

RECONSOLIDATION OF MEMORY IN OLDER ADULTS

By

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Approved by:

A handwritten signature in black ink, reading "Elizabeth L. Glisky", written over a horizontal line.

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Running head: RECONSOLIDATION OF MEMORY IN OLDER ADULTS

Reconsolidation of memory in older adults

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Abstract

Studies in younger adults have shown that memories can be changed when they are reactivated through the process of reconsolidation. There is also evidence that a context based reminder is crucial in the reconsolidation of memory. This study explores how the reconsolidation of memory may differ in older adults who have deficits in the binding of context and event information and demonstrates that reconsolidation of memory in older adults is different than in young adults.

Binding in Memory and Its Effects on the Reconsolidation Process

Although there has been a long standing belief that memories are permanently stored, recently, it has been shown that memories that have been consolidated and made permanent may be subject to change upon reactivation of that memory. The reactivation-induced reconsolidation of memory is the process in which memories are returned to a labile state in which they can then be altered. Reconsolidation effects have been shown in humans in conditioning (Galluccio, 2005) as well as procedural memories (Walker, Hobson, & Stickgold, 2003). Recently, a study by Hupbach, Gomez, Hardt, & Nadel, (2007) demonstrated that the modification of consolidated episodic memories also depends on the reactivation of that memory.

Participants in the Hupbach et al. study were taught a set of items on the first day. After a reminder, or no reminder on the second day, they were taught a second set of items. On the third day, their memory performance for the first list was tested. The results of this experiment showed that a subtle reminder puts the first list into a labile state so that the learning of the second list alters the memory of the first list. The experiment demonstrated the reconsolidation process proposed by Nader (2005) that involves three steps: the reactivation of a memory to return it to a labile state, the modification of an existing memory, and the reconsolidation of the memory over a period of time. It also eliminated the possibility that the effect might be due to simple source monitoring difficulties or retroactive interference by having a group of participants that are asked to recall objects from the second day on the third day. When asked to retrieve the items for the second list, they are able to accurately recall the objects without intrusions from the first list indicating that only the first list was modified. Further studies have shown that the type of cue that triggers reactivation is important. According to Chalfonte and Johnson, if different features of memory are bound together, then the reactivation of a specific feature of a memory

would allow this feature to become bound to new information (2006). Hupbach et al. demonstrated that the feature that is reactivated that may be critical in the reconsolidation of episodic memories may be context based reminder, specifically, the location of testing (Hupbach, Hardt, Gomez, & Nadel, 2008).

Studies on source memory have demonstrated that memory for content and context may rely on different parts of the brain (eg. Mc Intyre & Craik, 1987; Schacter, Kaszniak, Kihkstrom & Valdiserri 1991; Glisky, Polster, & Routhieaux, 1995) and that the ability to retain and retrieve source information is associated with efficient frontal lobe functioning (Craik, Morris, Morris, & Loewen 1990). Direct evidence of the relationship between frontal lobe functioning and source memory comes from studies that include patients with frontal lobe lesions. These participants showed more errors in source memory than the healthy controls, although memory for facts was the same for both groups (Janowsky, Shimamura, & Squire, 1989). Janowsky et al. (1989) found that some older adults make as many source errors as patients with frontal lobe lesions suggesting that this might be due to the declining frontal lobe functioning that is associated with normal aging. A great deal of research has shown that older adults have deficits in source monitoring when compared to younger adults (Ferguson, Hashtroudi, & Johnson, 1992; McIntyre et. al., 1987; Schacter et. al. 1991). Source monitoring in older adults also appears to be more affected by aging than fact or item memory (Ferguson et. al. 1992; Henkel, Johnson, & DeLeonardis, 1998; McIntyre et. al., 1987; Schacter et al., 1991).

Research suggests that the problem with source monitoring difficulties in older adults may be partly attributable to difficulties during encoding. Older adults with low frontal lobe functioning are able to properly encode and retrieve source information when they are instructed how to relate the source to the item during encoding (Glisky, Rubin, & Davidson, 2001).

However, in studies when individuals are required to focus on the source but not relate it to the item, source deficits are not eliminated (Schacter, Osowiecki, Kaszniak, Kihlstrom, & Valdiserri, 1994). Without instruction, older adults with low frontal lobe functioning may have problems initiating the processes important for binding memories so that perceptual and contextual cues may be encoded but may not be appropriately bound to the target event (Chalfonte & Johnson, 1996). They suggested that a combination of poor memory for the source and disrupted binding processes may be the reason why we see source monitoring difficulties in older adults.

Henkel et al. suggested that medial temporal lobe structures may also be important for the binding of different features of a memory. In this study, the older adults with deficits in medial temporal functioning performed poorly in a task that required them to integrate various features of a memory (1998). It is possible that both the medial temporal lobe and frontal lobes work together and are responsible for the binding of information. The medial temporal lobes may be directly responsible for the binding of different features of a memory in the hippocampus while the frontal lobes initiate the more strategic processes that ensure that all aspects of an experience are integrated during encoding.

