## Title
Morning light therapy in adults with Tourette's disorder



## Journal
Journal of Neurology, 269(1)

## ISSN
0340-5354

## Authors
Ricketts, Emily J
Burgess, Helen J
Montalbano, Gabrielle E
et al.

## Publication Date
2022

## DOI
10.1007/s00415-021-10645-z

HHS Public Access

Author manuscript

*J Neurol*. Author manuscript; available in PMC 2023 January 01.

Published in final edited form as:

*J Neurol*. 2022 January ; 269(1): 399–410. doi:10.1007/s00415-021-10645-z.

# Morning Light Therapy in Adults with Tourette's Disorder

**Emily J. Ricketts, Ph.D.**[1], **Helen J. Burgess, Ph.D.**[2], **Gabrielle E. Montalbano, B.S.**[1], **Meredith E. Coles, Ph.D.**[3], **Joseph F. McGuire, Ph.D.**[4], **Hardian Thamrin, M.A.**[1,5], **Dana L. McMakin, Ph.D.**[6,7], **James T. McCracken, M.D.**[1], **Mary A. Carskadon, Ph.D.**[8], **John Piacentini, Ph.D., ABPP**[1], **Christopher S. Colwell, Ph.D.**[1]

[1]Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, California, United States

[2]Department of Psychiatry, University of Michigan, Ann Arbor, Michigan, United States

[3]Department of Psychology, State University of New York at Binghamton, Binghamton, New York, United States

[4]Department of Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States

[5]Department of Psychology, Arizona State University, Tempe Arizona, United States

[6]Department of Psychology, Florida International University, Miami, Florida, United States

[7]Department of Neurology, Nicklaus Children's Hospital, Miami, Florida, United States

[8]Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, Rhode Island, United States

## Abstract

**Background:** Sleep disturbance is common among individuals with Tourette's Disorder (TD). Given that sleep is influenced by the circadian system, this study examined circadian rhythms and

Please direct all correspondence to Emily Ricketts, Ph.D., University of California, Los Angeles, Division of Child and Adolescent Psychiatry, 760 Westwood Plz., Los Angeles, CA 90024, (310) 825-2701 (Phone), 310-267-4925 (Fax), ERicketts@mednet.ucla.edu.

Author Contributions

Conceptualization: [Emily J. Ricketts, Ph.D., Meredith Coles, Ph.D., Mary Carskadon, Ph.D., John Piacentini, Ph.D., ABPP, and Christopher Colwell, Ph.D.]; Methodology: [Mary Carskadon, Ph.D., Helen Burgess, Ph.D., Emily J. Ricketts, Ph.D., John Piacentini, Ph.D., ABPP, and Christopher Colwell, Ph.D.]; Formal analysis and investigation: [Emily J. Ricketts, Ph.D., Joseph F. McGuire, Ph.D., Gabrielle E. Montalbano, B. S., and Hardian Thamrin, M.S.]; Writing - original draft preparation: [Emily J. Ricketts, Ph.D., Helen J. Burgess, Ph.D., and Christopher S. Colwell, Ph.D.]; Writing - review and editing: [Emily J. Ricketts, Ph.D., Helen J. Burgess, Ph.D., Gabrielle E. Montalbano, B.S., Meredith E. Coles, Ph.D., Joseph F. McGuire, Ph.D., Hardian Thamrin, M.S., Dana L. McMakin, Ph.D., James T. McCracken, M.D., Mary A. Carskadon, Ph.D., John Piacentini, Ph.D., ABPP, and Christopher S. Colwell, Ph.D.]; Funding acquisition: [Emily J. Ricketts, Ph.D.]; Resources: [John Piacentini, Ph.D., ABPP, and James T. McCracken, M.D.]; Supervision: [Helen J. Burgess, Ph.D., Dana L. McMakin, Ph.D., John Piacentini, Ph.D., ABPP, and Christopher S. Colwell, Ph.D.]

Ethics approval: The authors assert that all study procedures adhere to the ethical standards of the corresponding author's institutional ethics review committee and have been performed in accordance with the ethical standards outlined in the 1964 Declaration of Helsinki, and its subsequent revisions.

Consent to participate: Institutional ethics review committee-approved consent was obtained from all participants included in this study.

