

# D-KEFS ST identifies MS patients with a more severe cognitive decline



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## Background and aim

The Brief Repeatable Battery of Neuropsychological Test (BRB-NT), widely used to analyse cognitive functions in Multiple Sclerosis (MS), does not properly investigate the executive functions. To go beyond this limit, we explored whether Delis-Kaplan Executive Function System Sorting Test (D-KEFS ST) could help in detecting executive dysfunctions in early disease phases.

## Materials and Methods

**Patients** 137 MS patients were included in the study. Inclusion criteria were the diagnosis of Clinically Isolated Syndrome suggestive of MS or Relapsing-Remitting MS based on the McDonald Criteria and age >18 years; exclusion criteria were history of other medical illness, learning disability, alcohol or drug abuse and impaired vision and hearing. The study was approved by the Local Ethic Committee.

**Neuropsychological and Neurological evaluations** The BRB-NT, except for the Paced Auditory Serial Addition Test, two seconds version (PASAT 2), and the D-KEFS ST were administered by a neuropsychologist in agreement with the original manuals and normative data for Italian population. Self-evaluation questionnaires, i.e., the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ), the Fatigue Severity Scale (FSS) and the Beck Depression Inventory, Second Edition (BDI-II) were completed. Finally, EDSS was performed by trained neurologists.

**Statistical** For normally distributed variables the T test (when two groups were compared) or the ANOVA (for more than two groups comparison) were performed applying the Bonferroni's correction. For ordinal categorical variables the Mann-Whitney U test was performed, while for no ordinal variables, the Pearson's Chi square test was used. Linear correlation between variables was tested using the Pearson's single or multiple linear model when all variables were normally distributed. The significance level was set at  $p < 0.05$ .

## Results

**Demographical, clinical and neuropsychological features** Table 1 summarized clinical data and EDSS values of the overall population and in patient's subgroup. Based on disease duration (DD) (> 3 years), MS patients were divided in RRMS (78 patients) and CIS/eRRMS (59 patients). Moreover, MS patients were divided based on the detection of almost a failure in BRB-NT items ( $f$ BRB-NT vs normal BRB-NT,  $n$ BRB-NT) or in D-KEFS ST ( $f$ D-KEFS ST vs normal D-KEFS ST,  $n$ D-KEFS ST).

	Overall MS (137 pts)	CIS/eRRMS (59 pts)	p-values	RRMS (78 pts)	$f$ BRB-NT (83 pts)	p-values	$n$ BRB-NT (54 pts)	$f$ D-KEFS ST (19 pts)	p-values	$n$ D-KEFS ST (118 pts)
Age (years)	38.5±10.9 (18-68)	34.9±9.6 (18-55)	<0.001	41.2±11.0 (18-68)	40.6±11.0 (18-68)	<0.005	35.1±9.9 (18-56)	44.5±9.5 (21-60)	<0.01	37.5±10.8 (18-68)
Gender (M/F)	48/89	20/39	ns	28/50	31/52	ns	17/37	7/12	ns	41/77
Education (years)	12.8±3.7 (5-21)	13.8±3.8 (8-21)	<0.01	12.1±3.4 (5-20)	12.9±3.8 (5-21)	ns	12.6±3.4 (8-20)	11.9±3.8 (8-18)	ns	13.0±3.6 (5-21)
Disease Duration (years)	8.4±9.4 (0-42)	1.1±0.8 (0-3.0)	<0.0001	13.9±9.1 (3.1-42)	9.6±10.7 (0.1-42.1)	ns	6.7±6.7 (0.3-32.9)	15.0±13.4 (0.6-42.1)	<0.0001	7.4±8.2 (0.1-36.1)
EDSS median (range)	2.0 (0-7.0)	2.0 (0-6.0)	=0.05	2.5 (1.0-7.0)	2.5 (0-6.5)	ns	1.8 (0-7.0)	4.0 (1.5-6.5)	<0.05	2.0 (0-7)

Table 1. Clinical and disease parameters in overall population and subgroups.

