Relationship between sleep, fatigue and depression in pediatric multiple sclerosis

Tara Berenbaum, BSc[1,2], Stephanie A. Grover, MSc, CCRP[2], Samantha Stephens, PhD[2], Shelly Weiss, MD, FRCPC[1,4], Indra Narang, MEDSCI, MBBCH, FRCPCH, MD[3,4] and E. Ann Yeh, MD, MA, FRCPC, Dip ABPN[1,2,4]
(1)Division of Neurology, The Hospital for Sick Children, Toronto, ON, CA; (2)Department of Neurosciences and Mental Health, The Hospital for Sick Children, Toronto, ON, CA;
(3)Respiratory Medicine Division, The Hospital for Sick Children, Toronto, ON, CA; (4)Department of Paediatrics, University of Toronto, Toronto, ON, CA

BACKGROUND

- Fatigue and depression common in pediatric multiple sclerosis (MS)[1]
- Decreased quality of sleep known to be associated with fatigue and depression in adults with MS and healthy children[2,3]
- Prevalence of sleep problems in pediatric MS and their relationship with fatigue and depression is not well studied

OBJECTIVES

(1) To determine the prevalence of sleep problems in pediatric MS.

(2) To examine the relationship between sleep quality, fatigue and depression.

METHODS

Population:
- Participants were recruited from the Neuroinflammatory Clinic at the Hospital for Sick Children (HSC)
- Inclusion criteria: (1) Diagnosis of MS or monophasic acquired demyelinating syndrome (mono-ADS); (2) Age 5 to 17 and 11 months
- Exclusion criteria: (1) Attack within last 30 days; (2) Age <5 or ≥18

Questionnaires:
1. Child Sleep Habits Questionnaire (CSHQ) – subscales: bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep disordered breathing, daytime sleepiness
2. Child Behaviour Checklist Sleep Composite (CBCL)
3. Pediatric Multidimensional Fatigue Scale (PedsQL)
4. Center for Epidemiological Studies - Depression Scale for Children (CES-DC)

Thresholds:
- CSHQ: total score ≥41 used to identify potential sleep disorder; subscale score ≥mean+1SD of normative data used to identify type of sleep problem(s)
- CBCL: total score ≥1 indicated at least one self-reported sleep problem

Clinical data:
- Collected using a standardized data collection form (HSC Neuroinflammatory Registry). Data analyzed included: (1) Demographic information; (2) Expanded Disability Status Scale (EDSS); (3) disease duration; (4) annualized relapse rate (ARR)

Analysis:
- Differences between total scores in the two groups were analyzed (t-test or Mann-Whitney U)
- Relationship between sleep, fatigue and depression scores was examined (Spearman's correlations)
- Ethics approval was obtained from HSC REB (REB #1000005356)

RESULTS

Table 1. Demographics and disease characteristics

	MS (n = 23)	mono-ADS (n = 34)	p-value
Sex (# of females)	15	18	0.357
Age in years (mean ± SD)	16.11 ± 1.38	12.39 ± 3.20	<0.001*
Range	12.7-17.7	5.4-17.8	–
Disease duration in years (mean ± SD)	2.92 ± 2.29	4.05 ± 3.17	0.146
EDSS score (median (IQR))	1.5 (0.5)	1.0 (1.0)	0.001*
ARR (median (IQR))	0.7 (0.6)	–	–

*p<0.05 is considered statistically significant

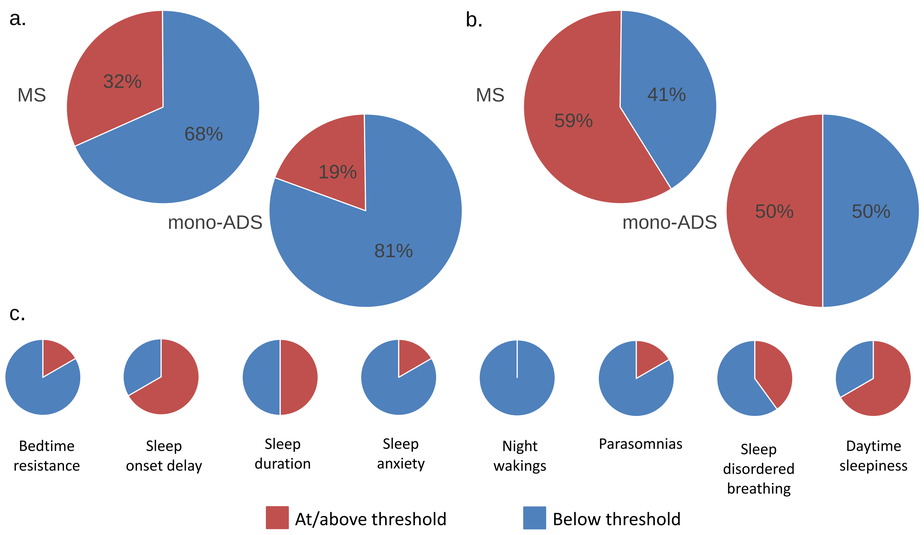

Figure 1. Prevalence of sleep problems. Proportion of MS vs. mono-ADS who met the threshold for a. CSHQ (p=0.341) and b. CBCL (p=0.423). c. Prevalence of specific types of sleep problems in MS who met threshold for CSHQ. *p<0.05 is considered statistically significant

