Performance on the Rey-Osterrieth complex figure test and the correlation with the magnetic resonance imaging brain lesion volume in multi-infarct versus small vessel disease dementia

Postignuća na Rey-Osterrieth testu složene figure i njihova povezanost sa volumenom ishemijskih lezija mozga vizualizovanih tehnikom magnetne rezonancije kod multi-infarktne demencije u odnosu na demenciju u okviru ishemijske bolesti malih krvnih sudova

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Abstract

Background/Aim. Regarding several cognitive domains, including visuospatial and visuoconstructional abilities, little is known about the differences between vascular dementia (VaD) subtypes, even in the most common subtypes, such as multi-infarct dementia (MID) and subcortical ischemic small vessel disease dementia (SSVD). This paper aimed to identify the differences between the performances on the Rey-Osterrieth Complex Figure (ROCF) test in MID and SSVD and correlate the ROCF scores in both groups with magnetic resonance imaging (MRI) ischemic lesion load. **Methods.** Sixty VaD patients with matching severity of dementia, age, and education were included in this study: 32 with SSVD and 28 with MID according to the NINDS-AIREN (*National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences*) neuroradiological criteria. A quantitative scoring system was performed. ROCF was given to all subjects in three test conditions: copy, immediate recall after 3 minutes, and delayed recall after 45 min. Magnetic resonance imaging (MRI) of the ischemic brain volumes of anterior and posterior lesions, left and right hemispheric lesions, left and right-sided basal ganglia lesions, and total lesion load (TLL) were calculated in both groups. **Results.** The MID group was more impaired than SSVD on ROCF copy ($p = 0.008$), immediate recall ($p = 0.005$) and delayed recall ($p = 0.001$). There were significant correlations between ROCF copy score and the TLL ($p < 0.05$) and posterior brain lesion volume ($p < 0.05$) in the MID group. **Conclusion.** The importance of visuospatial, visuoconstructional deficit and impairment of visual memory is disregarded in VaD subtypes. These impairments are more severe in MID than SSVD and the deficit of ROCF copying in MID patients correlates with posterior and total MRI lesion volume.

Key words:
dementia, vascular; cerebrovascular disorders; neurologic manifestations; neurologic examination; magnetic resonance imaging; memory disorders.

Apstrakt

Uvod/Cilj. U odnosu na kognitivne domene, uključujući i vizuospacijalne i vizuokonstrukcione sposobnosti, do sada su malo opisivane razlike između podtipova vaskualrne demencije (VaD), pa čak i kod najčešćih kao što su multi-infarktna demencija (MID) i demencija u okviru supkortikalne ishemijske bolesti malih krvnih sudova (SSVD). Cilj rada bio je da se utvrdi da li postoji razlika između obolelih od MID i SSVD u odnosu na postignuća na

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Rey-Osterrieth testu složene figure (ROCF), kao i da li postoji povezanost između postignuća na ROCF i volumena ishemijskih lezija na magnetnoj rezonanci (MR) mozga. **Metode.** U studiju je bilo uključeno 60 obolelih od VaD ujednačenih u odnosu na težinu demencije, starosnu strukturu i stepen obrazovanja, i u odnosu na NINDS-AIREN (*National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences*) neuroradiološke kriterijume. Grupa ispitanika je bila podeljena na grupu MID sa 28 bolesnika i grupu SSVD sa 32 bolesnika. Kod svih ispitanika izražen je kvantitativni skor kopiranja ROCF, neposredno prisećanje ROCF nakon 3 minuta i odloženo prisećanje ROCF nakon 45 minuta. Izračuniati su: volumen ishemijskih lezija mozga kod obe ispitivane grupe, volumeni anteriornih i posteriornih lezija, lezija leve i desne hemisfere, lezija bazalnih ganglija sa leve i desne strane i ukupni volumen lezija mozga. **Re-**

zultati. U grupi MID bilo je teže oštećenje nego u grupi SSVD na testu kopiranja ROCF (p = 0,008), neposrednog prisećanja (p = 0,005) i odloženog prisećanja ROCF (p = 0,001). U MID grupi pronađene su značajne povezanosti između kopiranja ROCF i volumena ukupnih (p < 0.05) i posteriornih lezija mozga (p < 0.05) na MR. **Zaključak.** Kod podtipova VaD zanemaren je značaj vizuospacijalnog i vizuokonstrukcionog deficita, kao i oštećenja vizuelnog pamćenja. Ova oštećenja su teža kod MID nego kod SSVD. Postoji povezanost deficita kopiranja ROCF sa volumenom ukupnih i posteriornih lezija na MR kod obolelih od MID.

