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The correlation between dyslipidemia and cognitive impairment in multiple sclerosis patients

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ABSTRACT

Background: A large number of multiple sclerosis [MS] patients suffer from cognitive dysfunction affecting their routine life in family and society. Investigating modifiable factors for cognition decline and controlling them, could improve the quality of life in MS patients. Therefore, the present study was aimed to evaluate the association between lipid profile components and cognition in MS patients.

Methods: A cross-sectional study was conducted on 50 Relapsing-Remitting MS (RRMS) patients referred to Sina hospital, Tehran, Iran. The definite diagnosis of MS was done based on the revised McDonald criteria. Data on demographic and clinical data of patients were obtained. 5 cc blood samples were taken from all subjects after 10-hour night fasting, and lipid profile components including LDL, HDL, triglyceride, and total cholesterol were evaluated. The Persian version of the Minimal Assessment of Cognitive Functions in MS [MACFIMS] battery was administered to assess the cognitive function. Spearman and Pearson correlation tests were applied to investigate the correlation between lipid profile components and MACFIMS subtests or clinical features of MS patients.

Results: The mean age of subjects was equal to 32.26 years old, and 85% of them were women. There was no significant correlation between MACFIMS subtests results with disease duration, patient's disability according to Expanded Disability Status Scale (EDSS), annual attack rate, and disease-modifying drug onset year (P value >0.05). A significant inverse correlation was found between greater serum total cholesterol and lower scores of Symbol Digit Modalities subtest [SDMT] (P value 0.02; r: -0.31), the Delis–Kaplan Executive Function System [DKEFS] sorting (P value 0.01; r: -0.34) and DKEFS-descriptive (P value 0.04; r: -0.28) subtests. This significant inverse correlation was also found in terms of the correlation between higher serum LDL and impairment in the case of DKEFS-sorting score (P value 0.05; r: -0.27), and DKEFS-descriptive score (P value 0.05; r: -0.27). No significant correlation was found in case of serum HDL or triglyceride and MACFIMS subtests (P value >0.05).

Discussion: Our findings proposed a possible correlation between the increased serum LDL cholesterol, serum total cholesterol and cognitive dysfunction among MS patients.

1. Introduction

Multiple sclerosis (Benton et al., 1994) is an inflammatory immune-mediated disorder mainly affecting young adults (Eskandarieh et al., 2016; Eskandarieh et al., 2018). This demyelinating disease of the Central Nervous System (CNS) is the second cause of disability after trauma and the first cause of non-traumatic neurologic disability in young population (Eskandarieh et al., 2016; Eskandarieh et al., 2018). Both environmental and genetic factors are proposed as MS risk factors (Eskandarieh et al., 2018). In the last decades, the MS prevalence and incidence has increased worldwide (Eskandarieh et al., 2018) including Tehran as the capital city of Iran. In 2017, the prevalence of MS was reported as 148.06 per 100,000 person with the mean onset age of 28.64 years old and female to male sex ratio of 3.03:1 (Eskandarieh et al., 2018).

The MS lesions may occur in various areas of brain such as periventricular, juxtacortical, infratentorial, etc., so MS patients may encounter with physical disability and cognitive impairments (Owji et al., 2019). More occurrence of MS in working-class population cause significant economic and social effects, and MS patients face with

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difficulties in routine living such as finding and sustaining a job or making social communication and sometimes they need lifetime supports (Eskandarieh et al., 2016; Owji et al., 2019). Epidemiological studies outlined the presence of cognitive dysfunction in 40–60% of MS patients (Owji et al., 2019). Cognitive dysfunction does not allow a uniform pattern in MS patients,and impairments more frequently affect sustained attention, verbal fluency, recent memory, visuospatial perception, and conceptual reasoning (Rao et al., 1991).

