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Reading, Writing, and Reserve: Literacy Activities are linked to Hippocampal Volume and Memory in Multiple Sclerosis

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Abstract

Consistent with basic research on enriched environments and the cognitive reserve literature, greater engagement in cognitive leisure activities during early adulthood has been linked to preserved memory and larger hippocampal volume in persons with multiple sclerosis (MS). Herein we investigated which specific types of cognitive leisure activities contribute to reserve. Reading-writing activities were positively linked to (a) hippocampal volume within independent samples of Italian (n=187) and American (n=55) MS patients, and (b) memory in subsamples of Italian (n=97) and American (n=53) patients with memory data. Art-music and games-hobbies did not contribute. Findings directly inform the development of targeted evidence-based enrichment programs aiming to bolster reserve against memory decline.

Keywords

multiple sclerosis; cognitive reserve; enriched environments; hippocampal volume; neurogenesis

INTRODUCTION

Consistent with the cognitive reserve hypothesis,[1,2] engagement in mentally-stimulating activities (e.g., reading, hobbies) during early adulthood is linked to (a) preserved memory[3-5] and (b) larger hippocampal volume[4] among persons with multiple sclerosis (MS). Larger hippocampal volume may represent a neuroanatomical basis for reserve in

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MS,[4] which is consistent with (a) capacity for adult neurogenesis within the human hippocampus,[6] and (b) the beneficial role of enriched environments in sustaining hippocampal neurogenesis.[7] (There is a broader literature on cognitive reserve in aging and MS reviewed elsewhere,[1,2] including two studies linking hippocampal volume in elders with intellectual enrichment estimated with education[8] and total engagement across various cognitive leisure activities.[9]) We now investigate which types of cognitive leisure (e.g., reading, music, games) are most related to preserved hippocampal volume and memory in two independent samples of MS patients (including a finer examination of previously-published findings[4]). Findings will inform the development of targeted enrichment programs specifically designed to build reserve against memory decline in MS patients.

METHODS

Patients

Independent samples consisted of (a) 187 Italian MS patients from our original publication[4] (109 women, age 43.9±10.6yrs, education 13.3±3.4, disease duration 13.0±8.4yrs, 135 relapsing-remitting [RR], 52 secondary progressive [SP], EDSS 3.2±2.0, median=2.5), and (b) 55 American MS patients (45 women, age 51.2±8.3yrs, education 15.3±2.3, disease duration 12.9±7.0yrs, 49 RRMS, 6 SPMS, Ambulation Index 2.3±2.4, median=1). Patients were without clinical exacerbations or corticosteroid use for at least four weeks. Patients reported cognitive leisure from their early 20s, so enrollment was limited to patients aged ≥25 years. Patients with pediatric-onset were excluded due to potential neurodevelopmental differences.[10] Studies were approved by institutional review boards at San Raffaele Hospital and Kessler Foundation. Written informed consent was obtained from patients.

Cognitive Leisure Activity

As described elsewhere,[4,5] patients reported frequency of participation in seven common cognitive leisure activities during early adulthood (see Table; see[5] for reliability and validity). Greater mean engagement across the seven activities has been linked to preserved memory[3-5] and hippocampal volume;[4] however, it is unknown which types of cognitive activity are most beneficial. To characterize types of cognitive activity, we performed a principal components analysis with oblique rotation on the seven activities in our total sample of 242 patients. Three separate components emerged (eigenvalues >1.0), accounting for 60.9% of the variance. As shown (Table), components corresponded to Reading-Writing, Art-Music, and Games-Hobbies. Based on these components, we computed three separate cognitive activity scores: means of (a) three Reading-Writing items (mean=3.2±0.9, median=3.0), (b) two Art- Music items (mean=2.1±1.1, median=2.0), and (c) two Games-Hobbies items (mean=2.7±1.0, median=2.5). Readers may contact JFS to receive a copy of the cognitive leisure scale.

Hippocampal Volume

A 3D T1-weighted fast field echo (slice thickness=1mm) was acquired in a 3.0 T Philips Intera scanner for Italian MS patients (see[4]). Normalized hippocampal volume was obtained using FIRST and then applying the volume scaling factor from SIENAX. For American MS patients, a 3D T1-weighted MPRAGE (slice thickness=1mm) was acquired in a 3.0 T

Siemens Skyra scanner. Normalized hippocampal volume was measured using the FreeSurfer brain segmentation program and then regression-adjusting for intracranial volume.

Memory

As described elsewhere,[4] memory data were available for a subsample of 97 patients within the Italian MS sample: measured as mean norm-referenced[11] performance across the Selective Reminding Test (SRT) and Spatial Recall Test. This tested subsample did not reliably differ from the untested subsample in age, education, disease duration, disease phenotype, EDSS, hippocampal volume, or any leisure activity type. For unknown reasons, there was a higher percentage of men within the tested (51.5%) versus untested (31.1%) subsample (p=.005). Mean norm-referenced z-score was −0.72±0.94 (24th percentile), with 17% of the sample <5th percentile. Memory was assessed in 53 of the 55 American MS patients with the SRT and Brief Visuospatial Memory Test, Revised (two other patients had incomplete data). Mean norm- referenced[11,12] z-score was −0.90±1.13 (18th percentile), with 28% of the sample <5th percentile.

