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Assessment of a Novel Visuospatial Memory Test

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An abstract of
A thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
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Abstract

Assessment of a Novel Visuospatial Memory Test

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Objective: Neuropsychological tests of learning and memory reliably detect verbal memory deficits following left temporal lobe damage but inconsistently detect visuospatial deficits following right temporal lobe damage. We devised a novel test using 3-dimensional shapes rather than traditional 2-dimensional drawings in an attempt to more sensitively measure visuospatial memory and right temporal lobe dysfunction.

Participants and Methods: Sixty healthy controls (30 male) were recruited into 3 experimental groups: 1) a control group (n=24; 12 male) completed the task under standard instructions and established a "normal" range of performance, 2) the verbal interference group (n=18; 9 male) completed the task while performing a verbally-based interference task (repeating the word "the"), 3) the visuospatial interference group (n=18; 9 male) completed the task while performing a visuospatial distraction task (following a moving shape). All three groups were given four learning trials to remember 12 towers, 6 gray towers intended to assess visuospatial memory and 6 color towers intended to assess verbal memory. Participants were instructed to encode stimuli by naming colors for the color towers or taking a mental picture for the gray towers. A recognition memory test was given immediately after trials 1 and 4, and after a 20-minute delay.

Results: Overall, we found no significant effects of group with the typical performance being similar for the two tower types on trial 1, but significantly better for the gray towers by trial 4 and after the delay. Although the verbal interference group showed this pattern of results, the visuospatial interference group performed significantly worse on the gray relative to the color towers on trial 1, similar on the two tower types on trial 4, and then significantly better for the gray towers at delay.

Conclusion: Overall, the interference tasks were minimally effective at impeding modality specific processing (i.e. verbal or visuospatial) given the lack of significant between group differences. Within this context, however, the visuospatial interference task did significantly affect performance on trial 1 which is what had been predicted.

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INTRODUCTION

Medial Temporal Lobe Memory System

The importance of medial temporal lobe (MTL) for learning and memory was first reported by Bekhterev in 1899 (Milner 1972), who noted that a patient with bilateral abnormalities in the region of the uncus, hippocampus, and adjoining medial temporal cortex showed severe memory impairment. However, the most compelling evidence for the importance of this region was established in the 1950's when a group of patients with bilateral surgical removal of the MTL showed profound and selective impairments in their ability to learn and remember new information (i.e. anterograde amnesia) despite preserved remote memories, technical skills, and general intelligence (Scoville and Milner 1957).

Subsequent work, using both humans and animals, delineated several MTL structures that are critical for normal learning and memory: the hippocampus (together with the dentate gyrus and subiculum) and the surrounding entorhinal, perirhinal, and parahippocampal cortices (Squire and Zola-Morgan 1991). These regions comprise what has become known as the medial temporal lobe memory system and are responsible for the conscious recollection of facts and events (declarative/explicit memory).

Material-Specific Memory Deficits After Unilateral Temporal Lobectomy

The MTL, especially the hippocampus, are vulnerable to the initiation and propagation of seizure activity and can lead to cognitive deficits, especially for learning and memory (Ben-Ari 2001; Schomer et al. 2001; Raspall et al. 2005; Leritz et al. 2006). The treatment of choice for intractable Temporal Lobe Epilepsy (TLE) has become surgical resection of these MTL structures, which has formed the basis of much of the current knowledge about the role of MTL structures in memory. Early findings of different patterns of deficits after unilateral MTL surgeries led to the development of the material specific model of memory which states that the dominant MTL, typically the left, is specialized for learning and remembering verbal information, whereas the nondominant MTL, typically the right, is specialized for learning and remembering visuospatial information (Milner 1972; Glosser et al. 1995; Martin 1999). This pattern of deficits is used to help lateralize seizure focus and obtain an idea of the risks of significant post-operative memory deficits (Schomer et al. 2001; McDermid Vaz 2004). Although research has supported the role of the left MTL in verbal learning and memory, recent findings have failed to demonstrate a similar relationship between right MTL and visuospatial learning and memory.

Verbal Memory Deficits After Left Medial Temporal Lobectomy

In an early study, 18 epileptic patients were tested pre- and post-surgically in order to clarify the nature of learning deficits associated with unilateral temporal lobectomy (Meyer and Yates 1955). Results from this study demonstrated significant impairments in the ability to learn verbal material presented in paired-associates as well as milder impairments on tasks assessing verbally based intellectual abilities in patients with a seizure focus in the left MTL. Patients with a seizure focus in the right MTL showed no such impairments. These deficits persisted when patients were reassessed at 1-year. A subsequent study that tested 86 post-surgical epileptic patients again demonstrated verbal learning deficits in patients following a left temporal lobectomy; however, this study found a gradual improvement in memory that began approximately 3 years post-surgery (Blakemore and Falconer 1967). This raises the possibility that patients developed compensatory strategies that allowed them to "work around" the deficits.

A more recent study has shown that resection of the structures surrounding the left hippocampus are sufficient to impair some forms of verbal learning and memory (Weintrob et al. 2007). Patients in this study were tested on arbitrary paired associate learning, semantically based (non-arbitrary) associative learning, and verbal list learning. Results from this study demonstrate that even when the hippocampus is preserved in a MTL surgery, resection of the left perirhinal and entorhinal cortex can still impair the ability to acquire arbitrarily related word pairs. However, when the perirhinal and entorhinal cortex were spared, no post-operative change in verbal learning was detected. Therefore, this study, through a more detailed anatomical analysis, concluded that different structures of the left MTL may contribute to different forms of verbal memory.

A meta-analytic review of 33 studies assessing verbal and visuospatial memory performance both before and after anterior temporal lobectomy further confirm the findings that verbal memory tasks are sensitive to left hemisphere dysfunction (Lee et al. 2002). Studies in this review used two Wechsler Memory Scale subtests, Logical Memory and Visual Reproduction subtests, as measures for verbal and visuospatial memory, respectively. Results from this meta-analysis demonstrated that left TLE patients performed worse on verbal memory tests then the right TLE patients before surgery and that this difference was larger after surgery. The findings reviewed above support the claim that verbal memory is lateralized in the left hemisphere and that verbal memory tasks are sensitive to left anterior temporal lobe dysfunction.

