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A comparison of cognitive performances between neuromyelitis optica spectrum disorder and multiple sclerosis patients in Indian context

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Abstract

Background: To compare the frequency and pattern of cognitive impairment in neuromyelitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS) patients.

Results: Twenty NMOSD and forty MS patients were included. Clinical and detailed neuropsychological assessment was done using frontal assessment battery and Kolkata cognitive battery supplemented with additional standard tests for different domains of cognitive functions. Domain wise tests were performed and compared. 15/20 (75%) NMOSD and 32/40 (80%) MS patients had cognitive impairment ($p = 0.65$). Executive function, verbal fluency, information processing speed, visuo-constructional ability, attention, complex calculation, and memory were more commonly involved in NMOSD in decreasing order. Compared to MS, the pattern was similar except that verbal fluency was more impaired in NMOSD. Expanded Disability Status scale (EDSS) correlated with cognitive involvement in NMOSD ($p = 0.02$) as against MS.

Conclusions: Executive function, verbal fluencies, and information processing speed were more affected compared to visual and verbal memory in NMOSD patients. The pattern of cognitive performance was similar in the MS group, even though clinical and radiological characteristics and pathophysiology is different, suggesting similar brain involvement.

Keywords: Neuromyelitis optica spectrum disorders, Multiple sclerosis, Cognitive impairment

Background

Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory and demyelinating condition of the central nervous system (CNS) characterized by optic neuritis and longitudinally extensive transverse myelitis. Currently, brain involvement in NMOSD is well recognized, and attacks on the brain may even occur as the first manifestation of NMOSD [1, 2]. NMOSD is caused by antibody (IgG)-mediated attack against Aquaporin 4

(AQP4), which is a bidirectional water channel protein on the foot process of astrocytes present all over CNS. This further sets up a cascade of reactions ultimately altering the synaptic plasticity of neurons. Cognitive impairment is considered to be an attack independent progressive symptom in NMOSD patients, presumably involving a similar phenomenon [3].

Cognitive impairment (CI) in NMOSD as seen in the contemporary studies is present in 30–70% of patients, predominantly involving alteration in attention, language, memory, processing speed, and executive function [3].

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In multiple sclerosis (MS), which is also an inflammatory demyelinating disorder of CNS, CI has been extensively studied and found to be present in 45–65% of the patients during the course of the disease [4]. The cognitive dysfunction in MS is usually subtle early in the course of the disease, although dementia has been observed in 20–30% of the severely impaired patients. The pattern of involvement is predominantly subcortical. In general, the cognitive domains involved are complex attention, information processing speed, verbal and visuo-spatial memory, and executive function; whereas language, semantic memory, and attention span are rarely involved.

There have been only a few studies till now documenting CI in NMOSD patients. Although no significant differences in the frequency and pattern of cognitive performance have been reported between NMOSD and MS patients [5–7], these results should be interpreted with caution due to the small sample size and variation in the test cut-offs considered indicative of CI.

Thus, in this study, we have compared the cognitive profile of NMOSD and MS patients to see if and how they differ. Moreover, we have looked for any association between the demographic factors, clinical disability, and MRI lesion load with the cognitive performance in each group.

Methods

A total of 20 NMOSD and 40 MS patients were recruited in the Department of Neurology, Bangur Institute of Neurosciences, Kolkata for one and a half year (March 2018–October 2019) for a cross-sectional study. MS was diagnosed by Revised McDonald's Criteria 2010 [8], and NMOSD was diagnosed by International Panel for NMO Diagnosis (IPND) criteria 2015 [9]. All patients who fulfilled the criteria and gave proper consent were included in the study after the acute phase was treated (at least 1 month and afterwards were in remission). The exclusion criteria were acute relapses of MS or NMOSD, comorbid neurological diseases other than NMOSD or MS, a history of psychiatric illness including depression, and alcohol and substance abuse. None of our patients had severe visual or physical disability, particularly of the dominant hand so as to restrict their performance of the cognitive tests. The parameters studied were current age, gender, educational level, disease duration, number of relapses, and disability which was measured by the Expanded Disability Status Scale (EDSS) [10], Oligoclonal band (OCB) in cerebrospinal fluid (CSF), and AQP4 positivity in serum (by cell based assay). This study was approved by the institutional Ethical Committee. Informed consent was obtained from all patients.