Several tools are available for assessment of cognition in MS patients (Owji et al., 2019). Comprehensive cognitive evaluations are time consuming and expensive (Eshaghi et al., 2012). Accordingly, in 2001, an expert panel of neuropsychologists proposed the Minimal Assessment of Cognitive Functions in MS (MACFIMS). MACFIMS is a 90-minute appropriate neurophysiological assessment battery with seven domains (Benedict et al., 2002) used largely for cognition evaluation in recent years. The Persian translation of MACFIMS has been validated in IRAN, in 2012 (Eshaghi et al., 2012).

Some pieces of evidence suggested that, there is an association between higher serum cholesterol and dementia through the increment of beta-amyloid plaques (Solomon et al., 2007; van Vliet, 2012). Elevated serum cholesterol is also noted as a risk factor for brain ischemia resulting in dementia (Panza et al., 2006). In a recent study, the prevalence of metabolic syndrome components in MS patients has been reported as follows: metabolic syndrome, elevated triglyceride, low level of serum high-density lipoprotein (HDL), and treated dyslipidemia were found to be by 30%, 28.8%, 31.4%, and 31.4% (Pinhas-Hamiel et al., 2015). To the best of our knowledge, there is no study on the association of lipid profile component and cognitive function in MS patients. But some studies outlined the association between dyslipidemia and higher disability and inflammation in MS patients (Gafson et al., 2018; Tettey et al., 2014).

Thus, the present study was aimed to investigate the association between lipid profile components including HDL, LDL, total cholesterol and triglyceride and cognitive function using the MACFIMS battery among Relapsing-Remitting MS (RRMS) patients.

2. Methods

2.1. Study population

To investigate the correlation between serum lipid profile and cognitive function among MS patients, a prospective cross-sectional study was performed at MS specialist clinic of Sina hospital, a tertiary care referral center in Tehran, Iran. 50 patients with definite diagnosis of RRMS according to the revised McDonald criteria (Thompson et al., 2018) were included in the present study through convenience sampling method.

RRMS patients were included in the study based on the following inclusion criteria: A) No history of chronic diseases such as diabetes, chronic liver or kidney diseases, cardiovascular diseases, and hormonal dysfunction or any other condition or medicine usage influencing the study results B) Not being in pregnancy or breast feeding status C) Not having clinical history of other neurologic or psychiatric diseases D) Not receiving corticosteroid in the past month E) No MS relapse during past month F) Not being on a special diet like vegetarian diet, weight loss diet G) No history of alcohol or drug abuse.

2.2. Patients' consent and protocol approval

Before entering the study, the main purpose of study was described for all subjects, and a written informed consent was obtained from all subjects.

The present study was approved by the Ethics Committee of Tehran University of Medical Sciences, and was registered with the ethics code of "IR.TUMS.MEDICINE.REC.1396.3129".

2.3. Demographic and clinical features of study population

Data on age (full years passed from birthday), Sex (male or female), and education level (years) were obtained by in-person interview. Clinical information such as disease duration (years passed from first disease onset), number of annual attack rate, disease-modifying drug (DMD) onset year (years passed from the first time that DMD was received), treatment (Interferon, Glatiramer acetate, Fingolimod, Rituximab, and Tysabri), and disease presentation (optic neuritis, paresis, myelitis, ataxia, diplopia, paresthesia, others) was collected from patient's clinical records. Disability status of the RRMS cases was evaluated using the Expanded Disability Status Scale (EDSS) by an expert neurologist.

2.4. Blood sampling

All subjects underwent at least a 10-hour overnight fasting before taking 5 cc blood samples from an antecubital vein. Serum HDL, LDL, total cholesterol and triglyceride were measured by enzymatic colorimetric assay (Pars-Asmun kits, Iran) using an auto analyzer (Hitachi 902, Japan).

Based on American Heart Association classification, dyslipidemia was defined as: total cholesterol >200 mg/dl, LDL cholesterol >130 mg/dl, HDL cholesterol <35 mg/dl, or triglycerides >150 mg/dl, or a combination of them (Kavey et al., 2003).

