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Correlation of MRI findings and cognitive function in multiple sclerosis patients using montreal cognitive assessment test

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Abstract

Background: Magnetic resonance imaging (MRI) has improved the diagnosis and management of patients with multiple sclerosis (MS). Montreal Cognitive Assessment (MoCA) is a brief, sensitive test that has been recommended by National Institute of Neurological Diseases and Stroke and Canadian Stroke Network (NINDS-CSN) as a reliable tool to detect mild cognitive impairments. This study aimed to evaluate the relationship between MoCA test and its sub-items with brain abnormalities in MRI of MS patients.

Methods: Based on MRI scans of 46 MS patients, third ventricle and white matter lesions volumes were measured. Disease duration and expanded disability status scale (EDSS) were recorded in each patient. In addition, cognitive domains of the patients were evaluated by Montreal cognitive assessment (MoCA) test. We analyzed data using t-test or Mann-Whitney U test, Pearson correlation coefficient, and non-parametric Spearman test. Furthermore, multiple linear regression model was applied to evaluate the association between cognitive indices and MRI characteristics.

Results: Among MRI indices, only severity of atrophy showed a significant difference between cognitively impaired and cognitively preserved patients. Third ventricular volume was significantly correlated with total MoCA score (p=0.003, r=-0.42), but none of the juxtacortical or periventricular lesions volume revealed significant relation with total MoCA score. However, using multivariate linear regression after adjustment for educational level and disease duration, there was a significant negative association between juxtacortical lesions volume and total MoCA score as well as naming and attention sub-items. Also, memory score was adversely associated with the third ventricular volume (p=0.03, r=0.31).

Conclusion: Cognitive disturbances detected by MoCA, may be associated with some pathological changes including atrophy, third ventricular volume, and juxtacortical lesion. MoCA, as a brief test, is not correlated with brain lesions volume in MS patients.

Keywords: Multiple Sclerosis, MRI, Cognitive Function, Lesions Volume, MoCA.

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Introduction

Cognitive impairment (CI) is a common neurological manifestation which develops in about half of multiple sclerosis (MS) patients even at early stages of the disease (1). The most neuropsychological impairments in these patients include information processing defect, attention complexity, and also memory loss (2,3). These defects may be even developed severely leading daily

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living activities and even social dysfunction (4). This CI not only can lead to patients' disability but also can adversely affect personal life and quality of life as well as impair psychological health leading high rates of depression and anxiety (5,6). On the other hand, detection CI at early stages can predict disability few years later (7). The cognitive dysfunction can be discovered based on related clinical and imaging evidence. In this context, CI may be evident in brain magnetic resonance imaging (MRI) as regional atrophy and neural lesions with the different locations and volumes that may be capable of predicting further neural worsening (8). MRI can be applied as a screening tool for these defects. Recent findings showed the role of cortical and white matter lesions in the development of CI (9,10). Hence, by developing quantitative brain imaging and neuropsychological testing tools, the quality and intensity of CI can be assessed more accurately. Accordingly, examining the relationship between volumes, the location of brain lesions and atrophy, with different sub-items of the cognition is so useful for the clinician to diagnosing CI in patients with MS and prevents more severity in cognitive performance. Montreal Cognitive Assessment (MoCA) is a brief, sensitive test that has been recommended by National Institute of Neurological Diseases and Stroke and Canadian Stroke Network (NINDS-CSN) as a reliable tool to detect mild cognitive impairments (MCI) (11). Also, in a study by Kaur et al., short version of MoCA showed as a quick screening battery to detect CI in MS patients (12).

However, this is a first study that evaluates MoCA test, as a brief neuropsychological battery in relation to MRI characteristics. We aimed to assess the relationship between MoCA test and evidence of MRI abnormalities in MS patients.

Methods

Subjects

In this cross-sectional survey, 46 consecutive outpatient subjects with MS were recruited. An expert neurologist rule out other mimickers of MS. Inclusion criteria were: clinically definite MS according to the 2010 revisions to the McDonald criteria (13), age 18 to 50 (to avoid age-related dementia) and the presence of brain lesions on MRI.

Exclusion criteria were: contraindication for MRI (pacemakers, metal implants, etc.), history of neurological or psychological problems or use of neuropsychological drugs, treatment with steroid during two months prior interviewing and patients with other brain pathology. The baseline characteristics including demographics, Expanded Disability Status Scale (EDSS) (14), educational level, and disease duration were collected by questionnaire. Also, written informed consent was obtained from all patients and study protocol was approved by institutional ethics committee.

Cognitive assessment

In this study, the Persian version of MoCA test (15) was employed in evaluating cognitive function. This questionnaire can assess more cognitive domains and is composed of more complex skills and is thus more sensitive than the Mini-Mental State Examination (MMSE) to diagnose mild CI. The MoCA assesses some cognitive domains including attention, concentration, executive functions (following the numbers, letters, words and abstract), delayed recalling, language (naming and sentence repetition), visuoconstructional skills (drawing cubic or watch), conceptual thinking, calculations, and orientation. The total possible score is 30 points; a score of 26 or above is considered normal. In those with an educational level lower than 12 years, one unit will be added to their score.