Neuropsychological assessment

The assessment was performed by trained neurologist under the guidance of psychologist, using frontal assessment battery (FAB) [11] and Kolkata cognitive battery (KCB) [12] supplemented with additional standard tests for different domains of cognitive functions. Attention was assessed using digit span forward, digit span backward, "A vigil" test, serial subtraction (e.g., 100-7, 20-3) as scored in Montreal cognitive assessment (MOCA) [13] and extended version of KCB. Information processing speed (IPS) was assessed using timed 100-7, timed trail A and timed trail B tests. IPS depends on time. For every unique population, there must be different normal variance of timing. To overcome this limitation, here we made our own time frame for IPS including control population and compared it with our patients. Language was assessed under spontaneous speech; comprehension namely single word, simple comprehension (asking to hold the pen or paper), complex comprehension (asking to hold pen and then the paper), and syntactic comprehension (using passive voice sentences); and fluency was assessed under category fluency (telling as many animal names in 1 min, fruit names in 1 min as possible, cut-off taken as 7), letter or lexical fluency asking to say as many words in 1 min as possible excluding proper nouns starting with a particular alphabet scoring as in FAB; repetition of single words, like eccentricity, Hippopotamus, unintelligible, statistician, used in patient's vernacular language scoring as in Addenbrooke's cognitive examination (ACE III) [14] and string of words, like no ifs, ands or buts, used in patient's vernacular language scoring as in MMSE; reading with or without comprehension seen by reading a passage and complex, silent, difficult words; writing assessed by asking to write a meaningful sentence; naming assessed by real object naming. Memory was assessed under verbal memory using word list memory task indicating immediate recall, delayed word list memory task, delayed recognition memory task, autobiographical and semantic memory, and scored as in KCB. Visual memory was assessed using brief visual memory test revised [15]. Visuo-constructional skill was assessed using 2D and 3D geometric figure drawing. Calculation was assessed as simple (single digit) and complex (double digits). Visuo-perceptual ability was assessed using dot counting and fragmented letters and scored as in ACE III. Praxis was assessed by asking to pantomime verbal command, imitate the examiner, pantomime seeing picture of the tool, pantomime using the actual tool, showing a picture, and asking what instrument was needed to push the nail further, which object would you use to keep your teeth clean and how would you do so. Gnosis was tested by identification of pictures of famous personalities, tools and objects, and their functions.

Executive function

Executive function was assessed using FAB, as well as individual subdomains as follows: abstraction was assessed using proverb interpretation and similarities; mental flexibility using trail making A and B (a shorter version as used in MOCA), go-no-go test; verbal fluency or lexical fluency as a part of FAB; judgement by asking real-life scenario questions; set shifting ability by Luria test (pattern as well as motor palm fist edge test); and planning by clock face drawing test scored as in ACE III.

Magnetic resonance imaging (MRI)

Radiological parameters were assessed by MRI 3 Tesla using Siemens magnetom verio 3T machine. The sequences studied were T1 (TR < 500, TE 15-20), T2 (TR 4000, TE 100), (FLAIR) fluid attenuated inversion recovery (TR 8000, TE 70-80, TI 2500), diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) mapping, short TI inversion recovery (STIR), gradient echo (GRE) of the brain, orbits, and spinal cord wherever relevant with or without gadolinium contrast. The parameters studied were number of lesions grouped as ≤ 4 , > 4 – ≤ 9 , > 9 , lesion location, and contrast enhancement.

The cognitive performance was estimated in the form of FAB score and number of cognitive domains involved and number of executive subdomains involved. Its association with demographic parameters, such as age, sex, and formal education; and clinical parameters, such as disease duration, number of relapses, EDSS, OCB positivity (for MS), and MRI lesion load, was calculated.

Statistical analysis

The data has been analyzed using SPSS (version 25.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data have been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables.

Two-sample *t* tests was used for a difference in mean involved independent samples or unpaired samples. Paired *t* tests were a form of blocking and had greater power than unpaired tests.

One-way analysis of variance (one-way ANOVA) was a technique used to compare means of three or more samples for numerical data (using the *F* distribution).

A chi-squared test (χ^2 test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, chi-squared test often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by chi-square test or Fischer's exact test, as appropriate.

Correlation was calculated by Pearson correlation analysis. The Pearson product-moment correlation

coefficient was a measure of the linear dependence between two variables *X* and *Y*. Explicit expressions that can be used to carry out various *t* tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a *t* distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a *t* value is determined, a *p* value can be found using a table of values from Student's *t* distribution. If the calculated *p* value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis. *p* value ≤ 0.05 was considered for statistically significant.

Results

The results have been summarized in Tables 1, 2, 3, 4, and 5.

