Journal of Child Neurology
1-6

DOI: 10.1177/0883073816636227
jcn.sagepub.com
SAGE

# Behavioral Symptoms in Pediatric Multiple Sclerosis: Relation to Fatigue and Cognitive Impairment

**Leigh Charvet, PhD[1], Bianca Cersosimo, BS[2], Colleen Schwarz, BS[1,2], Anita Belman, MD[1,2], and Lauren B. Krupp, MD[1,2]**

## Abstract

The emotional and behavioral problems associated with pediatric multiple sclerosis remain unclear. Participants with pediatric multiple sclerosis or clinically isolated syndrome (n = 140; ages 5-18 years) completed self- and parent ratings using the Behavioral Assessment System for Children, Second Edition, neurologic exam, the Fatigue Severity Scale, and neuropsychological assessment. Mean self- and parent-ratings on the Behavioral Assessment System for Children, Second Edition, were in the typical range across all scales. However, 33.1% indicated a clinically significant problem on a least 1 scale. Although the type of clinical problems varied across participants, attention problems, somatization, and anxiety were found to be most common. Disease features including duration, age of onset, neurologic disability, and fatigue did not distinguish those with and without clinical problems. However, cognitive functioning significantly predicted the presence of a clinical problem ($P = .02$). Pediatric multiple sclerosis is associated with a range of nonspecific emotional and behavioral clinical problems, occurring more frequently in those patients with cognitive involvement.

## Keywords

pediatric, multiple sclerosis, behavior, cognition, fatigue, BASC-2

Received May 15, 2015. Received revised January 2, 2016. Accepted for publication February 5, 2016.

The onset of multiple sclerosis (MS) during childhood and adolescence presents unique clinical challenges.[1] Pediatric (under age 18) onset is rare, with an estimated incidence of 0.2 to 0.6 per 100 000.[2] Although adult-onset MS is associated with increased risk for mood disorders and other psychiatric problems,[3] less is known concerning the psychiatric and psychosocial consequences in pediatric patients.

Initial studies of pediatric MS samples indicated that behavioral problems may be a frequent concern. Descriptive studies have found increased rates of mood disturbances, as reported by parents.[4] These disturbances potentially increase over the disease course.[5] Using semistructured psychiatric interviews, studies have reported elevated rates of mood and anxiety disorders[6] as well as depressive symptoms,[7] especially in those presenting with cognitive impairment and/or fatigue.

We sought to characterize the behavioral and emotional problems observed in a large consecutively recruited sample of pediatric MS patients, and to test whether these problems were associated with disease features or symptoms of fatigue or cognitive impairment. Problems were identified using the parent- and self-report forms of the Behavioral Assessment System for Children, Second Edition (BASC-2), a multi-item inventory that addresses adaptive skills, behavioral symptoms, externalizing problems, internalizing problems, and school problems. It is used to broadly screen for areas of clinical concern in children, adolescents and young adults.[8,9] Items present questions that allow participants to assess their adaptive and prosocial skills (eg, positive school functioning) as well as problem behaviors or feelings that may indicate the presence of a clinical disorder(s) (eg, inattention, mood disturbance). The BASC, Second Edition, is commonly used to screen and characterize these problems in youth with clinical diagnoses[8-10] as well as with healthy children in atypical situations.

[1] New York University MS Comprehensive Care Center, New York, NY, USA
[2] Department of Neurology, Stony Brook Medicine, Stony Brook, NY, USA

**Corresponding Author:**
Leigh Charvet, PhD, New York University MS Comprehensive Care Center, 240 East 38th Street, 20th Floor, New York, NY 10016, USA.
Email: Leigh.Charvet@nyumc.org

## Methods

Participants were consecutively recruited during outpatient clinical visits to the Lourie Center for Pediatric Multiple Sclerosis of Stony Brook Medicine in Stony Brook, New York between April 2006 and May 2014. This study was IRB approved and all individuals provided written, informed consent before participating. All participants were aged 18 years and younger, with those below the age of 18 presenting with symptom onset the prior year. All participants met criteria for a diagnosis of pediatric MS or clinically isolated syndrome,[11] with no other neurologic diagnosis. Those presenting with clinically isolated syndrome were included as, having had a clinical event consistent with MS, this group may be considered to represent those in the earliest stages of the disorder.[12] Participants with a current MS relapse, or who had received treatment with steroids within 1 month's time of cognitive assessment were excluded.