Ključne reči:
demencija, vaskularna; cerebrovaskularni poremećaji; neurološke manifestacije; neurološko ispitivanje; magnetna rezonanca, snimanje; pamćenje, poremećaji.

Introduction

The association between vascular brain lesions and cognitive deficits has been described over the past decades through the concept of vascular dementia (VaD) and vascular cognitive impairment [1–4].

The heterogeneity of VaD influenced the problem of classification and terminology within the category, in which numerous VaD subtypes are recognized [4–7]. Different etiologies, pathogenesis, and pathomorphological substrates in the VaD subtypes have affected the specificity of their cognitive profiles. The two most common VaD subtypes are large vessel disease dementia, or, as many authors call it, multi-infarct dementia (MID), and subcortical ischemic small vessel disease dementia (SSVD).

MID occurs most commonly as a result of multiple major cortical infarcts, and the impairments of cognitive functions in MID depend on the localization of infarction and include focal neuropsychological symptoms such as alexia, agraphia, acalculia, agnosia, apraxia, visuospatial and visuoconstructive disorders, and impairment of verbal and nonverbal memory.

The most common pathological substrate of SSVD includes subcortical lacunar infarcts and extensive white matter ischemic disease, which manifests as the lacunar state or the Binswanger's disease or their overlap. SSVD's cognitive profile is characterized by impairment of executive functions, decreased information processing speed, impaired attention and working memory.

Visuospatial skills involve the person's skill to identify the object visually, as well as to determine its localization, spatial coordinates, and relationships with other objects. Tests for assessing visuospatial abilities measure the subject's ability for visual discrimination, i.e. identification of the shape, the wholeness, details, understanding the similarities and differences in visual material, the ability to synthesize visual information, and the ability to imagine the object. Constructive praxia

implies the ability to assemble or organize parts into one whole. Impairments in this domain are reflected in free drawing and copy tests. Non-verbal topographic or visual memory is a complex process that relates to receiving, processing, storing, and recalling visual information.

The Rey-Osterrieth Complex Figure (ROCF) [8, 9] is widely used in assessing visuospatial abilities, construction praxia in two dimensions, and non-verbal memory [10], as well as in forming the strategy, planning, and organization. The performance on the ROCF can be assessed by quantitative and qualitative scoring. Successful copying of Rey's figure requires attention and concentration activation, the ability of visuospatial perception for identifying elements of the figure, and visuomotor coordination with the control of the executive system. All of this is associated with the activation of different brain zones, such as the right occipitoparietal lobe, the prefrontal lobe, the superior parietal lobule, and Brodmann's area V5 [11].

Although there are studies that do not report the importance of lateralization, visuospatial and visuoconstructive functions' impairments in stroke are mainly associated with lesions of the right hemisphere. Visuospatial and visuoconstructive deficits have been associated with infarction in the middle cerebral artery circulation, posterior lesions, occipital and parieto-occipital lesions, and bilateral posterior lesions.

All this points to the importance of strategic localization of ischemic lesions in the development of impairments of these cognitive functions, but so far there have been few reports of the differences between the VaD subtypes in relation to the mentioned neuropsychologic functions impairments.

The aim of this study was to examine whether MID and SSVD differed concerning the impairment of visuospatial and visuoconstructive abilities in two dimensions and visual memory using the ROCF test. This study also aimed to determine if there was a correlation between these impairments and the volume of ischemic lesion measured on magnetic resonance imaging (MRI).