More generally, the medial temporal lobes have been shown to have a vital role in the consolidation of episodic memory. Memory consolidation is the process in which acquired memories become permanently stored. According to all models of memory consolidation, memories are represented through different cortical regions and the medial temporal lobes are important for binding different aspects of a memory that are stored in the cortex together in order for the memory to be represented as a single event (Nadel et al, 2006). However, current theoretical debates on the consolidation of memory argue for a distinction between the neural mechanisms that mediate the transfer of explicit memories into long term memory. According to

the Standard Model of Memory Consolidation, memories are first dependent on the hippocampus but after time, connections between cortical regions become strengthened so that the hippocampus is no longer necessary in order to reactivate a memory. Multiple trace theory on the other hand, postulates that the retrieval of explicit memory is always dependent on the hippocampus. The process of reconsolidation supports Multiple Trace Theory because the reactivation of a stored memory should put the memory in a state where the medial temporal lobes are required for consolidating the new information and incorporating it into the old memory trace.

In this study, we are interested in learning whether the reconsolidation of memory works the same in a population of older adults; if it is different, why? Based on previous research in binding of source and events, source monitoring and frontal lobe deficits in older adults, it is possible that the reconsolidation process may be different in this population and may depend on the integrity of frontal and medial temporal lobe function.

If older adults with low frontal lobe functioning are not able to integrate the item and context of an event, then it is possible that a context-based reminder may not be efficient at integrating two memories. The reminder may not work at integrating the two memories because if a person did not originally integrate context and the target event then they could not use the context as a reminder to reactivate the first list when they learned the second list. If this is the case, then we would not expect to see a reconsolidation effect in the low frontal lobe functioning group resulting in an inability to integrate new information into the older list of objects. Alternatively, if the consolidation process itself is impaired because of reduced medial temporal lobe function, but the frontal lobe function is not impaired, we might expect memory to be somewhat poorer overall, but reconsolidation to be intact. Thus, we would expect an interaction

between our two neuropsychological groupings in the reminder group. We would not expect to see any differences in the number of intrusions recalled on Day 3 between the reminder and no reminder group in the low medial temporal lobe functioning group and do not expect to see intrusions in the high frontal lobe functioning group.

Another possibility is that older adults with low frontal and medial temporal lobe functioning may not bind either event to its context which could make it possible for the memories to become integrated without a reminder. In this case the reminder would not be useful in reactivating the memory so the new memory could become integrated with the old memory without a reminder. This would be a problem caused by encoding rather than retrieval because the participant would not have two separate representations of the two lists, instead, the two lists would be mixed together. Also, previous studies on encoding and retrieval of memories in older adults have not shown older adults to have problems during retrieval (Glisky, et. al. 2001) so we do not expect participants have a separate representation for each list but are merely confused about list each item came from.

Methods

Participants

A total of 22 community dwelling adults over the age of 65 without previous neurological problems that could impair cognitive functioning participated in the experiment. The participants were recruited from the subject pool from the Aging and Cognition Lab at the University of Arizona and were paid \$20 for participating. Each individual was given two scores based on previous neuropsychological testing, one representing performance on a group of tests associated with frontal lobe function and another representing performance on a group of tests associated with medial temporal lobe function. Tests included in the frontal lobe (FL) factor (Glisky et al., 1995) include the number of categories achieved on the modified Wisconsin Card Sorting Test (Hart, Kwentus, Wade, & Taylor, 1998), Mental Arithmetic from the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler, 1981), Mental Control from the Wechsler Memory Scale – III (WMS-III; Wechsler, 1997), Backward Digit Span from the WMS-III, and the total number of words generated on the Controlled Oral Word Association Test (Benton & Hamsher, 1976).

Neuropsychological tests used for the medial temporal lobe (MTL) factor (Glisky et al., 1995) that tap into medial temporal lobe processes include Logical Memory I, Verbal Paired Associates I, Faces I (all from WMS-III), Visual Paired Associates II (WMS-R, 1987), and Long-Delayed Cued Recall from the California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987).

Participants were assigned to each of the four groups that were created by crossing the FL and MTL factors. The four groups included: the high frontal-high medial temporal group (HH), high frontal-low medial temporal group (HL), low frontal-high medial temporal group (LH), and

low frontal-low medial temporal group (LL). Participants were placed into each group based on their score on each factor and whether they were above or below the mean. The scores for each factor represent the unweighted average of the z-scores from each of the component tests; variability attributable to age has been removed from these scores. There were seven participants in the HH group, four in the no reminder condition and three in the reminder condition, six participants in the HL group, three in each condition, five participants in the LL group, three in the no reminder condition and two in the reminder condition and 4 in the LH group, three in the no reminder condition and one in the reminder condition. Characteristics of each group are presented in Table 1 and separate one-way analyses of variance (ANOVAs) were conducted in order to test for differences in age, education, or scores on the Mini-Mental Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975) as a function of neuropsychological group. There were no differences between the high and low frontal groups in age ($F(1, 21)=.753$; $p>.05$), education ($F(1,21)=.239$; $p>.05$), or MMSE scores ($F(1,21)=1.692$; $p>.208$). There were no differences in the high and low medial temporal lobe groups in age ($F(1,21)=1.888$; $p>.05$) or education ($F(1,21)=4.325$ ($p>.05$)). We did find a difference between MMSE scores ($F(1,21)=6.316$; $p<.05$) with the high medial temporal group receiving a higher score than the low medial temporal lobe group, however, all of the participants received above a 27.