### Neurologic, Cognitive, and Fatigue Assessment

Neurologic assessment included confirmation of the diagnosis, date of symptom onset, and a neurologic examination that included the Expanded Disability Status Scale.[13] The majority of the participants also underwent neuropsychological evaluation at the same visit that the BASC, Second Edition, was administered. Neuropsychological evaluations used a battery of tests developed through consensus for use in the US Network of Pediatric MS Centers and reported as part of the national cross-sectional study,[14] assessing a broad range of areas including attention, executive functioning, and verbal and visual learning. Following the methods of the original cognitive study,[14] each test score was converted to an age-normative z score, with an average z score composite across measures representing cognitive functioning. Participants were determined to have cognitive impairment based on at least one-third of test scores falling 1 standard deviation or more below the age normative mean.

For a subset, fatigue was also measured using the self-reported Fatigue Severity Scale.[15] The Fatigue Severity Scale includes 9 items addressing fatigue severity and its influence on daily activities. Each item is rated along a 7-point scale, with higher ratings indicating more severe fatigue. In this manner, scores can range from 9 to 63. For adult samples, severe fatigue is suggested by scores >36; however, this has not yet been validated for younger patients.

Behavioral ratings were completed using the BASC, Second Edition, self- and parent-report forms (self-report of personality [SRP] and parent rating scales [PRS], respectively). Two SRP forms were used, each tailored toward a specific age group, ages 8 to 11 and ages 12 to 21. Similarly, 2 parent rating scales forms were designated for parents of children who were between the ages of 6 to 11 and 12 to 21. The length of the reports depended on the form administered, ranging from 134 to 160 items. Each item was either rated along a 4-point Likert-type scale ("never" to "almost always") or a "true or false" statement. All participants were English-speaking and reading; Spanish language forms were provided to parents who were primary Spanish speakers.

The BASC, Second Edition, includes clinical and adaptive functioning scales. Although there is some overlap, the individual scales vary from self- and parent-report forms, and also with age range. Each scale score is transformed to a *T* score (mean = 50, standard deviation = 10) based on the extensive age-normative database[10] with a normal distribution. Therefore, a scale *T* score falling 2 standard deviations from the normative mean represents the second percentile, indicating only 2% or less of the normative sample to have scored in that range. Scores in this range are considered to be "clinically significant."

Participants' BASC, Second Edition, profiles were scored (double entry) using BASC-2 ASSIST Software and generated using the program software referencing large normative databases (combined sex).[16] Only participants with profiles showing acceptable validity indices were included for analyses.

**Table 1.** Demographic and Clinical Characteristics.[a]

| | |
|---|---|
| Age, M ± SD (range) | 14.9 ± 2.6 (5 y 9 mo to 18 y) |
| Female, n (%) | 81 (57.6) |
| Race, n (%) | – |
| White | 75 (69.4) |
| African American | 21 (19.4) |
| Asian | 3 (2.8) |
| Mixed/other | 5 (4.6) |
| Hispanic ethnicity, n (%) | 32 (28.1) |
| Disease duration, M ± SD (range) | 1.6 ± 2.6 y (<1 to 10.1 y) |
| Age at symptom onset, M ± SD (range) | 12.5 ± 3.3 (2 y 4 mo to 17 y) |
| EDSS score,[13] median (range) | 1.0 (0.0 to 6.5) |

Abbreviations: BASC-2, Behavioral Assessment System for Children, Second Edition; EDSS, Expanded Disability Status Scale; M, mean; SD, standard deviation; SRP, self-report of personality; PRS, parent rating scales.
[a]Total n = 140 with 1 BASC-2 report: n = 128 with SRP form, n = 130 with PRS, and n = 119 with both SRP and PRS

### Analyses

Study data were collected and managed using REDCap electronic data capture tools hosted at Stony Brook Medicine[17] and analyses were completed using SPSS, version 22.0. A descriptive approach was used to determine whether there was any pattern of clinical concerns for the sample using the mean scores for the full group across both self-report of personality and parent rating scales. Next, the frequency of clinically significant scores was determined across individuals. Using group comparisons, we then tested whether any disease features or the symptoms of fatigue and cognitive impairment contributed to the likelihood of having a clinically significant score.

