Relationship of changes in physical activity to fatigue and depression in pediatric multiple sclerosis

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Background

- Fatigue and depression are common symptoms of pediatric multiple sclerosis (MS)[1].
- In pediatric MS, higher levels of physical activity are associated with lower disease burden and activity[2].
- The relationship between changes in physical activity, fatigue, and depression over time in pediatric MS remains unclear.

Objectives

- To describe the trajectory of fatigue, depression, and physical activity over time in MS in comparison to monophasic acquired demyelinating syndromes (mono-ADS) in the pediatric population
- To investigate the relationship between changes in physical activity and the evolution of fatigue and depression over time in pediatric MS

Methods

Patients

- Patients attending the Pediatric MS and Demyelinating Disorders Clinic at the Hospital for Sick Children (Toronto, Canada) were enrolled consecutively between September 1, 2013, and October 31, 2015.
- Patients were evaluated at baseline and at follow-up within 6-12 months.
- 56 patients (27 MS, 29 mono-ADS) fulfilling the following eligibility criteria were included in this study:
  - Age <18 years at baseline visit
  - Baseline visit within 5 years of clinical onset of disease
  - Stable diagnosis of MS or mono-ADS according to consensus criteria of the International Pediatric MS Study Group[3]
  - Baseline and follow-up visit occurring at least 30 days after a clinical relapse

Clinical Data

- Clinical data (onset date, Expanded Disability Status Scale [EDSS] scores, relapse date, and medication history) were extracted retrospectively from clinical records at baseline and follow-up.

Questionnaire Data

- Patients were administered a battery of standardized and validated self-report questionnaires at baseline and follow-up:
  - **Fatigue:** Pediatric Quality of Life Inventory (PedsQL™) Multidimensional Fatigue Scale[4]
    - 18-item inventory querying general, sleep/rest, cognitive, and total fatigue
    - Dimension score ≥12 or total score ≥36 are suggestive of moderate-to-severe fatigue
  - **Depression:** Center for Epidemiological Studies Depression Scale for Children (CES-DC)[5]
    - 20-item inventory querying depression
    - Scores ≥15 are suggestive of clinically significant depressive symptoms[6]
  - **Physical Activity**: Godin Leisure Time Exercise Questionnaire (GLTEQ)[7]
    - Four-item inventory of usual weekly physical activity, scored in metabolic equivalents (METs)
    - Quantifies strenuous, moderate, mild, and total physical activity
    - Health Contribution Score (HCS) is computed as the sum of the component scores for strenuous and moderate physical activity[7]

Statistical Analysis

- MS and mono-ADS cohorts were compared with respect to demographic, clinical, fatigue, depression, and physical activity characteristics.
- Normality of continuous variables was assessed with a Shapiro-Wilk test.
- Cohorts (MS *vs* mono-ADS) and time points (baseline *vs* follow-up) were compared with a *t*-test, Mann-Whitney *U*-test, Wilcoxon rank-sum test, chi-square test, or Fisher exact test, as appropriate.
- The relationship between fatigue or depression scores at follow-up and changes in physical activity in the MS cohort was evaluated with Spearman correlation analysis.
- Statistical analyses were performed with SPSS Statistics® version 22.0.

Consents and Approvals

- All patients provided informed consent for participation in this research.
- This study was approved by the SickKids Research Ethics Board.

Results

PATIENTS

Table 1. Cohort characteristics. Clinical and demographic features of MS and mono-ADS cohorts.

	MS (n=27)	Mono-ADS (n=29)	*p*
Female, *n*	20 (74.1%)	13 (44.8%)	0.033
Age at onset, median years (IQR)	13.7 (2.4)	10.2 (5.7)	<0.001
Age at baseline, mean years (IQR)	15.6 (3.4)	10.9 (6.2)	<0.001
Disease duration, median years (IQR)	2.0 (1.8)	2.0 (3.2)	0.501
Baseline to follow-up interval, median days (IQR)	243 (84)	334 (144)	0.034
EDSS, median (IQR)	1.5 (1.0)	1.0 (1.0)	0.238
Interval relapses, median (IQR)	0 (0)	--	--
Concurrent DMT at baseline, *n*	15 (55.6%)	--	--
Concurrent antidepressant at baseline, *n*	1 (3.7%)	0 (0.0%)	0.482
Concurrent fatigue medication at baseline, *n*	0 (0.0%)	0 (0.0%)	--

IQR, inter-quartile range; EDSS, Expanded Disability Status Scale; DMT, disease-modifying therapy

PHYSICAL ACTIVITY

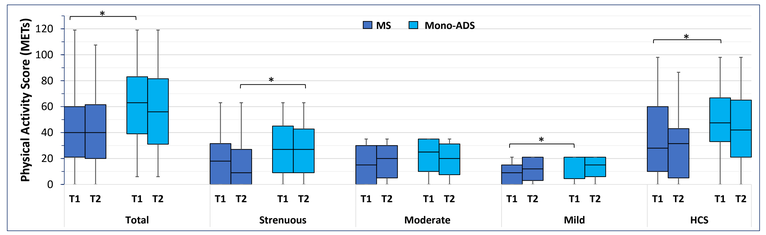

Figure 1. Physical activity. Median total, strenuous, moderate, and mild GLTEQ physical activity scores and Health Contribution Score (HCS) at baseline (T1) and follow-up (T2). (*p<0.05)

- MS patients reported lower total and mild physical activity, as well as HCS at baseline, and lower strenuous physical activity at follow-up (Fig. 1).

