MoL technique and how the VEs there were just exposed to would serve as their “virtual memory palaces”. Subsequently, participants encoded a total of three lists of 15 objects across the three VEs. Prior to viewing each list of objects, participants were told that the objects they were about to see belonged to one of three fictional-individuals (Otto, Pike, or Viola) and that they would later be asked to recall the list of items belonging to that individual, in the order in which they were originally presented. Following this encoding period, participants viewed screen recordings of their movements about each environment. Following this rehearsal period, participants were escorted to and placed in the scanner.

Once positioned in the scanner, participants were prompted to close their eyes and recall by list name (i.e. Otto, Viola, or Pike) and given a maximum of 2 minutes to do so. A beep signaled participants to initiate recall after their eyes were closed and a subsequent one alerted them that the recall period was complete, and they were free to open their eyes. Participants recalled each list a total of four times, twice in the original encoding order and, subsequently, twice in the reverse order. Participants were instructed to speak with as little movement as possible into a noise-cancelling microphone and encouraged to remember as many words as possible, even if they could not recall each object in its original encoding order.

Participants were then submitted to a task that assessed their spatial memory for landmarks by showing them either an allocentric or egocentric screenshot of one of the virtual environments with a purple star overlaid on the image and four landmarks choices positioned below the image (Figure 2). Participants were instructed to indicate which landmark they thought was located at the purple star by making a button press. Participants had 6s to respond. All landmarks were removed from the environment before creating the images. Participants completed a total of 48 trials (allocentric vs. egocentric; 8 trials; 3 worlds), randomly interleaved as a function of world and egocentric/allocentric.

Following the landmark task, participants were shown similar egocentric and allocentric viewpoints from each virtual environment. However, instead of a purple star on the screen, a purple arrow was displayed, pointing to either the top, bottom, left, or right of the image. Participants were instructed to indicate via a button press whether they thought the arrow was pointing North, South, West, or East. Crucially, in the allocentric condition, the image was rotated in 90-degree intervals such that the top of the screen was either N, S, W, or E (Figure 3). In the egocentric condition, the viewpoint of the screenshot was facing in either the N, S, W, or E direction as well. As such, participants had to first orient themselves so as to identify which direction was which and then use that bearing to complete the task. See Figure 4.11 for an example trial. Participants completed 96 trials of this task (egocentric vs. allocentric; 4 facing directions; 4 arrow directions; 3 worlds).

At the end of the scan, participants were shown a series of (24) 20 second videos taken from a first-person perspective as experimenters navigated about each of the virtual worlds. All videos started at one of the eight landmarks and moved towards the center of the environment and through to the landmark on the opposite cardinal point, barring any environmental constructs. Figure 5 illustrates example paths taken in Toon world. Videos were frame rate edited to ensure they were all 20s long.

### *fMRI Acquisition Parameters*

Magnetic Resonance Imaging (MRI) data were acquired with a 3.0T Siemens Magnetom Prisma Scanner at the UCLA Ahmanson-Lovelace Brain Mapping Center using a 64-channel head coil. We acquired a high-resolution T2-weighted anatomical scan acquired by magnetization-prepared 180 degrees radio-frequency pulses and rapid gradient-echo (MPRAGE). TR/TE = 2300ms/3ms. Resolution = 0.8x0.8x0.8 $mm^3$. For the functional portion of our task we acquired a series of T2*weighted blood-oxygen level dependent (BOLD) images by Echo Planar Imaging (EPI) with a multiband acceleration factor of 5. TR/TE = 1000/30ms; Flip angle = 60°; Slice thickness = 2.00mm; In-plane resolution = 2x2x2 $mm^3$; 65 interleaved axial slices, with an anterior-posterior phase encoding direction. In addition, we collected gradient field and magnitude maps and ran a brief 30s epi scan before the start of the experiment to calibrate the noise-cancelling microphone.

### *fMRI Data Preprocessing*

fMRI data pre-processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied: motion correction parameters were estimated using MCFLIRT (Jenkinson et al., 2002); non-brain removal using BET (Smith, 2002); grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor; high pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma=50.0s). B0 field unwarping was run with FEAT’s FUGUE using an EPI dwell time of .30ms. Given our fast TR, we opted to not include a slice-timing correction. We used FLIRT to align each participant’s BOLD timecourse to MNI space, first aligning each participant’s middle-timepoint BOLD image from each run to their MPRAGE, followed by aligning their MPRAGE to a 2mm MNI template, and finally applying run-specific transformation matrices to each BOLD image in the run. Prior to each analysis, voxelwise time-courses for each run were filtered using a Savitsky-Golay digital filter (Chen et al., 2004; Çukur et al., 2013; Press and Teukolsky, 1990) with a polynomial order of 3 and then z-scored across the temporal dimension.

### *fMRI Methods*

Our primary analysis of interest was to assess the degree with which there was a contextual reinstatement of encoding environment during the eyes-closed recall sessions. To obtain a metric of contextual reinstatement, we trained a nu-linear support vector machine (SVM; c=1; libSVM: Chang and Lin, 2011) classifier on all available BOLD data collected during the video viewing period (i.e. localizer). Specifically, we identified the middle third of the time course and averaged the images contained therein—creating an average BOLD pattern of activity. The classifier was given world labels (i.e. This data comes from when the subject was viewing videos from Toon World or Ruin World or Lagoon World) so that it could “learn” a representative brain pattern response to each world and form a v-dimensional decision boundary, where v is the number of voxels included, that separates world exemplars. We then probed the classifier with data from each TR of both the forward and reverse recall periods to see if it could “guess” which world was present in the subject’s BOLD data (i.e. which world the subject encoded the information in). Since the participants were recalling items following a list name cue (i.e. no explicit reminder of encoding environment), a successful classification using this procedure would imply that the participants were bringing back to mind the environment in which they originally encoded the information.

