

## Supplementary Materials

**Table S1.** Comparison of cognitive performances based on cerebellar involvement at baseline.

	Patients without cerebellar involvement			Patients with cerebellar involvement			P values*
Test	Raw (mean ± SD)	Adjusted (mean ± SD)	Equivalent (mean ± SD)	Raw (mean ± SD)	Adjusted (mean ± SD)	Equivalent (mean ± SD)	
<b>BDI*</b>	9.2 ±7.8	-	-	14.2±9.5	-	-	0.03
<b>Corsi Span</b>	5.2±1.4	4.9 ±1.3	2.9 ± 1.6	4.7±1.0	4.4±1.0	2.4±1.7	0.1
<b>Short story</b>	17.4±4.7	16.1 ±4.4	3.4 ±1.2	13.5±5.3	12.5±4.6	2.6±1.6	0.01
<b>Digit span forward</b>	6.1±1.1	5.8 ±1.1	3.5 ±0.9	5.5±1.2	5.2±1.0	2.9±1.3	0.08
<b>Digit span backward</b>	4.3±1.0	-	-	3.6±1.1	-	-	0.02
<b>Phonetic fluency</b>	37.1±10.1	34.4±9.4	3.2±1.1	30.3±9.2	28.8±9.5	2.5±1.3	0.03
<b>Semantic fluency</b>	48.2 ±11.6	46.0 ±11.2	3.6±0.9	42.6±12.7	41.4±11.3	3.2±1.1	0.05
<b>TMTa</b>	31.7±19.0	27.5±19.2	3.7±0.9	49.0±30.7	46.1±28.1	3.2±1.2	0.02
<b>TMTb</b>	79.6±55.5	69.8±59.0	3.6±1.2	109.8±68.0	109.2±64.4	3.0±1.4	0.05
<b>TMT b-a</b>	48.1±45.6	42.3±47.3	3.4±1.3	64.9±55.8	64.9±51.6	3.1±1.4	0.2
<b>Cognitive estimates</b>	13.5±4.2	13.5±3.6		16.6±3.8	16.24±3.8	-	0.01
<b>SDMT</b>	49.4±14.7	48.1±10.7	-	38.4±13.5	37.4±13.2	-	0.02
<b>Weigl test</b>	16.0±22.3	12.13 ±2.9	3.1 ±1.1	11.0±2.9	11.05±2.7	2.2±1.2	0.01
<b>Raven's matrices</b>	30.5±5.2	29.9±4.6	3.2±1.1	28.6±5.3	28.3±4.9	2.7±1.1	0.08
<b>PASAT 2' (errors)</b>	49.4±14.7	-	-	34.8±8.8	-	-	0.0005

\*pvalue obtained with Mann-Whitney test and referred to differences between equivalent values or when not available between adjusted or raw values

Abbreviations: BDI: SDMT: symbol digit modalities test; TMT: trail making test; PASAT. SD: standard deviation.

**Table S2.** Predictive factors at Ms diagnosis for long term cognition. N:65

		Beta	95% CI	P value
<b>Model*</b>	EDSS	-0.048	-0.134 – 0.087	0.469
	Cerebellum	0.135	-0.109 – 0.368	0.282
	WMLL	<b>0.265</b>	0.017 – 0.479	<b>0.036</b>
	Age	0.052	-0.009 – 0.014	0.667
	D.D	<b>0.293</b>	0.005 – 0.035	<b>0.01</b>
	E.L	<b>-0.320</b>	-0.073 - -0.012	<b>0.007</b>
	Any DMTs	-0.102	-0.337 - 0.131	0.382

\*Model considering cognition as a dependent variable and EDSS, cerebellum involvement, EDSS, WMLL, and educational level as independent variables. CI was defined with the presence of at least 2 severely altered tests at NPS evaluation at T1. **Abbreviations:** CI: cognitive impairment, DD: disease duration from the onset, DMT: disease modifying treatment, EDSS: expanded disability status score, EL: educational level, Ms: Multiple sclerosis, NPS: neuropsychological, WMLL= white matter lesion load