Visuospatial Memory Deficits After Right Medial Temporal Lobectomy

Kimura (1963) conducted one of the first studies showing that damage to the right MTL impaired visuospatial memory for unfamiliar, nonsense objects. In this experiment, pre- and post-operative patients with either a right or left seizure focus were given five different tests that required the recognition of letters, overlapping familiar figures, overlapping nonsense figures, familiar objects, and the number of dots immediately after their presentation. The subjects were also administered the Recurring Figures test, in which they were asked to recognize previously presented, unfamiliar designs. The right MTL group performed worse than the left MTL group, both pre- and post-operatively, on the recognition of nonsense figures and dots and on the Recurring Figures test. No such differences were found on the recognition of letters or overlapping familiar figures. On the recognition of familiar objects the right MTL group performed better post-operatively than the left MTL group. Overall, these results suggest that right MTL damage impairs the perception of unfamiliar visuospatial material (Nonsense Figures, Dots and Recurring Figures Tests), but not of familiar visuospatial material (Letters, Overlapping Familiar Figures, and Familiar Object Tests). Importantly, the unfamiliar and familiar stimuli differed in the degree of their verbal identification, which would be more dependent on the left MTL. Conversely, the unfamiliar stimuli were difficult to describe verbally and, as a result, were presumably less dependent on the left MTL. Therefore, this study mainly indicated that the right MTL is more sensitive to visuospatial material that is less amenable to verbal labeling.

Since Kimura's (1963) study, some of the most common visuospatial, neuropsychological tests have utilized similar unfamiliar, 2-dimensional stimuli in order to assess right MTL dysfunction. However, studies utilizing these tests have found inconsistent results. For instance, Martin et al. (1999) investigated the association between ^{1}H magnetic resonance spectroscopic imaging (MRSI)-detected neurochemical status of the hippocampus and neuropsychological measures in patients with TLE and found insignificant correlations between right hippocampal status and the Visual Reproduction (VR) subtest of the Wechsler Memory Scales (WMS), which uses 2 dimensional drawings. A recent meta-analytic review of 13 studies that investigated visuospatial memory performance in patients with right anterior temporal lobectomy (ATL) found 2-dimensional neuropsychological tests incapable of adequately explicating the effects of right ATL on visuospatial memory (McDermid Vaz 2004). While some neuropsychological measures indicated post-operative decreases in visuospatial memory, others showed improvements in performance following right ATL. Thus, recent studies using 2-dimensional stimuli for visuospatial memory tests do not uphold Kimura's (1963) earlier findings. Several researchers explain this inconsistency by suggesting that the test stimuli used to measure visuospatial memory may be susceptible to verbal encoding and, thus, insensitive to right MTL dysfunction.

Given this inconsistency, there is a need to identify other types of stimuli that may be more sensitive to right MTL damage or dysfunction. Examining the processes mediated by the right hemisphere and right MTL could help in developing such stimuli. In a study conducted by Maguire et al. (2001), positron emission tomography (PET) was used to investigate the patterns of brain activation associated with the intentional encoding and recognition of unfamiliar visuospatial stimuli. In general, the study found the right MTL to be specifically involved in the explicit learning and memory of complex visuospatial stimuli including buildings and landscapes.

In a study conducted by Smith and Milner (1981), patients with either left or right temporal lobectomies were tested on the incidental recall of objects and their location for both immediate and delay trials. This study is one of the few to date, that utilized 3-dimensional objects rather than 2-dimensional images for its testing stimuli. Sixteen small, namable toys were randomly assigned to different locations and the subjects were told to estimate prices of these objects. Immediately after this exposure, patients were asked to name as many of the objects they could remember. Following this object recall, subjects were given the sixteen toys and asked to place them in the correct location. After a twenty-four hour delay, object recall and object-location recall were reassessed. Both groups provided similar estimates for the prices of the objects; however, the left temporal lobectomy group performed significantly worse than the right temporal lobectomy group in the delayed recall of objects, indicating the greater dependence on verbally based information. Conversely, the right temporal lobectomy group showed impairments in both the immediate and delayed recall of the object’s location relative to the left group; thereby demonstrating the importance of right MTL in the learning and recall of spatial information.

Crane and Milner (2005) recently modified this approach by including multiple trials, reducing the number of test objects from 16 to 12, reducing the study time and the depth of processing required for each item, and introducing a 180° rotation from the study location to the testing location in order to examine the contributions of different MTL structures to object-location memory. In Experiment 1, healthy controls and patients with either a left or a right MTL surgery were given up to 10 study sessions to learn 12 objects and their locations. Memory was assessed immediately after each learning trial. Patients with a right MTL resection showed a trend toward memory impairments on trial 1 when compared to the control group. A 4 minute delay was introduced during experiment 2, in which the authors found impairments on immediate and delayed object-location recall in groups with right MTL group. Experiment 3 correlated postoperative MRI measurements of the tissue remaining in the MTL with the participants' performance during either Experiment 1 or 2. Here, the authors found the amount of right hippocampus remaining to be the best predictor of learning object location. Overall then, this study demonstrated that the right MTL plays an important role in the learning of object locations, while Experiment 3 indicated that the right hippocampus is critical in building a representation of an object's location.

Summary. While research has demonstrated a consistent relationship between performance on verbally based memory tests and left MTL dysfunction, an inconsistent relationship has been found between visuospatial memory tests and the right MTL dysfunction (McDermid Vaz 2004; Raspall et al. 2005). Based on the above literature, studies using 2-dimensional figures are not maximally sensitive to right MTL dysfunction, possibly due to the stimuli's vulnerability to verbal labeling (Chelune et al. 1991; Snitz et al. 1996; McDermid Vaz 2004). Instead, unfamiliar images resistant to verbal labels, complex visuospatial images, and 3 dimensional objects in space appear to be mediated by the right MTL. Thus, combining these three features into a single stimulus or group of stimuli may provide a more sensitive method through which functioning of the right MTL can be assessed.