Availability of data and material: The data that support the findings of this study are available from the corresponding author upon reasonable request.

sleep in adults with TD, and explored the possible benefit of short-wavelength wearable morning light therapy.

**Methods:** Participants were 34 adults with TD (n=14) and age- and sex-matched healthy controls (HC; n=20). Participants were screened using clinician-rated diagnostic and tic severity interviews, and procedures lasted 3 consecutive weeks. Participants completed a baseline week of actigraphy. Adults with TD completed two weeks of Re-Timer™ morning light therapy and continued actigraphy monitoring. Dim light melatonin onset (DLMO) phase assessment, tic severity interview, and measures of chronotype, sleep disturbance, daytime sleepiness, disability, depression, anxiety, and stress were completed at baseline and post-intervention.

**Results:** Adults with TD reported significantly greater eveningness and sleep disturbance relative to controls. Per wrist actigraphy, adults with TD exhibited significantly longer sleep onset latency, lower sleep efficiency, and greater sleep fragmentation than HC. Following morning light therapy there was significant advances in DLMO phase, but not self-report or actigraphy sleep variables. There were small, statistically significant decreases in tic severity and impairment. There were also significant reductions in daytime sleepiness, and self-reported anxiety, but not depression, stress, or disability. Participants reported minimal side effects and rated light therapy as acceptable and comfortable.

**Conclusions:** Findings showed some benefits following brief light therapy in TD; further exploration of the impact of spectral tuning the photic environment as part of treatment for TD subjects is warranted.

### Keywords

tic; circadian; melatonin; chronotype; actigraphy; sleep; sleepiness; depression; anxiety

## Introduction

Tourette’s disorder (TD) is a childhood-onset neurological condition involving multiple repetitive, involuntary movements and one or more vocalizations enduring for over a year, and associated with underlying basal ganglia thalamocortical dysfunction [1,2]. Beyond the hallmark features of TD, co-occurring psychiatric conditions often include ADHD, OCD, anxiety, and depression [3,4]. Sleep disturbance is also common, occurring in 11% to 16% of adults with TD [4,5]. Sleep problems in TD include difficulties falling asleep, night time awakenings, abnormal movements and tics during sleep, parasomnias, reduced sleep quality, and daytime sleepiness, and are associated with co-occurring psychiatric disorders and symptoms (i.e., ADHD, anxiety, obsessive-compulsive symptoms, and depression), increased tic severity, and female sex [6,7]. However, few objective studies have examined sleep in TD, particularly in adult samples.

The sleep-wake cycle is regulated in part by our circadian rhythm [8]. Circadian abnormalities (encompassing the sleep-wake cycle, and key circadian markers, including phase of melatonin, cortisol, and core body temperature), and delays or advances in chronotype (i.e., eveningness or morningness preference or timing) – the behavioral manifestation of circadian rhythms – are present in many neurological and psychiatric disorders [9–11]. However, there is a lack of research regarding circadian biology and

TD. Nevertheless, circadian delays and evening chronotype have been found in commonly co-occurring neurodevelopmental disorders, such as ADHD and OCD [12–14]. Given the shared deficits in inhibition of unwanted actions and basal ganglia thalamocortical circuitry among these three disorders, it is plausible that there may too be circadian delays in TD [2].

Light is a potent circadian entraining agent; thus, light therapy (LT) presents a powerful treatment to address circadian misalignment, with morning LT yielding circadian phase advances and evening light producing circadian phase delays [15]. LT can also positively affect sleep, mood, and alertness [16]. LT intervention has historically used a stationary box emitting white light to the retina at intensities ranging from 2,500 to 10,000 lux [17]. Although effective, adherence may be reduced by time constraints and the need to remain in front of the device for the session duration [18]. Further, research suggests that short-wavelength (i.e., blue-green) light may produce more robust circadian phase shifts at lower intensities and shorter durations than white light [19,20]. Guided by these data, researchers have developed the Re-Timer™, a wearable device emitting short-wavelength light [21]. Studies to date have shown that one week of morning Re-Timer™ LT was associated with a significant circadian phase advance in healthy adults relative to no-light control [21], and four weeks of morning Re-Timer™ LT in adults with probable post-traumatic stress disorder was associated with significantly greater reductions in symptoms of post-traumatic stress disorder and depression relative to sham-control (i.e., dimmed Re-Timer™ light) [22].