	Overall MS (137 pts)	CIS/eRRMS (59 pts)	P	RRMS (78 pts)	$f$ BRB-NT (83 pts)	p-values	$n$ BRB-NT (54 pts)	$f$ D-KEFS ST (19 pts)	p-values	$n$ D-KEFS ST (118 pts)
LTS c	45.2±13.8	41.8±13.3	ns	43.5±14.2	38.0±14.4	<0.0001	50.0±9.0	33.1±16.2	<0.005	44.3±12.8
LTS z	30 (22%)	13 (22%)	ns	17 (22%)	30 (36%)	<0.0001	0 (0%)	11 (58%)	<0.0005	19 (16%)
CLTR c	35.3±14.9	32.5±15.7	ns	32.6±14.3	26.3±14.5	<0.0001	42.2±9.3	21.9±15.8	<0.005	34.3±14.1
CLTR z	33 (24%)	14 (24%)	ns	19 (24%)	33 (40%)	<0.0001	0 (0%)	11 (58%)	<0.001	22 (19%)
SPART c	20.6±5.0	20.4±4.5	ns	20.5±5.4	18.8±5.3	<0.0001	23.0±3.1	16.6±4.5	<0.005	21.1±4.8
SPART z	32 (23%)	14 (24%)	ns	18 (23%)	32 (39%)	<0.0001	0 (0%)	10 (53%)	<0.005	22 (19%)
SDMT c	50.3±12.9	51.8±11.9	ns	48.9±13.5	45.0±11.5	<0.0001	58.1±10.6	36.3±12.9	<0.0001	52.4±11.4
SDMT z	31 (23%)	9 (15%)	ns	18 (23%)	27 (31%)	<0.0001	0 (0%)	14 (74%)	<0.0001	13 (11%)
PASAT c	41.4±11.8	38.3±11.6	ns	42.1±11.8	35.7±11.6	<0.0005	47.3±8.2	31.0±9.2	<0.001	41.7±11.6
PASAT z	37 (27%)	22 (37%)	ns	15 (19%)	37 (45%)	<0.0001	0 (0%)	10 (53%)	<0.05	27 (23%)
SRT-D c	8.8±2.7	8.3±2.5	ns	8.0±2.9	6.9±2.7	<0.0001	9.9±1.6	6.5±2.8	<0.005	8.4±2.6
SRT-D z	38 (28%)	15 (25%)	ns	23 (29%)	38 (46%)	<0.0001	0 (0%)	10 (53%)	ns	28 (24%)
SPART-D c	7.4±2.3	7.4±2.0	ns	7.1±2.4	6.5±2.4	<0.0005	8.4±1.6	5.2±2.0	<0.0005	7.6±2.2
SPART-D z	29 (21%)	12 (20%)	ns	17 (22%)	29 (35%)	<0.0001	0 (0%)	8 (42%)	ns	21 (18%)
WLG c	27.1±6.4	27.7±6.4	ns	26.6±6.4	25.6±6.5	<0.001	29.3±5.6	22.8±5.6	<0.005	27.8±6.3
WLG z	17 (12%)	7 (12%)	ns	10 (13%)	17 (20%)	<0.001	0 (0%)	6 (32%)	ns	11 (9%)
OV BRB-NT	83 (61%)	34 (58%)	ns	49 (63%)	83 (100%)	<0.001	0 (0%)	18 (95%)	<0.001	65 (55%)
D-KEFS ST FSC c	9.2±2.3	9.0±2.2	ns	8.9±2.4	8.2±2.3	<0.0001	10.0±1.8	5.4±2.8	<0.0001	9.5±1.6
D-KEFS ST FSC z	12 (9%)	5 (8%)	ns	7 (9%)	12 (14%)	<0.005	0 (0%)	12 (63%)	<0.0001	0 (0%)
D-KEFS ST FSD c	35.6±9.3	35.1±8.8	ns	34.5±9.7	31.8±9.3	<0.0001	39.1±7.4	19.9±10.6	<0.0001	37.1±6.5
D-KEFS ST FSD z	11 (8%)	5 (8%)	ns	6 (8%)	11 (13%)	<0.005	0 (0%)	11 (58%)	<0.0001	0 (0%)
D-KEFS ST SR c	35.6±10.6	36.5±9.4	ns	33.1±11.2	31.5±11.5	<0.0001	39.3±6.6	14.2±8.1	<0.0001	37.8±6.5
D-KEFS ST SR z	18 (13%)	5 (8%)	ns	13 (17%)	17 (20%)	<0.001	1 (2%)	18 (95%)	<0.0001	0 (0%)
OV D-KEFS ST	19 (14%)	5 (8%)	ns	14 (18%)	18 (21%)	<0.005	1 (2%)	19 (100%)	<0.0001	0 (0%)
MSNQ	17.0±11.9	14.6±11.3	<0.005	20.6±11.7	19.3±12.5	ns	15.7±10.6	26.2±14.2	<0.005	16.7±10.9
FSS	3.2±1.5	2.9±1.4	<0.005	3.6±1.6	3.5±1.5	ns	3.0±1.5	3.6±1.8	ns	3.3±1.5
BDI-II	8.0±7.8	10.4±8.7	0.3	8.9±7.0	10.6±8.4	ns	8.0±6.6	13.9±9.3	<0.005	8.8±7.3