Materials

List A and List B each consisted of 15 unrelated objects (see Table 2). The two groups of objects were counterbalanced so that half of the participants in each group received List 1 on the first day and the other half received List 2 on the first day in order to eliminate any effects that differences in task difficulty may have on the initial consolidation of the items.

Procedure

For this study, we used a similar experimental paradigm to the one used by Hupbach et al. (2007). Participants were informed that they would have to learn different lists of objects on different days. The three sessions took place on Monday, Wednesday, and Friday of the same week.

On Day 1 the experimenter took the objects out of a box one at a time and placed them in a blue basket. The participants were asked to name each item as it was shown to them and to try to remember the objects so that they could recall them later. After all of the items were presented, they were put away by the experimenter and the participants were asked to recall as many items as they could. This procedure was repeated until the participants could recall at least 13 of the 15 items on the list or until they had completed five learning trials.

The procedure on Day 2 differed for the two experimental groups. On Day 2 the participants in the context-reminder group were taken to the same room as Day 1 with a different experimenter. The participants in the no-reminder group were taken to a different room with a different experimenter. Participants in both groups were asked to learn a second list. This procedure differed from Day 1 so that the task did not serve as a reminder. All of the objects in the second list were placed in front of the participant. They were asked to name the objects and given 30 seconds to study the items. The items were then removed and the participant was asked to recall the items. If they recalled less than 13 items, the procedure was repeated until they could recall 13 items or more or until they had reached five trials.

On Day 3 the experimenter asked the participants to recall as many objects as they could from Day 1. If the participant was unable to recall anymore objects, they took a 30 second break during which the experimenter will engaged the participants in a conversation about an unrelated topic. They were then asked to recall the items again. This was repeated for four recall trials in

order to test the reliability of recall. The participant were asked whether they thought they would be tested on the first list and then took a brief questionnaire to see whether they had noticed whether or not they were tested by a different experimenter or in the same or different location during the learning trials. Testing materials and questionnaire are included in Appendix 1 and 2.

Results

Performance on Day 1

The number of learning trials that it took for participants to recall at least 13 of the 15 items on Day 1 were recorded. Participants who recalled less than 13 items on the fifth learning trial were given a score of 6. The average number of trials for all participants was 3.91 (SD=1.477). Participants in the high frontal group took an average of 4 trials (SD=1.58), the low frontal group average of 3.78 trials (SD=1.39), the high medial temporal group took an average of 3.18 (SD=1.25) and the low medial temporal group took 4.64 trials (SD=1.36). Differences between the reminder and no-reminder groups were analyzed using a t-test for independent groups. There were no significant differences between the number of trials it took for participants to recall 13 of the 15 items between the no reminder ($m=4.00$; $SD=1.53$) and the reminder group ($m=3.78$; $SD=1.48$) ($t=.340$, $p>.05$). Differences as a function of neuropsychological group were analyzed using a two separate one way ANOVAs. There was no difference between the number of trials between the low and high frontal groups ($F(1, 21)=.115$; $p>.05$). There was a significant difference between the number of trials for the low and high medial temporal groups ($F(1, 21)=6.809$; $p>.05$) such that the high MTL group took less trials to reach criterion than the low MTL group

Performance on Day 2

Analyses here are the same here as on Day 1. The average number of trials for all participants was 3.73 (SD=1.779). Participants in the high frontal group took an average of 3.77 trials (SD=1.96), the low frontal group average of 3.67 trials (SD=1.58), the high medial temporal group took an average of 2.55 (SD=1.37) and the low medial temporal group took 4.91 trials (SD=1.30). Differences between the reminder and no-reminder groups were analyzed using

a t-test for independent groups. There were no significant differences between the number of trials it took for participants to recall 13 of the 15 items between the no reminder ($m=3.85$; $SD=1.68$) and the reminder group ($m=3.56$; $SD=2.01$) ($t=.369$, $p>.05$). Differences as a function of neuropsychological group were analyzed using a two separate one way ANOVAs. There was no difference between the number of trials between the low and high frontal groups ($F(1, 21)=.017$; $p>.05$). There was a significant difference between the number of trials for the low and high medial temporal groups ($F(1, 21)=17.245$; $p>.05$) such that the high MTL group took fewer trials to reach criterion than the low MTL group.

Day 1 and Day 2 Comparison

We ran a repeated measures Analysis of Variance (ANOVA) using Day as the within subjects factor and frontal and medial temporal lobe groups as between subjects factors and found a Day by MTL interaction ($F(1,21)=3.899$; $p>.05$). The high MTL group performed significantly better on the second day compared to the first day. There was no interaction between the Days and FL group ($F(1, 21)=.008$; $p>.05$) or Day, FL, and MTL groups ($F(1,21)=.928$; $p>.05$)

Performance on Day 3:

The mean percent of items correctly recalled from List A and the mean percent of items falsely recalled from on Day 3 for all older adults and each neuropsychological groups for the two conditions will be displayed in Figures 1-5.