Only two case reports have examined the effects of LT in individuals with TD. Two adolescent males with TD received daily morning LT at 2,500 lux for 2 weeks, showing modest reductions in tic severity after six days, relative to a sham control administered 6 weeks later [23]. One adult female with persistent vocal tic disorder using morning LT at 10,000 lux daily (approximately 2 hours/day) for major depressive disorder, noted improved mood and tics after 6 weeks [24]. Although promising, more research is needed to establish the effects of LT in individuals with TD. The present study 1) evaluated the degree to which there are circadian delays and sleep disturbance in adults with TD relative to healthy controls (HC) at baseline, and 2) examined the extent to which short-wavelength wearable morning LT was associated with advanced circadian phase and improved sleep and clinical symptoms. Findings will help to elucidate the role of circadian rhythms in TD, and test a novel targeted, non-pharmacologic intervention.

## Methods

### Participants

Participants were 34 adults: 14 with TD ($n$=12, 85.7%) or persistent motor tic disorder ($n$=2, 14.3%), and 20 age- and sex-matched HC recruited through an academic medical center. Participants were 30.15 years of age (SD=7.48) and predominantly males (67.6%). There were no significant group differences in demographic characteristics (see Table 1). See Table 2 for clinical characteristics of adults with TD.

Inclusion criteria included an age of 22 to 50 years and English fluency. For the TD group, additional inclusion criteria included DSM-5 [1] diagnosis of TD or persistent (motor or vocal) tic disorder (PTD), Yale Global Tic Severity Scale (YGTSS) [25] total tic severity ≥

14 for Tourette's Disorder or ≥ 10 for PTD. Inclusion criteria for the HC group included no current or lifetime history of DSM-5 psychiatric disorders.

Exclusion criteria for adults with TD included lifetime diagnosis of bipolar disorder, psychosis, or pervasive developmental disorder; suicidality, severe depression or anxiety, or substance dependence present within the prior 6 months; current diagnosis of obstructive sleep apnea, restless leg syndrome, periodic limb movement disorder, or narcolepsy; use of prescribed or over-the-counter sleep medication within one month of study enrollment; and change in other psychotropic medication status or dose within one month of study enrollment.

HC were excluded for current or lifetime psychiatric disorders, including sleep disorders; and lifetime psychotropic medication use or prescribed or over-the-counter sleep medication use within one month of study enrollment. Exclusion criteria for both groups included intellectual functioning below the low average range (i.e., IQ score < 80); night shift work or travel across > 2 time zones in the past month; current pregnancy; and any medical or neurological condition likely to interfere in participation. We screened 18 adults with TD for eligibility. Four were ineligible due to: non-primary TS ($n$=2), recovery from surgery ($n$=1), and tic severity below cutoff ($n$=1). We screened 29 for eligibility for the control group. Seven were excluded due to early morning shift work ($n$=1), age discrepancy ($n$=1), and meeting diagnostic criteria for a psychiatric disorder ($n$=5); and two withdrew ($n$=2).

## Procedure and Measures

Individuals who appeared eligible following phone screening, completed an in-person screening evaluation. An interviewer assessed for psychiatric diagnosis (Mini International Neuropsychiatric Interview for DSM-5) [26], sleep disorders (Diagnostic Interview for Sleep Patterns and Disorders) [27], and tic symptom severity (YGTSS). A research coordinator administered a brief test of intellectual functioning [28]. Participants reported on sleep (Pittsburgh Sleep Quality Index) [29], chronotype (Morningness Eveningness Questionnaire-Revised) [30], negative affect (Depression Anxiety Stress Scale) [31], and disability (Sheehan Disability Scale) [32]. Following the screening assessment, eligible participants monitored their sleep for seven consecutive nights (see Sleep Monitoring section below), and returned, the day following the seventh night, for a dim light melatonin onset (DLMO) assessment to evaluate circadian phase. For adults with TD, this evaluation also included a clinical baseline assessment involving re-administration of the YGTSS and completion of self-report measures, including the Epworth Sleepiness Scale [33]. The day immediately following baseline, adults with TD began fourteen consecutive days of 1-hour morning LT, and continued to monitor sleep, followed by a post-intervention DLMO assessment and a clinical evaluation occurring on the final day of LT, assessing adverse effects (Light Effect Questionnaire) [34] and treatment perceptions of LT, adapted from a behavior therapy for TD trial [35]. See Online Resource 1 for measure descriptions. Participants received monetary reimbursement of up to $400.