There was no significant difference of mean age and gender ratio between two groups, although mean age MS patients and proportion of female subjects in NMOSD were higher. The MS patients had a higher education level ($p = 0.005$), a longer duration of disease ($p < 0.0001$), and a greater number of relapses ($p < 0.0001$). Moreover, MS patients had a higher EDSS compared to NMOSD patients ($p = 0.0091$) (Table 1).

The MS patients had a higher lesion load and brain involvement including supra- and infra-tentorial involvement. Larger number (60%) of the NMOSD patients had gadolinium enhancement on MRI suggestive of active lesions compared to MS patients (45%). OCB positivity among MS patients was 42.1% and AQP4 positivity among NMOSD group was 90% (Table 2).

Cognitive impairment was observed in equal proportion and in very large number of subjects. The primary domains involved in MS patients were executive function (95%), IPS (75%), and attention (70%). Praxis, gnosis, and visuo-perceptual ability (0 %) were not affected. In NMOSD group, the predominant domains involved were executive function (80%) and IPS (70%). Except for executive function which was more frequently affected in MS, the rest of the cognitive involvement did not yield any statistically significant difference between MS and NMOSD (Table 3).

Most affected executive subdomains involved in MS patients were mental flexibility (75%), set shifting (70%), and abstraction (55%) and verbal fluency (30%). The predominant executive subdomain involved in NMOSD patients was verbal fluency (80%), mental flexibility (70%), abstraction (60%), and set shifting (50%). The cognitive dysfunction profile between MS and NMOSD patients was found to be mostly similar except verbal fluency,

Table 1 General characteristics of NMOSD and MS patients

Characteristics	MS (n = 40)	NMOSD (n = 20)	P value
Age (mean ± SD)	34 ± 7.34	28.3 ± 11.21	0.0953
Female:male	1.5:1	2.3:1	0.5197
Formal education in years (mean ± SD)	15.52 ± 5.32	11.40 ± 13.31	0.0057
Duration in years (mean ± SD)	7 ± .14	2.12 ± 2.22	< 0.0001*
No. of relapses (mean ± SD)	2.75 ± 1.06	1.5 ± 1.68	< 0.0001*
EDSS	3.23 ± 1.94	2.65 ± 2.43	0.0091*

*p value ≤ 0.05 is considered significant

and visuo-perceptual ability was involved more in NMOSD patients. No statistically significant difference was noted in the executive profile between the two groups except for verbal fluency and judgement, while verbal fluency dysfunction was noted more frequently in NMOSD, and impairment in judgement was noted more in MS (Table 4).

It was found that in MS patients, MRI lesion load (negative), and OCB positivity had statistically significant correlation with FAB scores. Moreover, age (positive), formal education (negative), and OCB positivity had statistically significant association with number of cognitive domain involvement. Similarly, formal education and OCB positivity had significant association with number of executive subdomain involvement. Thus, in MS patients, CI was more commonly prevalent in older patients with lesser formal education and larger MRI lesion load and OCB positivity.

In NMOSD patients, the FAB score and number of cognitive domains involved have statistically significant association with female gender and EDSS; whereas number of executive subdomains did not have any statistically significant association with other characteristics. Due to inadequate patients in the AQP4 negative arm, correlation of cognitive decline with AQP4 positivity could not be obtained. Thus, NMOSD patients who are females having higher disability scores seem to have higher cognitive dysfunction (Table 5).

Discussion

In our study, we found that MS patients were mostly middle aged with female preponderance, having higher formal educational status, longer duration of disease, and mild disability. MRI showed a higher lesion load with predominant supra-tentorial burden, highest being in the periventricular location. Cognitive impairment was present in a significant proportion of patients;

Table 2 MRI characteristics of NMOSD and MS patients

Characteristics	MS (n = 40)	NMOSD (n = 20)	P value
MRI findings			
No. of lesions			< 0.0001*
≤ 4	2(5%)	16(80%)	
4–9	6(15%)	4(20%)	
≥ 9	32(80%)	0	
Lesion location			
Periventricular	40(100%)	4(20%)	< 0.0001*
Juxta cortical	22(55%)	4(20%)	0.0283*
Corpus callosal	28(70%)	2(10%)	< 0.0001*
Brain stem	18(45%)	0	0.0008*
Cerebellum	10(25%)	0	0.0096*
Area postrema	0	0	
Diencephalon	0	0	
Gadolinium enhancement	18(45%)	12(60%)	0.3138
OCB	16(42.1%)	2(10%)	0.002*
Anti-aquaporin 4	0	18(90%)	< 0.0001*