We leveraged both an informational based, functional-brain-mapping procedure (Searchlight; Sphere radius=5 voxels; Kriegeskorte et al., 2006) and ROI method to unveil which regions contained BOLD patterns of activity during both forward and reverse recall that yielded a successful classification when using the decision boundary formed during video-viewing. A group of ROIs were delineated by previous studies and automated meta analyses using the forward inference on search terms (Memory, Mental Imagery, Object-Category, Spatial Information, Spatial Attention, Context, Environment) using the Neurosynth database (Figure 5; Yarkoni et al., 2011). Another group of ROIs were defined based on their network membership (Default Mode, Visual, Ventral Attention, Dorsal Attention, Memory Retrieval, Fronto-Parietal) as a result of large-scale meta-analysis (Figure 5; Power et al., 2011).

We also leveraged an SVM within a searchlight brain mapping approach to make the following classifications: allocentric vs. egocentric in the landmark task, allocentric vs. egocentric in the orientation task, allocentric vs. egocentric collapsed across task, and landmark vs. orientation.

To determine significance for our single-subject analysis, we created a null-distribution using the binomial inverse of the cumulative distribution function. The center of the distribution was the expected chance accuracy (33% for environmental context given the three encoding environments). The number of TRs across both forward and reverse recall attempts was given as the total number of classifications conducted across all participants. We set a significance cutoff to be the top 5% of the distribution ($p<0.05$), which yielded a 41% accuracy threshold. Finally, we report regions where 50 contiguous voxels were assigned significant accuracy values, averaged across all TRs.

## Results

The participant recalled all words from all lists in the correct encoding order—an impressive 45 objects across the three lists.

When trained on the video viewing data, the searchlight brain mapping classification procedure unveiled a number of regions that, during recall, contained patterns of BOLD activity that was informative of which virtual environment the cued-list was encoded in. When applied to both forward and reverse recall, significant clusters revealed that the classifier relied most heavily on information in the R. Insula, L. Superior Temporal Gyrus (STG), R. Putamen, Bilateral Hippocampus, L. Retrosplenial, R. Rostrolateral Prefrontal Cortex (RLPFC), L. Visual Association area, and R. V5 (Table 1; Figure 6). Our distributed ROI analyses also revealed significant accuracy in the Visual Network and within the "Memory", "Mental Imagery", and "Spatial Information" NeuroSynth search terms.

Follow up analyses that independently tested the classifier on only reverse or forward recall revealed a set of mostly non-overlapping regions that contributed to the classifier's success. Specifically, the only regions whose BOLD data collected during recall that was informative as to the original encoding environment were the right putamen, right hippocampus, and right parahippocampus. Interestingly, reverse recall accuracy relied more heavily on the right hippocampus whereas forward recall depended on BOLD data in the left hippocampus. No significant accuracies were observed in the searchlight or ROI decoding attempts for: allocentric vs. egocentric in the landmark task, allocentric vs. egocentric in the orientation task, allocentric vs. egocentric collapsed across task, and landmark vs. orientation.

## Discussion

The current study, with its single subject, serves as a proof of concept that it is indeed possible to decode environmental encoding context during recall using fMRI. Briefly, participants were exposed to a series of three different VEs where they viewed lists of 15 objects and placed them about the environments, creating a virtual analog of the MoL. Participants were told that each list of objects belonged to one of three fictional individuals. The same day, participants were cued with a fictional individual's name in the scanner and asked to close their eyes and recall their list of objects in both the forward and reverse encoding order. Following this cued verbal recall, participants watched a series of videos taken from an egocentric perspective that moved about each of the VEs. Measures of contextual reinstatement were collected by training a SVM to form a decision boundary during video-viewing and presenting new exemplars collected during recall and determining which regions contained BOLD patterns of activity informative of which environment the information being recalled was originally encoded in. We focus briefly here on results that had significant decoding accuracy during both forward and reverse recall, since the process of interest (contextual reinstatement) should be equally present during both trial-types (and arguably more so during reverse recall).

The R. Insula yielded both the highest accuracy (50%) and the largest cluster extent (330 contiguous voxels). Meta analyses have revealed that the R. Insula is reliably activated when navigating about recently learned environments (like the VEs that were exposed to the participants the same day) over familiar environments (Spiers and Barry, 2015). Other research has shown that mental navigation along memorized routes activates the insula (Ghaem et al., 1997). This suggests that during recall, the participant was engaged in a process of placing themselves back in the recently learned environment and navigating about it to assist with their recall—an intuition that is solidified by the participant's response (they walked about the encoding environment) on the post-experimental questionnaire. Importantly, while the R. Insula has been associated with navigation and integrating interoceptive awareness (Simmons et al., 2013), our results suggest that information regarding environmental context is embedded within the neural code that is supporting the base computations necessary to imagine (and feel) oneself navigating about an environment.