List A recall

The number of items correctly recalled on Day 3 will be analyzed using 2x 2x2 between subjects ANOVA with the three factors: condition, FL and MTL. There were no significant differences in the percentage of items recalled between the reminder-no reminder conditions

($F(1,21)=.725$; $p>.05$), the high FL-low FL groups ($F(1, 21)=.022$; $p>.05$), the high MTL-low MTL groups ($F(1,21)=2.262$ $p>.05$). There were also no interactions between the FL and MTL groups ($F(1,21)=.001$; $p>.05$), the condition and the FL groups ($F(1,21)=.083$; $p>.05$), the condition and the MTL groups ($F(1,21)=.002$; $p>.05$) and the condition, FL and MTL groups ($F(1, 21)=.173$; $p>.05$).

Intrusions from List B

The number of intrusions recalled from Day 2 will be analyzed using 2x 2x2 between subjects ANOVA with the three factors: condition, FL and MTL. There were no significant differences in the percentage of intrusions recalled between the reminder-no reminder conditions ($F(1,21)=.578$; $p>.05$), the high FL-low FL groups ($F(1, 21)=.004$; $p>.05$), the high MTL-low MTL groups ($F(1,21)=2.262$ $p>.007$). There were also no interactions between the FL and MTL groups ($F(1,21)=.177$; $p>.05$), the condition and the FL groups ($F(1,21)=.083$; $p>.356$), the condition and the MTL groups ($F(1,21)=.044$; $p>.05$) and the condition, FL and MTL groups ($F(1, 21)=.177$; $p>.05$).

Discussion

The number of trials it took for the high MTL group to learn the 13 out of 15 items was significantly less than the low MTL group and their performance improves on the second day which is expected given the importance of the medial temporal lobes in the consolidation of memory. The experiment did not show the reconsolidation effect in the predicted direction.

All of the older adults, regardless of neuropsychological grouping are showing the same amount of intrusions and correct items recalled in the no reminder and the reminder conditions. It is possible that the sample sizes are too small to see an effect at this point. Although we do not see intrusions in the predicted direction, there is a difference in the way that the older adults are showing the reconsolidation effect when compared to the way the young adults performed the same task in the Hupbach et al. (2008) experiment. It is possible that the no reminder group reminded of the previous learning session on the second day which would cause them to reactivate their memory for the first list and modify it by adding new items. Although participants in the no reminder condition were testing in very distinct rooms, being in the same building and at the University of Arizona may have been a reminder for them. Unlike the young adults tested in the Hupbach et al (2007, 2008) studies, the older adults do not spend a considerable amount of time every week on the campus like the young adults. If this is the case, then being at the University may have been more salient to them than the distinction between the two rooms and the no reminder group would have been reminded of the previous session and performed the same as the reminder group. Another possibility is that the contextual information for the first list is no longer available at the time of retrieval so that it cannot be used to recall the first list separately from the second because neither list of objects is bound to an individual context. Future studies could focus on testing for the recall of Day 2 objects to see whether they

recall items from Day 1, if they do then this would indicate that their intrusions are due to source errors and not reconsolidation.

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Table 1

Characteristics of Older Adults as a Function of Neuropsychological Group

Variable	<i>High FL Function</i>				<i>Low FL function</i>			
	<u>High MTL function</u>		<u>Low MTL function</u>		<u>High MTL function</u>		<u>Low MTL function</u>	
	M	SD	M	SD	M	SD	M	SD
Age (years)	75.43	5.84	77.27	6.99	70.28	3.19	76.88	6.72
Education (years)	17.29	3.0	16.67	3.1	19.25	1.0	14.00	2.8
MMSE	29.71	.49	28.33	1.21	28.75	.96	28.20	1.30
FL score ^a	.34	.17	.20	.15	-.42	.29	-.79	.21
MTL score ^a	.58	.42	-.60	.35	.47	.40	-.65	.68

Note. FL=frontal lobe; MTL=medial temporal lobe; MMSE= Mini-Mental Status Examination; ^az scores (see text)

Table 2

<i>List A</i>	<i>List B</i>
Apple	Bow
Battery	Calculator
Book	Crayon
Cassette tape	Cup
Cellular phone	Feather
Comb	Flashlight
Dollar bill	Flower
Elephant	Glue
Toy pot	Key
Puzzle piece	Spoon
Rock	Sunglasses
Thread	Tea bag
Tissue	Tennis ball
Watch	Tooth brush
Zipper	Whistle