*p value ≤ 0.05 is considered significant

Table 3 Cognitive performance of NMOsD vs MS patients

Characteristic	MS	NMOsD	P value
FAB	14.35 ± .24	14.7 ± 2.56	0.7397
Cognitive impairment (CI)	32 (80%)	15 (75%)	0.65
Predominant domain involved	Executive	Executive/ IPS	
No. of domains involved	3.85 ± 1.85	3.5 ± 2.21	0.6579
Attention	28(70%)	10(50%)	0.3073
IPS	30(75%)	14(70%)	0.2563
Language	8(20%)	2(10%)	0.1793
Memory	10(25%)	8(40%)	0.2070
Calculation	22(55%)	10(50%)	0.0630
Visuo-construction	18(47.4%)	10(62.5%)	0.5929
Visuo-perceptual	0	2(11.1%)	0.0572
Praxis	0	0	
Gnosis	0	0	
Executive	38(95%)	14(70%)	0.006*

*p value ≤ 0.05 is considered significant

No statistically significant difference was noted in cognitive performance between the two groups except for executive dysfunction

executive function (mental flexibility), IPS, and complex attention were maximally affected.

The NMOsD patients in our study had a younger age, female majority, lower formal educational status, shorter duration of disease, less frequent relapses, and mild disability. MRI indicated lower lesion load but more active lesions. Cognitive impairment was present in a noticeable number of patients with predominant affection of executive function (verbal fluency, IPS, visuo-construction, attention, and calculation).

The trends of cognitive involvement in our study of MS patients were similar to previous studies by Rao et al. [4], Amato et al. [16], Rima et al. [17], and the COGIMUS group [18], but the percentage of involvement noted in the present study was quite high. This

Table 4 Executive profile of NMOsD vs MS patients

Characteristic	MS	NMOsD	P value
Predominant subdomain	Mental flexibility	Verbal fluency	
No. of subdomains involved	2.5 ± 1.13	2.9 ± 1.74	0.25
Abstraction	22(55%)	12(60%)	0.8543
Mental flexibility	30(75%)	14(70%)	0.7008
Verbal fluency	12(30%)	16(80%)	< 0.0001*
Judgement	2(5%)	0	0.04392*
Set shifting	28(70%)	10(50%)	0.3073
Planning	8(21.1%)	6(37.5%)	0.3470

*p value ≤ 0.05 is considered significant

No statistically significant difference was noted in the executive profile between the two groups except for verbal fluency and judgement

may be because of comprehensive assessment of patients and identification of even subtle cognitive impairment in various domains in the present study.

The educational status of the present study comprised of a mean of 15.52 years of formal education, graduates being the predominant group of patients. In the other studies, the years of formal education included 12.4 years in COGIMUS study [18], 11.44 in Amato et al. [16], and 15.9 years in Kaur et al. [19] study, while graduates were the predominant group in Rima et al. [17] group.

The mean duration from onset was 7 years and mean EDSS was 3.23 as compared to 14.2 years and 4.1 in Rao et al.'s study [4], 1.58 years and 1.98 in Amato et al. [16], 5 years and 1.8 in COGIMUS study [18], and 8.47 in Kaur et al. [19] and EDSS, and 3.15 in Rima et al. [17] group.

Negative correlation was found between FAB, age, and number of lesions on MRI which was statistically significant, probably because with increasing age and disease duration, there is cumulative accumulation of more lesions causing more axonal degeneration and brain atrophy.

Disease duration did not correlate with cognitive decline in a statistically significant manner in our present study as opposed to previous studies by Rao et al. and Amato et al. [4, 16]. Disease duration have been considered as a predominant factor in the development of cognitive impairment in CNS demyelinating disorders, but it may be influenced by other factors also. The plausible explanations would include the theory of cognitive reserve, severity of the disease itself, hemispheres involved in the disease process, locations of the lesions and impairment of the functions subserved by them, and involvement of white matter alone or associated grey matter affection. All the above-mentioned factors can affect the course of cognitive functions independent of the disease duration [20].

The duration of the disease is not predictive of whether a patient will have cognitive impairment. Although cognitive impairment tends to progress over time in MS, it can and does appear at any time during the course of the illness, even as the first symptom. Conversely, patients who have had MS for many years may be completely free of cognitive deficits. However, it is rare for cognitive changes to disappear completely once they have appeared.

