The Effects of Cognitive Impairment and Brain Atrophy on the Development of Depression in Patients with Multiple Sclerosis

Caitlyn Kelly, Jaeyeon Kweon, Carrie Pham, Shannin Moody, Deidre Devier PhD

Department of Neurology

Louisiana Health Sciences Center New Orleans

Introduction

Multiple sclerosis (MS) is an autoimmune, neurodegenerative disease characterized by the demyelination of axons within the central nervous system leading to the development of motor, sensory, and cognitive deficits. The cognitive impairment present in people with MS typically presents as deficits in complex attention, memory, and planning. 25-50% of patients with MS will develop depressive symptoms during their disease.[1] Depression can also affect aspects of cognition, particularly executive functioning, which can mimic the cognitive deficits seen in patients with MS. Previous studies have found that depressive symptoms appear more often in patients in the later stages of MS as compared to the earlier stages of the disease.[2]

The objective of this study was to determine if a correlation existed between the presence of cognitive deficits, depression, and the severity of MS, which was estimated by measuring the degree of atrophy found in the brains of patients with MS by analyzing MRI scans. It was hypothesized that depression would be predicted by greater levels of brain atrophy and cognitive impairment.

Participants with MS were administered the Symbol Digit Modalities Test (SDMT), a measure of information processing speed, and the Center for Epidemiological Studies Depression Scale (CES-D), a measure of depressive symptoms. T-scores were calculated for the SDMT and a score of ≤40 was considered impaired compared to norms provided by the test makers. On the CES-D, a score of 16 or above classified a patient as at risk for a diagnosis of depression. Participants' clinical MRI scans dated within a year of administration of the tests were analyzed and the width of the third ventricle was measured. Third ventricle width was measured by hand using FreeSurfer software. The axial slice with the longest segment of the third ventricle was chosen and a vertical line was drawn along the length. We then measured the length of the segment, divided that in half, and drew a horizontal line halfway down and used its length to represent the width. Both inter-rater and intra-rater reliability were calculated using intraclass correlation.

References:

[1]Patten SB, Marrie RA, Carta MG. Depression in multiple sclerosis. Int Rev Psychiatry. 2017 Oct;29(5):463-472. doi: 10.1080/09540261.2017.1322555. Epub 2017 Jul 6. PMID: 28681616.

[2]Feinstein, A., Magalhaes, S., Richard, JF. et al. The link between multiple sclerosis and depression. Nat Rev Neurol 10, 507–517 (2014). https://doi-org.ezproxy.lsuhsc.edu/10.1038/nrneurol.2014.139.

Participant Demographics

n	84
Male	16 (19.0%)
Female	68 (81.0%)
Age	46.71 ± 12.487
Highest Level of Education (years)	14.63 ± 2.823
Baseline Visit Minus Diagnosis Date (months)	129.69 ± 114.670
White	56 (66.7%)
Black or African American	26 (31.0%)
American Indian / Alaskan Native	1 (1.2%)
Hispanic or Latino	1 (1.2%)
Non-Hispanic or Latino	82 (97.7%)

Comparison of Impaired and Non-Impaired Groups

	Impaired	Non-Impaired	*p*
Male	17%	21%	0.584
Female	83%	79%	
Age	45	48	0.230
Highest Level of Education	13.8	15.5	0.005

Correlational Results

Correlation between baseline SDMT score, 3rd ventricle width, and CES-D at Years 1 and 2.

Whole Group

		Baseline SDMT	3rd Ventricle Width
3rd Ventricle Width	Pearson Correlation	-0.614	—
	p	0.000	—
	n	65	—
CES-D (Year 1)	Pearson Correlation	-0.066	-0.288
	p	0.703	0.098
	n	36	34
CES-D (Year 2)	Pearson Correlation	-0.176	-0.336
	p	0.423	0.137
	n	23	21

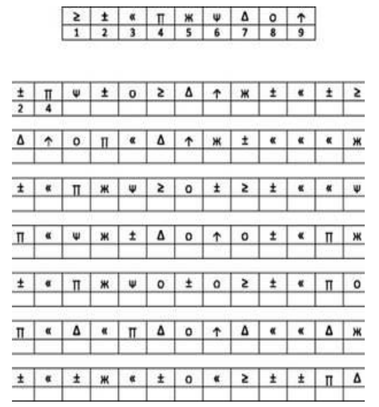
Impaired vs. Non-Impaired

		Baseline SDMT		3rd Ventricle Width	
		Impaired	Non-Impaired	Impaired	Non-Impaired
3rd Ventricle Width	Pearson Correlation	-0.653	-0.407	—	—
	p	0.000	0.011	—	—
	n	27	38	—	—
CES-D (Year 1)	Pearson Correlation	0.199	0.117	-0.510	-0.398
	p	0.495	0.603	0.090	0.067
	n	14	22	12	22
CES-D (Year 2)	Pearson Correlation	-0.022	0.070	-0.921	-0.348
	p	0.973	0.782	0.079	0.171
	n	5	18	4	17

Logistic Regression Results

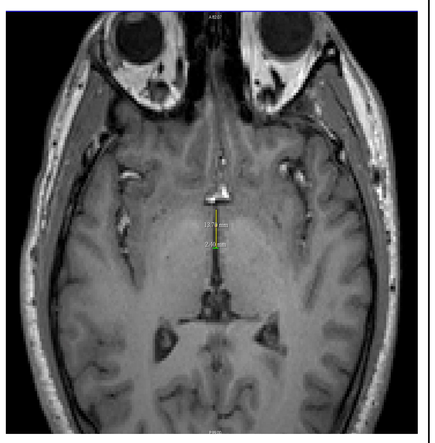
A logistic regression analyzing the effect of baseline SDMT, 3rd ventricle width, and disease duration on levels of depression at Year 1 resulted in a B value of -0.405 and a significance of 0.374.

SDMT



Patients were given 90 seconds to correctly pair as many symbols with their associated digit as they could.

MRI of 3rd Ventricle



Statistical Methods

The statistical analyses were done using SPSS. An ANOVA test was used to compare the demographic data of the impaired and non-impaired groups. The Logistic Regression was done using SPSS. The ICC for inter-rater reliability was 0.972

Conclusions

When analyzing the participant demographics, it was found that the impaired and non-impaired groups did not differ significantly with respect to sex or age, but did differ in terms of education. The impaired group had fewer years of education than the non-impaired group. These results are consistent with the concept of cognitive reserve, which states that more years of advanced education serve as a buffer that allows individuals to tolerate higher levels of damage to the central nervous system due to neurodegenerative processes before becoming symptomatic.

The results of the correlational studies showed that there was no significant relationship between depression at Year 1 and Year 2 and baseline SDMT score or 3rd ventricle width in either the impaired or non-impaired groups. This was supported by the results of the Logistic Regression, which found no significant predicative effect of baseline SDMT score, 3rd ventricle width, or disease duration at baseline on the development of depression at Year 1. Based on these results the hypothesis would be rejected. However, this study was limited by small sample sizes (partially because of the COVID-19 pandemic) and a limited amount of data on the presence of depression at baseline, so a repeat of the experiment with a larger number of patients would be useful in coming to a more definitive conclusion.