## Results

### Demographic and Clinical Factors

A total of 140 participants completed at least 1 report form of the BASC, Second Edition. The majority of the sample (n = 108, 77.1%) met criteria for relapsing remitting MS and the remainder were diagnosed with clinically isolated syndrome (n = 32, 22.9%). Sample characteristics are demonstrated in Table 1.

### Cognitive Functioning

Of the full sample with BASC, Second Edition, reports, 120 also completed the neuropsychological assessment. A total of n = 38 (37.1%) were classified as having cognitive impairment (n = 32 multiple scleroses vs n = 6 clinically isolated syndromes). This rate of impairment is consistent with what was found in the larger US Network sample (32%).[14] The mean composite *z* score (lower scores indicating greater impairment)

**Table 2.** Cognitive and Fatigue Symptom Measures in Sample Subsets.

| | MS | CIS | Total | Typical range |
|---|---|---|---|---|
| Cognitive functioning[a] | | | | |
| n | 91 | 20 | 120 | |
| Composite z score, M ± SD (range) | –0.37 ± 0.78 (–3.40 to 1.88) | –0.11 ± 0.72 (–1.37 to 2.20) | –0.31 ± 0.77 (–3.40 to 2.20) | 0.00 ± 1.00 (–1.00 to 1.00) |
| Fatigue Severity Scale[15] | | | | |
| n | 46 | 20 | 66 | |
| Self-report, M ± SD (range) | 30.06 ± 14.37 (9 to 53) | 32.70 ± 13.78 (12 to 72) | 30.86 ± 14.14 (9 to 72) | 20.70 ± 6.30 (<27) |

Abbreviations: CIS, clinically isolated syndrome; M, mean; MS, multiple sclerosis; SD, standard deviation.
[a]Cognitive functioning composite z score, with lower values indicating greater impairment; tests in battery were the Wechsler Abbreviated Scale of Intelligence, including Vocabulary and Matrix Reasoning subtests,[18] Wechsler Intelligence Scale for Children–Fourth Edition,[19] and Wechsler Adult Intelligence Scale–Fourth Edition–Digit span,[20] Contingency Naming Test,[21] California Verbal Learning Test–Child[22] or second edition,[23] Beery-Buktenica Developmental Test of Visual-Motor Integration–6th edition,[24] Wechsler Abbreviated Scale of Intelligence Matrix Reasoning,[18] Expressive One Word Picture Vocabulary Test,[25] Wechsler Individual Achievement Test–II,[26] Wechsler Abbreviated Scale of Intelligence,[18] Delis-Kaplan Executive Functioning System Trail Making Test–motor speed condition,[27] Pediatric Quality of Life Inventory–Multidimensional Fatigue Scale[28]; see Julian et al.[14]

for the full sample was $z = –0.31 \pm 0.77$, indicating average range of functioning overall. Although the MS participants had overall lower cognitive functioning than the clinically isolated syndrome participants, this difference was not significant (mean $z$ score of $–0.37 \pm 0.78$ vs $–0.12 \pm 0.71$, $P = .12$).

## Fatigue

A total of n = 66 participants also completed the Fatigue Severity Scale, indicating mild to moderate levels of fatigue overall (Table 2).

*Behavioral symptoms at the group level.* Of the 140 participants with BASC, Second Edition, data, n = 128 had completed self-report forms and n = 130 had parent-report forms completed, whereas n = 119 had both self- and parent-report forms completed. Figure 1 illustrates the mean scores for each of the clinical scales for the self-report of personality and parent rating scales for the sample as a whole. As shown, no mean score on any clinical scale for self- or parent-report forms fall outside of the typical range (all mean $T$ scores between 45 and 55).