Table 2. Neuropsychological scores in overall population and subgroups.

## Conclusions

Our data demonstrate that a subgroup of MS patients (14%) has got impaired executive functions. This can be observed even in early disease phases in 8% of the patients. Executive functions, that are not explored by BRB-NT, are associated with a worse perceived quality of life and concern abilities that may be relevant also for therapeutic compliance, such as planning, problem solving and decision making, should be assessed by D-KEFS ST in all MS patients.

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1) Between CIS/eRRMS and RRMS, no difference in corrected BRB-NT or D-KEFS ST scores was observed (Table 2). In both groups, an exponential correlation was observed between the number of failed BRB-NT tests and the percentage of failure in D-KEFS ST ( $r^2$  value: 0.975, Figure 1).

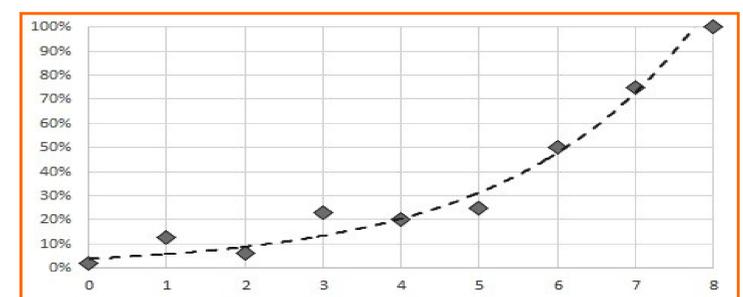


Figure 1. Number of failed BRB-NT tests correlates with the percentage of failure in D-KEFS ST.

- Only SDMT mildly correlated to D-KEFS ST.
- Except for age, no difference was found between  $f$ BRB-NT and  $n$ BRB-NT in any other demographical data (Table 1). Furthermore, MSNQ, FSS and BDI-II scores did not differ within the two groups (Table 2).
- Compared to  $n$ D-KEFS ST,  $f$ D-KEFS ST were older, had longer disease duration and higher EDSS (Table 1). BDI-II and MSNQ presented higher values in  $f$ D-KEFS ST (Table 2). Finally,  $f$ D-KEFS ST presented a mean of 4 failed items of BRB-NT. The frequency of  $f$ D-KEFS ST increased with age ( $p < 0.05$ ) but not with DD ( $p = 0.4$ ).