Methods

The study included 60 patients aged 50 to 80 years, with probable VaD according to the NINDS-AIREN (National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences) criteria [12], with 8 to 16 years of education. The study was prospective and randomized. The sample of patients with VaD was divided into two groups according to the operationalized NINDS-AIREN neuroradiologic criteria [13] for vascular dementia: MID comprising 28 patients (17 men and 11 women) and SSVD comprising 32 patients (23 men and 9 women). The study included patients with mild and moderate dementia according to the Mini-Mental State Examination Test (MMSE) [14] score 15–25. The study did not include patients with deep paresis or plegia of the dominant hand, visual and hearing impairments, and patients who have aphasia, delirium, outpatients and inpatients treated at the Clinic for Neurology, Clinical Center of Vojvodina in Novi Sad.

The standard procedure for copying the Rey-Osterrieth Complex Figure (ROCF) was applied [8, 9]. Visuospatial and visuoconstructive abilities in two dimensions were evaluated using the ROCF copy, immediate recall after 3 minutes, using the ROCF immediate recall, and delayed recall after 45 minutes, using the ROCF delayed recall. All 18 ROCF elements in all three attempts to draw ROCF were scored as follows: 2 points for correct and well-placed figure; 1 point for correct and poorly placed figure; 1 point for deformed or incomplete figure, or recognizable and well placed; 0.5 points for deformed or incomplete, or recognizable and poorly placed figure; 0 points for missing or unrecognizable figure. The maximum score was 36. Lower scores indicated a lower performance. To evaluate the accuracy of the elements of the figure, Taylor descriptive criteria were used [15].

Visualization of cerebral ischemic lesions was done with the Siemens Avanto II apparatus (Erlangen, Germany), with the magnitude of the magnetic field of 1.5 Tesla, and the 3T Trio-Team in the interval of up to 3 months from the date of the neuropsychological testing. The study excluded patients who were in the acute phase of the stroke.
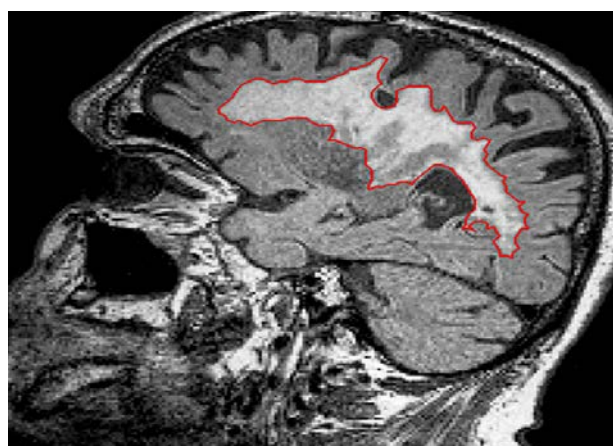
For determining the volume of ischemic lesions, the following protocol was used: FLAIR (Fluid attenuation inversion recovery) sequence in the sagittal plane, slice thickness of 1 mm; between sequences 144 and 191, 1 mm thick slices were used, depending on the volume of the cranium; diffusion sequences (B = 0; 500; 1000) in the transversal plane with calculated ADC map (apparent diffusion coefficients), 5 mm thick, in order to exclude the presence of acute infarction.

Neuroradiological criteria and volume calculation were made by a neuroradiologist who was ignorant of the information on the neurological status or neuropsychological profile of the patient.

Calculating the lesion volume on MRI slices was done by a semi-automated method, using the non-commercial software program MIPAV (Medical Image Processing Analysis and Visualization) [16]. The MIPAV program was used to analyze each individual FLAIR sagittal MRI slice in the DICOM (Digital Imaging and Communications in Medicine) format.

The MIPAV is designed to automatically isolate the ischemic area from the surrounding, intact parenchyma, based on the difference in the signals of the changed and unchanged brain parenchyma. This is made possible by using the FLAIR (Fluid-attenuated inversion recovery) MRI sequence that optimally displays changed parenchyma in the form of a high signal (ischemia, gliosis, myelin destruction) and preserved parenchyma, which has an intermediary signal. Figure 1 shows an example of mapping ischemic parenchyma in a patient with leukoaraiosis.

Fig. 1 – Mapping ischemic parenchyma in a patient with leukoaraiosis.

