

Fatigue predicts progression of disease in newly diagnosed multiple sclerosis

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Objectives: Multiple Sclerosis (MS) is a chronic disease with a great heterogeneity of course, varying from benign to highly disabling forms. Clinical predictors at disease onset are only partially known. We evaluated if cognitive function in newly diagnosed patients could play a role as predictor of disability within an observation interval of two years.

Materials and Methods: we enrolled 22 subjects satisfying McDonald 2010 criteria for MS from June 2012 to May 2013 at the Multiple Sclerosis Center of Bergamo. Each patient underwent a multidimensional assessment comprehensive of neuropsychological tests (BRB, MMSE, Clock Drawing, Verbal Fluency, Digit Span, Corsi, EBN, Rivermead Behavioural Memory, TMA, TMB, Stroop, Attentive Matrices, Raven's Progressive Matrices, Tower of London, Rey Complex Figure Test, WCST), evaluation of depression, anxiety, sleep, fatigue and quality of life (BDI, STAI-Y, PSQI, ESS, FSS, MSQOL-54), measures of motor function and disability (9HPT, TWT, EDSS). Relapses rate and EDSS scores were detected two years later. Subjects were classified as PROGRESSIVE (MS-PRO) or NOT PROGRESSIVE (MS-NO PRO) respectively by a EDSS score increased or stable within an observational interval of two years.

Results: in our cohort, after two years by diagnosis, 10 subjects got worse (MS-PRO), 12 were stable (MS-NO PRO). Disability at disease onset was similar in both groups (EDSS mean=1.5), whereas, as expected, relapses in the first two years were greater in MS-PRO (1.5±1.4 vs 0.3±0.8 in MS-NO PRO, p<0.05) (Table 1). Results of cognitive tests were all suprathreshold and comparable (Table 2), whereas fatigue complains were denounced more often in MS-PRO (4.2±1.2 vs 2.6±1.2 in MS-NO PRO, p<0.05), independently by other confounding factors, such as anxiety, depression and lack of sleep (Table 3). Impaired motor skills were detected in MS-PRO, but only concerning the ambulation (TWT: 10.5±1.3 vs 9.3±1.1 in MS-NO PRO, p<0.05) (Table 1).

Table 1. Demographic and clinical characteristics

	MS-NO PRO N° 12				MS-PRO N°10				p value
	%	median	mean	sd	%	median	mean	sd	
Gender (female)	66.7				70.0				0.867
Age		31.0	30.8	6.9		32.5	36.1	10.3	0.162
Relapses (N°)		0	0.3	0.8		1.5	1.5	1.4	0.017
EDSS		1.5	1.5			1.5	1.5		
TWT		9.2	9.3	1.1		9.9	10.5	1.3	0.049
9HPT right		17.7	17.9	1.9		18.9	20.0	3.8	0.138
9HPT left		19.2	19.6	2.8		19.9	22.6	10.1	0.742

Table 2. Neuropsychological profile

	MS-NO PRO N° 12				MS-PRO N°10				p value
	%	median	mean	sd	%	median	mean	sd	
Education		13.0	12.2	3.6		13.0	13.7	2.7	0.314
MMSE		30.0	29.2	1.3		29.0	29.4	0.5	0.614
Clock Drawing		10.0	9.1	1.7		10.0	9.5	0.7	0.512
BRB									
SRT-LTS		53	51.7	9.5		46.2	48.5	12.5	0.509
SRT-CLTR		32.1	36.0	17.0		37.1	38.8	16.1	0.696
SPART		22.2	21.5	5.1		19.1	19.1	3.4	0.236
SDMT		61.3	60.4	8.4		53.3	54.3	8.9	0.114
PASAT 3		45.0	44.1	6.6		44.5	42.4	12.0	0.962
PASAT 2		32.8	31.1	9.1		33.2	35.9	10.1	0.326
SRT-D		8.9	9.0	1.4		8.9	9.3	2.1	0.707
SPART-D		8.6	7.9	2.3		7.2	7.1	2.2	0.446
WLG		25.1	23.9	5.8		26.5	25.8	6.5	0.49
WCST		43.0	59.2	34.9		42.4	59.5	36.8	0.833
Digit Span forward		5.5	5.8	0.9		5.3	4.9	1.1	0.187
Digit Span backward		5.0	5.4	1.4		4.0	4.4	1.3	0.11
Corsi		5.6	5.4	1.0		5.1	5.2	0.9	0.691
Rivermead1		11.0	11.0	1.0		11.5	10.8	1.7	0.853
Rivermead2		22.0	21.5	1.3		22.5	21.6	2.7	0.475
Tower of London		32.0	31.6	2.0		29.0	29.4	4.7	0.169
Phonemic fluency		31.0	35.5	9.9		36.5	35.7	11.1	0.958
Rey Figure copy		31.3	30.8	2.6		32.3	31.8	1.7	0.323
Rey Figure recall		15.3	15.6	7.1		18.5	17.4	4.6	0.794
Raven's Matrices		37.8	31.4	2.1		31.5	31.0	2.8	0.659
TMTA		30.0	33.4	13.8		33.5	34.1	11.5	0.459
TMTB		94.0	85.5	28.5		96.0	84.9	30.8	0.732
Attentive Matrices 1		10.0	9.8	0.4		10.0	9.8	0.4	0.849
Attentive Matrices 2		36.8	37.4	3.5		39.9	39.3	3.0	0.188
Stroop Test 1		23.0	24.1	4.3		22.4	23.2	7.7	0.621
Stroop Test 2		1.8	2.0	1.4		1.3	1.2	0.9	0.203

Table 3. Neuropsychiatric symptoms

	MS-NO PRO N° 12			MS-PRO N°10			p value
	median	mean	sd	median	mean	sd	
BDI	5.0	6.8	6.2	10.5	13.6	12.5	0.115
STAI-y Trait	59	40.9	11.7	45.5	45.4	12.9	0.401
STAI-y State	39.5	41.2	13.0	52.0	47.9	12.7	0.236
PSQI	4.5	5.0	2.7	5.0	6.5	4.0	0.306
ESS	5.5	5.9	3.9	6.0	7.2	4.1	0.469
MSQOL-54f	78.7	76.0	15.6	60.9	62.8	21.0	0.105
MSQOL-54m	83.0	75.9	16.1	62.7	62.1	22.4	0.11
FSS	2.2	2.6	1.2	4.3	4.2	1.2	0.015

References:

Gajofatto A., Calabrese M., Benedetti M.D., and Monaco S.. Clinical, MRI, and CSF markers of disability progression in Multiple Sclerosis. Hindawi Publishing Corporation Disease Markers, Volume 35 (2013), Issue 6, Pages 687–699.

Discussion and conclusions:

Fatigue complains, even subclinical, at onset of MS could predict the following progression of disease in term of physical disability, especially if they are distinct from depressive and anxiety disorders.

Further clinical longitudinal observation and a larger sample are needed to confirm these findings.