*Behavioral symptoms across individuals.* At the individual profile level, there was a high frequency of scales rated in the clinically significant range. Across the sample, 29.9% and 34.1% of the self-report of personality and parent rating scales profiles, respectively, had at least 1 scale in the clinically significant range, indicating approximately one-third of the sample having a clinical concern and that the parents were slightly more likely to indicate the presence of a behavioral concern. Figure 2 shows the rates of clinically significant scores for the self- and parent-report form composite scales.

*Comparison of self- and parent-reports.* Parents reported clinically significant problems at generally the same rate as were reported by the participants themselves (16.2% vs 14.7%). More than 5% of parents reported clinically significant scores in 8 different scales, whereas participant self-reports only highlighted 6 clinically significant scales of dysfunction (Figure 2). Both parent and participant reports seemed to agree on scales of dysfunction that occurred at higher frequencies, such as problems with attention, somatization, and hyperactivity.

*Predictors of BASC, Second Edition, clinical elevations.* Those participants with at least 1 clinically significant scale elevation (self-report of personality or parent rating scales, n = 34 or 33.1%) were compared to those with profiles in the typical range across demographic and clinical features. Among the demographic features, gender but not age, race, or ethnicity trended toward significant association with the presence of a clinical problem: 62% of the girls versus 28% of the boys, $\chi^2(1, N = 96) = 4.17$, $P = .04$ (all other $P$s > .12).

MS and clinically isolated syndrome participants did not significantly differ in rates of clinically significant elevations for either the parent rating scales (35.0% vs 30.0%, respectively, $P = .72$) or self-report of personality (28% vs 34%, $P = .51$). Further, between those with and without at least 1 clinically significant elevation, there were no significant differences in age, age of onset, disease duration, Expanded Disability Status Scale, or fatigue (all $P$s > .12). However, the clinical elevation group had significantly lower cognitive functioning (mean composite $z$ score $= –0.69 \pm 0.78$ vs $–0.18 \pm 0.74$, $P = .007$). Cognitive functioning (composite $z$ score) and fatigue (Fatigue Severity Scale score) were not significantly related, $r = 0.09$, $P = .48$, consistent with its unique association to the presence of a cognitive problem. Finally, those meeting criteria for cognitive impairment were significantly more likely to have at least 1 clinically significant problem, $\chi^2(1, N = 113) = 5.56$, $P = .02$.

# Discussion

In this large and consecutively evaluated sample, one-third (33.1%) of those diagnosed with pediatric MS or clinically isolated syndrome had clinically significant elevations on at least 1 self- or parent-reported BASC, Second Edition, clinical scale. However, no one scale consistently emerged to characterize the MS group's behavioral symptoms as a whole. Taken

