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Recovery from Proactive Semantic Interference in Mild Cognitive Impairment and Normal Aging: Relationship to Atrophy in Brain Regions Vulnerable to Alzheimer's Disease

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Abstract

Background—There is growing evidence that proactive semantic interference (PSI) and failure to recover from PSI may represent early features of Alzheimer's disease (AD).

Objective—This study investigated the association between PSI, recovery from PSI, and reduced MRI volumes in AD signature regions among cognitively impaired and unimpaired older adults.

Methods—Performance on the LASSI-L (a novel test of PSI and recovery from PSI) and regional brain volumetric measures were compared between 38 cognitively normal (CN) elders and 29 older participants with amnestic mild cognitive impairment (MCI). The relationship between MRI measures and performance on the LASSI-L as well as traditional memory and non-memory cognitive measures was also evaluated in both diagnostic groups.

Results—Relative to traditional neuropsychological measures, MCI patients' failure to recover from PSI was associated with reduced volumes in the hippocampus (rs = 0.48), precuneus (rs = 0.50); rostral middle frontal lobules (rs = 0.54); inferior temporal lobules (rs = 0.49), superior parietal lobules (rs = 0.47), temporal pole (rs = 0.44), and increased dilatation of the inferior lateral ventricle (rs = −0.49). For CN elders, only increased inferior lateral ventricular size was associated

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SUPPLEMENTARY MATERIAL

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with vulnerability to PSI (rs = −0.49), the failure to recover from PSI (rs = −0.57), and delayed recall on the Hopkins Verbal Learning Test-Revised (rs = −0.48).

Discussion—LASSI-L indices eliciting failure to recover from PSI were more highly associated with more MRI regional biomarkers of AD than other traditional cognitive measures. These results as well as recent amyloid imaging studies with otherwise cognitively normal subjects, suggest that recovery from PSI may be a sensitive marker of preclinical AD and deserves further investigation.

Keywords

Alzheimer's disease; LASSI-L; memory; mild cognitive impairment; MRI; proactive interference; semantic interference

INTRODUCTION

With the aging of the population and related rise in incidence of Alzheimer's disease (AD), there has been increasing interest in the development of more sensitive neuropsychological measures for the early detection of cognitive impairment. One such measure, the Loewenstein-Acevedo Scales for Semantic Interference and Learning (LASSI-L) [1], is a cognitive stress paradigm that employs controlled learning and cued recall to maximize the storage and retrieval of 15 targets belonging to three semantic categories (fruits, articles of clothing, and musical instruments). A distinguishing feature of the LASSI-L is that following the administration of the original target words it provides the opportunity to determine the effects of proactive semantic interference (PSI: old learning interfering with new learning) and recovery from semantic interference (the ability to recover from PSI effects, learning a second list of targets over an additional trial). Maximum recall of the original targets, PSI and recovery from PSI have been shown to be very sensitive in discriminating between older adults with mild cognitive impairment (MCI) and those who are cognitively normal (CN) and to have good test-retest reliabilities [1, 2]. Equally important, among community-dwelling older adults who scored normally on traditional neuropsychological measures, deficits in recovery from PSI have been shown to have strong associations with amyloid load in the precuneus, posterior cingulate regions, and whole brain [3]. Findings of strong associations between PSI and recovery from PSI, and amyloid load in regions vulnerable to AD pathology, raises the possibility that LASSI-L measures may detect early cognitive changes associated with neurodegeneration associated with amyloid deposition in early AD. The previous study also explored the association of brain amyloid that may be more sensitive than other standard neuropsychological measures, where only weak or no associations were found.

While brain amyloid load represents an early risk factor for subsequent clinical AD, reductions in regional brain volumes, measured by magnetic resonance imaging (MRI), may provide a better measure of the actual neurodegeneration associated with the AD cascade. Holland et al. [4] and Dickerson et al. [5] have identified several brain regions (identifiable on MRI) which may represent a signature of the neurodegeneration that is present in the early stages of AD. In this study, we compared participants who were diagnosed with MCI or CN to evaluate the relationships between the volumes of these AD signature brain regions

and performance on the LASSI-L and other widely-used memory and non-memory measures.