The L. STG finding, which was in the more posterior portions, near the TPJ, was also found (albeit contralaterally) to support contextual reinstatement in a previous data set collected using these same VEs and similar method (video-viewing data trained a classifier that was later tested on mnemonic retrieval; Chapter 5). The STG was found in the same meta-analysis to be associated with familiar environments over novel ones (Spiers and Barry, 2015), which may reflect the relative familiarity the participants had with the VEs that same day. Additionally, the TPJ is also involved in working memory (Anticevic et al., 2010) and functionally connected with the hippocampus during memory retrieval, but not during encoding (Huijbers et al., 2011). The STG has been shown to be more active when using distal cues to navigate about a maze as compared to shuffled distal cues that provided no information (Marsh et al., 2010), which could suggest that the participant was using nearby landmarks to navigate themselves about the environment during recall. Entirely in line with our findings, the L. STG has been posited to contribute to the formation of allocentric representations through the processing of categorical spatial relations (van Asselen et al., 2008), which strengthens our claim that the information being retrieved was intimately encoded alongside the context, by way of creating explicit binding to the spatial scaffolding of the environment (i.e. spatial relations).

Lesions to the putamen have shown impairment in spatial navigation (Whishaw et al., 1987b, 1987a). Combined with the classic purported function of the putamen in regulating and planning movement (Kimura, 1990) and its role in stimulus-action association learning (Haruno and Kawato, 2006), our results could indicate that contextual information is present in the putamen, assisting with computations necessary to complete the task (i.e. spatially navigate to loci where an action (placement) occurred). Also involved in spatial navigation is our finding in the L. retrosplenial cortex. Importantly, during mental navigation attempts, activity in Retrosplenial cortex was capable of decoding environmental context (Chapter 5), much like in the current study. Given its role in memory, navigation, and imagination (see Vann et al. (2009) for review), its not surprising that recruitment of the retrosplenial cortex was necessary to complete the task at hand. However, our finding that contextual information is embedded within its pattern of BOLD activity as it computes imagined navigation is novel.

Given that the data used to test the classifier was collected while participants were engaged in recall, a recruitment of the hippocampus is to be expected given long-standing observations of its involvement in retrieval processes (see Addis and Schacter (2012) and Rissman and Wagner (2012) for review) and its preference for recently acquired spatial knowledge (Spiers and Barry, 2015), especially when spatial associations have been formed in a way that allows for successful navigation (Hartley et al., 2003). In line with our task demands, the hippocampus is known to be recruited as a participant searches for paired-associate places of a previously seen objects (Lee et al., 2016). Crucially, the hippocampus is also important for learning the layout of new virtual environments (Wolbers and Büchel, 2005), a finding that supports its classic role in constructing and maintain spatial representations of an environment (O'Keefe and Nadel, 1978). The hippocampus was also unveiled as containing information allowing for the successful decoding individual episodic memory traces, defined by cued imagined recall of video clips viewed before the scan (Chadwick et al., 2010). Furthering support for its role in reinstatement, the hippocampus has been shown to be active when previously learned information is recalled in its original form (Giovanello et al., 2009; Xu et al., 2010). While the hippocampus has been shown to be sensitive to environmental size and geometry (Baumann and Mattingley, 2010; Muller et al., 1987) and fine-grain spatial information, especially for recent over remote spatial knowledge (Hirshhorn et al., 2011), including a participant's current location in an VE (Hassabis et al., 2009), no human research, to our knowledge, has shown that contextual environment can be decoded during recall. Simple contextual reinstatements (auditory-reward conditioned stimuli) have been observed in the rodent hippocampus (Fuchs et al., 2005) and shown to modulate if an environment is associated with fear (Ji and Maren, 2007; Moita et al., 2004), suggesting a potential role for the hippocampus in supporting context. Taken together, our findings suggest a role for the hippocampus in leveraging contextual information to retrieve place-object associations, while also supporting the base computations permitting successful imagined navigation.

Decoding mental imagery of places has been shown to activate corresponding stimulus-specific brain regions (O’Craven and Kanwisher, 2000). As such, our visual association finding (which replicates previous contextual-environment decoding during mental imagery (Chapter 5), is sensible; mental images can be decoded from activity patterns in visual cortex (Albers et al., 2013), suggesting a potential role for visual cortex as a “blackboard” (Bullier, 2001) that is used during both bottom-up stimulus processing and top-down internal generation of mental content. Also, Ishai et al. (2000) showed that decoding perceptual images was driven by activity in right-lateralized visual areas, whereas the decoding of visual imagery was more left-dominant, which lines up with our left-lateralized results. A similar logic can be extended to our V5 findings, which has been implicated in motion imagery (Goebel et al., 1998) and may suggest a role for V5 in inferring imagined movement necessary for navigation.

Finally, our R. RLPFC finding may have arisen due to the region’s likely role in mediating context-dependent integration (Cocchi et al., 2013) and its suggested part in manipulating domain-specific details (Wendelken et al., 2012). Given that RLPFC is involved in switching between stimulus-oriented and stimulus-independent thought (Gilbert et al., 2005), it could be that our RLPFC results indicate its role in assembling environment-specific information in both perceptual and imagery tasks, presenting similar patterns of activity each time and, thus, emerging from our analysis technique which was sensitive to exactly such operations.

Taken together, our results suggest that there exists brain regions whose pattern of BOLD activity during recall mirror that of their perceptual activity when viewing videos of VEs that were previously used to encode the recalled information. Specifically, our results illustrate a presence of contextual information within regions thought to support navigation and memory, given the strategy employed by our participant (navigating the original encoding environment to retrieve in accordance with the MoL strategy)—suggesting an incorporation of visuospatial content within processes responsible for supporting domain-invariant cognitive function. Future research will need to be conducted to unveil if recall processes that rely on different cognitive processes aside from memory (e.g. reasoning on previously acquired information) carries a signature of contextual reinstatement in regions supporting such processes and whether the degree of contextual reinstatement accounts for individual differences in memory retrieval.