**Sleep Monitoring.—**Participants wore an actigraph (Actiwatch Spectrum Pro, Philips Respironics, Amsterdam, Netherlands) on their non-dominant wrist for the duration of the

study to measure movement and light, which was recorded in 30-second epochs using a medium sensitivity movement-detection threshold. Participants were instructed to press a marker on the actigraph to indicate bedtime (i.e., time in bed with the intention of falling asleep) and rise time (i.e., time out of bed). Participants were also instructed to record their bedtimes, rise times, and other sleep variables using a daily sleep diary, in addition to text messaging bedtimes and rise times to the lab as a backup sleep record. Bedtimes and rise times were not fixed. This information was used to schedule the DLMO assessment and inform actigraphy scoring. A trained scorer processed actigraphy using Philips Actiware version 6.0.9, according to existing procedures [36], which suggest setting the bounds of the rest interval (i.e., time in bed, and time out of bed) based on the marker, followed by sleep diary bedtimes and rise times, then light and activity information. A second scorer reviewed all rest intervals for accuracy. The software yielded sleep start and end times, used to calculate sleep mid time (often used as an estimate of circadian phase) [37], sleep onset latency (the duration in minutes between time in bed and sleep start time), total sleep time (the total number of minutes scored as sleep within the rest interval), and sleep continuity measures, including wake after sleep onset (the total minutes spent awake following sleep onset), number of wake bouts (the total number of continuous blocks of epochs in which each epoch is scored as wake during the time spent in bed), sleep efficiency (total sleep time divided by time in bed multiplied by 100), and fragmentation index (a sum of the percentage of the sleep period that is spent moving and the percentage of consecutive epochs with no movement) [38]. Actiwatch actigraphs have exhibited good validity against polysomnography (i.e., sleep electroencephalography) [39,40].

**Dim Light Melatonin Onset Assessment.—**DLMO, referring to the time at which melatonin levels begin to rise in the evening, is a reliable marker of circadian phase [41,42]. During this assessment, participants remained in a dimly lit (i.e., < 5 lux), windowless room within our facility for 6.5 hours (from 5.5 hours prior to average bedtime until one hour after). Saliva samples were collected every 30 minutes using salivettes, beginning after 30 minutes of dim light exposure. Saliva samples were placed on ice during the assessment, stored at −20° C, and later shipped overnight in dry ice to SolidPhase, Inc. (Portland, Maine) for batch analysis. There, the samples were thawed and centrifuged prior to performing radioimmunoassay analysis of salivary melatonin concentration (pg/mL) using Bühlmann kits. DLMO was established using both a fixed threshold of 3 pg/mL, and a 3k threshold, which accounts for interindividual variability in melatonin production and is calculated by summing the mean plus two standard deviations of the first three low daytime melatonin concentrations just prior to the evening rise [43]. DLMO was set to the clock time at which pg/mL of melatonin crossed and remained above the threshold for at least an hour. See Online Resource 2 for more information.

**Light Therapy.—**LT began the morning following the baseline DLMO assessment. Participants were provided a wearable device, the Re-Timer™ (https://www.re-timer.com/), which emits blue-green (500nm wavelength) light at *low* (315 lux lm/$m^2$ and 143 irradiance μW/$cm^2$) or *high* (506 lux lm/$m^2$ and 230 irradiance μW/$cm^2$) settings. Participants were instructed to wear the device on the high setting for 1 hour daily upon awakening at their average rise time (calculated from baseline reported rise times). However, if this average

rise time was deemed too late to allow the participant to adhere to LT procedures while maintaining their regular activity schedule, the rise time was shifted up to one hour earlier prior to treatment outset. Wake times were not fixed during LT [44]. Participants were given adjustable straps to improve stability of the device placement. Participants were informed they could perform routine activities (e.g., eating, watching television, reading) while using the device. They were told they may begin to feel sleepy earlier in the evening than is typical, and were encouraged to go to bed earlier if they felt sleepy. Participants were also instructed to refrain from sleeping in during the weekends or drinking caffeine after 3:00 pm. Participants were encouraged to refrain from napping during LT. However, they were advised that, if feeling very sleepy, they should nap after 12 pm, so as not to counteract LT. Participants received phone calls on days 1 through 3, with subsequent text messages to prompt use of the device at the specified time. Participants completed a LT tracking form assessing time of LT onset and offset. In addition, an actigraph with straps removed was affixed to the inside of the device with velcro to monitor light and movement to determine times it was turned on and in use.