METHODS

Sixty-seven older adult participants from an NIH-funded and IRB approved investigation at the University of Miami Miller School of Medicine were evaluated using a standard clinical assessment protocol consisting of the Clinical Dementia Rating Scale (CDR) [6] and the Mini-Mental Status Examination (MMSE) [7]. Memory and other cognitive complaints were assessed by clinicians who were blind to the neuropsychological test results and had formal training in administering the CDR and MMSE. All participants were community-dwellers, independent in their activities of daily living, had knowledgeable collateral informants, and did not meet DSM-V criteria for Major Neurocognitive Disorder, active Major Depression, or any other neuropsychiatric disorder. In cases where there was evidence of cognitive decline by history and/or clinical examination, the clinician scored the Global CDR as 0.5 and a probable diagnosis of MCI, pending the results of formal neuropsychological testing. A standard neuropsychological battery was then administered uniformly across groups independently of the clinical examination. The neuropsychological battery included the Hopkins Verbal Learning Test-Revised (HVLT-R) [8], National Alzheimer's Coordinating Center (NACC) delayed paragraph recall [9], Category Fluency [10], Block Design of the WAIS-IV [11], and the Trail Making Test (Parts A and B) [12].

Criteria for CN participants (n = 38)

After an extensive clinical interview with the participant and the informant, an individual was considered cognitively normal if there were: a) no subjective memory or other cognitive complaints by the participant or collateral informant (e.g., Have you had any difficulties with memory or thinking?); b) no evidence by extensive clinical evaluation or history of memory or other cognitive decline; c) Global CDR score of 0 rated by the clinician; d) all memory and non-memory neuropsychological measures scored within normal limits relative to age and education related norms as determined by an experienced neuropsychologist (this was typically less than 1.0 SD below normative values for all tests).

Criteria for MCI (n = 29)

On the basis of the same clinical interview and performance on the neuropsychological tests, an individual was considered to have MCI if there was: a) subjective memory complaints by the participant and/or or collateral informant; b) evidence by clinical evaluation or history of memory or other cognitive decline; c) Global CDR score of 0.5; d) one or more memory measures 1.5 SD or below normal limits relative to age and education related norms.

Loewenstein-Acevedo Scales for Semantic Interference and Learning

The LASSI-L is a novel measure that employs controlled learning and cued recall to maximize storage of a list of to-be-remembered target words that targets represent three semantic categories. Test-retest reliabilities of the LASSI-L have been shown to be high in previous studies, and the accuracy of classification of MCI patients versus cognitively normal elderly participants exceeded 90% [1, 2]. A distinguishing aspect of this measure is

the presentation of a second list of to-be-remembered words which share the same semantic categories in the first list, eliciting a considerable amount of proactive interference. Unlike other memory paradigms, the individual is again administered this second list of words to measure recovery from proactive semantic interference. The specific elements of the test are described below.

The examinee is instructed to remember a list of 15 common words that are fruits, musical instruments, or articles of clothing (five words per category). The person is asked to read the words from the target list aloud, as each word is presented individually at 4-s intervals. In the unlikely event that the person cannot correctly read the word, the word is read by the examiner and the examinee is asked to repeat the word. If a person does not know one of the words (also unlikely), the examiner tells the person what category the word belongs to (e.g., “Lime is a fruit.”) and the person is asked to repeat the word. After the person has read all 15 words, they are asked to recall the words. After free recall has ended, the examinee is presented with each category cue (e.g., clothing) and asked to recall the words that belonged to that category (LASSI-L A1).