Present Study's Goals

Since previous research has found unfamiliar images, complex visuospatial images, and 3 dimensional objects in space to be more dependent on right MTL than the left, the present study created novel, complex, 3-dimensional objects to assess visuospatial memory. We predict that these objects will be difficult to label verbally and, as a result, will be a more sensitive measure of visuospatial learning and memory deficits than the traditional 2-dimensional drawings. Moreover, we created the test stimuli and corresponding instructions to promote the use of either a verbally- or visuospatially-based strategy to further dictate participants' encoding strategy. After establishing normal performances on this test, we recruited two additional groups, who were subjected to either a verbal or visuospatial interference task with the expectation that these would affect performance on one stimulus type while leaving the other intact.

METHODS

Subjects

A total of 60 healthy participants, who had not been diagnosed with any neurological disease and had no history of learning disorder or serious mental illness, were recruited from the Emory University community. A group of 24 subjects (12 male) completed the novel visuospatial memory test under standard test instructions (i.e. the Control group) in order to establish a "normal" range of performance. The remaining 36 subjects were alternately assigned to either a verbal or a visuospatial interference group. These tasks are described in further detail below.

In addition to the novel visuospatial memory test, all participants completed the Information subtest of the Wechsler Adult Intelligence Scale -III, which provides a gross estimate of the participant's IQ given its strong correlation with Full Scale IQ; the California Verbal Learning Test – II (CVLT-II), which measures verbal learning and memory; and the Beck Depression Inventory – 2, which assesses the presence and severity of current depressive symptoms. They were also screened for color blindness using the Quantitative Color Vision Test, PV-16.

Experimental Stimuli

Test stimuli were created by stacking six small rectangular wooden blocks to create a "tower" that was 3.8 inches tall (Figure 2). Although the orientation of each block could be the same (i.e. parallel) or different (i.e. perpendicular) as the previous block, the placement was varied so that, at most, only 2/3 of any two blocks overlapped. This created a series of irregular outcroppings that should make verbal labeling difficult. Differences between the layout of these towers were calculated using the number of different placements (i.e. which portions of the blocks overlapped), orientation (parallel or perpendicular), and color (when appropriate) of each block in relation to the block below it as well as across all towers. The mean difference both within each group (i.e. gray and color) and across groups ranged from

5.11 to 5.42 (0=identical, 6=completely different). Thus, all stimuli were considerably different from one another. Thirty-six of these towers were created, 12 of which (6 gray, 6 colored) served as targets while the remaining 24 (12 gray) served as distracters during the recognition portions of the test.

For half of the towers, each block was painted one of six different colors: blue, green, orange, yellow, purple, or red and are referred to hereafter as the color towers (Figure 1). The order of the colors was randomized across towers and checked to ensure that no more than two colors were repeated in the same order between towers. These towers were created to encourage verbal processing since previous research demonstrated that recognition memory for cross-categorical colors (i.e. different colors) is dependent on verbal processing and, thus, sensitive to verbal interference (Roberson and Davidoff 2000). Furthermore, a study using positron emission tomography (PET) showed increased activation in the left temporal, frontal, and parietal lobes during the retrieval of cross-categorical colors (Chao and Martin 1999).

The remaining towers were painted a uniform gray (i.e. gray towers) in order to minimize any identifiable cues that could facilitate verbal labeling, thereby encouraging visuospatial processing.

Experimental Procedure

A total of four learning trials were given during which each of the 12 target stimuli were shown for 5 seconds. Test instructions were provided to maximize the use of verbal or visuospatial encoding strategies. The participants were instructed to, *"Remember each of the towers you are about to see. Some of them will have many different colors and some of them will just be gray. It will be easier for you to* *remember the color towers by focusing on the colors and naming them to yourself. You won't be able to do this with the gray towers, so try to take a mental picture of those towers so you can remember them later."*

A recognition memory test was given immediately after trials 1 and 4, and after a 20-minute delay. For all 3 recognition memory tests, the 12 target towers were presented with 12 distracter towers (6 gray, 6 colored). A different set of distracter towers was used on trials 1 and 4. Half of the distracters from each list (i.e. 3 gray, 3 color from each list) were used as distracters following the delay. During the recognition memory test, towers were randomly presented one at a time and the participants were asked whether or not they had been asked to remember that specific tower (i.e. Yes/No). An overview of this test design is show in Figure 2.

Verbal Interference Group

Subjects in this group were read standard test instructions but required to say the word "the" once every second during trials 1-4 in an attempt to disrupt verbal processing. This task was meant to place minimal demands on attention. Participants started saying "the" ten seconds before the first tower was presented and continued until ten seconds after the last tower was presented. This task was designed to impede verbal processing and was only performed during the study portions of trials 1-4.

Visuospatial Interference Group

Subjects in this group were read standard test instructions but were required to follow a black rectangle as it appeared at random locations on a computer screen in between tower presentations. All towers were placed directly in front of this screen and the location of the rectangle changed every second. Participants again began this task 10 seconds before the first tower was presented and continued it 10 seconds after the last tower was presented. This task was designed to impede visuospatial processing and was only performed during the study portions of trials 1-4.

Experimental Test Scoring

On each recognition test (i.e. trials 1, 4, and delay), the number of true-positive (TP) and false-positives (FP) were totaled. In order to control for any response bias, d' was calculated by determining the proportion of TP and FP, converting this to a normalized z-score, and then subtracting FP from TP.

Statistical Analysis

One-way analysis of variance (ANOVA) was used to assess between group differences in demographic variables (age and education), estimated intellectual abilities (Information subtest), current mood (BDI-2), and verbal learning (CVLT-II Trial 1-5 and CVLT-II delay). D-prime scores were used to assess group performances on the experimental memory test. A mixed model (3 group) 3 (time) x 2 (tower type) repeated measures ANOVA (RM ANOVA) was used to compare group differences in performance. Given our apriori hypotheses that the interference tasks would impede within group performance for one tower type, but not the other, we performed a 3 (time) x 2 (tower type) RM ANOVA with post-hoc t-tests to assess differences in performance between the tower types at each time point within each group (i.e. verbal and visuospatial interference).