The volume of ischemic lesions was calculated by multiplying the surface of the ischemic area. The volume was automatically calculated with the MIPAV program using the 1 mm MRI slices with the obtained volume of the ischemic lesion in mm^3. By dividing the product by 1,000, the volume of the lesion in milliliters was obtained. For both study groups, the following parameters were calculated: the volume of right-sided lesions (MRI right), the volume of left-sided lesions (MRI left), the volume of anterior or prerolandic lesions (MRI anterior), the volume of posterior or postrolandic lesions (MRI posterior), the volume of basal ganglia on the right (MRI BG right) and the volume of basal ganglia on the left (MRI BG left).

The research was conducted in accordance with the Ethical Principles of Medical Research Involving Human Subjects – the World Medical Association Declaration of Helsinki and with the consent of the Ethics Committee of the Medical Faculty of the University of Novi Sad and the Ethics Committee of the Clinical Center of Vojvodina.

As part of the descriptive statistics, data were presented in the form of arithmetic mean, standard deviation, median, and range. At the level of inferential statistics, the significance of the difference between the investigated groups was tested with the Student *t*-test. In the case of disturbed normality of distribution, Mann-Whitney *U*-test

was used to determine the differences between the groups. The correlation between the tested parameters (performance on the ROCF and volumetric measures of brain damage) was determined by Spearman's rank correlation coefficient since the distribution of the volume variables significantly deviated from the normal distribution. Statistical data were processed using the statistical software package SPSS (SPSS 17.00 for Windows).

Results

There was a statistically significant difference in all three subtests of the ROCF test (copy, immediate recall, and delayed recall) between MID and SSVD patients (Table 1). Additionally, the SSVD group had a statistically significantly higher average ROCF score in all three subtests than the MID group.

Regarding the descriptive parameters of brain injury volume on MRI (Table 2), there was a higher average volume of the ischemic lesion in the right cerebral hemisphere compared to the left one in MID patients and posterior compared to anterior parts. On average, SSVD patients had a higher volume of lesions in the right cerebral hemisphere compared to the left one, and anterior compared to posterior parts. On average, SSVD patients had the smallest lesion volumes in the left-sided basal ganglia.

There was a statistically significant moderate negative correlation between MRI total brain lesion volume with ROCF copy score (-0.484) and MRI volume of posterior lesions with ROCF copy score (-0.455) in MID patients (Table 3). No other correlations in MID patients were statistically significant. In SSVD patients, there was a statistically significant moderate positive correlation between MRI total brain lesion volume with ROCF immediate recall score (0.490) and MRI posterior lesion volume with ROCF immediate recall score (0.424) (Table 4). No other correlations in SSVD patients were statistically significant.

Table 1

Mean score differences on the Rey-Osterrieth Complex Figure (ROCF) test between patients with multi-infarct dementia (MID) and subcortical small vessel disease dementia (SSVD)

Test recall	MID (n = 28)	SSVD (n = 32)	p
	mean ± SD	mean ± SD	
ROCF copy*	8.27 ± 7.60	13.31 ± 6.69	0.008
ROCF immediate recall[†]	2.61 ± 3.10	4.59 ± 3.00	0.005
ROCF delayed recall*	1.95 ± 1.82	4.30 ± 3.07	0.001

SD – standard deviation; *Student's _t_-test; [†]Mann-Whitney _U_-test.

Table 2

Descriptive parameters of magnetic resonance imaging (MRI) ischemic brain injury volume in patients with multi-infarct dementia (MID) and subcortical small vessel disease dementia (SSVD)

Parameter	MID (n = 24)			SSVD (n = 28)		
	range	median	mean ± SD	range	median	mean ± SD
MRI total	1.3–146.1	53.0	59.8 ± 43.3	0.3–42669.0	17.0	3948.6 ± 9271.9
MRI anterior	0.2–121.7	21.7	26.0 ± 30.1	0.6–30247.0	66.0	2758.0 ± 6672.0
MRI posterior	0.0–98.7	24.7	28.6 ± 28.3	0.0–17282.0	496.5	2685.5 ± 4116.8
MRI left	0.0–141.2	13.5	25.8 ± 35.9	0.0–13989.0	1407.5	3050.5 ± 3914.8
MRI right	0.0–145.6	22.4	33.6 ± 42.1	0.0–32610.0	656.0	3360.6 ± 6472.4
MRI BG left	0.0–313.0	0.0	13.8 ± 63.8	0.0–1784.0	1.0	214.1 ± 399.6
MRI BG right	0.0–1.3	0.0	0.1 ± 0.3	0.0–4353.0	1.4	297.5 ± 884.6

BG – basal ganglia; SD – standard deviation.