The examinee is then presented with the target stimuli for a second learning trial with subsequent cued recall to strengthen the acquisition and recall of the List A targets, providing maximum storage of the to-be-remembered information (LASSI-L A2). Following this trial, the participant is introduced to a semantically related list (i.e., List B) which is then presented in the same manner as List A targets. List B consists of 15 words which are different from List A, five that belong to each of the three categories used in List A (i.e., fruits, musical instruments, and articles of clothing). Following the presentation of the List B words, the person is asked to freely recall the List B words; this assesses proactive interference effects (LASSI-L B1). Then, each category cue is given and they are asked to recall each of the List B words that belonged to each of the categories. List B words are presented again, followed by a second category-cued recall trial. This second learning trial for the new list allows the assessment of the ability to recover from the initial semantic interference effects (LASSI-L B2). This recovery from proactive interference is a feature of the LASSI-L that is not assessed by any existing list-learning measure. Previous investigations of amyloid in non-demented community-dwelling elders [3] have shown that the most important LASSI measures related to amyloid load is List B1 cued recall (susceptibility to proactive interference) and List B2 cued recall (recovery from proactive interference) as well as a measure of maximum storage and recall of the initial A2 targets (List A2).

MRI measurements

Subjects underwent MRI scanning using a Siemens Skyra 3T MRI scanner at the University of Miami Applebaum MRI Center. Brain parcellation was obtained using a 3D T1-weighted sequence (MPRAGE) with 1.0 mm isotropic resolution. FreeSurfer Version 5.3 software (http://surfer.nmr.mgh.harvard.edu) was employed to assess atrophy in AD signature regions [4, 5, 13], including the hippocampus, entorhinal cortex, precuneus, posterior cingulate gyrus, inferior temporal gyrus, temporal pole, superior parietal lobe, middle caudal gyrus, superior frontal gyrus, and posterior cingulate gyrus. We also included the volume of the

inferior lateral ventricles, a sensitive index of atrophy in surrounding brain regions which are affected early in AD. Larger inferior volume size is indicative of greater ventricular dilatation and is inversely correlated measures such as the hippocampus and other brain regions.

Given the high degree of association between corresponding structures in the right and left hemispheres of the brain, homologous structures (e.g., precuneus, inferior temporal lobules) were added together and normalized using intracranial volume).

Statistical analyses

The data was analyzed using SPSS (Version 22). Group comparisons were conducted using a series of one-way analyses of variance. Within MCI and CN groups separately, we associated LASSI-L and traditional memory and non-memory measures with different regions on the MRI. As in previous studies [3, 14] we employed Spearman Rank order correlation coefficients (since these non-parametric measures are 1) not dependent on normal distribution of neuropsychological and MRI variables which are difficult to ascertain with modest sample sizes and 2) are less sensitive to the effects of outlier values.

We had an *a priori* hypothesis that LASSI-L List B1 Cued Recall and List B2 Cued recall, which has been particularly sensitive to medial temporal lobe atrophy and amyloid load in previous studies [2, 14], would be related to AD sensitive regions such as the hippocampus and precuneus in participants with aMCI. However, the current study included ten different AD related MRI regions and six different memory subtests. Conservative approaches such as the Bonferroni Correction reduces statistical power and frequently leads to enhanced family Type 2 error rates (failing to detect true differences in test-wise contrasts) and fails to discriminate between *a priori* and *post-hoc* examinations of the data [19]. As such, we wanted to limit the potential for Type 2 errors but wanted more stringent criteria of $p < 0.01$ for each-test-wise contrast to reduce the probability of family-wise Type 1 errors. We further conducted an analysis of the false discovery rate (FDR) with individual adjustment of individual p-values. We only considered corrected p-values of $p < 0.05$ corrected for FDR using methods by Benjamini and Hochberg [20]. Since using a test-wise alpha of $p \leq 0.01$ and adjusting p-values for FDR yielded identical findings, we employed the former approach in presentation of the data (See Table 2).

RESULTS

As indicated in Table 1, there were no statistically significant differences between CN and MCI participants with regards to age, education, or gender distribution. MCI participants had significantly lower volumes in the hippocampus, inferior lateral temporal lobule, superior parietal lobule, precuneus, and superior frontal lobule as well as increased volume of the inferior lateral ventricles. Not surprisingly, HVLT-R Total Recall [$F(1,64) = 40.00$; $p < 0.001$], HVLT-R Delayed Recall [$F(1,64) = 79.78$ $p < 0.001$], and NACC delayed story passages [$F(1,64) = 44.36$; $p < 0.001$] produced the highest F-values in group comparisons since the HVLT-R and NACC passages were used in conjunction with the clinical evaluation to assign participants to diagnostic groups. The LASSI-L was not employed in diagnostic determination and MCI patients scored lower than CN participants on LASSI-A2 cued