### Figure Captions

**Figure 1.** A) The five Virtual Environments (VEs) created for this study using OpenSim Software. Toon World, Ruin World, and Lagoon World were used for encoding. Viewpoints within encoding environments reveal the participant's starting location in the southmost area of the world, facing North. Avatar Island was used to familiarize participants with navigation within our VEs and Moon World was used to exposure participants to the object-placement technology. All environments rested within a 64 x 64 grid region border. B) The 24 landmarks placed in the eight cardinal locations (N,S,W,E,NW,NE,SW,SE) along the perimeter of each of the three encoding VEs. The figure's arrangement of each landmark reflects their placement in each environment. Landmark names are as follows, starting with the landmark in the upper left corner (i.e. NW) and moving clockwise for each environment: Toon (slide, penguin pool, mushrooms, lollipop tree, Tetris blocks, water pipes, flamingo pool, doghouse), Ruin (fish fountain, treasure chests, giant telescope, armillary sphere, large bell, red flags,

sun plaque, bubbling cauldron), Lagoon (fern statue, horse saddle, giant cactus, kayak, two curvy chairs, surfboard, fireplace, ridged planters). C) Tokens collected by participants upon their first entries into each VE. Tokens varied as a function of world: coins in Toon World, rings in Ruin World, and shells in Lagoon World. Each world contained 20 tokens and a Heads Up Display (HUD) indicated a participant's progress as they collected each of the tokens D) Placement HUD, which allowed participants to view 3D rendering of objects and click on them to place them ina discrete location within the environment.

**Figure 2.** A) An example allocentric task where a purple star appears in place of the "Red Flags" landmark in Ruin World. B) The same task and landmark as A, but from an egocentric perspective.

**Figure 3** A) An example allocentric task where a purple arrow appears in the downward position in Lagoon World. The map has been shifted 180 degrees, such that North is at the bottom of the screen, making the correct direction of the arrow pointing in the North direction. B) The same task and direction as A, but from an egocentric perspective that is looking in the North direction, making the arrow pointing to the North.

**Figure 4.** An allocentric view of Toon World. Each color denotes the path a virtual camera took when creating the 20s videos used in the fMRI localizer. Each path was used twice: once from each landmark on the path

**Figure 5.** Example distributed ROIs from the Visual Network (defined by meta analysis: Power et al. (2011)) or Neurosynth automated meta-analysis search terms (Yarkoni et al., 2011). Search terms are displayed to the left of each array of images. Z-score

represents the forward-inference in the automated meta-analysis. All voxels with a non-zero z-score were included in the analysis.

**Figure 6.** Whole brain averaged searchlight maps from when the classifier was trained on fMRI data collected while the subject viewed 30s video clips from each virtual world and subsequently tested on recall data where subject was cued by a list name unrelated to the world name. The classifier was tasked with guessing "Which World" the subject had encoded the information they were currently retrieving in after having been trained on the patterns of activity displayed during the video viewing trials. Thus, chance was 33%. We only display results that survived a 50% lower threshold cutoff as determined by a $p<0.05$ from a binomial cumulative distribution function.

**Figure 7.** Distributed ROI (either defined by meta-analyses (Power et al., 2011) or neurosynth search terms (Yarkoni et al., 2011)) decoding accuracies from when the classifier was trained on fMRI data collected while the subject viewed 30s video clips from each virtual world and subsequently tested on recall data where subject was cued by a list name unrelated to the world name. The classifier was tasked with guessing "Which World" the subject had encoded the information they were currently retrieving in after having been trained on the patterns of activity displayed during the video viewing trials. Thus, chance was 33%. We highlight results that survived a 50% lower threshold cutoff as determined by a $p<0.05$ from a binomial cumulative distribution function.

## Table Captions

**Table 1.** Significant searchlight results for decoding environmental context when the classifier was trained on a video-localizer and tested during free recall.