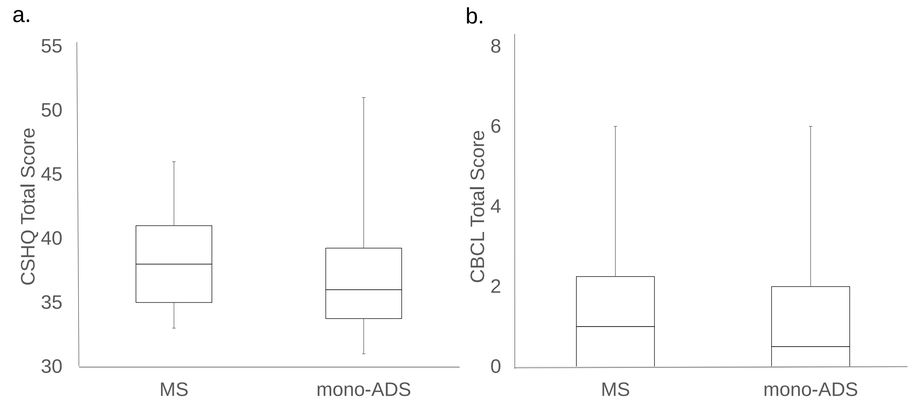

Figure 2. Differences in sleep problems. Median total scores in MS vs. mono-ADS for a. CSHQ (p=0.070) and b. CBCL (p=0.423). *p<0.05 is considered statistically significant

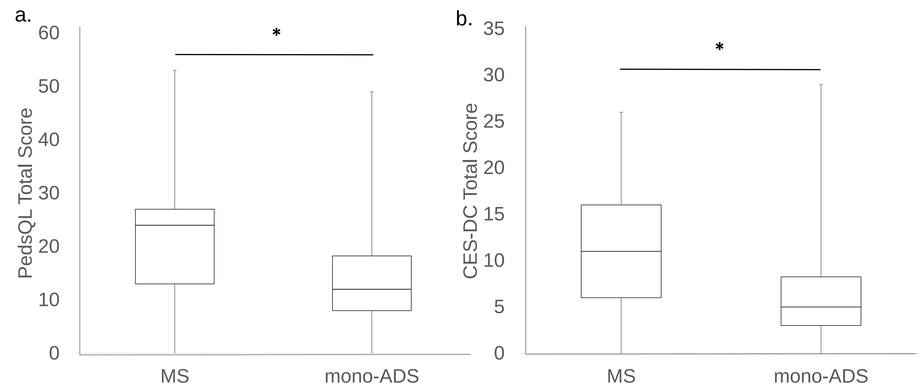

Figure 3. Differences in fatigue and depression. Median total scores in MS vs. mono-ADS for a. PedsQL (p=0.019) and b. CES-DC (p=0.016). *p<0.05 is considered statistically significant

Table 2. Correlations controlled for age

	MS		mono-ADS	
	R	p-value	R	p-value
Sleep (CSHQ) & Fatigue (PedsQL)	0.427	0.087	**0.647**	**<0.001**
Sleep (CSHQ) & Depression (CES-DC)	0.112	0.669	**0.683**	**<0.001**
Sleep (CBCL) & Fatigue (PedsQL)	-0.078	0.766	**0.496**	**0.012**
Sleep (CBCL) & Depression (CES-DC)	0.015	0.955	**0.577**	**0.003**
Fatigue (PedsQL) & Depression (CES-DC)	**0.525**	**0.030**	**0.776**	**<0.001**

* p<0.05 is considered statistically significant

CONCLUSIONS

- It is clear that MS group reported experiencing sleep problems and was at risk for the development of sleep disorders. The most prevalent types of sleep problems in MS were sleep onset delay, sleep duration and daytime sleepiness.
- However, there were no statistically significant differences in the overall prevalence of sleep problems between the two groups.
- MS group reported higher fatigue and depression scores than mono-ADS, as previously shown.
- Higher sleep problem scores were associated with increased fatigue and depression scores in mono-ADS, but not MS.
- Reasons for this are unclear but reinforce the role that ongoing disease activity may play in fatigue and depression in youth with MS.
- Objective measures of sleep (e.g. actigraphy) may be more sensitive to the identification of sleep problems and could provide further insight into the nature of the relationship between sleep, fatigue and depression in youth with MS.

ACKNOWLEDGEMENTS/DISCLOSURES

This project has been funded by the SickKids Research Institute and the SickKids Foundation. The authors would like to thank Dr. Yeh's research team and the staff of the Neuroinflammatory clinic for all of their help and support with this project. The authors have nothing to declare.

REFERENCE

1. Parrish J et al. Fatigue and depression in children with demyelinating disorders. Journal of Child Neurology 2013, 28(6):713-8
2. Chaput J-P, Gray CE, Poitras VJ, et al. Systematic review of the relationships between sleep duration and health indicators in school-aged children and youth. Applied Physiology, Nutrition, and Metabolism 2016;41:S266-S282.
3. Attarian HP, Brown KM, Duntley SP, Carter JD, Cross AH. The relationship of sleep disturbances and fatigue in multiple sclerosis. Archives of Neurology 2004;61:525-528.