retrieval [F (1,65) = 20.42; $p < 0.001$], LASSI-B1 cued retrieval [F(1,65) = 14.96; $p = 0.001$], and LASSI-B2 cued retrieval [F(1,65) = 20.27; $p < 0.001$]. There were also differences favoring CN participants with regards to Category Fluency [F(1,65) = 9.81; $p < 0.003$] and Trails B [F(1,65) = 28.40; $p < 0.001$], and a trend for Block Design [F(1,64) = 4.50; $p < 0.04$]. There were no group differences with regards to Trails A [F(1,65) = 3.12; $p = 0.08$].

Relationship between LASSI-L and other cognitive measures and MRI variables among MCI participants

We examined the relationship between volumetric MRI measures and traditional Spearman Rank Order Correlation coefficients because they are not dependent on the underlying distribution of normality and are less sensitive to outliers [3]. As previously mentioned, because of multiple MRI and neuropsychological contrasts and to reduce the potential for family-wise alpha error, each test-wise comparison was set at $p \leq 0.01$ to reduce the possibility of spurious errors of inference.

As depicted in Table 2, for MCI participants, of all of the memory measures, lower scores on LASSI-L B2 recall (reflecting difficulties in recovery from proactive interference) were associated with decreased volumes in the precuneus (rs = 0.50; $p = 0.003$), hippocampus (rs = 0.48; $p = 0.004$), inferior temporal lobules (rs = 0.49; $p = 0.004$), superior parietal lobule (rs = 0.47; $p = 0.005$), rostral middle frontal (rs = 0.54; $p = 0.001$), and temporal pole (rs = 0.44; $p = 0.008$), and with increased inferior lateral ventricle dilatation (rs = −0.49; $p = 0.004$). The inferior temporal lobule was also associated with Delayed NACC Passage Recall (rs = 0.51; $p = 0.002$). Relationship between these cognitive areas and other brain regions can be found in Supplementary Table 1

When the relationship between MRI volumetric measures and non-memory measures were considered, category fluency scores were positively associated with inferior temporal lobe volume (rs = 0.49; $p < 0.003$). Performance on Block Design of the WAIS-IV, Trails A and Trails B were not related to any of the volumes of any of the MRI measures.

Relationship between LASSI-L and other cognitive measures and MRI variables among cognitively normal participants

Table 3 shows the relationship between cognitive and MRI measurements to 38 CN elders. The only brain region that was related to cognitive measures was the inferior lateral ventricle which was most strongly related to susceptibility to LASSI-L B2 cued recall (rs = −0.57; $p < 0.001$), B1 Cued Recall (rs = −0.49; $p < 0.001$), and HVLT-R Delayed Recall (rs = −0.48; $p < 0.007$). Additional analyses indicated that there were no associations between non-memory measures and other volumetric measures of the brain at $p \leq 0.01$.

DISCUSSION

This study relates performance on a novel cognitive test that measures recovery from PSI to atrophy in signature brain regions associated with AD. The strongest and most consistent relationships were found on the LASSI-L measure sensitive to recovery from PSI (Cued B2 Recall), among aMCI patients and decreased volumes in the precuneus, hippocampus,

rostral middle frontal lobules superior parietal lobules, inferior temporal lobules, and temporal pole, with correlation coefficients statistically significant at $p < 0.01$ ranging between 0.44 and 0.54. There was also a statistically significant association between dilatation of the inferior lateral ventricles and Cued B2 recall. It should be noted that an identical pattern of results emerged the FDR for the 60 contrasts with a test-wise alpha of $p < 0.05$ was calculated using the procedure developed by Benjamini and Hochberg [20]. Additionally, in *post-hoc* tests we examined List B2 cued recall was expressed as a ratio of initial List A2 cued recall of the LASSI-L, the obtained correlations with the precuneus, rostral middle frontal lobules, superior parietal lobules inferior temporal, hippocampus, and inferior lateral ventricle all remained statistically significant at $p < 0.05$ or less. This is strongly suggestive that a measure tapping the failure to recover from PSI (after adjusting for initial learning) may be specifically related to atrophy in a number of AD related brain regions.