Figure 1

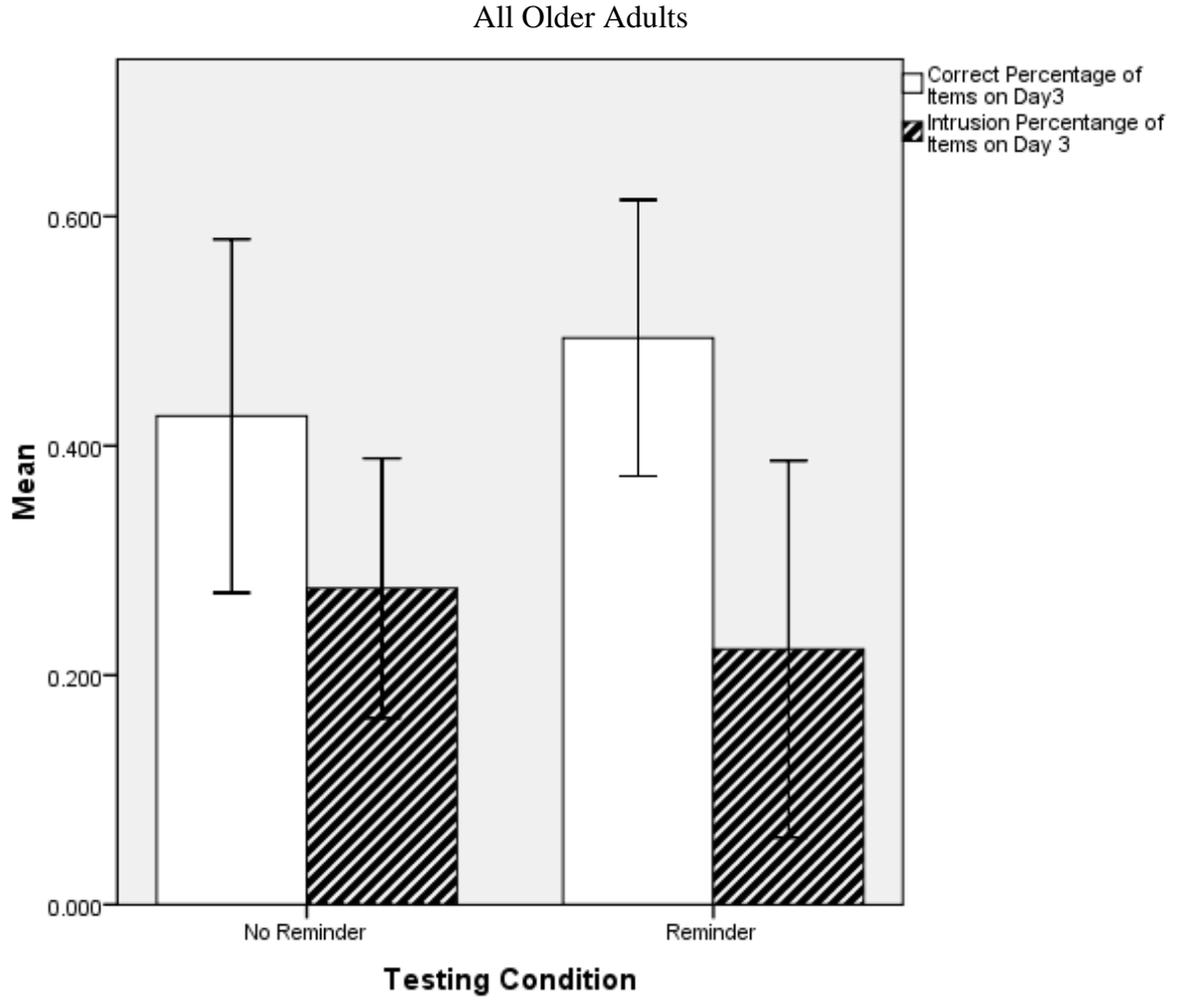


Figure 2

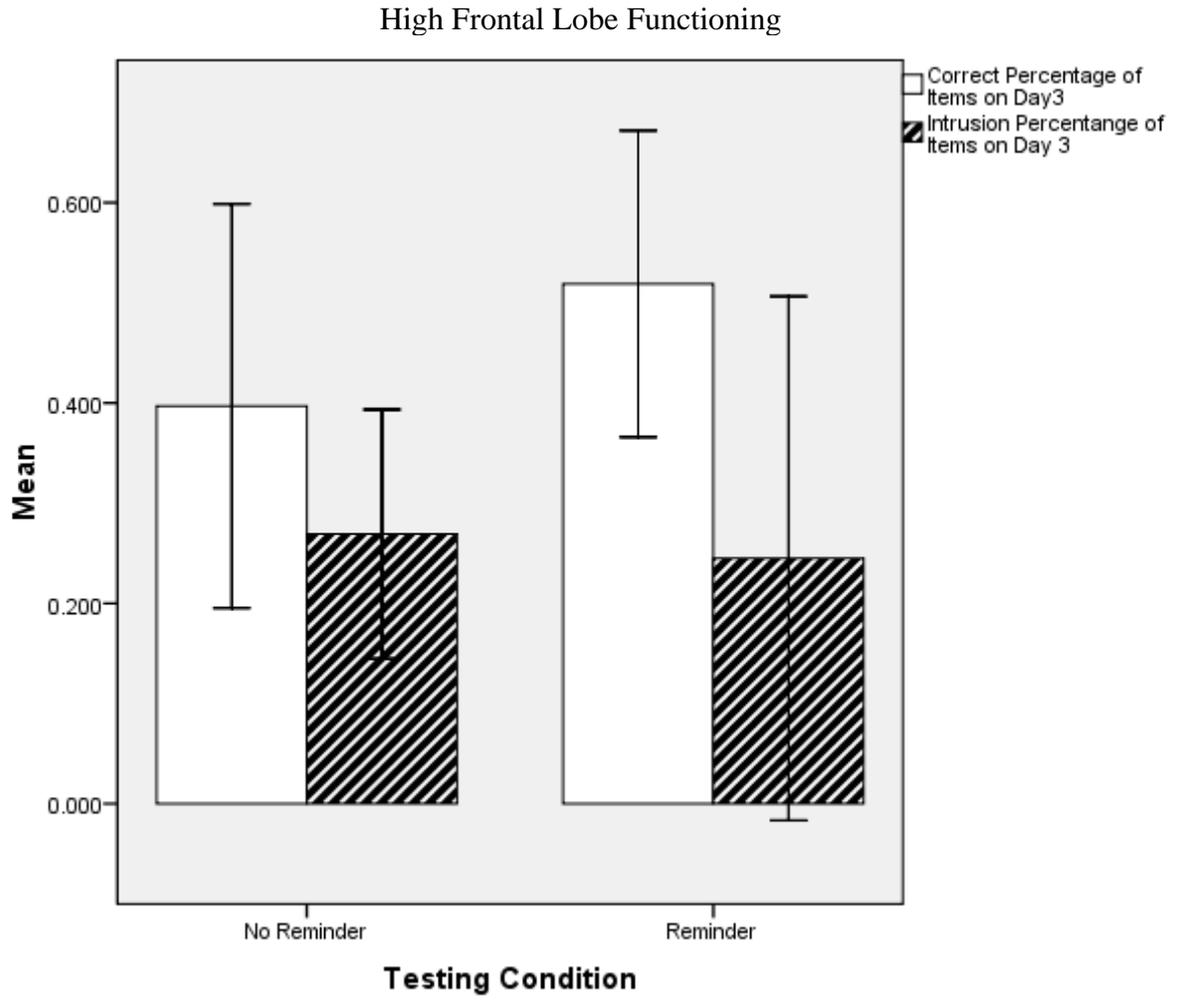