2.5. Cognitive assessment

To assess the cognitive function, Persian version of MACFIMS battery, validated in Iran in 2012 (Eshaghi et al., 2012) was administered. MACFIMS battery (Benedict et al., 2002) is previously published consisting of 7 subtests including the California Verbal Learning Test second edition (CVLT-II) (Delis et al., 2001), the Paced Auditory Serial Addition Test (PASAT) (Gronwall, 1977), the Symbol Digit Modalities Test (SDMT) (Smith, 1982), the Brief Visuospatial Memory Test-Revised (BVMT-R) (Benedict, 1997), the Controlled Oral Word Association Test (COWAT) (Benton et al., 1994), the Delis–Kaplan Executive Function System (DKEFS) (Delis et al., 2001) sorting Test, and the Judgment of Line Orientation Test (JLO) (Benton et al., 1994). DKEFS descriptive Test, CVLT-II-delayed recall and BVMT-R-Delayed recall were also used.

The range of scores which could be obtained from MACFIMS subtests are as follows: CVLTII: 0–80; CVLT-II-delay: 0–16; SDMT: 0–110; BVMT-R: 0–36; BMT-R-delay: 0–12; COWAT: 0- undetermined; PASAT: 0–60; D-KEFS-sorting: 0–16; D-KEFS-Description: 0–64, and JLO: 0–30. Greater score in each subtest means better cognitive function (Benedict et al., 2002).

2.6. Statistical analysis

All data were analyzed using IBM SPSS software ver.22 (IBM Corp., Armonk, N.Y., USA), and were reported as mean ± Standard Deviation (SD). The normality of variables was tested using the Kolmogorov-Smirnov test. In case of variables which Kolmogorov-Smirnov test was significant ($P < 0.05$), data analysis was done using non-parametric tests, and in case of variables which Kolmogorov-Smirnov test was not significant, parametric tests were applied. Triglyceride, total cholesterol, HDL cholesterol, CVLT-II, PASAT, SDMT, CVLT-delay, D-KEFS-description score, BVMT-R, COWAT was normal and LDL cholesterol, EDSS, DMD, Disease duration, D-KEFS-sorting score, BVMT-delay, and JLO had not normal distribution. The correlation between two variables was analyzed by Spearman's rank-order correlation (non-parametric test) or Pearson correlation tests (parametric test). The difference between scores of MACFIMS subtests between two groups of dyslipidemia and non-dyslipidemia was assessed using Two-Sample t-Test (parametric test) or Mann-Whitney U Test (non-parametric test). P value < 0.05 was considered as statistically significant.

Table 1
Baseline characteristics of participants.

Variables		
Female gender[a]		42 (84%)
Age (years)[b]		35.26 (7.62)
Education (years)[b]		13.5 (2.88)
Disease duration (years)[b]		5.89 (4.06)
EDSS[b]		0.86 (1.20)
Annual attack rate (number)[b]		2.28 (1.97)
DMD onset year (years)[b]		4.50 (3.15)
Treatment[a]	NO treatment	1 (2%)
	Interferon	17 (34%)
	Glatiramer acetate	12 (24%)
	Fingolimod	9 (18%)
	Rituximab	3 (6%)
	Tysabri	8 (16%)
Disease presentation[a]	Optic neuritis	14 (28%)
	Paresis	10 (20%)
	Myelitis	1 (2%)
	Ataxia	1 (2%)
	Diplopia	8 (16%)
	Paresthesia	14 (28%)
	Others	2 (4%)

EDSS: Expanded Disability Status Scale; DMD: disease modifying drug.
[a] These data are presented as number (percent).
[b] These data are presented as mean (standard deviation).

