Dystonia is one of the most common movement disorders in children and is characterized by abnormal, often repetitive movements and/or postures. Individuals with dystonia also commonly experience nonmotor symptoms, such as psychiatric comorbidities, chronic pain, cognitive deficits, and disruptions to sleep. Sleep disturbances and fatigue are particularly debilitating, in some instances correlating more strongly with quality of life than the motor manifestations of dystonia. Most data regarding sleep in pediatric movement disorders are derived from children with cerebral palsy (CP), whose dyskinetic/dystonic subtype is the most common cause of acquired dystonia. Between 25% and 80% of children with CP are affected by sleep disorders, precipitated by sequelae of CP such as upper airway obstruction, epilepsy, and postural limitations. Insomnia and excessive daytime sleepiness have been shown to negatively impact the quality of life of children with CP. Despite a clear association with quality of life and function, with a promising potential to serve as objective biomarkers of disease burden and treatment efficacy, sleep metrics are not routinely assessed in children with dystonia.

Actigraphs are wearable three-axis accelerometers that objectively quantify movement over multiday recordings and provide a unique opportunity to characterize activity in children with dystonia. In particular, actigraphs reliably
measure sleep parameters and complement individually reported and polysomnographic data.9,10 When sleep was quantified using actigraphs among children with CP, the children were found to have shorter sleep duration and poorer sleep efficiency than typically developing children.10,11 However, despite previous studies on CP, no similar investigations have been performed in pediatric dystonia. In addition, while deep brain stimulation (DBS) has been demonstrated to improve dystonia severity as measured by the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS),11–13 no studies to date have objectively quantified changes in sleep post-DBS treatment. In this study, we used actigraphs to compare sleep duration of children with dystonia and typically developing controls, as well as before and after DBS treatment. These findings highlight an underreported aspect of morbidity in pediatric dystonia caused by sleep disturbances and provide a compelling rationale to integrate actigraphy in the clinical monitoring of symptom severity and treatment effect.

Methods

Study Design

Children aged 1–18 years with generalized dystonia, including both genetic and acquired forms of dystonia, were consecutively recruited from the Movement Disorders and Deep Brain Stimulation clinic at the Hospital for Sick Children in Toronto, Canada. Children with other movement disorders such as chorea, tremor, and ataxia were excluded from this analysis. Typically developing age- and sex-matched children were recruited as a control group. Dystonic participants were asked to wear an actigraph on the most affected wrist (as determined by the clinical treatment team) and control participants on the dominant wrist for 14 consecutive days. Dystonia patients underwent a clinical dystonia severity assessment using the BFMDRS.13 BFMDRS motor and disability (BFMDRS-M and BFMDRS-D, respectively) subscores were included in the analysis.

For dystonia patients who were treated with globus pallidus internus (GPi) DBS, BFMDRS and actigraph data were collected before electrode implantation, as well as after implantation and optimization of DBS settings by the treatment team. This study received approval from the Institutional Research Ethics Board of the Hospital for Sick Children, Toronto, Canada, and all study protocols complied strictly with the principles outlined in the Declaration of Helsinki by the World Medical Association.

Actigraphs

Motor activity and temperature were collected continuously for 14 days at 100 Hz using an Axivity AX3 (Axivity Ltd.). Patients were instructed to wear the actigraph at all times for the duration of recording.

Data Processing

Actigraph data were processed using the R package GGIR (version 2.9–0. https://cran.r-project.org/web/packages/GGIR/).14 Auto-calibration of raw accelerometer data was performed, followed by calculation of the Euclidean norm minus one (ENMO) for all time points as previously described.15 Briefly, ENMO is defined as the magnitude of the vector sum of x-, y-, and z-axis accelerations (measured in units of gravitational acceleration 9.81 m/sec^2) with gravity subtracted:

\[
ENMO = \sqrt{a_x^2 + a_y^2 + a_z^2 - 1}
\]

ENMOS were averaged over 5-second epochs and negative values were rounded up to zero. We used the default nonwear detection algorithm implemented by GGIR, based on a 0.013g standard deviation and 0.05g range threshold in at least 2 of 3 axes, applied to overlapping 60-minute windows. Detection of sleep duration was performed using the Heuristic algorithm looking at distribution of change in z-angle (described by van Hees et al., based on sustained inactivity, defined as periods of at least 5 minutes in which the angle between the wrist-worn actigraph and the z-axis changes less than 5°) occurring during the sleep window.16 In the absence of a sleep diary, the sleep window is algorithmically determined using a threshold for the rolling median of z-angle over 5-minute windows, as detailed in van Hees et al.17 First and last nights of recordings were excluded from sleep analyses and only afternoons/evenings (noon to noon periods) with more than 16 hours of valid data were included.

Statistical Analysis

One-way ANOVA and chi-square tests were used to compare demographic variables between groups. Fisher’s exact test was used to compare frequency of pharmacotherapy and botulinum toxin therapy between DBS- and non–DBS-treated groups. The Mann-Whitney U-test was used to compare BFMDRS scores between the two groups. The pairwise Student t-test was used to compare BFMDRS scores before and after DBS surgery. Pearson correlation was used to quantify strength of correlation between sleep time and BFMDRS score, as well as improvement in sleep and BFMDRS score post-DBS. All statistical analyses were conducted using Python 3.8.8 and SciPy 1.10.1.

Results

Patient Demographics

A total of 22 children with dystonia were included; there were 16 nonsurgical patients and 6 patients who underwent GPi-DBS. Ten age- and sex-matched controls were also included. Demographic and clinical variables are summarized in Table 1. There were no significant differences between the groups in terms of age, sex, etiology of dystonia, treatment with pharmacotherapy or botulinum neurotoxin injection, and BFMDRS scores (Table 1).