RESULTS

The three groups were well matched in that no significant group differences were seen in participants' age, education level, performance on the Information SS, CVLT-II trials 1-5 or delay, or BDI-2. The mixed-model RM ANOVA showed significant main effects of time ($F_{2, 114} = 34.2$; $p < 0.001$; partial eta^2 = 0.55) and tower type ($F_{1, 57} = 22.9$; $p < 0.001$; partial eta^2 = 0.29) but not group ($F_{2, 57} = 0.84$; $p = 0.44$). There was a significant time by tower type interaction ($F_{2, 114} = 17.3$; $p < 0.001$; partial eta^2 = 0.33), but no significant interactions with group (time by group: $F_{4, 114} = 1.7$; $p = 0.15$; partial eta^2 = 0.05; tower type by group: $F_{2, 57} = 0.6$; $p = 0.58$; partial eta^2 = 0.02). Although a possible trend was evident, the three-way interaction between time, tower type, and group failed to reach statistical significance ($F_{4, 114} = 2.0$; $p = 0.09$; partial eta^2 = 0.08). Since no significant group effects were seen, we performed paired t-tests to assess differences in performance for the 2 types of tower at each time point. Here, we found the three groups performing similarly on the 2 types of towers on trial 1 (Figure 3; $t(59) = -1.6$, $p = 0.11$) but were significantly more accurate on the gray towers than the color towers during trial 4 and the delay ($t(59) = 4.3$, $p < 0.001$ and $t(59) = 5.3$; $p < 0.001$, respectively).

Despite the lack of statistically significant differences between the three groups, our initial hypothesis predicted within group differences in the groups performing interference tasks. We, therefore, assessed within group differences for the control group, the verbal interference group, and the visuospatial interference group.

Control Group

The control group's performance was assessed in order to establish the "normal" pattern of performance on the test. The overall pattern of results is consistent with those described above. Specifically, participants became more accurate over the course of the test, as reflected by the significant main effect of time (Figure 4; $F_{2, 46} =$

16.5; $p < 0.001$; partial eta^2 = 0.42). There was also a significant main effect of tower type ($F_{1, 23} = 6.5$; $p = 0.02$; partial eta^2 = 0.22) as well as a time by tower type interaction ($F_{2, 46} = 6.2$; $p = 0.004$; partial eta^2 = 0.21). These findings are explained by the similar performances for the gray and color towers during trial 1 ($t(23) = -1.01$, $p = 0.3$), but the significantly better performance for the gray towers on trial 4 and after the delay ($t(23) = 2.9$, $p = 0.007$ and $t(23) = 2.1$, $p = 0.05$, respectively).

Verbal Interference Group

The verbal interference group became more accurate over the course of the test, as reflected by the significant main effect of time (Figure 5; $F_{2, 34} = 7.0$; $p = 0.003$; partial eta^2 = 0.29). There was also a significant main effect of tower type ($F_{1, 17} = 10.8$; $p = 0.004$; partial eta^2 = 0.39) wherein they demonstrated similar performance during trial 1 ($t(17) = 1.4$, $p = 0.18$) but significantly better performances for the gray compared to the color towers during trials 4 ($t(17) = 2.8$, $p = 0.01$ and the delay ($t(17) = 2.4$, $p = 0.03$). No time by tower type interaction was seen in this group ($F_{2, 34} = 2.6$; $p = 0.09$; partial eta^2 = 0.14).

Visuospatial Interference Group

For the visuospatial interference group, analyses revealed main effects of time (Figure 6; $F_{2, 34} = 14.8$; $p < 0.001$; partial eta^2 = 0.47) and tower type ($F_{1, 17} = 5.8$; $p = 0.03$; partial eta^2 = 0.26) as well as a significant time by tower type interaction ($F_{2, 34} = 11.3$; $p < 0.001$; partial eta^2 = 0.40). Performance on the gray towers was significantly worse than on the color towers on trial 1 ($t(17) = -2.4$, $p = 0.03$), equivalent for the two tower types on trial 4 ($t(17) = 1.6$, $p = 0.12$), and significantly better for the gray towers after the delay ($t(17) = 6.5$, $p < 0.001$) (i.e. when the interference was no longer present). Thus, the overall pattern of results was different than for the other two groups.

DISCUSSION

The objective of this study was to devise a novel visuospatial memory test that was more sensitive to right MTL damage. We used novel, complex 3 dimensional objects and test instructions to encourage more of a verbal (color towers) or visuospatial (gray towers) processing approach. We predicted that interference tasks affecting verbal or visuospatial processing would impede performance on the color or gray towers, respectively.

Overall, we found that all groups performed similarly on the different portions of the experimental test. The characteristic performance, exemplified by the control group, was similar for the two tower types on trial 1, but significantly better for the gray towers than the color towers on trial 4 and delay. This performance may possibly be due to the more challenging encoding strategy for the color towers (i.e. remembering the order of 6 different colors) than for the gray towers (i.e. taking a mental picture).

The verbal interference group’s overall pattern of performance was generally analogous to that of the control group in that they performed similarly for the two tower types on trial 1, but significantly better for the gray than the color towers on trial 4 and the delay. These similarities may be explained in a number of ways. First, it is possible that the verbal interference task did not meaningfully impede verbal processing given the simplicity of the interference task. Second, the towers were designed to be highly dependent on visuospatial processing. So, although the participants were instructed to use the color names to remember the color towers, trying to remember the order of 6 different colors for 6 different target towers may have been too challenging. Instead, the participants may have relied on a more visuospatial approach to encoding these towers. They may have focused on remembering the differing shapes of the 6 target color towers rather than memorizing the order of the colors, thus explaining why the verbal interference task did not impede performance on these towers.

The overall pattern of performance in the visuospatial interference group (Figure 6) was different from the other two groups. Participants in the visuospatial interference group performed significantly better on the color towers than the gray towers on trial 1, which is consistent with our predictions and indicates that the visuospatial interference task did initially impede visuospatial processing. This finding is also consistent with a previous study that used a single trial experiment to demonstrate impairments in object-location recall in patients with right MTL resection (Smith and Milner 1981). Therefore, using a single trial assessment may be more sensitive to right MTL damage than multiple trial assessments since it could limit the use of compensatory mechanisms that would be used on subsequent learning trials. On trial 4, participants in the visuospatial interference group showed similar performances for the two tower types whereas the other groups performed significantly better on the gray blocks. This suggests that the visuospatial interference task limited the differential benefit in performance for the gray towers relative to the color towers. Nonetheless, these participants did show significant improvement from trial 1 to 4 for both tower types, possibly because they simply stopped performing the interference task (i.e. they no longer followed the rectangle across the screen). Alternatively, they could have begun concentrating “harder” and focused more intently on the stimuli while still performing the interference task. Finally, they may have applied verbal labels to both tower types which would have limited any visuospatial processing or interference effects. After the delay, however, the visuospatial interference group showed significantly better performance on the gray towers than the color, which is the same pattern as the control and verbal interference groups.