2.7. Results

Considering the inclusion and exclusion criteria, finally 50 RRMS cases with the mean age of 32.26 years old were enrolled in the study. 85% of subjects were female. The most prescribed disease-modifying drug (DMD) was Interferon (34%), followed by Glatiramer acetate (24%). The average years passed from the first onset of disease was equal to 4.5 years, and subjects had a mean of 0.86 for EDSS. The most common disease presentation was optic neuritis and paresthesia with the equal percentage of 28%. Table 1 presents the baseline characteristics of subjects. Data on cognitive features and lipid profile of patients are shown in Table 2.

As reported in Table 3, correlation analysis between lipid profile components and clinical features of subjects including disease duration, disability status, annual attack rate, and DMD onset years did not reveal any significant results (*P*value >0.05).

Table 2
Descriptive statistics of participants (patients with multiple sclerosis).

Variables		
Lipid profile	Cholesterol (mg/dl)	181.58 (38.58)
	LDL (mg/dl)	109.76 (34.12)
	HDL (mg/dl)	49.8 (11.95)
	Triglyceride (mg/dl)	110.98 (41.18)
MACFIMS subtests	CVLT-II	53.34 (9.03)
	PASAT	45.16 (9.25)
	SDMT	45.62 (12.96)
	CVLT-II-delayed recall	11.28 (3.02)
	BVMT-R	23.46 (6.88)
	D-KEFS-Descriptive	26.60 (10.89)
	D-KEFS-Sorting	7.32 (3.66)
	COWAT	26.22 (8.84)
	BVMT-R-Delayed recall	9.70 (3.05)
	JLO	19.56 (6.04)

All data are presented as mean (standard deviation).
LDL: low-density lipoprotein; HDL: high-density lipoprotein.
MACFIMS: Minimal Assessment of Cognitive Function in Multiple Sclerosis.
CVLT-II: California Verbal Learning Test second edition; PASAT: Paced Auditory Serial Addition Test; SDMT: Symbol Digit Modalities Test; BVMT-R: Brief Visuospatial Memory Test-Revised; D-KEFS: Delis–Kaplan Executive Function System; JLO: Judgment of Line Orientation Test; COWAT: Controlled Oral Word Association Test.

Table 3
The correlation between lipid profile and participant's clinical features.

	Disease duration	EDSS	Annual attack rate	DMD onset year
Cholesterol	0.22 (0.17)	0.13 (0.21)	0.85 (0.02)	0.72 (0.05)
LDL	0.50 (0.09)	0.19 (0.18)	0.78 (0.03)	0.30 (0.14)
HDL	0.95 (−0.00)	0.56 (−0.08)	0.79 (−0.03)	0.38 (0.12)
Triglyceride	0.86 (0.02)	0.19 (0.18)	0.70 (0.05)	0.36 (−0.13)

Data are presented as *P* value (*r*), calculated by Spearman correlation test.
LDL: low-density lipoprotein; HDL: high-density lipoprotein.
EDSS: Expanded Disability Status Scale; DMD: Disease modifying drug.

The correlation between cognitive features of patients according to subtests of MACFIMS battery and lipid profile components including serum total cholesterol, LDL, HDL, and triglyceride is presented in Table 4. A significant inverse correlation was found between serum total cholesterol and visual processing speed of subjects based on SDMT subtest with *P* value: 0.02; and *r*: −0.31. In the case of D-KEFS-Description score measuring a variety of verbal and nonverbal executive functions, a higher score was significantly correlated with lower level of serum total cholesterol (*P* value: 0.01; *r*: −0.34), and lower serum LDL (*P* value: 0.05; *r*: −0.27). Similar results were found for the subtest of D-KEFS-Sorting score. Significant negative correlations were found between D-KEFS-Sorting score and serum level of total cholesterol (*P* value: 0.04; *r*: −0.28), and serum LDL (*P* value: 0.05; *r*: −0.27).

No significant correlation was observed between CVLT-II, PASAT, CVLT-delayed recall, BVMT-R, COWAT, BVMT-Delayed recall, and JLO subtests of MACFIMS battery and lipid profile components (*P* value >0.05).

There were no significant differences in MACFIMS subtests scores between two groups of dyslipidemia and non-dyslipidemia (Table 5).