**Table S3.** Motor disability and prognostic factors. Group comparison and correlation analyses.

	a) EDSS<4 (N49)	b) EDSS≥4 (N16)	p- value a) vs b)	MSSS T1 (N65)	ARMSS T1 (N65)	EDSS T1 (N65)
<b>Age at onset;</b> mean±SD	31.06 ± 9.53	34.94 ± 7.48	0.1	<i>r:0.26 p:0.03</i>	r:-0.18 p:0.1	r:0.14 p:0.2
<b>Age at diagnosis;</b> mean±SD	34.20 ±10.23	40.0 ± 7.46	<b>0.03</b>	<i>r:0.29 p:0.01</i>	r:-0.12 p:0.3	r:0.22 p:0.08
<b>Age at T1; mean±SD</b>	45.84 ± 9.25	54.19± 5.02	<b>0.0008</b>	<i>r:0.34 p:0.005</i>	r:0.008 p:0.9	<i>r:0.38 p:0.01</i>
<b>Sex (% of grand total)</b>						
Female	56.06%	18.18%	0.9	2.7±2.3 vs 2.4±2.1	3.9±2.5 vs 3.6±2.4	2.9±2 vs 2.7±1.9
Male	19.70%	6.06%		p0.6	p0.7	p0.6
<b>Educational level;</b> mean±SD	12.22±2.82	11.69±3.86	0.7	r:-0.07 p:0.5	r:-0.003 p:0.9	r:0.09 p:0.4
<b>BDI; mean±SD</b>	10.09±8.94	14.31±7.28	<b>0.03</b>	<i>r:0.36 p:0.003</i>	<i>r:0.24 p:0.049</i>	<i>r:0.36 p:0.003</i>
<b>Dd from onset</b> mean±SD	15.41 ± 6.61	19.56 ± 7.15	<b>0.03</b>	r:0.02 p0.8	r:0.17 p0.1	<i>r:0.31 p:0.01</i>
<b>Dd from diagnosis</b> mean±SD	12.24 ± 6.36	14.50 ± 5.06	0.1	r:-0.02 p0.8	r:0.18 p0.1	<i>r:0.26 p0.03</i>
<b>ARR mean±SD</b>	0.47 ± 0.49	0.6 ± 0.32	0.08	r:0.20 p0.1	<i>p:0.43 p0.006</i>	r:0.21 p0.09
<b>EDSS at T0;</b> mean±SD	0.93± 0.84	1.81± 0.99	<b>0.003</b>	<i>r:0.54 p&lt;0.0001</i>	<i>r:0.49 p&lt;0.0001</i>	<i>r:0.51 p&lt;0.0001</i>
<b>EDSS at T1;</b> mean±SD	1.85± 0.86	6.03 ±1.04	<b>&lt;0.0001</b>	-	-	-
<b>MSSS at T1;</b> mean±SD	1.52 ± 1.09	6.13 ± 1.42	<b>&lt;0.0001</b>	-	-	-
<b>ARMSS at T1;</b> mean±SD	2.74 ± 1.68	7.16 ± 1.30	<b>&lt;0.0001</b>	-	-	-
<b>Recovery from onset (% of grand total)</b>						
Yes	50.7%	10.7%		2.1±1.7 vs 3.5±2.7	3.2±2.1 vs 4.7±2.7	3.4±2.4 vs 2.5±1.6
no	24.6%	13.8%	0.9	<i>p0.049</i>	<i>p0.03</i>	p0.1
<b>Type of onset (% of grand total)</b>						
Sensory/pyramidal	12.3%	40%				
Brainstem/cerebellar	4.6%	7.7%				
Optic neuritis	4.6%	18.5%				
Myelitis	3.1%	9,2%	p:0.8	p:0.7	p:0.2	p:0.6
<b>Type of MS at T0 (% of grand total)</b>						
RR	75%			2.6±1.9 vs 7.7±0.	3.5±2.2 vs 8.6±0.2	2.6±1.5 vs 7.1±0.2
PP	18.7%	0%		<i>p&lt;0.0001</i>	<i>p&lt;0.0001</i>	<i>p&lt;0.0001</i>
		6.2%	<i>p:0.0003</i>			
<b>Type of MS at T1 (% of grand total)</b>						
RR	71.8%					
PP	0%	3.1%				
	3.1%	6.2%				