Limitations

There are a few possible reasons why we found no significant group effects. First, the interference tasks may not have successfully impeded verbal or visuospatial processing and other, more demanding, tasks may show large effects. Second, our study may have been undersized to detect significant between-group differences. This may be especially relevant given our use of neurologically healthy individuals who could have applied compensatory strategies to facilitate task performance when one type of processing was impeded via interference. Our initial patient data (see below) support this conclusion.

A final limitation in regards to task design is that the stimuli were created to be heavily dependent on visuospatial processing and, as a result, may require minimal verbal mediation. If true, lesions to the right MTL should substantially affect performance whereas those to the left MTL should have smaller effects. While performing the current study, we also began collecting data from patients who had undergone a unilateral amygdalohippocampectomy (AH). To date, we have 5 left AH and 4 right AH. Not only do these patients perform differently than the neurologically healthy participants, but the right AH generally have more difficulty on both tower types. For the gray towers (Figure 7), both patient groups appear to perform similarly on trials 1 and 4, but their performances remain below that of the healthy individuals, which suggests that any hippocampal damage is sufficient to impede performance on this test. After the delay, however, the right AH patients appear to have difficulty retaining the information whereas the left AH patients do not.

For the color towers (Figure 8), the right AH patients are initially performing better than the left AH, which is consistent with expectations. However, performance of the left AH patients remain stable over the remainder of the test whereas the right AH patients perform at essentially chance level. Within the context of the limited effects of verbal interference, this finding again suggests that the towers primarily require visuospatial processing, which the left AH patients were still able to perform. Conversely, the right AH effectively applied verbal labels on trial 1 but, because of the complexity of this approach (i.e. remembering 6 lists of the same 6 colors) were unable to maintain this performance. They were also unable to utilize visuospatial processes to help maintain or facilitate performance, which resulted in their poor performances. Although caution is obviously warranted in interpreting data based on such small groups, the overall results are promising and support our experimental design.

Future Directions

It is suggested that future studies change certain aspects of the experimental test to better assess verbal learning and memory. For instance, learning the order of 6 different colors for each color tower may have been too overwhelming for the participants, possibly explaining their poor performance on these towers when compared to the gray towers. Future studies should decrease the number of different colors present on the color towers to make verbal processing less challenging. Furthermore, the color towers not only varied in the order of the 6 colors, but also varied in the arrangement of each individual block, thus adding a visuospatial component to these towers. Future studies may want to create the color towers by keeping the arrangement of each block consistent and only varying the order of the different colors instead. This will encourage a more verbal processing approach. It might also be worthwhile to assess the sensitivity of this experimental test using a single learning trial rather than multiple learning trials to prevent participants from adapting a verbally based approach to encoding the test stimuli. Lastly, these same manipulations should be attempted in patients who are both pre- and post-surgical in order to identify the sensitivity and specificity of these techniques.

	Age (SD)	**Education (SD)**	**Information SS (SD)**	**CVLT-II 1-5 Total (SD)**	**CVLT-II Delay (SD)**	**BDI-2 (SD)**
Control (n=24)	20.4 (1.1)	14.4 (0.9)	14.4 (1.9)	61.7 (7.2)	13.7 (1.8)	6.0 (6.3)
Verbal Interference (n=18)	19.8 (1.6)	13.5 (1.3)	14.9 (2.4)	60.8 (5.9)	13.6 (1.8)	7.8 (6.0)
Visual Interference (n=18)	20.7 (2.1)	14.1 (1.5)	14.0 (1.6)	58.7 (6.4)	13.1 (2.2)	5.8 (3.9)
p-value	0.23	0.09	0.41	0.36	0.61	0.48

Table 1. Group characteristics. No between group differences exist for any of the above variables. SD = standard deviation; Information SS = Information scaled score; CVLT-II = California Verbal Learning Test – II; BDI – 2 = Beck Depression Inventory – 2.

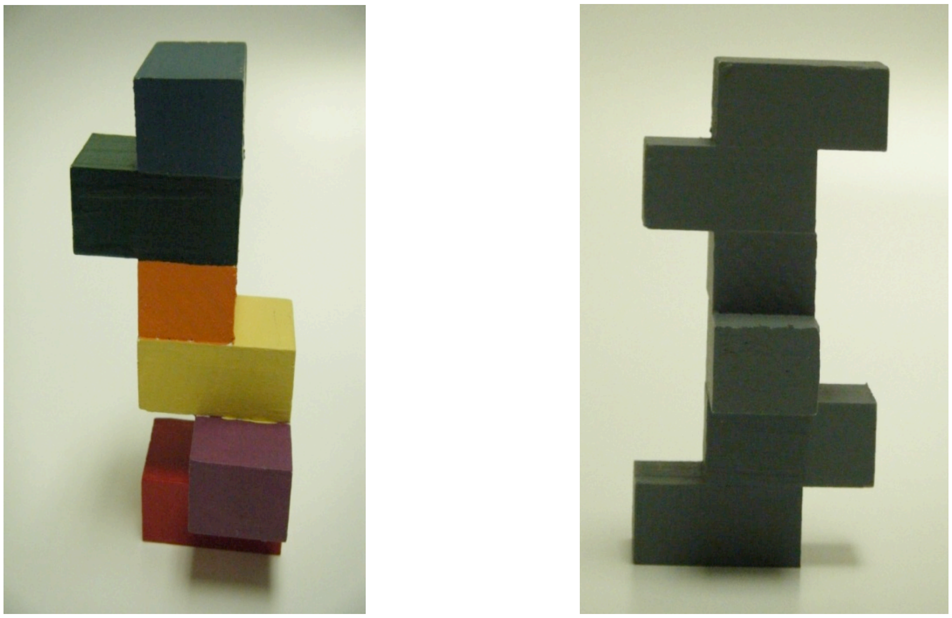

Figure 1. Examples of the experimental stimuli used. Color towers (left) were created to encourage verbal processing. Participants were instructed to recite the colors to themselves in order to help remember these towers. Gray towers (right) were created to encourage visuospatial processing. Participants were told that these towers were difficult to label verbally and, instead were instructed to take a mental picture of these towers.

