The EDSS integration with the Brief International Cognitive Assessment for Multiple Sclerosis and Orientation Tests (iEDSS)

Saccà F[1], Costabile T[1], Carotenuto A[1], Lanzillo R[1], Moccia M[1], Pane C[1], Russo CV[1], Barbarulo AM[2], Casertano S[2], Rossi F[2], Signoriello E[2], Lus G[2], Brescia Morra V[1]

[1]Department of Neurosciences, Odontostomatological and Reproductive Sciences, University Federico II, Naples, Italy; [2]University of Campania Luigi Vanvitelli, Department of Clinical and Experimental Medicine, Naples/Italy

BACKGROUND

• Cognitive impairment (CI) affects about 40–60% of MS subjects, and involves all the disease subtypes and tends to progress over time, sometimes independently of the accumulation of physical disability. CI is often underrated but it can have an important negative impact on patient everyday activities, employment, social activities, and quality of life.
• The most commonly used instruments to estimate cognitive dysfunction in MS patients are the Brief Repeatable Battery (BRB) and the Minimal Assessment of Cognitive Function in MS (MACFIMS). Both tests explore different cognitive domains in MS, but they last 45 to 90 minutes.
• The Brief International Cognitive Assessment for MS (BICAMS) takes about 15 minutes, and can be administered by health care professionals who are not necessarily cognitive specialists.
• Despite cognitive tests have been validated in Multiple Sclerosis (MS), a neuropsychological evaluation is not implemented in the Expanded Disability Status Scale (EDSS) scoring.The aim of our study was to propose a quick and objective method to measure the Cerebral Functional Score (CFS) of the EDSS, and to evaluate its impact on the EDSS score on a large cohort of MS patients.

METHODS

• We used the BICAMS and orientation tests (OTs) to measure the Cerebral Functional System (CFS) score, and to evaluate its impact on the EDSS (Table 1). We compared EDSS calculated as usual (Native-EDSS) and after the integration of the BICAMS and OT (iEDSS).
• We performed a multivariate logistic regression analysis to test the effect of age, age at onset, disease duration, sex, education, and native-EDSS on two dependent categorical variables: impaired-BICAMS (three normal tests = 0, at least one altered test = 1), improvable-EDSS (Native- and iEDSS are equal = 0; Native- and iEDSS are different = 1).
• We performed an ordinal multivariate logistic regression analysis in order to determine whether the previous factors and covariates were related to the BICAMS severity (number of altered tests.

RESULTS

• We tested 604 MS patients with BICAMS, OTs, and EDSS (Table 2)
• 384 patients (63.6%) had at least one altered test at the BICAMS.
• Older age, lower education, higher native-EDSS, and male gender, were independently associated with at least one impaired BICAMS test. (Table 3)
• Native-EDSS was different from NPS-EDSS (-0.112; p<0.001) in 99 patients (16%).
• When considering patients with a Native-EDSS ≤4.0, the proportion of miscalculated EDSS was 25%.
• One-year follow-up data were available for 306 patients and showed a mismatch between Native-EDSS and iEDSS in 15% of patients, and in 22.6% of patients with an EDSS ≤4.0

Table 1. Definitions of Cerebral Functional Scores

CFS	Kurtzke - EDSS	NEUROSTATUS	iEDSS
0	Normal	None	All three BICAMS tests are normal. No disorientation.
1	Mood alteration only (does not affect EDSS score)	Signs only: not apparent to patient and / or significant other	One impaired BICAMS test. No disorientation.
2	Mild decrease in mentation	Mild: patient and/or significant other report mild changes in mentation. Examples include: capable of handling routine daily activities, but unable to tolerate additional stressors; reduced performance; tendency toward negligence due to obliviousness or fatigue.	Two impaired BICAMS tests. No disorientation.
3	Moderate decrease in mentation	Moderate: abnormalities on brief mental status testing, but still oriented to person, place and time	Three impaired BICAMS test. No disorientation.
4	Marked decrease in mentation (chronic brain syndrome)	Marked: not oriented in one or two spheres (person, place or time), marked effect on lifestyle	Disorientation in one or two spheres, independent of BICAMS.
5	Dementia, or chronic brain syndrome, severe or incompetent	Dementia confusion and/or complete disorientation	Disorientation in three spheres, independent of BICAMS.

CFS = Cerebral Functional Score; EDSS = Expanded Disability Status Scale; BICAMS = Brief International Cognitive Assessment for Multiple Sclerosis.

Table 2. Demographics

Parameter	Value
Age at enrolment, years ± SD (range)	42.5 ± 11.3 (15–73)
Female, n (%)	399 (66.1)
Disease duration, years ± SD (range)	12.9 ± 8.9 (0.1–45.4)
EDSS, score ± SD (range)	3.52 ± 1.9 (0–7.5)
Education, years ± SD (range)	12.7 ± 3.7 (3-24)
Disease form RR, n (%)	509 (85.4)
Disease Modifying Therapy	
Interferon beta 1-a s.c.	97
Interferon beta 1-a i.m.	60
Interferon beta 1-b	56
Glatiramer acetate	25
Dimethylfumarate	55
Teriflunomide	41
Fingolimod	159
Natalizumab	106
Alemtuzumab	1
Cyclophosphamide	1
No therapy	3

SD = Standard Deviation; EDSS = Expanded Disability Status Scale

Table 3. Multivariate Logistic Regression

Logistic Regression of Impaired BICAMS			
Factors	OR	CI 95%	Significance (p)
Age (years)	1.021	1.004, 1.039	0.014
Gender (male)	1.507	1.035, 2.195	0.033
Education (years)	931	0.887, 0.977	0.004
EDSS	1.242	1.117, 1.379	0.001
Ordinal Logistic Regression of BICAMS severity			
Disease duration (years)	1.019	1.000, 1.037	0.045
Gender (male)	1.382	1.012, 1.888	0.042
Education	922	0.886, 0.960	0.001
EDSS	1.271	1.164, 1.388	0.001
Logistic Regression of improvable-EDSS			
Gender (male)	1.657	1.022, 2.686	0.040
Education	892	0.835, 0.954	0.001
EDSS	756	0.600, 0.952	0.017

EDSS = Expanded Disability Status Scale; BICAMS = Brief International Cognitive Assessment for Multiple Sclerosis; NPS-CFS = Neuropsychological assisted Cerebral Functional Score; OR = Odds Ratio; CI 95% = 95% Confidence Interval; OR of the Ordinal Logistic Regression refer to the probability of being in the group with the higher score in the NPS-CFS (score = 3).

CONCLUSIONS

The use of brief neuropsychological tests leads to a more accurate CFS assessment in two-thirds of patients, and to a more accurate disability measurement at baseline and follow-up (25% less mistakes in patients with EDSS≤4.0) The iEDSS may help recognize cognitive impairment in everyday clinical practice, and correctly assess No Evidence of Disease Activity (NEDA) during follow-up.