Statistical Analyses

Hierarchical regression predicted normalized hippocampal volume with demographics entered in step one (age, sex, education, disease duration, phenotype) and the three types of cognitive leisure (Reading-Writing, Art-Music, Games-Hobbies) entered in step two. Next, the same hierarchical regression was used to predict memory. Analyses were performed separately for Italian and American samples. To be thorough, we also repeated these same analyses within a total combined sample, with sample entered as an additional covariate.

RESULTS

Italian Sample

After controlling for covariates in block one (R^2=.153), greater engagement in Reading-Writing activities during early adulthood was the only leisure predictor of normalized hippocampal volume (r_p=.222, p=.003, Figure 1a). Art-Music r_p=.022, p=.766) and Games-Hobbies (r_p=.009, p=.907) did not contribute. Within the memory subsample, after controlling for covariates (R^2=.354), greater engagement in Reading-Writing (r_p=.253, p=.016, Figure 1b) and Games-Hobbies (r_p=.218, p=.039) was independently linked to better memory, whereas Art-Music was unrelated to memory (r_p=−.101, p=.343).

American Sample

Results were consistent with findings from the Italian sample. Controlling for covariates (R^2=.060), greater engagement in Reading-Writing activities was the only leisure predictor of normalized hippocampal volume (r_p=.334, p=.020, Figure 1c), whereas Art-Music r_p=.037, p=.804) and Games-Hobbies (r_p=−.021, p=.890) did not contribute. Controlling for covariates (R^2=.177), there was a trend whereby greater engagement in Reading-Writing (r_p=.266, p=.073, Figure 1d) was linked to better memory, whereas Art-Music (r_p=.−.027, p=.858) and Games-Hobbies (r_p=−.002, p=.989) were unrelated to memory.

Combined Sample

Within a total combined sample (n=242), Reading-Writing activities were the only predictor of hippocampal volume (r_p=.204, p=.002), with no link to Art-Music (r_p=.031, p=.640) or Games-Hobbies (r_p=.020, p=.760). Within the combined memory subsample (n=150), Reading-Writing was the only leisure type linked to memory (r_p=.288, p=.001), as neither Art- Music (r_p = −.044, p = .602) nor Games-Hobbies (r_p = .132, p = .117) were reliable predictors.

DISCUSSION

We identified reading and writing activities as the type of cognitive leisure most related to larger hippocampal volume and better memory in two independent samples of MS patients (although the link between Reading-Writing and memory within the smaller American sample only trended toward significance). The consistency of our findings across geographically and linguistically diverse samples with different imaging parameters and memory tests supports the robustness of our results. Basic research has shown that animals must learn from enriched environments to sustain hippocampal neurogenesis.[13] That is, many new hippocampal neurons are lost unless they are integrated into functional hippocampal networks, and successful hippocampally-mediated learning (e.g., spatial learning, not classical conditioning) supports survival of new neurons. In humans, most knowledge acquisition (new learning) after high school is accomplished through literacy (i.e., reading),[14] which may explain the relationship between reading-writing activity and hippocampal volume reported herein. Although such activities as playing a musical instrument or engaging in games or hobbies may also involve learning, such learning may be quantitatively less and/or qualitatively different (e.g., procedural rather than hippocampally-mediated).

Relative to basic experimental research, the observational nature of our work represents a lower level of evidence. We interpreted our results in the context of basic research on neurogenesis and enriched environments;[7] however, it is possible that reading and writing activities during early adulthood are linked to (a) larger premorbid hippocampal volume or (b) lower subsequent risk for hippocampal atrophy. Experimental work is needed to investigate the causal link between intellectual enrichment and increased hippocampal volume and memory in MS patients. Such research will be critical in determining whether cognitive reserve against memory decline can be bolstered, thereby providing a much-needed high level of evidence for (a) recommendations to engage in cognitive activity, and (b) the cognitive reserve hypothesis more generally. Based on our findings, such experiments of cognitive enrichment to preserve memory may maximize their efficacy by focusing on reading and writing tasks that promote new learning.