FATIGUE

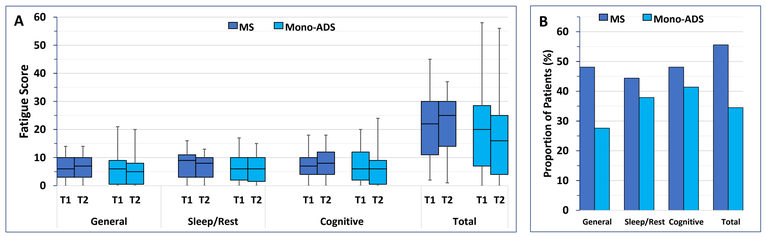

Figure 2. Fatigue. (A) Median dimension-specific and total PedsQL™ fatigue scores at baseline (T1) and follow-up (T2). **(B)** Proportion of patients with interval increase in fatigue score.

- Fatigue scores at baseline and follow-up were similar between MS and mono-ADS patients (Fig. 2A).
- For all dimensions of fatigue, a greater proportion of MS patients reported interval worsening of fatigue scores compared to mono-ADS (Fig. 2B).

DEPRESSION

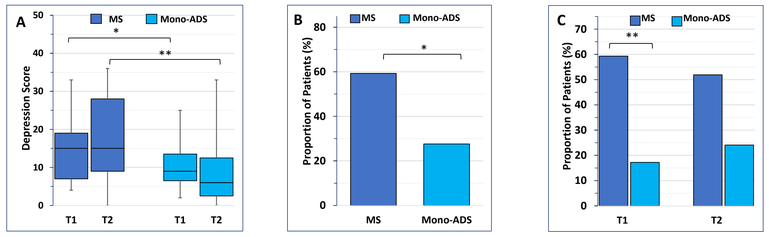

Figure 3. Depression. (A) Median CES-DC depression scores at baseline (T1) and follow-up (T2). Proportion of patients with **(B)** interval increase in depression score and **(C)** depression scores meeting criteria for significant depressive symptoms at baseline (T1) and follow-up (T2). (*p<0.05, **p<0.01)

- The MS cohort reported significantly higher baseline and follow-up depression scores compared to the mono-ADS cohort (Fig. 3A).
- A greater proportion of MS patients reported interval worsening in depression score compared to the mono-ADS cohort (Fig. 3B).
- A greater proportion of MS patients fulfilled criteria for significant depression compared to mono-ADS patients at baseline (Fig. 3C).

CORRELATES OF FATIGUE AND DEPRESION

Table 2. Association of fatigue and depression with physical activity in MS. Spearman correlation analysis of physical activity scores (interval change) and fatigue or depression scores (at follow-up) in the MS cohort. Correlation coefficients, ρ, are shown with p-values in parentheses. Significant correlations are highlighted.

	Total PA	Strenuous PA	Moderate PA	Mild PA	HCS
General Fatigue	**-0.499 (0.008)**	**-0.567 (0.002)**	-0.257 (0.195)	-0.066 (0.743)	**-0.536 (0.004)**
Sleep/Rest Fatigue	**-0.504 (0.007)**	**-0.444 (0.020)**	**-0.417 (0.031)**	-0.165 (0.410)	**-0.539 (0.004)**
Cognitive Fatigue	-0.091 (0.650)	-0.194 (0.332)	-0.005 (0.981)	0.263 (0.185)	-0.167 (0.405)
Total Fatigue	**-0.428 (0.026)**	**-0.483 (0.011)**	-0.238 (0.231)	0.016 (0.939)	**-0.483 (0.011)**
Depression	-0.349 (0.074)	**-0.396 (0.041)**	-0.173 (0.388)	0.197 (0.326)	**-0.416 (0.031)**

PA, physical activity; HCS, Health Contribution Score

- In the MS cohort, significant negative correlations were observed between interval changes in physical activity scores (total physical activity, strenuous physical activity, moderate physical activity, and health composition score) and follow-up scores for fatigue (general fatigue, sleep/rest fatigue, and total fatigue) and depression (Table 2).

Conclusions

- Fatigue and depression are common in pediatric MS. Depression in this population may be more frequent and may fluctuate over brief periods of follow-up (<12 months).
- Children with MS may be less likely than those with mono-ADS to participate in regular physical activity.
- An increase in physical activity (particularly strenuous physical activity) is associated with lower self-reported fatigue and depression in children with MS.
- Limitations of this study include the small sample size and its observational design. Future randomized, controlled studies may clarify the putative causal relationship between changes in physical activity and fatigue or depression in this population.
- Physical activity represents a modifiable behaviour that may potentially ameliorate fatigue and depression in pediatric MS.

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