Total lesion load correlated with cognitive impairment is similar to our study, but we could not find significant correlation between EDSS and cognitive impairment as with some previous studies like that of Rao et al. [4], probably because EDSS is more so a marker of physical disability, and the substrate for the same is different from that of cognitive function.

Table 5 Association between demographic, clinical, and MRI characteristics and cognitive dysfunction in MS and NMOSD patients

Characteristic	MS (FAB)		NMOSD (FAB)		MS (no. of cognitive domains involved)		NMOSD (no. of cognitive domains involved)		MS (no. of executive subdomains involved)		NMOSD (no. of executive subdomains involved)	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Age	-.315	.048	-.309	.185	.446	.004	.197	.404	.309	.053	.238	.311
Gender (female)	NA	.339	NA	.009	NA	.068	NA	.009	NA	.086	NA	.531
Formal education in years	.301	.051	.385	.093	-.358	.023	-.263	.261	-0.632	<.0001	-.283	.227
Disease duration	-.021	.898	.284	.224	.158	.332	-.029	.902	.219	.175	.044	.854
No. of relapses	.146	.368	.233	.323	-.125	.443	-.060	.802	-.279	.175	-.114	.633
EDSS	.101	.534	-.704	.001	-.097	.550	.514	.020	-.134	.410	.240	.308
MRI lesion load	-.386	.014	-.040	.867	.268	.094	.232	.325	.292	.068	.176	.457
OCB positivity	NA	.012	NA	NA	NA	<.0001	NA	NA	NA	<.0001	NA	NA

The associations were calculated by Pearson's correlation coefficient and chi square tests. *r* value is correlation coefficient. *p* value ≤ 0.05 considered statistically significant

Physical disability is likewise not predictive of cognitive impairment, and cognitive changes can occur even when physical symptoms are absent or very mild. Moreover, patients with substantial physical disability may be free of cognitive changes. It does appear, however, that if a patient has had MS for a long time and is severely disabled physically, the probability of cognitive impairment is increased to some extent.

The OCB positivity had positive correlation with FAB, cognitive, and executive impairment in MS patients which was statistically significant. The reason for the same can be higher disease activity indicated by intrathecal immunoglobulin synthesis.

The cognitive profile of NMOSD patients was similar to the previous international studies by Blanc et al. (2008) [5], Blanc et al. (2012) [21], Saji et al. [6], and He et al. [22], although executive involvement was much more in our study. The presence of brain lesions in MRI was 50% which was more than previous studies probably implying some association between the same and cognitive dysfunction. Also, in this study, definition of cognitive dysfunction was not the same as the above-mentioned studies since we took into account even subtle changes in the cognitive domains. Moreover, the ethnicity and educational status as well as age of presentation may have influenced the difference. In our study, the domains of verbal fluency and visuo-perceptual ability were more impaired in NMOSD patients compared to MS patients, whereas executive dysfunction was the most commonly affected domain in both the groups unlike previous studies. The reason for the same could be the educational background as well as the detailed executive examination of all the subdomains in the present study so as to identify the subtle cognitive impairments, if any. Moreover, the overall cognitive profile of the patients was in fitting with the subcortical type

of cognitive impairment as is expected in these demyelinating conditions of the brain. The major studies on comparative cognitive profiling of MS and NMOSD have been summarized in Table 6 [6, 7, 23–25].

There has been previous documentation that despite the MS patient being younger, they had more impairment in variable cognitive domains compared to NMOSD probably attributed to the left superior temporal gyrus volume loss. However, our study results differed to those previous findings. The probable explanation could be related to the fact that though MS ultimately leads to cortical atrophy which indicates grey matter involvement, but both MS and NMOSD are primarily disorder of white matter (which primarily builds the primer of cognitive network) and thus it is not unusual to have a similar type of cognitive impairments. Moreover, no particular pattern of cognitive impairment is expected in NMOSD. Owing to the diverse cerebral involvement in NMOSD, the varying degree of cognitive impairments may be noted ranging from mild to florid multidomain impairment and will depend on the hemispheric involvement and location of the lesion. Thus, it can serve as another potential explanation for no particular difference in pattern of cognitive impairment except executive dysfunction between NMOSD and MS [26]. The highlight of the study is that a majority of patients of demyelinating disorders have some cognitive dysfunction however subtle, which can be detected by comprehensive cognitive assessment. Since the predominant age group affected is that of the high functioning youth and adult population involved in cognitively challenging jobs, hence even subtle cognitive dysfunction in the domains of attention, information processing speed, and executive function, which were primarily affected in our study, can lead to decreased productivity and occupational disability of these

