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Impaired cognition without behavioral problems in pediatric clinically isolated syndrome (CIS)

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Objective

To characterize cognitive and behavioral functioning in children younger than 18 years of age with clinically isolated syndrome (CIS).

Background

Pediatric MS is diagnosed when the onset of the disease occurs before age 18 and has a rare incidence [1]. Clinically isolated syndrome (CIS) refers to the first demyelinating event and represents the earliest clinical stage of the disease process. In adults, there is an estimated 57% rate of conversion from CIS to MS within two years [2].

Cognitive impairment is estimated to occur in one-third of children with MS but the rate of impairment in pediatric CIS is unknown. Cognitive impairment has been reported in adults with CIS, but at a lesser frequency than MS [3]. This study describes the cognitive function of 44 pediatric CIS patients evaluated in the US pediatric MS network.

Methods

Patients were evaluated between 2006 and 2011 at one of six Pediatric MS Centers of Excellence cross country (University of California, San Francisco; Mayo Clinic, Rochester, Minnesota; University of Alabama Birmingham; State University of New York at Buffalo, New York; Stony Brook Children's Hospital, Stony Brook, New York; Massachusetts General Hospital, and Partners HealthCare, Boston, Massachusetts).

Participants were considered eligible for analyses if they were diagnosed with pediatric CIS (onset prior to 18 years). They were also required to be relapse-free and off all steroids at least one or more months from the time of cognitive testing. All participants completed at least 9 of the 11 neuropsychological tests shown in Table 1.

Impairment ratings were determined from 25 scores derived from the tests using age-stratified normative data. The traditional benchmark definition for mild impairment was used, defined as a score falling at least 1 SD deviation below the normative mean, with moderate impairment requiring scores 2 SDs or more below population norms.

Impairment per participant was computed from the sum of the number of impaired test scores divided by the total number of completed test scores (25). A participant was considered impaired when this proportion of impaired scores was greater than one-third. Table 2 shows the characteristics of the sample.

Table 1. Neuropsychological Evaluation Measures

Domain	Measure
Behavioral Functioning	BASC-2, parent rating and self-report forms
Verbal Functioning/ Reading/Language	WASI Vocabulary WIAT-II Pseudoword Decoding Expressive One Word Vocabulary Test
Attention/Working Memory/ Speeded Processing	Digit Span Test Coding/Digit Symbol
Executive Functioning	Contingency Naming Test DKEFS Trail Making Test
Verbal Learning and Recall	California Verbal Learning Test-C/II
Visuospatial Functioning	Beery-Buktenica Visuomotor Integration Test
Fine Motor Speed/Coordination	Grooved Pegboard

Table 2. Clinical & Demographic Features (n=44)

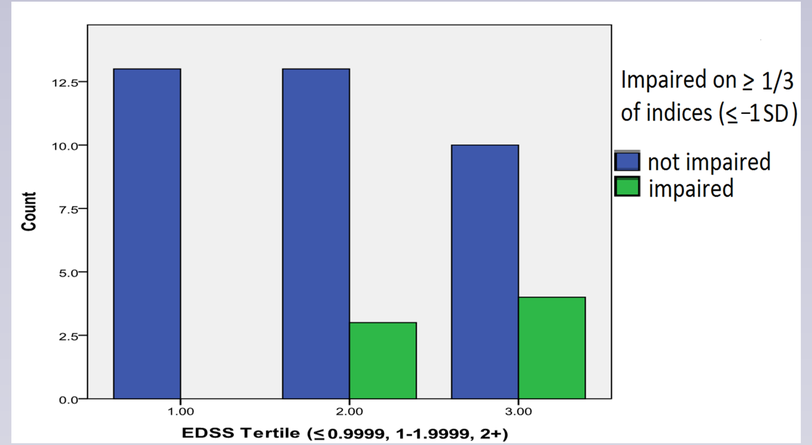
Age, M ± SD (years)	14.8 ±2.6
Female, n (%)	24 (55)
Caucasian, n (%)	35 (80)
African American, n (%)	4 (9)
Asian, n (%)	2 (4)
Mixed/Other, n (%)	3 (7)
Hispanic, n (%)	15 (34)
Disease Duration, M ± SD (years)	0.8 ± 1.7
Age Symptom Onset, M ± SD (years)	14.0 ± 3.0
EDSS score, median (range)	1.0 (0-6.5)
NP indices ≤ -1 SD, median (range)	4 (0-17)
One-third of NP indices ≤ -1 SD, n (%)	8 (18)

Results

The 44 participants who met eligibility criteria had a mean of 14.8± 2.6 years of age, an average interval between symptom onset and evaluation of 0.8±1.7 years, and a median Expanded Disability Status Scale (EDSS) of 1.3 (range 0 to 6.5).

A total of eight (18%) with CIS met criteria for cognitive impairment. Impairment was most frequently found on tests of visuomotor integration (57%) and speeded information processing (34%). Clinically elevated behavioral symptoms were most frequently reported on parent ratings of depression (n=5, 11%), anxiety (n=4, 9%) and somatization (n=4, 9%). The number of BASC-2 scales (parent rating and self-report) rated in the clinically significant range was not associated with number of cognitive tests impaired (r=.02, p>.94), EDSS (r=.20, p>.43), or presence or absence of overall cognitive impairment.

Figure 1. Cognitive Impairment Increases with Neurologic Disability



Conclusions

- Cognitive impairment can be identified in pediatric CIS.
- The cognitive domains most frequently affected are visuomotor integration and speeded information processing.
- Cognitive impairment in CIS is not associated with parent or patient behavioral ratings.

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