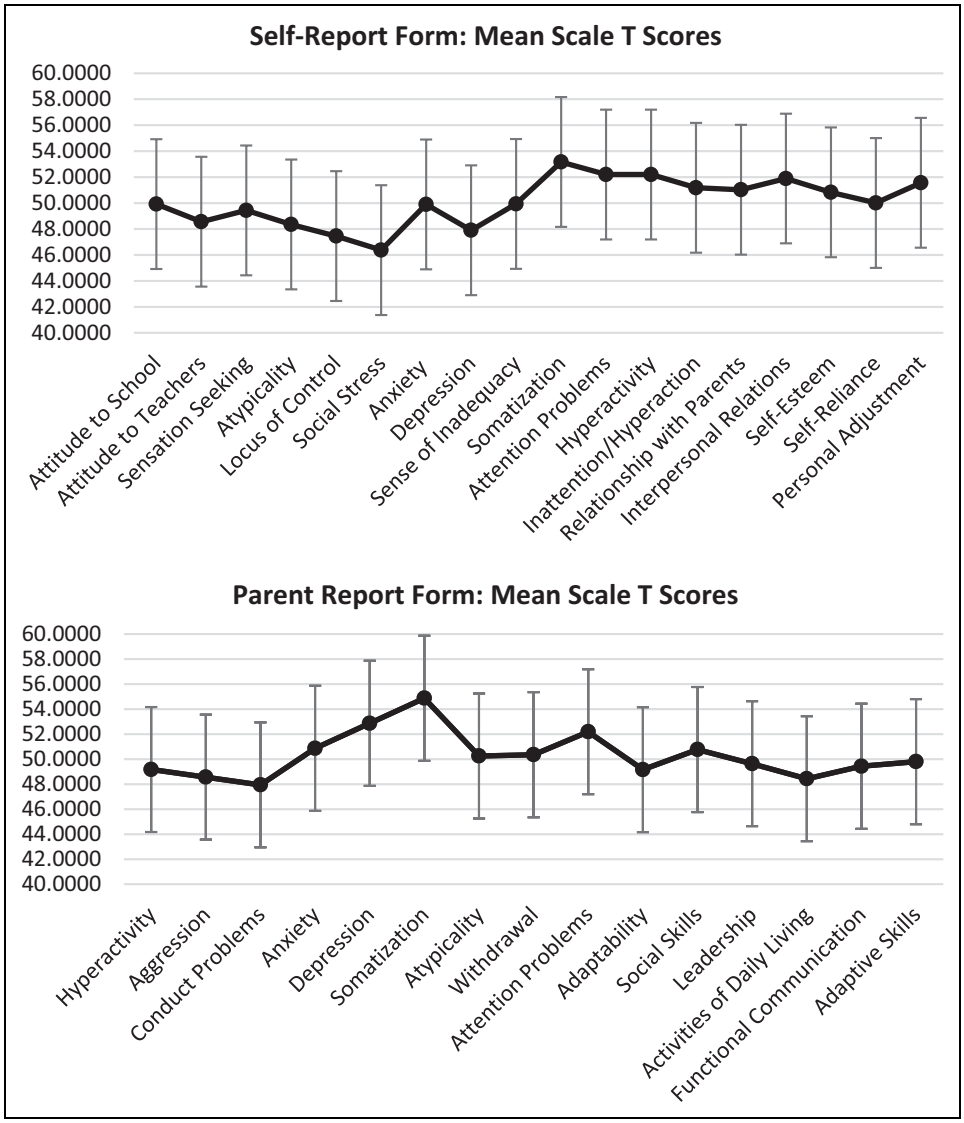


**Figure 1.** Mean scale T scores for self- and parent-report forms.

together, these findings indicate frequent clinically significant behavioral and emotional problems in pediatric MS.

Participants self-reported slightly lower rates of impairment than was reported by their parents, but both indicated similar problem areas of attention problems, somatization, and anxiety with other internalizing problems. Attention problems may indicate awareness and experience of the influence of MS on cognition, as information processing is the earliest and most common type of impairment.[29] Anxiety and internalizing symptoms in general may indicate concern with the diagnosis and future disease course, and problems related to living with a medical diagnosis during childhood. Elevations on the somatization scale are likely to reflect, at least in part, the symptoms of MS as they are experienced.

Age, age of onset, and disease features of duration and severity (Expanded Disability Status Scale) were not associated with behavioral ratings on either self- or parent-reports. Among the symptoms measured, cognitive impairment, but not fatigue, was a significant predictor of BASC, Second Edition, impairment.

The current findings are generally consistent with prior studies that have used the BASC, Second Edition, to characterize behavioral issues in smaller samples. Only 1 study has found clinical elevations in the BASC, Second Edition, for a MS sample, and only in parent-report scales measuring depression and anxiety.[30] The other 2 studies[7,31] found all self- and parent-reports to fall within the typical range, but with elevations relative to healthy control participants. In a study focused on depression and fatigue in pediatric demyelinating disorders (children diagnosed with MS, n = 36, and acute disseminated encephalomyelitis, n = 13), Parrish and colleagues[7] found that parents reported their children to have more depressive symptoms than parents of healthy control participants (with no difference in self-reported depression ratings between the demyelinating disorder group and healthy controls). Till and colleagues[30] compared a Canadian sample of 31 consecutively recruited pediatric multiple scleroses participants to 31 controls and found that although both groups' mean scale scores were within the typical