3. Discussion

The increased cholesterol level was found to be associated with cognitive impairment in MS patients. This finding is important as it is a modifiable factor meaning that, the reduction of cholesterol level can prevent the forthcoming complications. The relationship between blood lipid and cholesterol and cognitive impairments has also been reported in dementia. The elevated cholesterol level in middle age has been shown as one of the causes of dementia at higher ages, because cholesterol contributes in production of beta-amyloid plaques (Solomon et al., 2007; van Vliet, 2012)

Another study also found that, an increase in LDL level increases the brain Aβ N-42 levels. The increase in the blood lipid and cholesterol also causes ischemia in the brain, as a risk factor for dementia (Panza et al., 2006).

The effect of the increased blood cholesterol on MS disease has also been studied. The specific lipid concentrations within VLDL sub-fractions have been shown to be associated with the degree of disability, as well as pre-inflammatory factors in MS patients (Gafson et al., 2018). Another study also found that, lipid profile has a direct effect on the disability of MS patients (Tettey et al., 2014).

In another study, a correlation was reported between the levels of cholesterol, TG and LDL, and the degree of disability. In addition, an increase in HDL has been found to be accompanied by a decrease in enhancing the plaques presented in MRI images (Weinstock-Guttman et al., 2011). Another study conducted in our center also showed that, BMI could be associated with cognitive impairments in MS patients, reflecting the role of obesity and lipid profile in cognitive impairments among MS patients (Owji et al., 2019).

In line with the negative effect of lipid profile on MS, the effects of lipid lowering drugs on this disease have also been studied. In a study carried out in 2017, a high dose of simvastatin was found to have a

Table 4
The correlation between lipid profile and MACFIMS tests.

	CVLT-II	PASAT	SDMT	CVLT-delayed recall	BVMT-R	COWAT	D-KEFS-Description score	D-KEFS-Sorting score	BVMT- R-Delayed recall	JLO
Cholesterol	0.14 (−0.21)	0.60 (−0.08)	**0.02 (−0.31)**	0.17 (−0.19)	0.58 (−0.08)	0.21 (−0.17)	**0.01 (−0.34)**	**0.04 (−0.28)**	0.27 (−0.15)	0.72 (0.05)
LDL	0.98 (0.00)	0.89 (−0.02)	0.22 (−0.17)	0.49 (−0.09)	0.68 (−0.05)	0.41 (−0.11)	**0.05 (−0.27)**	**0.05 (−0.27)**	0.17 (−0.19)	0.81 (0.03)
HDL	0.34 (−0.13)	0.95 (−0.01)	0.79 (−0.05)	0.98 (−0.00)	0.69 (0.05)	0.36 (−0.13)	0.99 (−0.00)	0.95 (0.00)	0.46 (0.10)	0.95 (−0.00)
Triglyceride	0.45 (−0.10)	0.79 (−0.04)	0.26 (−0.16)	0.80 (−0.03)	0.26 (−0.16)	0.70 (0.05)	0.52 (0.09)	0.55 (0.08)	0.17 (−0.19)	0.34 (0.13)

Data are presented as *P* value (*r*), calculated by Spearman correlation test for nonparametric variables and Pearson correlation test for parametric variables.
LDL: low-density lipoprotein; HDL: high-density lipoprotein.
MACFIMS: Minimal Assessment of Cognitive Function In Multiple sclerosis.
CVLT-II: California Verbal Learning Test second edition; PASAT: Paced Auditory Serial Addition Test; SDMT: Symbol Digit Modalities Test; BVMT-R: Brief Visuospatial Memory Test-Revised; D-KEFS: Delis–Kaplan Executive Function System; JLO: Judgment of Line Orientation Test; COWAT: Controlled Oral Word Association Test.

Table 5
The difference in MACFIMS subtests scores between two groups of dyslipidemia and non-dyslipidemia.