Delayed recall of the NACC story passage and performance on the Category Fluency test were significantly related to atrophy in the inferior temporal lobules. The recovery from PSI and its association with the hippocampus, precuneus, superior parietal lobules, temporal pole, inferior lateral ventricles, and superior parietal lobule was not observed with any other memory or non-memory measure.

These results are of particular interest given our previous findings that failure to recover from PSI was strongly associated with amyloid load in the precuneus and whole brain in neuropsychologically normal, but elderly (and therefore, at-risk) community-dwelling elders [3] Recently, Miners, Palmer, and Love [15] found that decreased perfusion in the precuneus is an early finding in AD. Indeed, Lundstrom, Ingvar, and Peterson [16] highlight the importance of the precuneus in source memory and its relationship and connectivity to a number of brain regions involved in cognitive processing. The relationship between failure to recover from PSI and dysfunction of the precuneus and other brain structures including the superior parietal lobule is worthy of further research.

Our findings that MCI participants had significantly lower volumes in several AD signature regions, particularly the hippocampal regions, are consistent with a number of studies that show that structural changes within these regions occur in the early neurodegenerative disease process [5, 17].

An interesting finding in the current investigation is the strong and specific associations between LASSI-L B1 (susceptibility to PSI), LASSI-B2 (inability to recover PSI), HVLT-Delayed recall, and larger inferior lateral ventricle size among CN participants. Although enlarged ventricles are not specific to AD and is seen in normal aging, there is increasing evidence that early ventricular changes may be a feature of pre-symptomatic AD (see Apostolova et al. [18]).

As attention is focused on identification of cognitive deficits in pre-clinical stages of neurodegenerative disorders such as AD, it would seem important to use cognitive tests, such as the LASSI-L, which employ a stress paradigm to detect subtle deficits, among older adults who may have little or no cognitive impairment on traditional neuropsychological

measures. While previous studies have shown that measures such as the PSI, have been associated with amyloid load [3, 14], the LASSI-L is unique, relative to other cognitive measures, in that it has a second recall trial which measures the ability to recover from the initial effects of PSI. This study indicates that this ability to recover from PSI is associated with atrophy across a wider spectrum of signature regions. Future studies are required with larger groups of subjects, representing diverse ethnic/cultural groups, to replicate the present results and to determine whether PSI and recovery from PSI are predictive of longitudinal changes in cognition and specific biomarkers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

LASSI-L	Loewenstein-Acevedo Scales for Semantic Interference and Learning
HVLT-R	Hopkins Verbal Learning Test-Revised
NACC	National Alzheimer's Coordinating Center

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Table 1

Demographic information, neuropsychological and MRI values for cognitively normal and mild cognitive impairment patients