## Figures

### Figure 1. Virtual environments and accompanying software

**Figure 2. Allocentric vs. Egocentric Landmark Task**

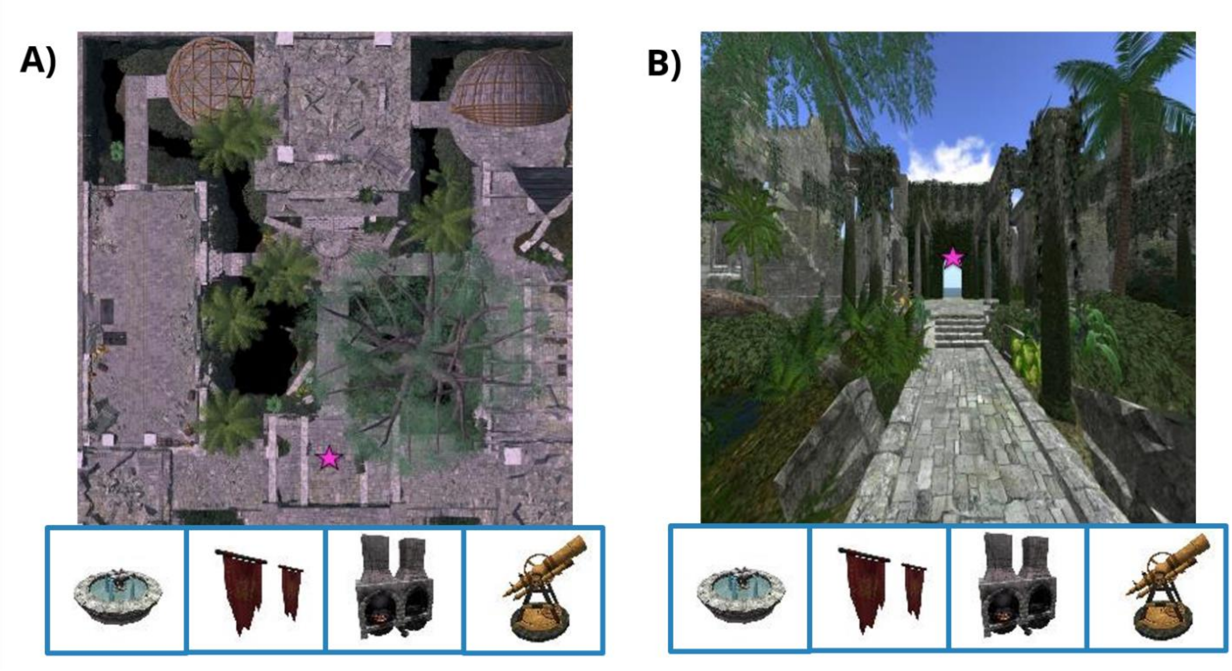


**Figure 3. Allocentric vs. Egocentric