Variables	LDL			HDL			Triglyceride			Total cholesterol		
	>130 mg/dl n: 12	<130 mg/dl n: 38	*P*	<35 mg/dl n: 5	>35 mg/dl n: 45	*P*	>150 mg/dl n: 9	<150 mg/dl n:41	*P*	>200 mg/dl n: 16	<200 mg/dl n: 34	*P*
CVLT-II	55.5 ± 8.3	52.66 ± 9.2	0.24	51.6 ± 11.4	53.49 ± 9	0.73	52.33 ± 10.1	53.56 ± 8.9	0.74	51.13 ± 9.7	54 ± 8.6	0.33
PASAT	48.11 ± 8.5	44.24 ± 9.4	0.31	39.5 ± 11.7	45.47 ± 9	0.38	47 ± 4.5	44.74 ± 10	0.37	45.5 ± 9.4	45 ± 9.3	0.89
SDMT	47.25 ± 12.2	45.11 ± 13.3	0.41	44.6 ± 15.7	45.05 ± 12.6	0.95	44.7 ± 13.4	45.8 ± 13	0.81	40.53 ± 12.9	47.21 ± 12.2	0.1
CVLT-delayed recall	11.83 ± 2.8	11.1 ± 3.1	0.53	10.6 ± 4.8	11.4 ± 2.9	0.73	11.56 ± 3.6	11.2 ± 2.9	0.79	10.33 ± 3.4	11.68 ± 2.9	0.19
BVMT-R	25.25 ± 5	22.89 ± 7.3	0.39	21.8 ± 10	23.6 ± 6.6	0.98	22.56 ± 8.2	23.66 ± 6.7	0.9	23.47 ± 7	23.3 ± 7	0.93
COWAT	26.33 ± 7.6	26.18 ± 9.3	0.56	26.8 ± 12.2	25.95 ± 8.7	0.76	26 ± 10	26.27 ± 8.7	0.77	23.93 ± 7.9	27.03 ± 9.2	0.42
D-KEFS-Description score	26.75 ± 8.8	26.5 ± 11.6	0.91	31.2 ± 10.7	25.81 ± 10.9	0.33	28.67 ± 12.6	26.15 ± 10.6	0.59	23.4 ± 11.9	28.15 ± 10.4	0.2
D-KEFS-Sorting score	6.92 ± 2.4	7.45 ± 4	0.85	7.8 ± 2.7	7.23 ± 3.8	0.46	7.33 ± 3.3	7.32 ± 3.8	0.66	6 ± 3.1	7.94 ± 3.8	0.16
BVMT- R-Delayed recall	10 ± 2.3	9.61 ± 3.3	0.75	9.4 ± 4	9.74 ± 3	0.76	9.33 ± 3.5	9.78 ± 3	0.9	9.67 ± 2.8	9.71 ± 3.2	0.57
JLO	20.33 ± 7.2	19.31 ± 6.2	0.49	22 ± 6.9	19.44 ± 6.4	0.47	19.11 ± 9	19.67 ± 5.8	0.9	18.87 ± 7.8	20.03 ± 5.8	0.82

Data are presented as mean ± Standard Deviation (SD).
LDL: low-density lipoprotein; HDL: high-density lipoprotein.
MACFIMS: Minimal Assessment of Cognitive Function In Multiple sclerosis.
CVLT-II: California Verbal Learning Test second edition; PASAT: Paced Auditory Serial Addition Test; SDMT: Symbol Digit Modalities Test; BVMT-R: Brief Visuospatial Memory Test-Revised; D-KEFS: Delis–Kaplan Executive Function System; JLO: Judgment of Line Orientation Test; COWAT: Controlled Oral Word Association Test.
P was calculated using Two-Sample t-Test (parametric test) or Mann-Whitney U Test (non-parametric test).

positive effect on the frontal lobe function and the physical quality-of-life of patients with secondary progressive MS (Chan et al., 2017). This is consistent with our findings regarding the effect of blood lipid on cognitive impairments in MS patients.