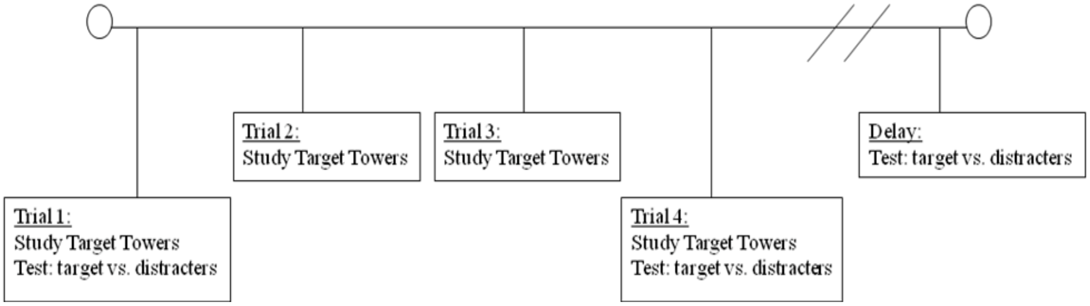

Figure 2. Basic Experimental Design. Four learning trials were administered using each of the 12 target towers (6 color and 6 gray). A recognition memory test, consisting of 12 targets and 12 distracters, was given immediately after trials 1 and 4, and after a 20-minute delay.

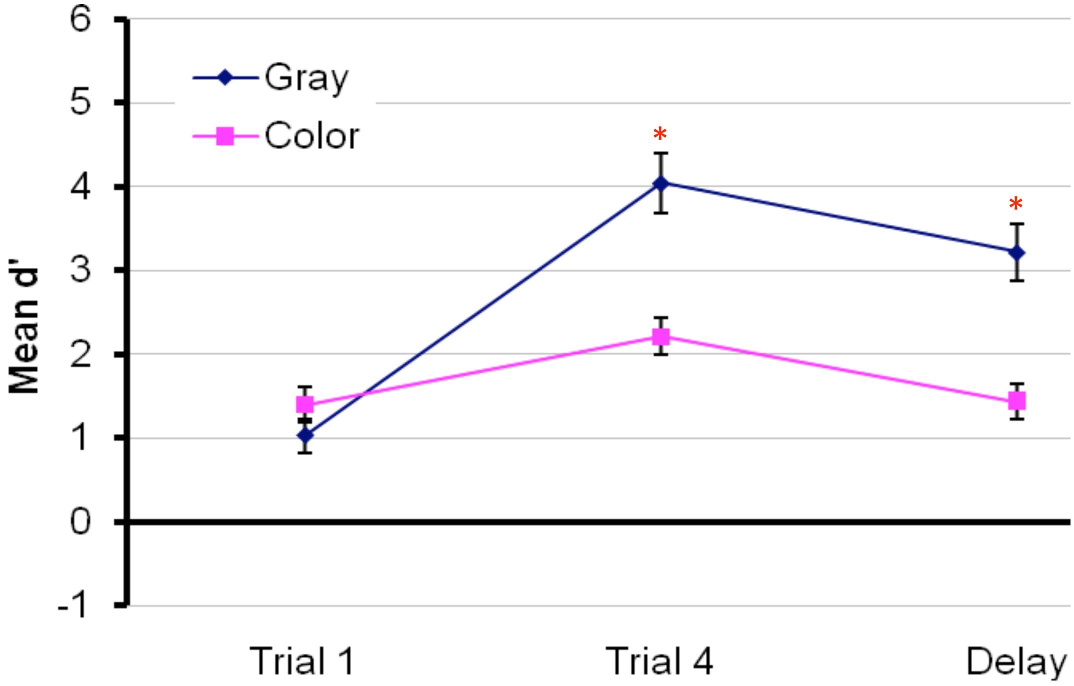

Figure 3. Combined group performance on the novel visuospatial memory test. Although participants performed similarly on trial 1 ($p = 0.11$), performance was significantly better for the gray towers on trial 4 and delay ($p < 0.001$ and $p < 0.001$, respectively).