Table 3

Spearman's rank correlation coefficient between the Rey-Osterreith Complex Figure (ROCF) score and magnetic resonance imaging (MRI) volumetric brain lesions in patients with multi-infarct dementia (MID)

| MRI	ROCF copy	ROCF immediate recall	ROCF delayed recall
MRI total	-0.484*	-0.245	-0.228
MRI anterior	-0.198	0.007	0.088
MRI posterior	-0.455*	-0.387	-0.262
MRI left	-0.091	-0.188	-0.305
MRI right	-0.378	-0.140	-0.027
MRI BG left	-0.131	-0.058	0.158
MRI BG right	-0.117	-0.005	0.033

BG – basal ganglia; *$p < 0.05$.

Table 4

Spearman's rank correlation coefficient between the Rey-Osterreith Complex Figure (ROCF) score and magnetic resonance imaging (MRI) volumetric brain lesions in patients with subcortical small vessel disease dementia (SSVD)

MRI	ROCF copy	ROCF immediate recall	ROCF delayed recall
MRI total	-0.005	0.490[†]	0.298
MRI anterior	0.006	0.283	0.313
MRI posterior	0.054	0.424*	0.354
MRI left	0.123	0.198	0.205
MRI right	-0.012	0.294	0.132
MRI BG left	0.235	0.092	0.140
MRI BG right	0.177	0.275	0.048

BG – basal ganglia; *$p < 0.05$; [†]$p < 0.01$.
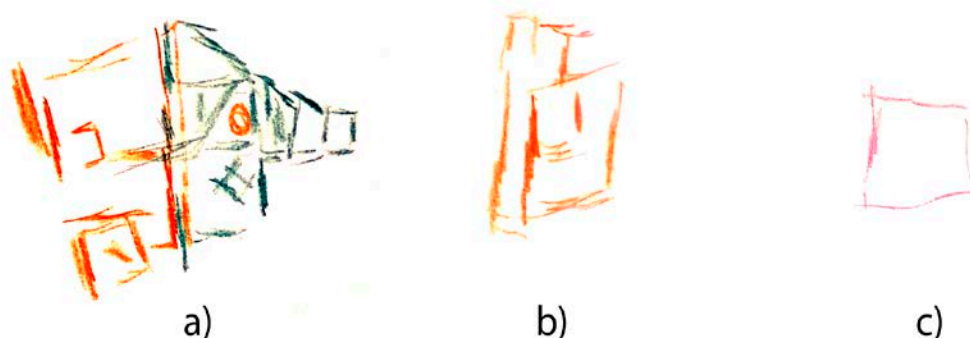
Fig. 2 – An example of a copy (a), immediate recall (b), and delayed recall (c) of Rey-Osterreith Complex Figure (ROCF) in subcortical ischaemic small vessel disaese dementia (SSVD) patient

Figure 2 represents an example of severe impairment in the visuospatial domain, the deficit of visuoconstructional praxia with perseverations, as well as the deficit of immediate and delayed recall ROCF in patients with SSVD.

Discussion

The aim of this study was to compare whether there were differences in the performance on the ROCF test between patients with MID and those with SSVD, matched for gender, age structure, education, and severity of dementia. The study also aimed to assess whether there was a correlation between ROCF performance and the volume of brain ischemic lesions.

The ROCF test is recommended for assessing visuospatial abilities as a part of the 60-minute protocol in examining cognitive functions in vascular cognitive impairment [17, 18].

Our results confirmed that patients with VaD had deficits in visuospatial and visuoconstructive abilities and visual memory [19].

Our data showed that both the MID and SVDD groups had low scores on the ROCF copy, which means that both groups had problems with visual perception, organization, assembling the whole, and data processing. However, since the scores on immediate and delayed recall were low as well, it indicated a problem with coding and storing visual information.

Although vascular dementia is the second most common among dementias, the results of neuropsychological studies are not unambiguous in terms of specifying a clear neuropsychological profile associated with vascular brain damage [19]. Considering that the differences in the deficits of numerous cognitive functions [20] have not yet been clearly defined between VaD subtypes, the characteristics of the visuospatial impairment are not sufficiently defined either, nor is the deficit of constructional praxis in VaD subtypes.