Direction Task**

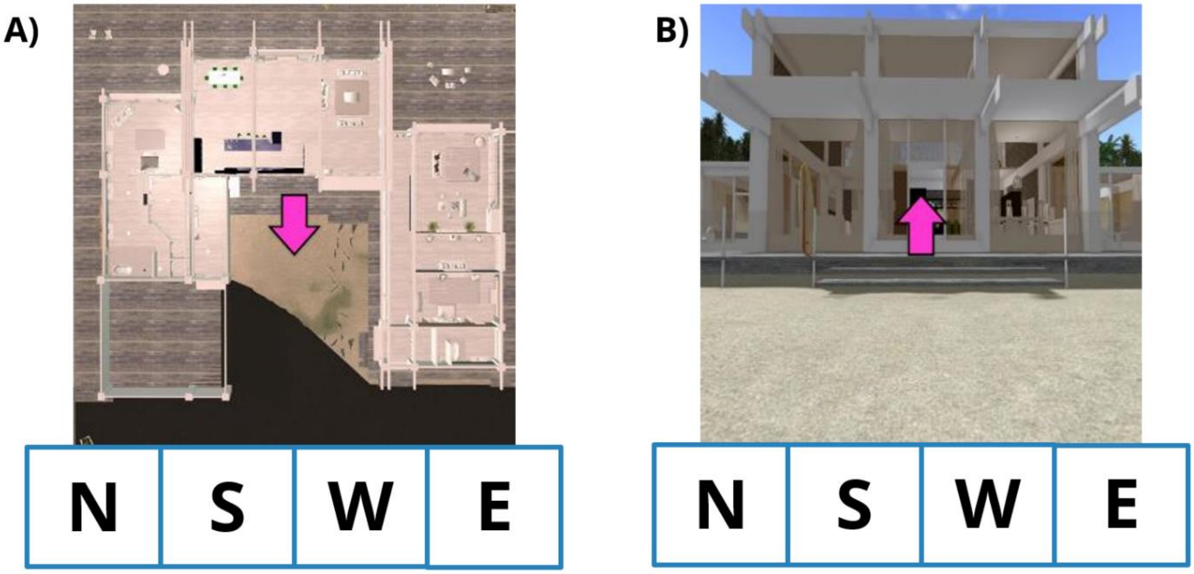


**Figure 4. Virtual camera paths**

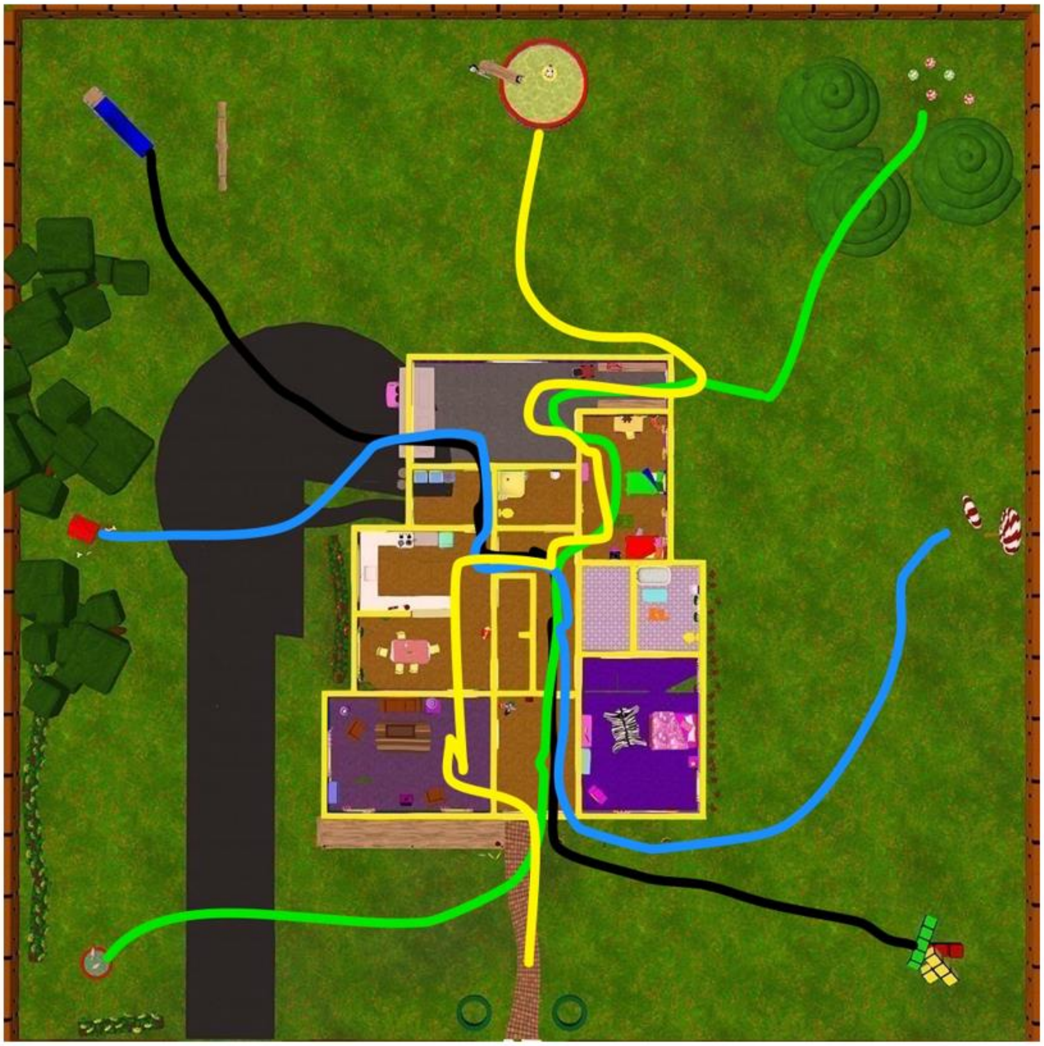
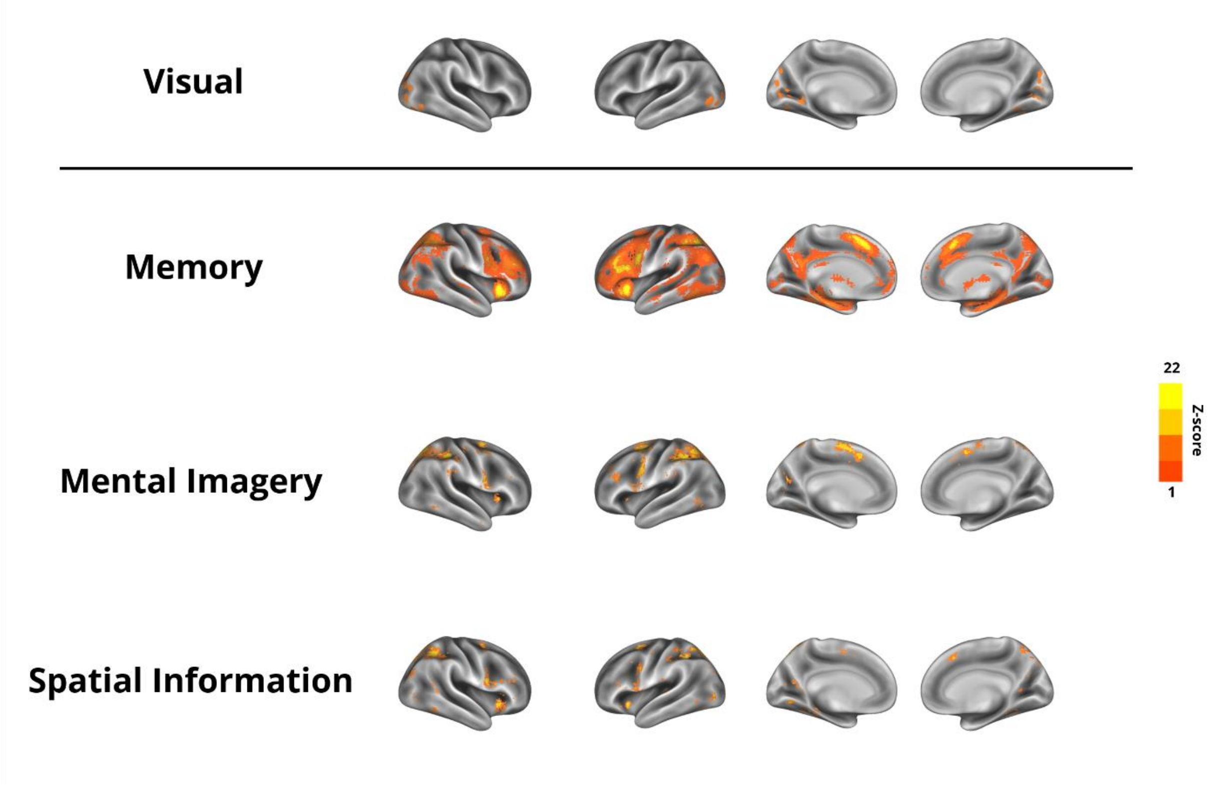
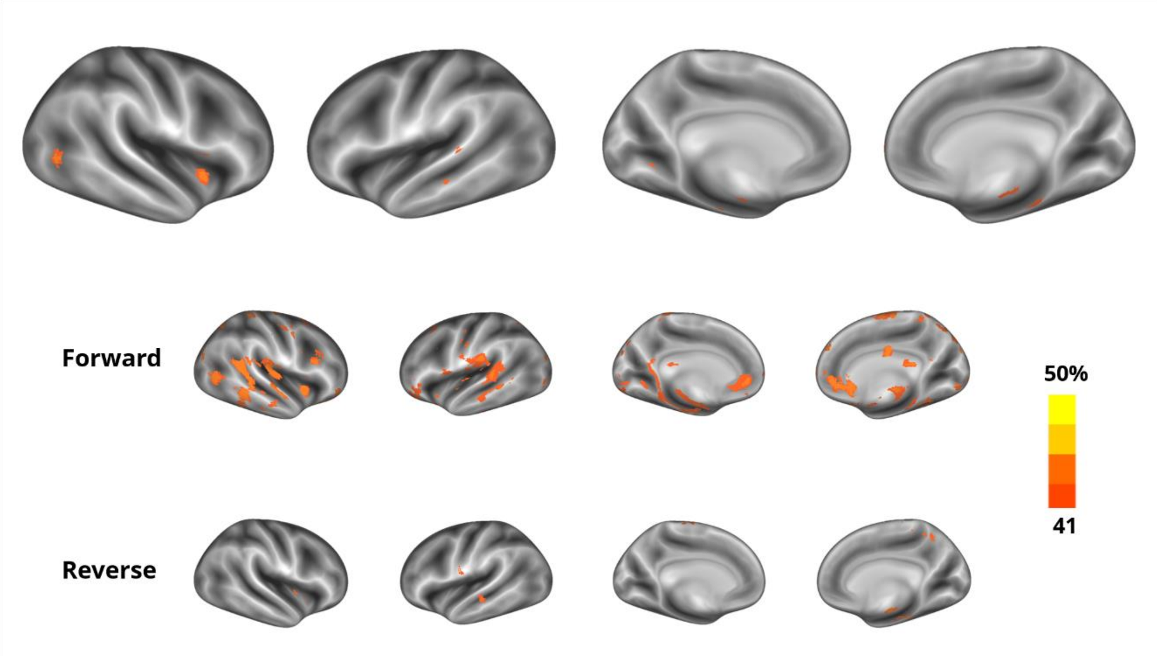