Figure 3

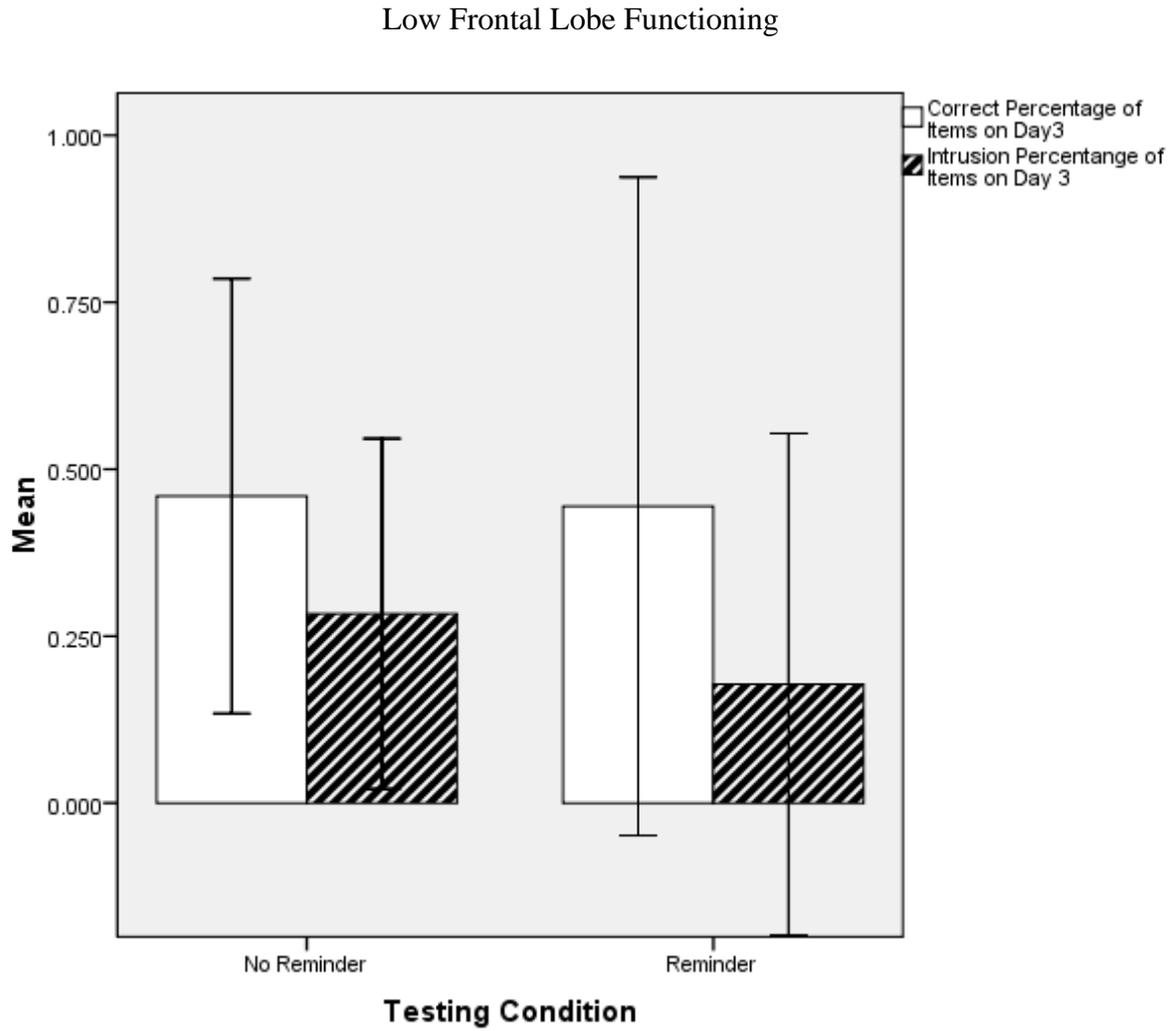


Figure 4