	Cognitively Normal (*n* = 38)	MCI (*n* = 29)	F or χ^2	*p*-value
Age	74.1 (SD = 7.7)	73.7 (SD = 7.0)	0.05	0.818
Education	14.7 (SD = 3.6)	14.6 (SD = 3.5)	0.02	0.904
Gender	68.4 % female	51.7 % female	1.29	0.256
Ethnicity				
White Non-Hispanic	71.1%	65.5%	0.51	
Hispanic	21.1%	27.6%	(Fisher Exact Test)	
African-American	7.9%	6.9%		
MMSE	28.7 (SD = 1.6)	26.9 (SD = 2.4)	13.99	<0.001
HVLT-R Total Recall	24.2 (SD = 4.6)	17.3 (SD = 4.0)	40.00	<0.001
HVLT-R Delay Recall	8.9 (SD = 2.2)	4.0 (SD = 2.2)	79.78	<0.001
NACC Delay Passage	12.3 (SD = 3.4)	6.7 (SD = 3.4)	44.36	<0.001
LASSI-L A2 Cued Recall (Maximum Storage)	13.1 (SD = 1.5)	11.2 (SD = 1.9)	20.42	<0.001
LASSI-L B1 Cued Recall (Susceptible to PSI)	7.5 (SD = 2.8)	5.1 (SD = 2.1)	14.96	<0.001
LASSI-L B2 Cued Recall (Recovery from PSI)	11.2 (SD = 2.5)	8.5 (SD = 2.4)	20.27	<0.001
Hippocampal Volume	0.0054 (SD = 0.0008)	0.0048 (SD = 0.0008)	9.74	<0.003
ERC Volume	0.0022 (SD = 0.0003)	0.0022 (SD = 0.0004)	0.66	0.421
Inferior Lateral Ventricle	0.0008 (SD = 0.0006)	0.0011 (SD = 0.0006)	4.66	0.035
Precuneus Volume	0.0120 (SD = 0.0013)	0.0114 (SD = 0.0012)	3.48	0.067
Posterior Cingulate Volume	0.0039 (SD = 0.0005)	0.0038 (SD = 0.0005)	2.65	0.108
Temporal Pole Volume	0.0031 (SD = 0.0005)	0.0030 (SD = 0.0006)	0.78	0.381
Inferior Temporal Volume	0.0125 (SD = 0.0012)	0.0118 (SD = 0.0014)	5.08	0.028
Superior Parietal Lobe	0.0161 (SD = 0.0015)	0.0152 (SD = 0.0012)	6.86	0.011
Superior Frontal Lobe Volume	0.0259 (SD = 0.0025)	0.0247 (SD = 0.0022)	3.80	0.056
Middle Frontal Lobe Volume	0.0184 (SD = 0.002)	0.0177 (SD = 0.0016)	2.26	0.128

MMSE, Mini-Mental State Examination; HVLT-R, Hopkins Verbal Learning Test-Revised; NACC, National Alzheimer's Coordinating Center; LASSI-L, Loewenstein-Acevedo Scales for Semantic Interference and Learning; ERC, entorhinal cortex.

Table 2

Associations between MRI volumes and LASSI-L and other memory measures for 29 MCI participants

	LASSI-L A2 Maximum Storage	LASSI-B1 Vulnerable to Proactive Interference	LASSI-B2 Vulnerable to Recovery from Proactive Interference	HVLT-R Total Recall	HVLT-R Delayed Recall	NACC Delayed Passage Memory
Hippocampal Volume	rs = 0.37 * (p = 0.024)	rs = 0.33 * (p = 0.042)	**rs = 0.48** ** (p = 0.004)	rs = 0.23 (p = 0.113)	rs = 0.04 (p = 0.422)	rs = 0.16 (p = 0.203)
Inferior Lateral Ventricle	rs = −0.30 (p = 0.058)	rs = −0.32 * (p = 0.047)	**rs = −0.49** ** (p = 0.004)	rs = −0.17 (p = 0.184)	rs = 0.03 (p = 0.434)	rs = −0.06 (p = 0.371)
Precuneus Volume	rs = 0.03 (p = 0.446)	rs = 0.25 (p = 0.100)	**rs = 0.50** ** (p = 0.003)	rs = −0.02 (p = 0.454)	rs = −0.15 (p = 0.226)	rs = 0.02 (p = 0.464)
Inferior Temporal Volume	rs = 0.25 (p = 0.095)	rs = 0.37 * (p = 0.024)	**rs = 0.49** ** (p = 0.004)	rs = 0.30 (p = 0.058)	rs = 0.22 (p = 0.125)	**rs = 0.51** ** (p = 0.002)
Superior Parietal Lobe Volume	rs = 0.18 (p = 0.173)	rs = 0.33 * (p = 0.042)	**rs = 0.47** ** (p = 0.005)	rs = −0.07 (p = 0.352)	rs = −0.04 (p = 0.415)	rs = −0.01 (p = 0.473)
Superior Frontal Volume	rs = 0.01 (p = 0.480)	rs = 0.19 (p = 0.168)	rs = 0.18 (p = 0.176)	rs = 0.30 (p = 0.056)	rs = 0.09 (p = 0.315	rs = −0.07 (p = 0.369)
ERC Volume	rs = 0.26 (p = 0.090)	rs = 0.003 (p = 0.494)	**rs = 0.31** (p = 0.107)	rs = −0.14 (p = 0.237)	rs = 0.04 (p = 0.421)	rs = 0.24 (p = 0.102)
Posterior Cingulate Volume	rs = 0.20 (p = 0.153)	rs = −0.09 (p = 0.321)	rs = 0.24 (p = 0.239)	rs = 0.07 (p = 0.359)	rs = 0.22 (p = 0.123)	rs = 0.13 (p = 0.251)
Temporal Pole Volume	rs = 0.07 (p = 0.359)	rs = 0.30 (p = 0.57)	**rs = 0.44** ** (p = 0.008)	rs = 0.06 (p = 0.377)	rs = 0.03 (p = 0.441)	rs = −0.07 (p = 0.364)
Rostral Middle Frontal Volume	rs = 0.27 (p = 0.077)	rs = 0.40 * (p = 0.016)	**rs = 0.54** ** (p = 0.001)	rs = 0.15 (p = 0.222)	rs = −0.04 (p = 0.427)	rs = 0.09 (p = 0.320)