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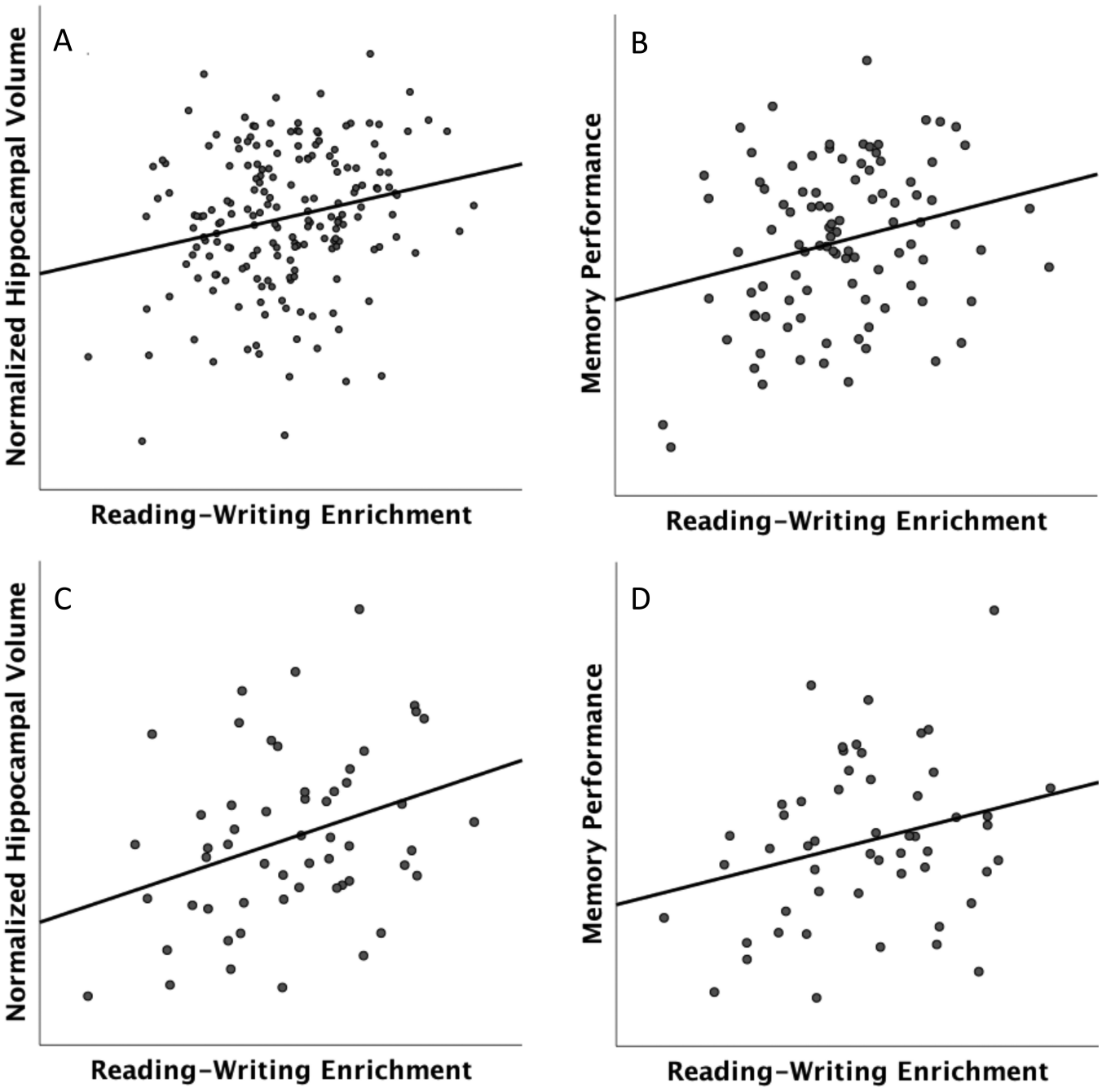

FIGURE.

Scatterplots depict partial correlations (controlling for demographics) between normalized hippocampal volume and reading-writing enrichment in Italian (A) and American (C) MS patients, and partial correlations (controlling for demographics) between memory performance and reading-writing enrichment in Italian (B) and American (D) MS patients.

TABLE

Principal components analysis of cognitive leisure activities

Three components derived corresponded to Reading-Writing, Art-Music, and Games-Hobbies (eigenvalues of 1.72, 1.37, and 1.34, respectively). Note that patients endorsed the frequency with which each activity was performed during their early 20s as daily (5), several times per week (4), several times per month (3), several times per year (2), or once per year or less (1). Patients were instructed to "only report on activities that were performed for leisure, not activities performed to fulfill educational or occupational requirements." These PCA results informed creation of variables representing the three different types of activity. Reading-Writing was the mean frequency across the three items loading on that component (in bold). Art-Music and Games-Hobbies were means of the two items loading on each of these components, respectively.

	Cognitive Leisure Activity Components		
Cognitive Leisure Activities	**Reading-Writing**	**Art- Music**	**Games-Hobbies**
Read books	**.687**	.116	.177
Read magazines or newspapers	**.727**	−.283	−.094
Produce non-artistic writing (e.g., newsletter, diary, essays)	**.682**	.164	.042
Produce art (e.g., painting, poetry, sculpture)	.351	**.701**	−.048
Play a musical instrument	−.192	**.831**	.003
Play structured games (e.g., board games, cards, crossword puzzles)	−.020	−.142	**.795**
Participate in hobbies (e.g., model building, gardening, web design)	.058	.103	**.760**