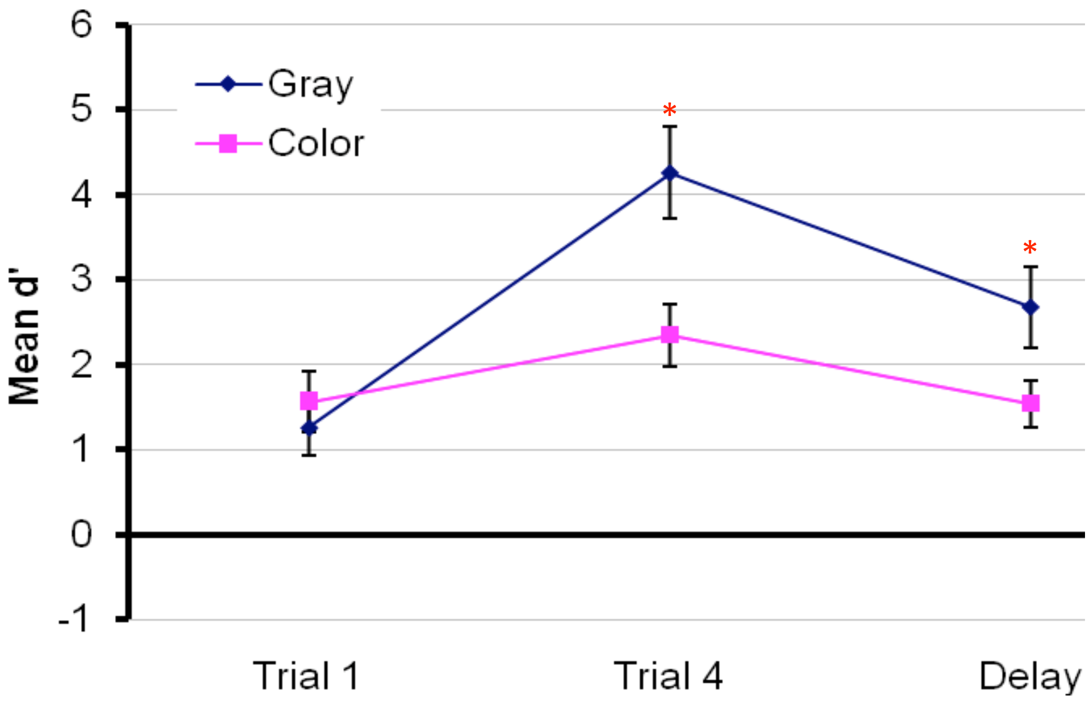

Figure 4. Control group performance on the novel visuospatial memory test. Although participants performed similarly on trial 1 (p = 0.3), performance was significantly better for the gray towers on trial 4 and delay (p = 0.007 and p = 0.05, respectively).

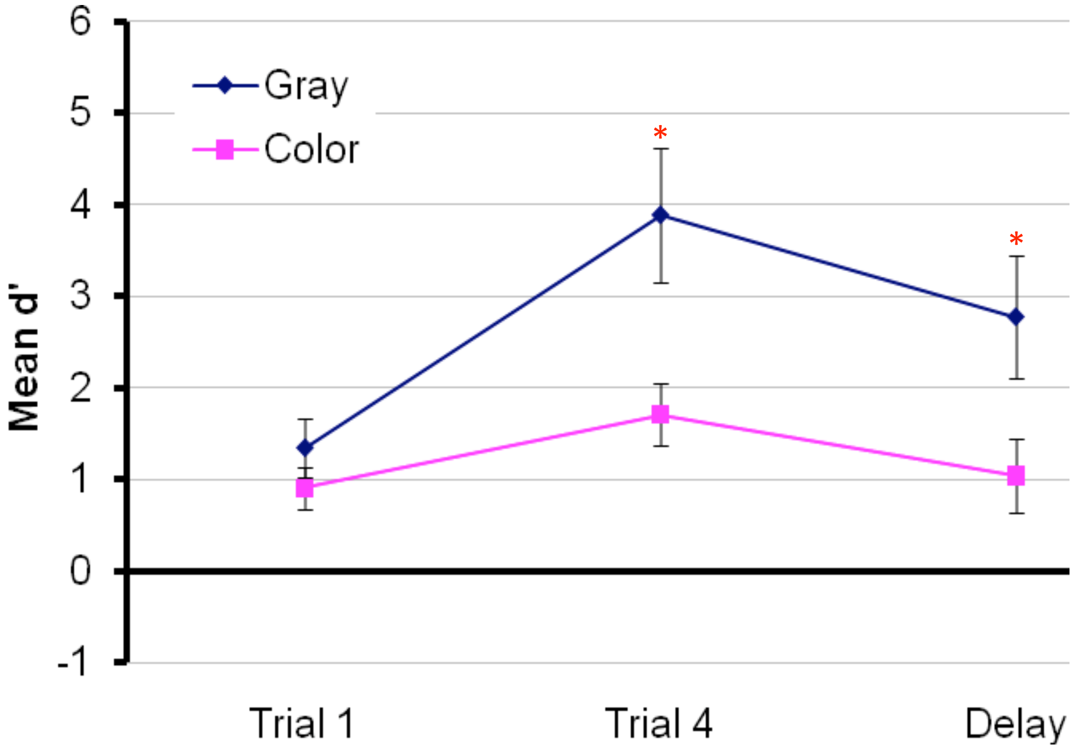

Figure 5. Verbal interference group performance on the novel visual memory test. Although participants performed similarly on trial 1 (p = 0.18), performance was significantly better for the gray towers on trial 4 and delay (p = 0.01 and p = 0.03, respectively).

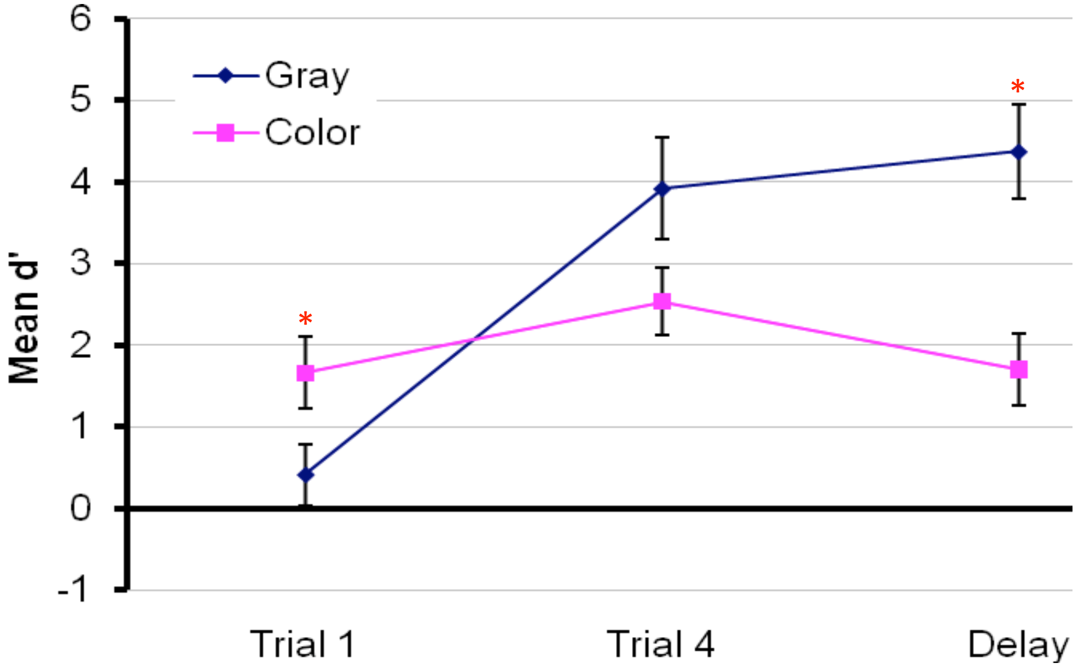

Figure 6. Visual interference group performance on the novel visuospatial memory test. Although the participants perform significantly better on the color towers than the gray towers on trial 1 ($p = 0.03$), they perform similarly on trial 4 ($p = 0.12$) and their performance reverses over the course of learning trials where they perform significantly better on the gray towers than the color towers after the delay ($p < 0.001$).