The heterogeneity of VaD [21, 22], multiple classifications, and diagnostic criteria influence interpreting the results of neuropsychological studies in VaD. However, it was observed that between VaD subtypes, executive functions were more frequently impaired in small vessel dementia compared to large vessel and mixed dementia and that visuospatial and language deficits were more commonly expressed in large vessel dementia (37.1% versus 15.5%) [20].

Our study indicated that patients with MID have more severe impairment of visuospatial and visuoconstructive abilities, but also a more severe deficit of visual memory, compared to those with SSVD.

The lesion volumetry in the MID group on MRI showed a higher lesion volume in the right cerebral hemisphere than in the left, as well as in the posterior regions compared to the anterior ones. Even though the volume threshold was not the subject of the research in this study, patients with very small lesion volumes were also analyzed. This can indirectly confirm the results of earlier studies [23, 24], which in the

context of association between cognition and imaging parameters in VaD, emphasize greater importance of localization than the volume of ischemic lesions. Here, the strategic localizations include the dominant angular gyrus, the territory of the anterior cerebral artery and posterior cerebral artery, the territory of the upper-middle cerebral artery, left anterior corona radiata artery, basal ganglia, bilateral medial thalamus, dominant nucleus caudatus, anterior capsula interna, hippocampus, amygdala, and basal forebrain.

However, some imaging studies also showed contradictory results in the correlation between the infarct location and dementia [24, 25]. The stated result of our study may indirectly indicate the importance of other parameters, such as the total number of lesions, lesion size, and bilaterality of infarction.

The association between the volume of total and posterior ischemic lesions and performance on the ROCF copying test was found in the MID group. However, in all other investigated domains in this group, as well as in SSVD, no statistically significant negative correlation was found between the performance on the ROCF and volumetric measures. A possible reason for the absence of the correlations in the present study is the insufficient sensitivity of standard MRI techniques since studies using advanced neuroimaging techniques have shown significant correlations with cognitive impairment in VaD, especially in SSVD.

In agreement with earlier studies [26, 27], our results found an association between cognitive impairment and the volume of ischemic lesions. However, it should be taken into account that the volume of functional loss may be more important because it involves the effect of deafferentation of the cortex.

The association between visuospatial and visuoconstructive deficits with the right hemispheric infarction and posterior lesions [28] was confirmed, but our study also anticipated the importance of MRI posterior ischemic volumes. Lower performance in the MID group on the ROCF copy was associated with MRI posterior volumes and the total lesion load, indicating the association between diffuse lesions and the visuospatial and visuoconstructive deficits in MID.

The low ROCF performance in SSVD in our study is in accordance with the published data that have shown that visuoconstructive deficits occur in subcortical white matter lesions, as well as in diffuse brain lesions and small infarctions [29, 30]. Although it was not included in our study, the qualitative analysis is important in assessing the copying, immediate, or delayed recall of ROCF. Nevertheless, indicative low ROCF scores in SSVD, as our results present, are also important and are most likely a part of the dysexecutive syndrome, which is the leading deficit in SSVD. It may occur as a feature of interruption of the frontal–subcortical circles, within diffuse changes of the white matter and lacunae with a predilection for subcortical frontal regions.

A moderate positive correlation was found between the total lesion load and ROCF immediate recall in the SSVD group, as well as between the posterior lesion volume and ROCF immediate recall. This result could generally reduce the significance of the ischemic lesions' volume on MRI in terms of visual memory deficits in patients with SSVD.

Study limitations encompass insufficient sensitivity of volumetric measurements with a standard MRI technique and lack of CSF and imaging biomarkers of amyloid pathology. Therefore, patients with mixed pathology could not have been excluded.

Conclusion

In patients suffering from multi-infarct dementia of mild to moderate severity, there is a more severe impairment of visuospatial and visuoconstructive abilities in two dimensions, as well as a more severe impairment of immediate and delayed visual memory, compared to patients with mild to moderate subcortical ischemic small vessel disease dementia. In patients with multi-infarct dementia, there is a correlation between lower ROCF copy scores with a higher total lesion load and a larger volume of posterior lesions.

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