Clinical Outcomes

After DBS, mean BFMDRS-M scores improved from 73.3 ± 17.5 to 57.6 ± 19.7 (p = 0.006, pairwise t-test). No significant change was observed in BFMDRS-D scores (22.8 ± 5.6 before DBS vs 23.2 ± 5.3 after DBS; p = 0.17, pairwise t-test). Three children showed a clinically significant improvement in their BFMDRS-M score, defined as a
reduction of at least 16.6%.

Of 6 children implanted with DBS, 5 had postimplantation actigraphy up to 5 months postoperatively while the remaining child was assessed 18 months after implantation.

Data Quality

Figure 1 displays a representative night’s single vector magnitude gravity subtracted (SVMgs) and z-angle data for a single patient pre- versus post-DBS. All actigraphs were successfully auto-calibrated using GGIR. Five recordings of dystonia patients were excluded due to lack of at least 1 night with 16 hours of valid data (excluding first and last nights); subsequent analyses were performed on the remaining 14 nonsurgical and 4 DBS-implanted patients. Average daily nonwear time and number of valid nights per recording were not significantly different between control and dystonic actigraphs (1.88 hours vs 0.99 hours, p = 0.18; and mean 9.6 days vs 10.73 days, p = 0.06, respectively; Mann-Whitney U-test).

Sleep and Activity Levels

Patients with dystonia slept fewer hours per night on average compared with typically developing controls (mean 6.23 hours vs 7.43 hours; p = 0.009, Mann-Whitney U-test) (Fig. 2A). Sleep time was negatively correlated with the BFMDRS score, although the association did not reach statistical significance (Pearson r = −0.421, p = 0.073) (Fig. 2B). Waking time after sleep onset, or time awake between initial sleep onset and final morning awakening, was not significantly different between patients with dystonia and controls (1.20 hours vs 0.98 hours; p = 0.28, Mann-Whitney U-test).

Four of 6 patients with dystonia undergoing DBS had sleep data recorded before and after surgery, while recordings from the other 2 children were omitted because of actigraph noncompliance (Fig. 2C). DBS treatment improved sleep significantly in patient 18 when recorded 83 days postimplantation (6.97 hours pre-DBS vs 8.99 hours post-DBS; p < 0.001, Mann-Whitney U-test), although other patients did not experience a significant improvement in daily sleep duration. Change in participants’ mean sleep duration postimplantation across all valid nights was significantly associated with postimplantation improvement in BFMDRS scores (Pearson r = −0.965, p = 0.035) (Fig. 2D).

Discussion

In this study, we used actigraphy to record multiday sleep data in children with dystonia, including those undergoing Gpi-DBS. We demonstrated that children with dystonia have shorter average sleep duration compared with matched, typically developing controls and that sleep deficit may be associated with disease severity. In addition, while DBS did not significantly improve sleep in our cohort, changes in sleep correlated with improvement in dystonia after DBS treatment. To our knowledge, this is the first study using actigraphy to quantify sleep in children with dystonia.

We found that sleep duration is reduced in pediatric
Dystonia and tends to be shorter in more severe cases. Previous studies of sleep in pediatric movement disorders focused on children with CP, in whom sleep disorders are prevalent due to muscle spasms, pain, and comorbid epilepsy. Among patients with CP, those with dyskinetic/dystonic CP were more likely to have disordered sleep than those with spastic CP, particularly disordered sleep-wake transitions, impaired sleep maintenance, and hyperhidrosis. In agreement with our findings, actigraphy studies of sleep in patients with CP have demonstrated that while largely milder cases (i.e., ambulatory, Gross Motor Function Classification Scale level I or II) sleep an adequate amount per night, children with CP overall have shorter measured sleep duration than typically developing children.

Sleep duration increased after GPi-DBS in 1 of 4 children with complete data. GPi-DBS has been reported to improve both subjectively reported and polysomnographic measures of sleep in the context of Parkinson disease, although these findings were often nonsignificant due to small sample sizes. Similarly, because of the heterogeneity of our sample, greater numbers are necessary to make generalizable conclusions regarding the effect of GPi-DBS on sleep. However, in support of such an effect, we found that patients with greater response to GPi-DBS experience greater improvement in sleep.

The strength of our findings is limited by our sample size and single-center cohort. Participants varied in compliance with actigraphs, and data were lost to nonwear time. In addition, we did not control for medication effects or DBS settings, which were individually tailored to patients’ clinical needs. Despite these limitations, this novel study is the first to use actigraphy to objectively quantify sleep parameters in pediatric dystonia, particularly in the context of treatment with DBS. Our results suggest that sleep disturbances are prevalent in children with the disease, and these children should be actively screened to improve their quality of life.

**FIG. 2.** A: Box plot showing comparisons between patients with dystonia and controls. Interquartile ranges (IQRs) are shown with whiskers to 1.5 IQR. B: Linear regression showing that sleep time is negatively correlated with BFMDRS score. The solid line represents least-squares linear regression. C: Box plot showing comparisons of sleep data before and after DBS treatment. D: Least-squares linear regression showing that postimplantation sleep duration is associated with postimplantation improvement in BFMDRS scores. ns = nonsignificant. *p < 0.01; **p < 0.001; Mann-Whitney U-test.
Conclusions

Sleep duration, as measured by wrist-worn actigraphs, is reduced in pediatric dystonia and showed a trending correlation with dystonia severity. While DBS treatment of dystonia patients was inconsistent in improving sleep duration, reduction in symptom severity correlated with increased sleep duration in these patients. These findings are a proof of concept for objective quantification of dystonia severity using wrist-worn actigraphs. In addition, actigraphy can be used to measure response in quality of life measures to DBS treatment.

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References