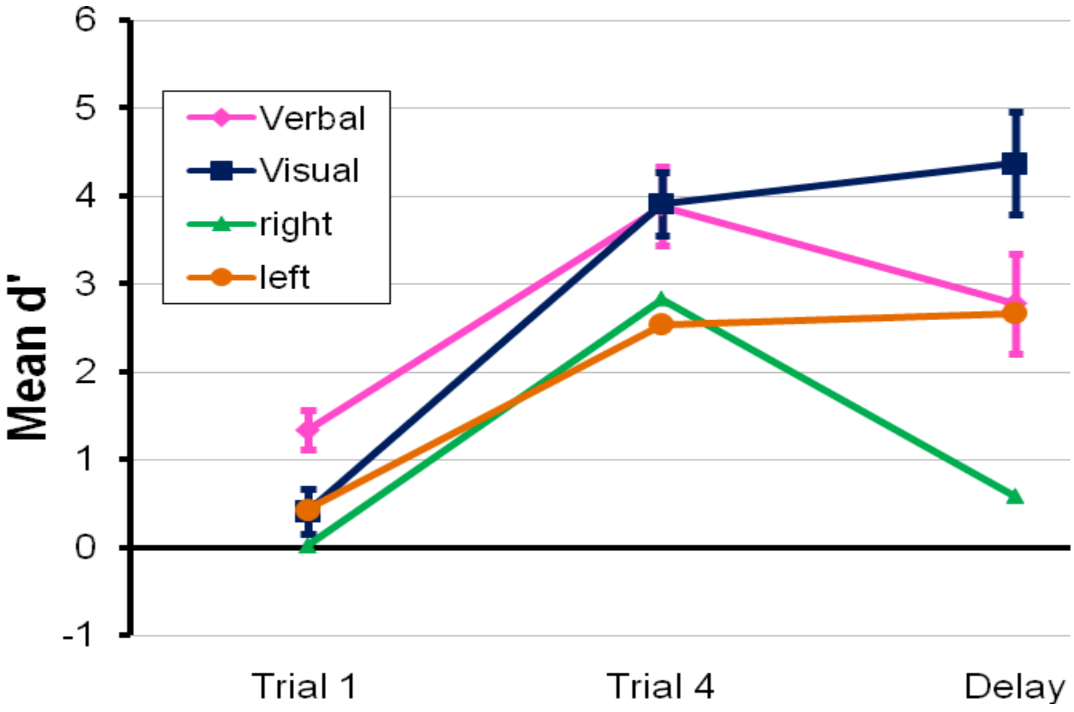

Figure 7. Performance of amygdalohippocampectomy (AH) patients on the gray towers. Both patient groups appear to perform similarly on trials 1 and 4, but their performances remain below that of the healthy individuals. After the delay, however, the right AH patients appear to have difficulty retaining the information whereas the left AH patients do not. Verbal = Verbal interference group; Visual = Visuospatial interference group; right = Right AH patients; left = Left AH patients.

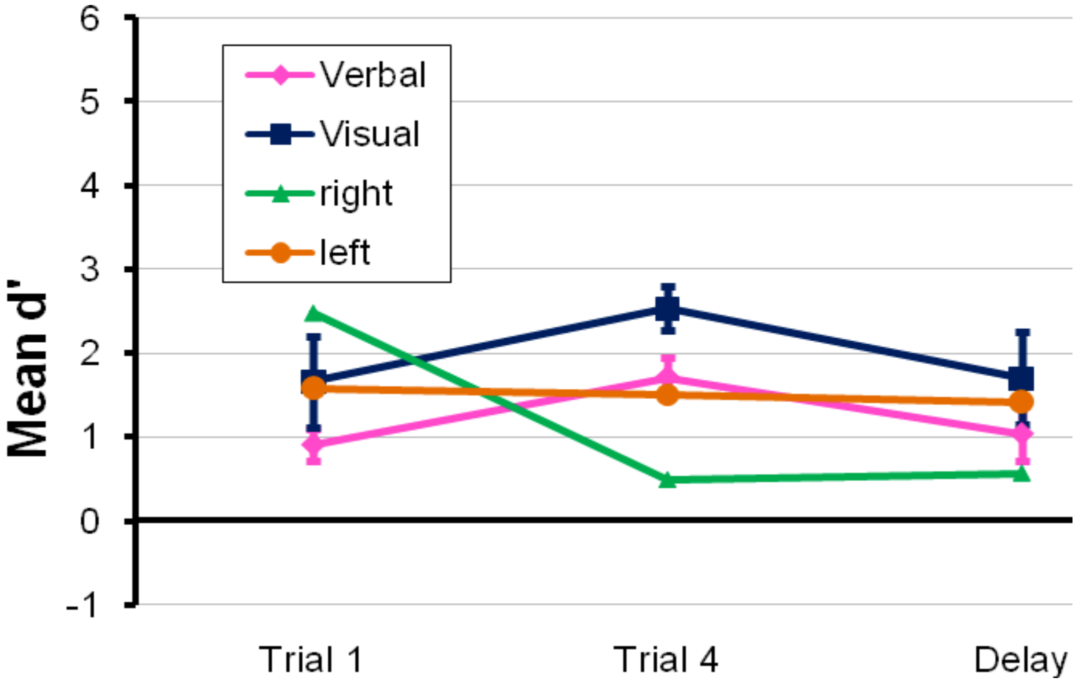

Figure 8. Performance of amygdalohippocampectomy (AH) patients on the color towers. The right AH patients are initially performing better than the left AH; however, performance of the left AH patients remain stable over the remainder of the test whereas the right AH patients perform at essentially chance level. Verbal = Verbal interference group; Visual = Visuospatial interference group; right = Right AH patients; left = Left AH patients.

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