* $p < 0.05$;

** p < 0.01: Correlation coefficients represent Spearman Rank Order Correlation Coefficients. Due to multiple contrasts and to reduce the possibility of family-wise Type 1 errors, the criteria for statistical significance is **$p \leq 0.01$. LASSI-L, Loewenstein-Acevedo Scales for Semantic Interference and Learning; HVLT-R, HopkinsVerbal Learning Test-Revised;NACC, National Alzheimer's Coordinating Center; ERC, entorhinal cortex.

Table 3

Associations between MRI volumes and LASSI-L and other memory measures for 38 cognitively normal participants

	LASSI-L A2 ***(Maximum Storage)***	**LASSI-B1** ***(Vulnerable (to Proactive (Interference) Proactive***	**LASSI-B2** ***(Vulnerable to Recovery from Interference)***	**HVLT-R Total Recall**	**HVLT-R Delayed Recall**	**NACC Delayed Passages**
Hippocampal Volume	rs = 0.18	rs = 0.28 *	rs = 0.28 *	rs = 0.07	rs = 0.23	rs = −0.33 *
Inferior Lateral Ventricle	rs = −0.33 *	**rs = −0.49** ***	**rs = −0.57** ***	**rs = −0.39** **	**rs = −0.48** ***	rs = −0.28 *
Precuneus Volume	rs = 0.12	rs = 0.15	rs = 0.15	rs = 0.21	rs = 0.07	rs = −0.25
Inferior Temporal Volume	rs = −0.56	rs = 0.004	rs = −0.02	rs = −0.02	rs = −0.08	rs = −0.25
Superior Parietal Lobe Volume	rs = 0.14	rs = 0.27 *	rs = 0.21	rs = 0.22	rs = 0.23	rs = −0.01
Superior Frontal Volume	rs = 0.26	rs = 0.19	rs = 0.19	rs = 0.22	rs = 0.23	rs = −0.14
ERC Volume	rs = 0.26	rs = 0.14	rs = 0.11	rs = 0.03	rs = 0.21	rs = −0.04
Posterior Cingulate Volume	rs = 0.09	rs = 0.26	rs = 0.24	rs = 0.05	rs = 0.12	rs = −0.27
Temporal Pole Volume	rs = 0.20	rs = 0.06	rs = 0.20	rs = 0.08	rs = 0.12	rs = −0.02
Middle Frontal Volume	rs = −0.16	rs = 0.11	rs = 0.17	rs = 0.16	rs = 0.17	rs = −0.12

Correlation coefficients represent Spearman Rank Order Correlation Coefficients. Due to multiple contrasts and to reduce the possibility of family-wise Type 1errors, the criteria for statistical significance is ** $p \leq 0.01$. LASSI-L, Loewenstein-Acevedo Scales for Semantic Interference and Learning; HVLT-R, Hopkins Verbal Learning Test-Revised; NACC, National Alzheimer's Coordinating Center; ERC, entorhinal cortex.

* $p \leq 0.05$,

*** $p \leq 0.001$.