

Cognition in Multiple Sclerosis (MS) Across the Lifespan



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Objective

To use a highly sensitive, computerized brief cognitive assessment in individuals with MS across the adult and pediatric age range.

Background

Few cognitive studies have compared pediatric and adult MS patients, and are often evaluated with different tests. We evaluated a large group of MS participants across the life span using two cognitive screening assessments: the Brief International Cognitive Assessment in MS (BICAMS) and the Cogstate Brief Battery.

The BICAMS measure is a clinical screen developed by an international committee and measures the domains considered to be most affected by MS (information processing speed, visual and verbal learning). Regression-based normative data for those 18 and older can be obtained through its website www.bicams.net. Here, we adapted the BICAMS approach to extend its use to those younger than 18 by using a different verbal learning measure.

The computerized Cogstate Brief Battery is often used in clinical trials and was developed for sensitive detection of cognitive impairment and repeated assessment to identify cognitive change. Cogstate can be administered for ages six and older, and offers the strength of an extensive normative database (>50,000 participants) for children aged 10 years and older. The BICAMS and Cogstate batteries take approximately the same time to administer.

Methods

Participants were either consecutively-recruited during routine outpatient visits (pediatric-onset) or through their participation in other ongoing clinical studies (adult-onset). The BICAMS approach includes three measures: SDMT (information processing), BVMT-R (visual learning) and a verbal list learning measure. While originally intended for use with the California Verbal Learning Test-II, here this was substituted with either the Selective Reminding Test (SRT) or the Rey Auditory Verbal Learning Test (RAVLT). Both alternate measures provide multiple forms for repeat assessment and one version for use across the age range.

The Cogstate Brief Battery includes four measures: Detection Task (simple reaction time), Identification Task (choice reaction time), One Card Learning Task (visual learning), and One-Back Task (working memory). For all measures, scores of one standard deviation or more below the published age-based normative data were considered impaired; having one or more impaired scores counted as an impaired assessment.

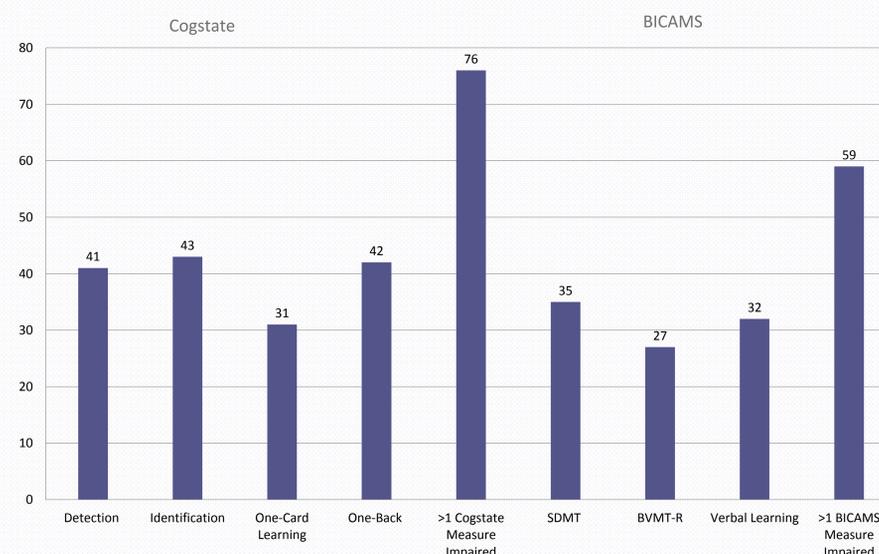
Table 1. Demographic and Clinical Features (n=172)

Female v. Male	67% vs. 33%
Age (mean SD, range)	27 ± 16 (8 to 69) years
Race	65% White, 22% African American, 13% Other
Hispanic	26%
Pediatric v. Adult Onset	n=108 (63%) v. n=64 (37%)
EDSS	0.0 to 8.0, median 2.0
Disease Duration	7±8 years (<1 to 45) years
Subtypes	RRMS n=155 SPMS n=12, PPMS n=1 CIS n=2, RIS n=3

Results

As shown in Figure 1, the Cogstate speeded information processing measures of simple (Detection) and choice (Identification) reaction time and working memory (One Back) were more sensitive to detecting cognitive impairment compared to the learning measure (One Card Learning). These measures had the highest impairment rates overall. The speeded information processing measure the SDMT was the most sensitive of the BICAMS measures.

Figure 1. Percent of Sample Impaired on Cogstate Brief Battery and BICAMS (n=172)



Results (continued)

Of the 172 participants, a total of 122 completed both the full BICAMS and the Cogstate assessments. There was a higher impairment rate on Cogstate than BICAMS with 91% agreement on impaired cases.

As would be expected, older age significantly correlated with higher EDSS ($r=0.59$) and disease duration ($r=0.72$). Neither age nor disease duration correlated significantly ($p<.01$) with any of the Cogstate or BICAMS measures. While not significant, the adult-onset participants performed more poorly than the pediatric-onset participants across all measures. This difference was greatest on the simple reaction time task (Cogstate Detection). Here, the slower performance in the adult- vs. pediatric-onset participants approached significance (mean age normative z score = -1.13 vs. -0.79, $p=0.09$).

Conclusion

- Cognitive impairment was found to be frequent across all ages, ranging from 58 to 76% of the sample.
- Speeded processing measures are the most sensitive to detecting MS-related cognitive impairment.
- The computerized Cogstate battery detects impairment more frequently than BICAMS, with high agreement between both approaches.
- A common standardized cognitive assessment can be applied to individuals with MS across the lifespan.

References

1. Benedict, R.H., et al., *Brief International Cognitive Assessment for MS (BICAMS): international standards for validation*. BMC Neurol, 2012. **12**: p. 55.
2. Julian, L., et al., *Cognitive impairment occurs in children and adolescents with multiple sclerosis: results from a United States network*. J Child Neurol, 2013. **28**(1): p. 102-7.
3. Langdon, D.W., et al., *Recommendations for a Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS)*. Mult Scler, 2012. **18**(6): p. 891-8.
4. Maruff, P., et al., *Validity of the CogState brief battery: relationship to standardized tests and sensitivity to cognitive impairment in mild traumatic brain injury, schizophrenia, and AIDS dementia complex*. Arch Clin Neuropsychol, 2009. **24**(2): p. 165-78.