SP	15.6%	<i>p</i> :<0.0001	<i>p</i> :<0.0001	<i>p</i> :<0.0001	<i>p</i> :<0.0001
<b>Spinal (% of grand total)</b>			3.1±2.5	4.1±2.4	3.0±2.0
Yes	43.1%	16.9%	vs 2±1.8	vs 3.2±2.4	vs 2.5±1.8
No	32.3%	7.7%	p0.06	p0.09	p0.2
<b>Cerebellar (% of grand total)</b>			3.5±2.7	4.8±2.5	3.6 ±2.3
Yes	23.1%	16.6%	vs 2.0±1.8	vs 3.1±2.2	vs 2.3 ± 1.6
No	52.3%	7.7%	<i>p</i> 0.049	<i>p</i> 0.005	<i>p</i> 0.040
<b>Gd+ (% of grand total)</b>			2.6±2.3	3.4±2.4	2.8±1.9
Yes	33.8%	15.4%	vs 2.7±2.3	vs 4.2±2.4	vs 2.9±2
no	41.5%	9.2%	p0.7	p0.2	p0.8
<b>WMLL (% of grand total)</b>			3.2±2.5	4.3±2.5	3.2±2.1
Yes	36.9%	13.8%	vs 2-0±1.9	vs 3.2±2.4	vs 2.5±1.8
No	38.5%	10.8%	<i>p</i> 0.03	<i>p</i> 0.049	p0.08
<b>DMT at T1 (% of grand total)</b>			2.1±1.7	3.4±2	2.3±1.5
Yes	46.9%	7.6%	vs 3.3±2.7	vs 4.2±2.8	vs 3.4±2.4
No	28.7%	16.7%	p0.07	p0.3	<i>p</i> 0.049
<b>Any DMT exposure in the past (% of grand total)</b>			2.5±2 vs	3±2.3	2.5±1.9
Yes	51.5%	18.2%	2.8±2.4	vs 4.1±2.4	vs 3±2
No	24.2%	6.1%	p0.4	p0.08	p0.4
<b>OCB (% of grand total)</b>			3±2vs2.5±1.5	2.7±2.4 vs 2.1±1.6	3.9±2.5vs 3.2± 2.3
Yes	65.6%	21.9%	p0.7	p0.8	p0.5
No	10.9%	1.6%			

Group comparison; test used: Mann–Whitney and Kruskal–Wallis tests for continuous variables; Chi-Squared test and Fisher test for categorical variables. **Abbreviations:** ARMSS: age-related MSSS, ARR: annualized relapse rate, DD: disease duration, DMT: disease-modifying treatment, EDSS: expanded disability status score, Gd: gadolinium, OCB: oligoclonal bands, Ms: Multiple sclerosis, MSSS: MS severity score, WMLL: white matter lesion load

**Table S4.** Predictive factors at Ms diagnosis for long-term motor disability. N:65

	Beta	95% CI	P value
<b>Model*</b>			
MS Type at T0	0.500	1.890-4.709	0.000
MS Type at T1	0.192	-0.833 – 1.371	0.042
DMT at T1	0.038	-0.212 – 0.420	0.513
DD from onset	-0.001	-0.041 – 0.040	0.987
Cerebellum	0.075	-0.187 – 0.798	0.219
WMLL	0.031	-0.343 – 0.592	0.597
Age at diagnosis	-0.084	-0.061 - 0.027	0.438
Age at T1	0.145	-0.018 – 0.083	0.204
EDSS at T0	0.239	0.251 – 0.761	0.000

\*Model considering EDSS at T1 as a dependent variable and EDSS at diagnosis, cerebellum involvement, WMLL, MS phenotype at diagnosis and T1 , DMT at T1, disease duration from the onset, age at diagnosis, and at T1 as multiple independent variables. **Abbreviations:** DD: disease duration, DMT: disease-modifying treatment, EDSS: expanded disability status score, Ms: Multiple sclerosis, WMLL= white matter lesion load