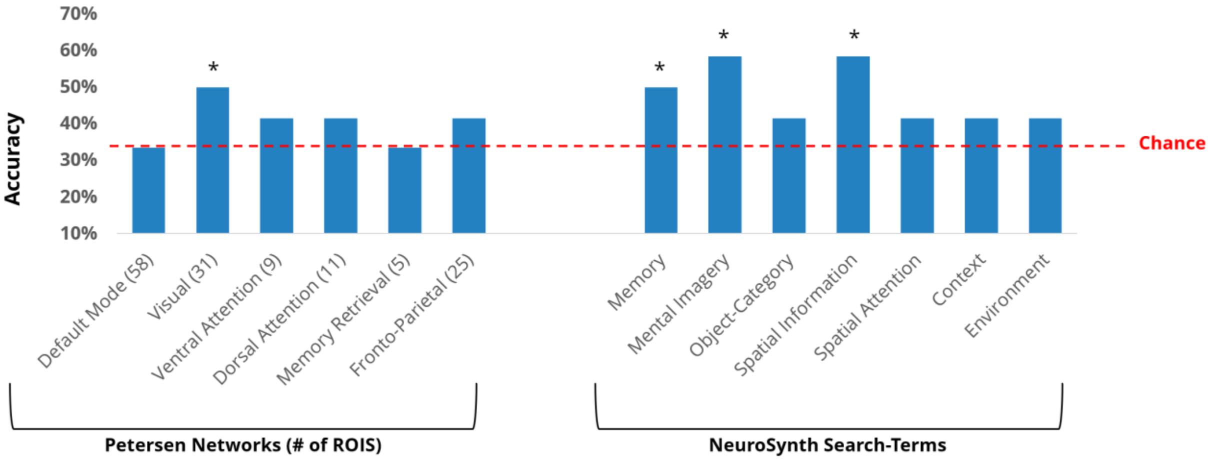
**Figure 5. Distributed ROIs use for analysis**



## Figure 6. Searchlight classification results

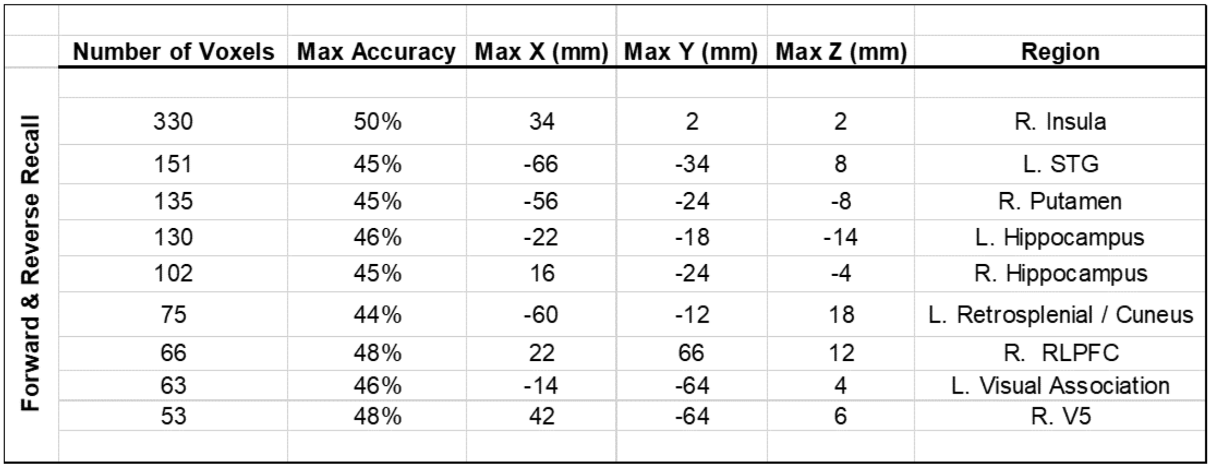


## Figure 7. Distributed ROI results



## Tables

### Table 1. Significant searchlight results for decoding environmental context when the classifier was trained on a video-localizer and tested during free recall.