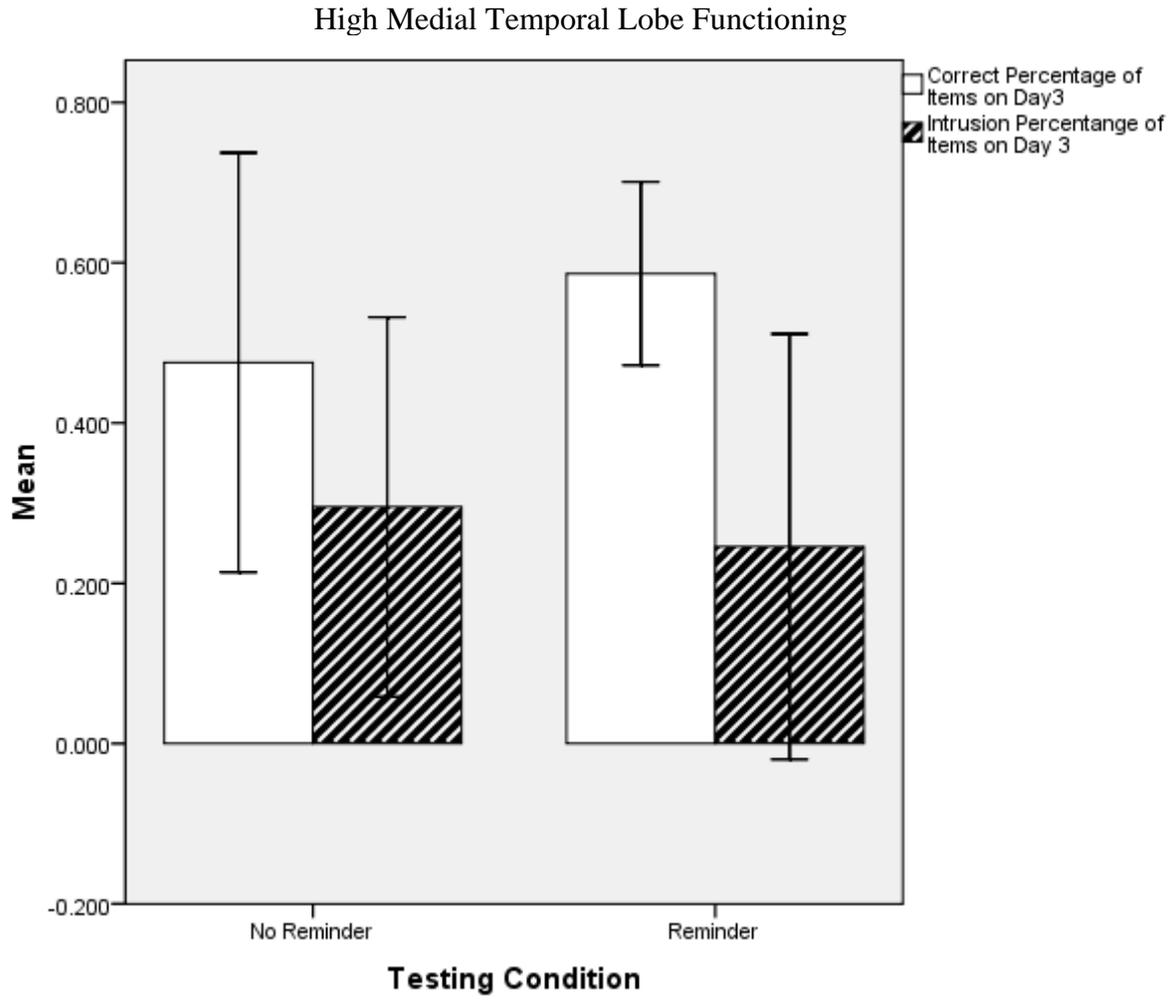
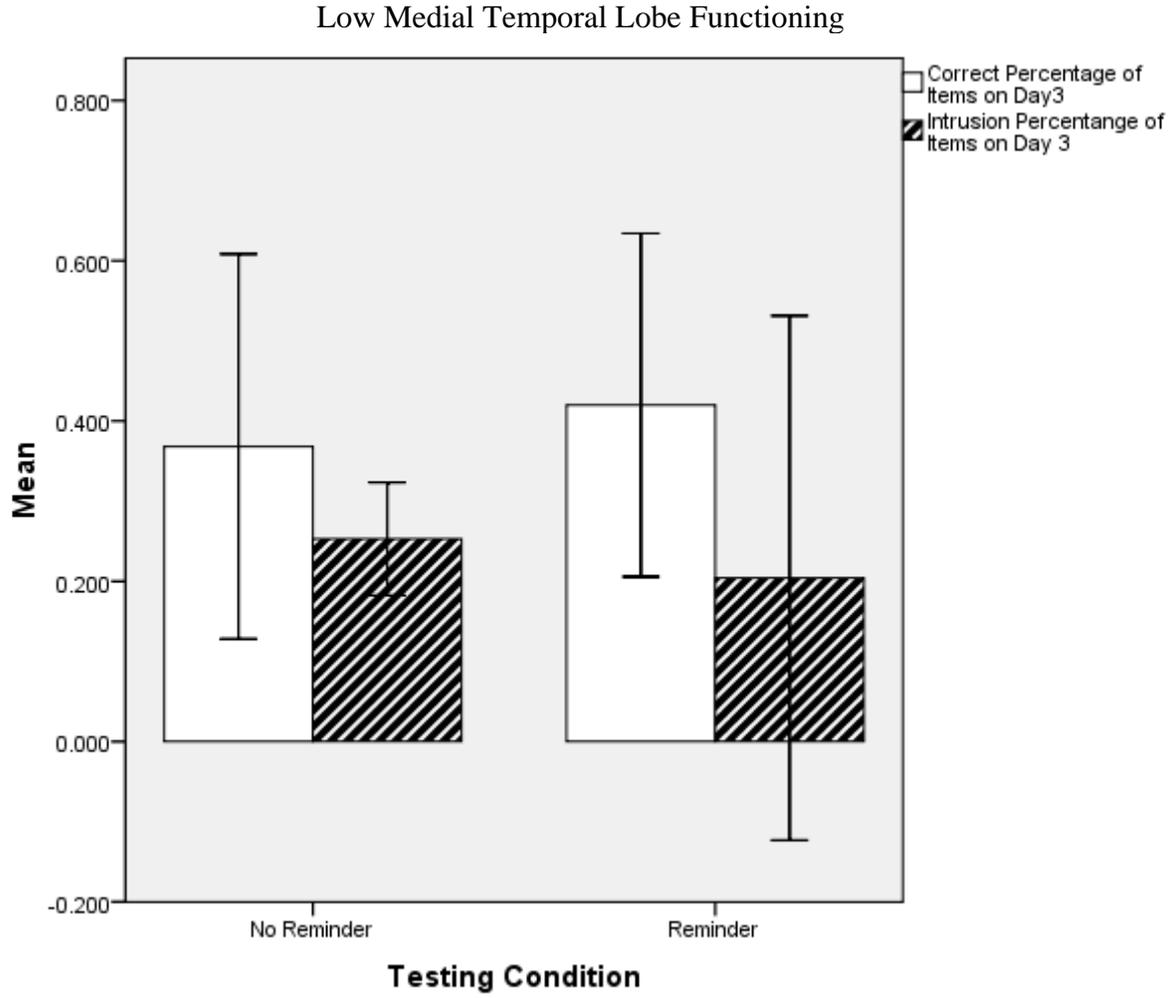