Image Acquisition

A 1.5-T MRI device (Siemens, Avanto, Germany) was used to acquire images on Fluid-attenuated inversion recovery (FLAIR) sequence. All MRI scans were prepared with following metrics: Axial, 2D FLAIR, TR/TE=2500/100, matrix=

20*240, the field of view=220.

Image Analysis

Brain lesions were classified to two regions consists of juxtacortical and periventricular. Juxtacortical lesions are defined as lesions that are in sub-cortex of the brain, and lesions that are close to the ventricle are recognized as periventricular.

An expert neuroradiologist who was unaware of the cognitive test results, obtained quantitative measurements by use of Medical Image Processing Analysis and Visualization (MIPAV) software version 7.0.1 available at http://mipav.cit.nih.gov/

Lesions and third ventricle were outlined semi-automatically. Subsequently, volumes were calculated by the following formula:

Volume=Cross Section Area×Slice thickness.

Also, the severity of cortical atrophy was reported as none, mild, moderate and severe based on the visual scale (16).

Statistical Analysis

Results were expressed as mean (SD) for quantitative variables and by frequency and percentage for categorical variables. Continuous variables were compared using a t-test for normally distributed data and Mann-Whitney U test for non-normal data. The correlation between quantitative variables was examined by the Pearson correlation coefficient or non-parametric Spearman test. Multiple linear regression model was used to investigate the association between cognitive indices and MRI characteristics.

For the statistical analysis, the statistical software SPSS 20 was used. A P-value less than 0.05 was considered statistically significant.

Results

A total of 46 relapsing-remitting (RRMS) subjects were included in the study with the mean±SD age of 32.5 ± 8.21yrs (age range: 19-49yrs), mean±SD educational level 10.8 ± 4.22yrs, and mean±SD disease duration 18.7 ± 10.74 months. Of them, 28.3% (n=13) were male and 71.7% (n=33) were female. The mean±SD EDSS was also 1.0 ± 0.90 (EDSS median: 1.0 and range 0-4.0). Regarding changes in MRI, the mean±SD volume of periventricular lesions was 3875.8 ± 4411.67mm^3, the mean±SD volume of juxtacortical lesions was 2325.7 ± 2341.92mm^3 and the mean±SD volume of the third ventricle was 15468.8±7563.50 mm^3. In the evaluation of the severity of atrophy, 28.3% (n=13) of subjects didn't show this abnormality while mild, moderate and severe atrophy was revealed in 47.8%, 19.6%, and 4.3%, respectively.

The mean±SD total MoCA score was 22.1±4.09 ranged 15-30. Among study individuals, only 12 patients (26.1%) had normal cognitive status (MoCA total score equal or higher than 26). Comparing MS groups with and without CI showed similarity in male gender distribution (21.7% versus 6.5%, p=0.77), as well as in mean age (33.8 ± 8.36 yrs versus 28.7 ± 6.66 yrs, p=0.061). However, those with normal cognitive status had significantly higher educational level (14.0 ± 1.90yrs versus 9.7± 4.25yrs, p=0.002), lower disease duration (11.7±6.75 versus 21.1±10.85 years, p = 0.007), and lower mean EDSS (0.5±0.58 versus 1.2±0.94, p=0.030).

Table 1. MRI findings in MS patients with and without cognitive impairment

MRI finding	Group	Mean	SD	p
Periventricular lesion volume (mm^3)	cognitively impaired	3537.86	3497.98	0.38
	cognitively preserved	4833.18	6446.70	
Juxtacortical lesion volume (mm^3)	cognitively impaired	2646.11	2427.30	0.11
	cognitively preserved	1417.92	1882.90	
Supratentorial lesion volume (mm^3)	cognitively impaired	6183.97	5289.56	0.97
	cognitively preserved	6251.11	7831.56	
Third ventricular volume (mm^3)	cognitively impaired	16720.80	7815.56	0.06
	cognitively preserved	11921.63	5675.06	

There was no difference in lesions volume as well as the third ventricular volume between the patients with and without CI (Table 1).

Also, those with CI had more severe atrophy when compared with those who had normal cognition so in the groups with and without CI, mild atrophy was found in 55.9% and 25%, moderate in 23.5% and 8.3%, and severe in 5.9% and 0.0%, respectively (p=0.007).

Based on the correlation coefficients, there was a relationship between cognitive function and MRI and we showed an adverse association between the third ventricular volume and some cognitive indices (Table 2).

Also, there was a negative association between the volume of juxtacortical lesions and attention score (r=-0.32, p=0.03) (Table 3).