| | Number of Voxels | Max Accuracy | Max X (mm) | Max Y (mm) | Max Z (mm) | Region |
|---|---|---|---|---|---|---|
| Forward & Reverse Recall | 330 | 50% | 34 | 2 | 2 | R. Insula |
| | 151 | 45% | -66 | -34 | 8 | L. STG |
| | 135 | 45% | -56 | -24 | -8 | R. Putamen |
| | 130 | 46% | -22 | -18 | -14 | L. Hippocampus |
| | 102 | 45% | 16 | -24 | -4 | R. Hippocampus |
| | 75 | 44% | -60 | -12 | 18 | L. Retrosplenial / Cuneus |
| | 66 | 48% | 22 | 66 | 12 | R. RLPFC |
| | 63 | 46% | -14 | -64 | 4 | L. Visual Association |
| | 53 | 48% | 42 | -64 | 6 | R. V5 |

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## General Summary

The work presented in this dissertation provides neurocognitive insights to the determinants of enhanced mnemonic recall. Of particular insert were the behavioral outcomes and neural correlates of memory encoding phenomena that result in reliable alterations in memory strength during recall: 1) preferential recall of information that is associated with behavioral salience; 2) enhanced mnemonic capacity when information is encoded within the scaffolding of spatial environments.

Chapter 1 used Diffusion Tensor Imaging to examine whether individual differences in anatomical connectivity within reward and fronto-temporal circuits are associated with value-induced modulation of memory. Results suggest that when presented with a reward value-indicating cue, communication between the Nucleus Accumbens and Ventral Tegmental Area may act as a gating mechanism to determine if elaborative encoding processes, as facilitated by the Uncinate Fasciculus, will be upregulated to preferentially bolster the encoding of words that follow high-value associations.

Chapter 2 set the stage for the remainder of the research conducted within the dissertation by reviewing the literature and positioning Virtual reality (VR) as an ecologically valid medium for fMRI investigations of memory. We hypothesized that contextual reinstatement (i.e. an initial binding of information to a spatial environment that is later expressed during recall) was underlying the efficacy of the MoL. This notion was tested in several stages. First, Chapter 3 demonstrated that the MoL could be successfully conducted within an objectifiable medium (i.e. VR) and that removing one’s ability to explicitly bind items to an environment context resulted in depreciated effectiveness of the technique. Results also revealed an intimate relationship between spatial memory for objects seen in a virtual environment and verbal recall strength for those items. Additionally, strategies for the re-utilization of a virtual environment were explored in Chapter 4, revealing a role for elaborative encoding (i.e. associating two objects with one another in addition to the environmental backdrop) in reducing forgetting when encoding multiple lists of information in the same virtual environment.

The next stage in hypothesis testing relied on a successful decoding of environmental context from mental imagery. Chapter 5 revealed a vast set of cortical regions that supported the decoding of environmental context and path-directionality as participants viewed videos from and mentally navigated within a series of three virtual environments. Results revealed cortical regions concerned with the contents of visual consciousness and motion sensitivity during perception and those concerned with spatial navigation and orientation during mental imagery, suggesting the inclusion of content-specific information within regions that support basic navigational functioning. Interestingly, there was minimal overlap in cortical regions supporting both perceptual and mental distinctions. Regions more classically associated with mnemonic retrieval were unveiled during contextual-reinstatement analyses, which we postulate could reflect a memory-enhanced processing signal that more closely reflects the original encoding brain-state.

This success allowed for a final test of the hypothesis: is it possible to decode environmental encoding context during recall? Chapter 6's results suggest that there exists brain regions whose pattern of BOLD activity during recall mirror that of their perceptual activity when viewing videos of VEs that were previously used to encode the recalled information. Specifically, our results illustrate a presence of contextual information within regions thought to support navigation and memory, given the strategy employed by our participant (navigating the original encoding environment to retrieve in accordance with the MoL strategy)—suggesting an incorporation of visuospatial content within processes responsible for supporting domain-invariant cognitive function.

Taken together, the results presented in this dissertation contribute meaningfully to discussions concerning the neurocognitive determinants of memory enhancement. Behavioral results indicate a definitive role for both reward and spatial context in reliably manipulating the selectivity and capacity of memory, respectively. Neuroimaging results reveal that a) individual differences in execution of value-directed remembering strategies can be explained by the integrity of reward and semantic encoding white matter pathways and b) the implementation of the MoL mnemonic instantiates a robust signature of encoding environment, which is decodable from regions involved in spatial processing and mnemonic retrieval during recall, suggesting an intimate binding of to-be-remembered information with encoding environment. Importantly, with the use of VR and behavioral paradigms aimed at exploiting the naturally occurring memory enhancing phenomena of value-directed-remembering and spatially-augmented-learning, this dissertation presents a suite of technology that is inherently easy to implement and which could be theoretically extended to educational environments rehabilitation centers to assist those with learning disabilities or memory disorders.