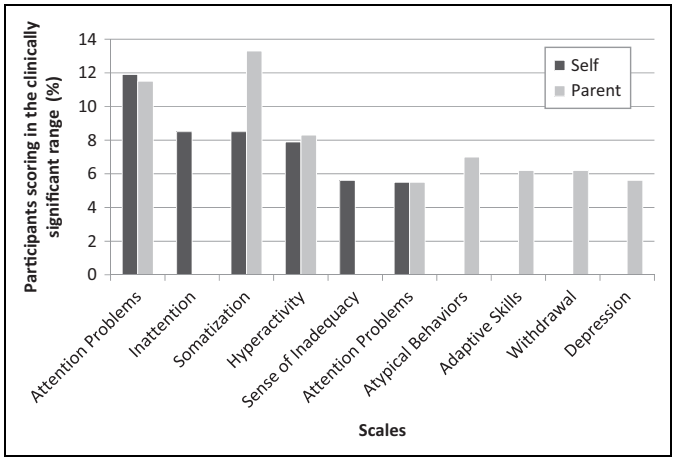


**Figure 2.** Scales with >5% Clinically Significant Ratings.

(nonclinical) range, the MS group had more frequently reported problems. Self-reported problems included inattention/hyperactivity and lower self-reliance, and parent-reported problems included depression, higher somatization, and lower adaptive functioning when compared to controls. Overall, these studies suggested that behavioral problems were generally related to elevated symptoms such as fatigue,[7,30,31] but without strong relation to other disease features including years of disease,[32] Expanded Disability Status Scale,[13] or imaging markers.[33,34]

Although we found cognitive impairment to be linked to higher risk of behavioral problems, the mechanism of the risk remains unclear. Cognitive impairment is a common feature of both adult[35,36] and pediatric MS,[14,33,37] reported in approximately 30% of patients across varying samples and methods. Of the studies including both cognitive and behavioral measures, findings have been variable. In a subset of these participants who also received psychiatric interviews,[6] those who were concurrently diagnosed with an anxiety or mood disorder had the highest frequency of cognitive impairment. Parent-reported depression has also been reported as a predictor of poorer executive functioning.[31] However, other studies have found an absence of a strong relation between behavioral problems and cognitive performance.[7,14] Future studies may be designed to specifically test hypotheses concerning the direct link between cognitive involvement of MS and the resulting emotional and behavioral problems. For example, cognitive difficulties may increase the disease burden on a daily basis, therefore raising overall stress. Or, certain types of cognitive impairment such as executive dysfunction may contribute to poorer emotional and behavioral control.

There are several limitations to the current study. No healthy control participants were available for comparison. It is important to note that prior studies have found more subtle differences between the MS and healthy control groups even when group averages were within the nonclinical range.[7,30] Instead, our study focused on the frequency of clinically significant elevations in reference to the normative data provided by the BASC, Second Edition, scoring system. Also, including a comparison group with other neurologic disorders as well as general medical illness[38-41] would allow us to isolate any risk factors related to behavior and emotional functioning unique to pediatric MS patients.[7] Although we included fatigue measurement in a subset, it would have been useful to include these measures for the full sample. Additional symptom inventories would be helpful as well to better understand the full impact of the disease.

Despite these limitations, it is clear that nonspecific behavioral problems are a frequent occurrence in this pediatric MS sample, and that the presence of cognitive impairment elevates this risk. Future studies should focus on the specificity of the association between cognitive impairment and behavioral problems for pediatric MS or pediatric central nervous system disorders, as well as the overall more general effects of chronic illness in childhood.[42] The behavioral, cognitive, and physical changes of pediatric MS clearly impact a child's life. Early detection can hopefully lead to the provision of support services to ease burden for patients and their families.

## Acknowledgments

We would like to thank Dana Serafin for her role in data collection, test administration, and data entry. Michael Porter and Nikita Gupta also assisted with scoring, data entry, and management.

## Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Lourie Foundation, Inc; National Multiple Sclerosis Society (grant number PP2106, 10020073405); NIH (grant number R01NS071463); and the Slomo and Cindy Silvian Foundation.

## Ethical Approval

This study and related data collection were approved by the Institutional Review Board of Stony Brook Medicine, Stony Brook, New York, #2011-1362. Informed consent was obtained from all participants' parent/legal guardians and, when appropriate, assent was obtained from participants.

## References

1. Krupp LB, Tardieu M, Amato MP, et al. International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis and immune-mediated central nervous system demyelinating disorders: revisions to the 2007 definitions. *Mult Scler*. 2013;19:1261-1267.
2. Langer-Gould A, Zhang JL, Chung J, Yeung Y, Waubant E, Yao J. Incidence of acquired CNS demyelinating syndromes in a multiethnic cohort of children. *Neurology*. 2011;77:1143-1148.
3. de Cerqueira AC, Semionato de Andrade P, Godoy Barreiros JM, Teixeira AL, Nardi AE. Psychiatric disorders in patients with multiple sclerosis. *Comprehensive Psychiatry*. 2015;63:10-14.
4. MacAllister WS, Boyd JR, Holland NJ, Milazzo MC, Krupp LB. The psychosocial consequences of pediatric multiple sclerosis. *Neurology*. 2007;68:S66-S69.
5. Amato MP, Goretti B, Ghezzi A, et al. Cognitive and psychosocial features in childhood and juvenile MS: two-year follow-up. *Neurology*. 2010;75:1134-1140.