Figure 5



Appendix 1

Subject #
Date of Birth:

Group:
Location:

M/F

Presenter:
Test Date:

Learning Session Day _____

<i>Item</i>	1 st Immediate Memory	2 nd Immediate Memory	3 rd Immediate Memory	4 th Immediate Memory	5 th Immediate memory
Bow					
Calculator					
Crayon					
Cup					
Feather					
Flashlight					
Flower					
Glue					
Key					
Spoon					
Sunglasses					
Teabag					
Tennis Ball					
Toothbrush					
Whistle					

Subject #
Date of Birth:

Group:
Location:

M/F

Presenter:
Test Date:

Learning Session Day _____

Item	1 st Immediate Memory	2 nd Immediate Memory	3 rd Immediate Memory	4 th Immediate Memory	5 th Immediate memory
Apple					
Battery					
Book					
Cassette Tape					
Cellular Phone					
Comb					
Dollar Bill					
Elephant					
Pot/Pan					
Puzzle Piece					
Rock					
Thread					
Tissues					
Watch					
Zipper					

Subject #
 Date of Birth:
 Day 3 Recall (Friday)

Group: M/F
 Location:

Presenter:

Test Date:

Order	1st Trial	2nd Trial	3rd Trial	4th Trial
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				

Did you expect that you had to recall the items from Day 1/2 today?

Appendix 2

Subject #:

Group:

Date:

Experimenter:

1. Did you learn list 1 and 2 in the same location or different locations?
(Please circle one answer)

SAME / DIFFERENT / UNCERTAIN

2. Did you learn List 1 and 2 from the same experimenter or from different experimenters? (please circle one answer)

SAME / DIFFERENT / UNCERTAIN

Subject #:

Group:

Date:

Experimenter:

3. Describe where you learned List 1.

4. Describe where you learned List 2.

5. Describe the experimenter who taught you List 1.

6. Describe the experimenter who taught you List 2.