Table 6 Comparison of cognitive impairment with international studies

Study name	Country	Sample size	Aquaporin 4 positivity	Main finding
Cho et al. 2018 [22]	Korea	14 NMOSD vs. 21 HCs	13/14	-Patients perform significantly worse in attention/working memory, processing speed, executive function, and visuo-spatial processing -CI in patients associated with local efficiency, regional efficiency, and nodal clustering coefficient of two disrupted subnetworks
Fujimori et al. 2017 [23]	Japan	12 NMOSD vs 14 MS	12/12	-Impairment in perceptual organization, working memory, and processing speed -Compared to MS less CI
Seiji et al. 2013 [6]	Japan	14 NMO vs 17 MS vs 37 HCs	14/14	-57% CI compared to HC significant cortical neuron density decrease in layers II, III, and IV -Cognitive deficits in sustained attention, concentration, speed of information, processing, and verbal memory
Vanotti et al. 2013 [7]	Argentina	14 NMOSD vs 17 MS vs 14 HCs	NR	-57% CI compared to HC dysfunctions in verbal fluencies and attention -Compared to MS similar pattern of dysfunction
Moore et al. 2016 [24]	UK	42 NMOSD vs 42 MS vs 42 HCs	30/42	-67% CI substantial cognitive and psychiatric comorbidities in NMOSD -Compared to MS greater psychological burden, but similar CI prevalence and profiles
Present study	India	20 NMOSD vs 40 MS	18/20	-75% CI executive function, verbal fluency, information processing speed, visuo-constructural ability, attention, complex calculation, and memory involved. -Compared to MS similar pattern of involvement. -Compared to MS verbal fluency and visuo-perceptual ability was more impaired

patients. A baseline and periodic assessment of cognitive function in these patients are therefore imperative for their professional well-being as well as timely intervention.

A smaller sample size without long-term follow-up and healthy controls, absence of recognized standard cognitive battery, and unavailability of newer MRI modalities to measure brain volume loss and functional deficit were the limitations of the study.

Conclusions

Cognitive impairment, although subtle, is present in significant number of patients with NMOSD and MS. The cognitive performances of MS and NMOSD patients are similar even though their clinical and radiological presentations are varied and different. Age at presentation, educational status, EDSS, MRI lesion load, and OCB positivity may influence the cognitive dysfunction in these patients. Standardized cognitive batteries, long-term follow-up studies and larger registries are needed for better understanding and management of this parameter.

Abbreviations

NMOSD: Neuromyelitis optica spectrum disorder; CNS: Central nervous system; AQP4: Aquaporin 4; CI: Cognitive impairment; MS: Multiple sclerosis; IPND: International Panel for NMO Diagnosis; EDSS: Expanded Disability Status Scale; OCB: Oligoclonal band; FAB: Frontal assessment battery; KCB: Kolkata cognitive battery; MOCA: Montreal cognitive assessment; IPS: Information processing speed; ACE: Addenbrooke's cognitive examination; MMSE: Mini-Mental State Exam; MRI: Magnetic resonance imaging; FLAIR: Fluid attenuated inversion recovery; DWI: Diffusion-weighted imaging; ADC: Apparent diffusion coefficient; STIR: Short T1 inversion recovery; GRE: Gradient echo; ANOVA: Analysis of variance; COGIMUS: Cognitive impairment in multiple sclerosis

Acknowledgements

None.

Authors' contributions

SK, GG, and SDu were involved in patient care, data entry, and maintaining the demyelination registry. The initial concept and design of the study was generated by SK, GG, AB, and SDu. Literature search was done by SK and SDu. SK wrote the first draft which was subsequently edited by SDa and SDu. The statistical analysis was carried out by SK and SDu. The draft was critically reviewed by SDu, GG, and AB from its initial stage. Expert opinion from AP and BR improved the quality of the final manuscript substantially. All the authors read and agreed upon the final form of the manuscript before submission.

Funding

No funding was received to assist with the preparation of this manuscript.

Availability of data and materials

All authors confirm the availability of data and materials.

Declarations

Ethics approval and consent to participate

Approval was obtained from the ethics committee of Institute of Post-graduate Medical Education & Research, Kolkata, India. The procedures used in this study adhere to the tenets of the Declaration of Helsinki (Ethics Committee reference number ECR/35/Inst/WB/2013/RR-16). Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Patients signed informed consent regarding publishing their data and photographs.

Competing interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Received: 22 March 2021 Accepted: 4 July 2021

Published online: 21 July 2021

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