Using multiple linear regression model with the presence of baseline confounders, none of the baseline characteristics including educational level and disease duration as well as none of the cognitive domains was associated with the volume of supratentorial lesions (juxtacortical and periventricular). Similar regression model also showed no associations between baseline characteristics and cognitive domains with the periventricular lesions volume. In this regard, two cognitive domains of naming (beta=-1639.9, 95%CI:-2693.10 to -16.76, p=0.01) and attention (beta=-842.70, 95%CI:-1469.23 to -216.17, p=0.01) were negatively associated with juxtacortical lesions volume. In addition, total MoCA score was adversely related to juxtacortical lesions volume (beta=-284.09, 95% CI:-506.19 to -61.99, p=0.01) adjusted for years of education.

Among years of education and different domains of cognition, only memory was adversely associated with severity of atrophy (beta=-0.22, 95% CI:-0.41 to -0.04, p=0.01). Overall, severity of brain atrophy was negatively associated with total MoCA score (beta=-0.08, 95% CI:-0.16 to -0.01, p=0.01). Among cognitive domain, memory was negatively associated with third ventricular volume (beta = -1908.25, 95% CI:-3585.85 to -230.65, p=0.02).

Discussion

We attempted to assess the relation between cognitive function in MS patients and MRI evidence regarding changes in the brain, third ventricle as well as lesion's volume, using a brief battery. In this study, although there was no difference in volume of lesions between the patients with and without CI, but patients with CI experienced more severe atrophy when compared with subjects who had a normal cognitive state. Moreover, adverse associations between attention score, the frequent complaint, and the volume of juxtacortical lesions were revealed. This is in accordance with the recent study by Yildiz et al. that showed an association between attention difficulties and white matter lesion volume

Table 2. Bivariate correlations between third ventricular volume and some cognitive indices

		MoCA Score	Visuoconstruntional	Naming	Memory	Attention	Language	Abstraction	Orientation
Third Ventricular Volume (mm^3)	r	-0.42	-0.32	-0.27	-0.31	-0.31	-0.01	-0.24	0.005
	p	(0.003)	(0.03)	(0.06)	(0.03)	(0.04)	(0.94)	(0.11)	(0.97)

Table 3. Bivariate correlations between periventricular and juxtacortical lesions volume with some cognitive indices

		MoCA Score	Visuoconstructional	Naming	Memory	Attention	Language	Abstraction	Orientation
Periventricular lesions Volume	r	0.03	-0.05	-0.05	-0.15	0.003	0.26	-0.003	0.11
	p	(0.82)	(0.69)	(0.73)	(0.31)	(0.98)	(0.07)	(0.98)	(0.48)
Juxtacortical lesions Volume	r	-0.25	-0.21	-0.21	-0.31	-0.32	-0.03	-0.04	0.12
	p	(0.08)	(0.16)	(0.16)	(0.03)	(0.03)	(0.79)	(0.75)	(0.42)

(17). Although MS is classically considered a white matter disease, but by pathological and imaging assessment, abnormal changes in gray matter and in brain volume can also be demonstrated in this disorder. Besides, it has been revealed that in MS patients, abnormal changes in both white and gray matters may lead to significant CI while demyelination in white matter alone may be associated with a moderate level of CI. It indicates the more critical role of changes in gray matter in occurring this impairment. On the other hand, the involvement of grey matter in MRI indicates a close relationship between CI and pathological changes in gray matter in MS patients (18). Moreover, many studies have shown that CI is correlated with brain lesion volume, as well as brain atrophy. Various neuroimaging techniques are now employed to identify the increased risk for CI in MS patients (19). However contradictory results in some reports may be dependent to difference in age of the study population, the stage of disease, different MRI protocol, and different cognitive batteries. In a study by Calabrese and colleagues on RRMS patients, 34.3% subjects showed some degree of impairment in cognition. In their study, no difference was fond in T2-hyperintense white matter lesion volumes between MS patients groups with and without CI. But there was a meaningful difference in other MRI indicators including the number and the volume of cortical lesions and volume of grey matter across the two MS groups, as well (20). Assouad et al. study, superimposed neurological relapses was present in 61% of cases. In their observation, multiple periventricular lesions and also severe atrophy resulted in widening of the third ventricle were observed in half of the affected patients with CI compared to healthy controls (21). In our study, we found that third ventricular volume, as well as severity of atrophy, showed significant association with memory score. In another study by Rocca et al., impaired cognition was the main manifestation in 47% of MS subjects that was associated with decreased recruitment of the right dorsolateral prefrontal cortex when compared to MS patients with preserved cognitional ability (22). Furthermore, contrary similar to our study, in Yaldizli et al. study, CI index was correlated with T2- and T1-lesion volume and also with whole brain volume, while the correlation between the severity of CI and other parameters including disease duration and EDSS score was significantly weaker (23).

Our study has some limitations. First, the study sample size was small; second, FLAIR sequence, is not useful for evaluating lesions in the posterior fossa which may play a role in cognitive dysfunction (24); and the third, 2D MRI images have some shortcoming in estimating volumes correctly.

Conclusion

In conclusion, this study showed that some domains of MoCA may be correlated with some pathological changes reflected by atrophy, third ventricular volume, and juxtacortical lesions. However brief cognitive screening tool is not correlated with imaging indices related to lesions volume in RRMS patients.

Acknowledgments

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