6. Weisbrot D, Charvet L, Serafin D, et al. Psychiatric diagnoses and cognitive impairment in pediatric multiple sclerosis. *Mult Scler*. 2014;20:588-593.
7. Julian L, Serafin D, Charvet L, et al. Cognitive impairment occurs in children and adolescents with multiple sclerosis: results from a United States network. *J Child Neurol*. 2013;28:102-107.
8. Kamphaus RW, Reynolds CR. Behavior assessment system for children—second edition (BASC-2): Behavioral and Emotional Screening System (BESS). Pearson, 2007.
9. Reynolds CR, Kamphaus RW. BASC-2: Behavior assessment system for children. Corsini Encyclopedia of Psychology. Online. New York: John Wiley & Sons, Inc, 2004.
10. Reynolds CR, Kamphaus RW. BASC-2 Behavior Assessment System for Children Second Edition Manual Supplement for the Clinical Report. Bloomington, MN: Pearson, 2010.
11. Krupp LB, Banwell B, Tenembaum S. Consensus definitions proposed for pediatric multiple sclerosis and related disorders. *Neurology*. 2007;68:S7-S12.
12. Kuhle J, Disanto G, Dobson R, et al. Conversion from clinically isolated syndrome to multiple sclerosis: A large multicentre study. *Mult Scler*. 2015;21:1013-1024.
13. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33: 1444-1452.
14. Julian L, Serafin D, Charvet L, et al. Cognitive impairment occurs in children and adolescents with multiple sclerosis: results from a United States network. *J Child Neurol*. 2013;28:102-107.
15. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol*. 1989;46:1121-1123.
16. Reynolds CR, Kamphaus RW. *A Clinician's Guide to the BASC*. New York: The Guilford Press; 2002.
17. Paul A. Harris, Harris Robert Taylor, Robert Thielke, Jonathon Payne, Nathaniel Gonzalez, Jose G. Conde. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381.
18. Corporation TP. *The Wechsler Abbreviated Scale of Intelligence*. San Antonio, TX: Harcourt Assessment; 1999.
19. Watkins MW, Smith LG. Long-term stability of the Wechsler Intelligence Scale for Children—fourth edition. *Psychol Assess*. 2013;25:477-483.
20. Wechsler D. Wechsler Adult Intelligence Scale–Fourth Editon. 2008.
21. Anderson P AV, Northam E, Taylor HG. Standardization of the Contingency Naming Test: a measure of reactive flexibility. *Clin Neuropsychol*. 2000;1:247-273.
22. Delis D KJ, Kaplan E, Ober B. *California Verbal Learning Test–Children's Version (CVLT-C)*. San Antonio, TX: Psychological Corporation; 1994.
23. Delis D, et al. *California Verbal Learning Test Manual: Second Edition, Adult Version*. San Antonio, TX: Pearson; 2000.
24. Beery KE, Buktenica NA, Beery NA. *Beery-Buktenica Developmental Test of Visual-Motor Integration*. Minneapolis, MZ: NCS Pearson; 2006.
25. Gardner MF. *Expressive One-Word Picture Vocabulary Test*. Novato, CA: Academic Therapy Publications; 1979.
26. Wechsler D. *Wechsler Individual Achievement Test 2nd Edition (WIAT II)*. London: The Psychological Corp; 2005.
27. Delis DC, Kaplan E, Kramer JH. *Delis-Kaplan Executive Function System (D-KEFS) examiner's manual*. San Antonio, TX: The Psychological Corporation; 2001b:1-218.
28. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the Pediatric Quality of Life Inventory. *Med Care*. 1999;37:126-139.
29. Hughes AJ, Denney DR, Lynch SG. Reaction time and rapid serial processing measures of information processing speed in multiple sclerosis: complexity, compounding, and augmentation. *J Int Neuropsychol Soc*. 2011;17:1113-1121.
30. Till C, Udler E, Ghassemi R, Narayanan S, Arnold DL, Banwell BL. Factors associated with emotional and behavioral outcomes in adolescents with multiple sclerosis. *Mult Scler*. 2012;18:1170-1180.
31. Holland AA, Graves D, Greenberg BM, Harder LL. Fatigue, emotional functioning, and executive dysfunction in pediatric multiple sclerosis. *Child Neuropsychol*. 2014;20:71-85.
32. Banwell BL, Anderson PE. The cognitive burden of multiple sclerosis in children. *Neurology*. 2005;64:891-894.
33. Till C, Ghassemi R, Aubert-Broche B, et al. MRI correlates of cognitive impairment in childhood-onset multiple sclerosis. *Neuropsychology*. 2011;25:319-332.
34. Till C, Deotto A, Tipu V, et al. White matter integrity and math performance in pediatric multiple sclerosis: a diffusion tensor imaging study. *Neuroreport*. 2011;22:1005-1009.
35. Amato MP, Portaccio E, Goretti B, et al. Relevance of cognitive deterioration in early relapsing-remitting MS: a 3-year follow-up study. *Mult Scler*. 2010;16:1474-1482.
36. Achiron A, Barak Y. Cognitive impairment in probable multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2003;74:443-446.
37. Amato MP, Goretti B, Ghezzi A, et al. Cognitive and psychosocial features of childhood and juvenile MS. *Neurology*. 2008;70: 1891-1897.
38. Thompson E, Kline E, Reeves G, Pitts SC, Bussell K, Schiffman J. Using parent and youth reports from the Behavior Assessment System for Children, Second Edition to identify individuals at clinical high-risk for psychosis. *Schizophr Res*. 2014;154:107-112.
39. Caruso NC, Radovanovic B, Kennedy JD, et al. Sleep, executive functioning and behaviour in children and adolescents with type 1 diabetes. *Sleep Med*. 2014;15:1490-1499.
40. Ensign J, Maricle DE, Brown C, Mayfield JW. Psychosocial subtypes on the behavior assessment system for children, second edition following pediatric traumatic brain injury. *Arch Clin Neuropsychol*. 2012;27:277-292.
41. Wolfe-Christensen C, Mullins LL, Stinnett TA, Carpentier MY, Fedele DA. Use of the Behavioral Assessment System for Children 2nd Edition: Parent Report Scale in pediatric cancer populations. *J Clin Psychol Med Settings*. 2009;16:322-330.
42. Taylor HG, Albo VC, Phebus CK, Sachs BR, Bierl PG. Postirradiation treatment outcomes for children with acute lymphocytic leukemia: clarification of risks. *J Pediatr Psychol*. 1987;12: 395-411.