Statins has been found to reduce the whole-brain atrophy in MS patients compared to placebo (Chataway et al., 2014). In general, findings confirmed the negative effect of cholesterol on the cognitive abilities of patients with MS. Cognitive impairments are one of the most serious symptoms in MS patients starting from the very beginning of the disease (Owji et al., 2019). The overall rate of these disorders is between 40-60% in patients with MS. Unfortunately, despite the high prevalence of these disorders, not much attention has been paid to the daily treatment of these patients (Moghadasi et al., 2016).

On the other hand, drug treatments cannot have a positive effect on these disorders and only cognitive rehabilitation can positively influence these impairments. So, paying attention to the risk factors and preventing such disorders are very important.

Despite the significant inverse correlation between greater serum lipids levels and MACFIMS subtests scores, no significant differences were founded in scores of MACFIMS between two groups of dyslipidemia and non-dyslipidemia in the present study. Due to the main goal of study, which was investigating the correlation between dyslipidemia and cognitive impairment in MS patients, this study was performed in cross-sectional design. So, as you can find in Table 5, when we divided study participants into two groups of hyperlipidemia and non-hyperlipidemia almost 80% of patients had normal lipid status. The non-significant differences of MACFIMS scores between two groups could be referred to this unequal distribution of patients between groups and small sample size of participants in each group. Further case-control design investigation by appropriate sample size is needed to evaluate the difference of cognition between dyslipidemia and non-dyslipidemia patients.

4. Conclusion

The results of the study indicated that, the increased blood cholesterol level has a negative effect on cognitive impairments in MS patients. Considering that, hyperlipidemia is one of the modifiable risk factors, attention to this risk factor and its improvement can be effective in preventing cognitive impairments in MS patients.

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This study did not receive any founding.

Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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Supplementary materials

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References

Benedict, R.H., Fischer, J.S., Archibald, C.J., Arnett, P.A., Beatty, W.W., Bobholz, J., et al., 2002. Minimal neuropsychological assessment of Ms patients: a consensus approach. Clin. Neuropsychol. 16 (3), 381–397.

Benedict, R.H., Fischer, J.S., Archibald, C.J., Arnett, P.A., Beatty, W.W., Bobholz, J., et al., 2002. Minimal neuropsychological assessment of MS patients: a consensus approach. Clin. Neuropsychol. 16 (3), 381–397.

Benedict R.H. Brief visuospatial memory test–revised: professional manual: par; 1997.

Benton, A.L., Sivan, A.B., deS Hamsher, K., Varney, N.R., Spreen, O, 1994. Contributions to Neuropsychological Assessment: A Clinical Manual. Oxford University Press, USA.

Chan, D., Binks, S., Nicholas, J.M., Frost, C., Cardoso, M.J., Ourselin, S., et al., 2017. Effect of high-dose simvastatin on cognitive, neuropsychiatric, and health-related quality-of-life measures in secondary progressive multiple sclerosis: secondary analyses from the MS-STAT randomised, placebo-controlled trial. Lancet Neurol. 16 (8), 591–600.

Chataway, J., Schuerer, N., Alsanousi, A., Chan, D., MacManus, D., Hunter, K., et al., 2014. Effect of high-dose simvastatin on brain atrophy and disability in secondary progressive multiple sclerosis (MS-STAT): a randomised, placebo-controlled, phase 2 trial. Lancet 383 (9936), 2213–2221.

Delis D.C., Kaplan E., Kramer J.H. Delis-Kaplan executive function system: examiners manual: psychological corporation; 2001.

Eshaghi, A., Riyahi-Alam, S., Roostaei, T., Haeri, G., Aghsaei, A., Aidi, M.R., et al., 2012. Validity and reliability of a Persian translation of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS). Clin. Neuropsychol. 26 (6), 975–984.

Eskandarieh, S., Heydarpour, P., Minagar, A., Pourmand, S., Sahraian, M.A, 2016. Multiple sclerosis epidemiology in east Asia, south east Asia and south Asia: a systematic review. Neuroepidemiology 46 (3), 209–221.

Eskandarieh, S., Allahabadi, N.S., Sadeghi, M., Sahraian, M.A, 2018a. Increasing prevalence of familial recurrence of multiple sclerosis in Iran: a population based study of Tehran registry 1999–2015. BMC Neurol. 18 (1), 15.

Eskandarieh, S., Molazadeh, N., Moghadasi, A.N., Azimi, A.R., Sahraian, M.A, 2018b. The prevalence, incidence and familial recurrence of multiple sclerosis in Tehran, Iran. Mult. Scler. Relat. Disord. 25, 143.

Gafson, A.R., Thorne, T., McKechnie, C.I.J., Jimenez, B., Nicholas, R., Matthews, P.M, 2018. Lipoprotein markers associated with disability from multiple sclerosis. Sci. Rep. 8 (1), 17026.

Gronwall, D., 1977. Paced auditory serial-addition task: a measure of recovery from concussion. Percept. Mot. Skills 44 (2), 367–373.

Kavey, R.-E.W., Daniels, S.R., Lauer, R.M., Atkins, D.L., Hayman, L.L., Taubert, K, 2003. American heart association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. Circulation 107 (11), 1562–1566.

Moghadasi, A.N., Pourmand, S., Sharifian, M., Minagar, A., Sahraian, M.A, 2016. Behavioral neurology of multiple sclerosis and autoimmune encephalopathies. Neurol. Clin. 34 (1), 17–31.

Owji, M., Ashraf-Ganjouei, A., Sahraian, M.A., Bidadian, M., Ghadiri, F., Moghadasi, A.N, 2019. The relationship between cognitive function and body mass index in multiple sclerosis patients. Mult. Scler. Relat. Disord. 32, 37–40.

Panza, F., D'Introno, A., Colacicco, A.M., Capurso, C., Pichichero, G., Capurso, S.A., et al., 2006. Lipid metabolism in cognitive decline and dementia. Brain Res. Rev. 51 (2), 275–292.

Pinhas-Hamiel, O., Livne, M., Harari, G., Achiron, A, 2015. Prevalence of overweight, obesity and metabolic syndrome components in multiple sclerosis patients with significant disability. Eur. J. Neurol. 22 (9), 1275–1279.

Rao, S.M., Leo, G.J., Bernardin, L., Unverzagt, F, 1991. Cognitive dysfunction in multiple sclerosis.: I. Frequency, patterns, and prediction. Neurology 41 (5), 685–691.

Smith A. Symbol digit modalities test: western psychological services Los Angeles. Spreen, O & Strauss, E(1998) a compendium of neuropsychological tests (2nd ed) new. 1982.

Solomon, A., Kareholt, I., Ngandu, T., Winblad, B., Nissinen, A., Tuomilehto, J., et al., 2007. Serum cholesterol changes after midlife and late-life cognition: twenty-one-year follow-up study. Neurology 68 (10), 751–756.

Tettey, P., Simpson Jr., S., Taylor, B., Blizzard, L., Ponsonby, A.L., Dwyer, T., et al., 2014. An adverse lipid profile is associated with disability and progression in disability, in people with MS. Mult. Scler. 20 (13), 1737–1744.

Thompson, A.J., Banwell, B.L., Barkhof, F., Carroll, W.M., Coetzee, T., Comi, G., et al., 2018. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 17 (2), 162–173.

van Vliet P. Cholesterol and late-life cognitive decline. J. Alzheimer's Dis. 2012;30 Suppl 2:S147–62.

Weinstock-Guttman, B., Zivadinov, R., Mahfooz, N., Carl, E., Drake, A., Schneider, J., et al., 2011. Serum lipid profiles are associated with disability and mri outcomes in multiple sclerosis. J. Neuroinflammation 8, 127.