**Statistical Analysis—**SPSS 26.0 was used to conduct analyses. Descriptive statistics, chi-squared tests of independence and independent samples t-tests were performed to characterize the sample. The TD and HC groups were compared on baseline PSQI global score, actigraphy variables, MEQ total score, 3k and 3 pg/mL DLMO thresholds (see Online Resource 3 for details), in addition to the phase angle (i.e., time interval) between clock time of 3k and 3 pg/mL DLMO thresholds and sleep mid time using the Mann-Whitney U test. This test was selected to account for the skewed distribution of sleep onset latency, wake after sleep onset, number of wake bouts, sleep fragmentation, and PSQI global score variables. The exact significance (two-tailed) corrected for ties was used to obtain the p-value. Bivariate Pearson correlations were performed to evaluate associations among measures.

Repeated measures linear mixed modeling (LMM) was performed to evaluate change in actigraphy variables. LMM is optimal as it accounts for missing data, small sample sizes, and nonparametric distributions [45]. Sleep start time, sleep onset latency, wake after sleep onset, number of wake bouts, and sleep efficiency were log transformed due to their skewed distribution. LMM was performed with timepoint entered as a fixed effect and repeated effect. An autoregressive heterogeneous covariance structure of order 1 was specified to account for reduced correlation between data points with increasing distance between assessment timepoints [46], and maximum likelihood specified as the method of estimation.

The Wilcoxon Signed Rank Test was used to evaluate change in PSQI global score, ESS, MEQ, clock time of 3k and 3 pg/mL DLMO thresholds (see Online Resource 3 for details), YGTSS total, motor, and vocal tic severity scores, YGTSS impairment score, DASS depression, anxiety, and stress totals, and SDS total. This test was selected to account for the skewed distribution of baseline YGTSS vocal tic score and post-intervention YGTSS impairment score. Bivariate correlations tested relationships between change in DLMO and change in clinical measures. Descriptive statistics summarized LT side effects, adherence, and acceptability. Self-reported LT perceptions were reviewed to gauge feasibility.

## Results

### Adults with TD exhibited sleep disturbance and eveningness relative to HC.

Based on self-report, adults with TD had greater self-reported sleep disturbance (PSQI global score; $U$=29.00, $p$<.001) relative to HC. As measured by actigraphy (see Table 3), adults with TD exhibited significantly longer sleep onset latency ($U$=29.00, $p$<.001), poorer sleep efficiency ($U$=65.00, $p$=.01), and greater sleep fragmentation ($U$=78.00, $p$=.046). There were no significant group differences in sleep start time, sleep mid time, sleep end time, wake after sleep onset, number of wake bouts, or total sleep time ($p$=.38–.84).

Adults with TD reported significantly greater eveningness compared to HC ($U$=57.50, $p$=.01; see Figure 1); however, there were no significant group differences in DLMO as evaluated using the 3k ($U$=73.00, $p$=.56) and 3 pg/mL methods ($U$=91.00, $p$=.57; See Table 3). See Online Resource 3 for sensitivity analyses for 3k and 3 pg/mL DLMO thresholds. There were no significant group differences (Table 3) in phase angle between sleep mid time (per actigraphy) and DLMO, using 3k ($p$=.56) or 3 pg/mL methods ($p$=.11). See Online Resource 4 for Pearson bivariate correlations among measures.

### LT associated with advances in DLMO and reduced daytime sleepiness in adults with TD.

There were no improvements in sleep or advances in sleep mid time per actigraphy ($p$s: .09–.92; See Online Resource 5). Daytime sleepiness significantly decreased ($Z$=−2.06, $p$=.04). However, there were no significant changes in morningness-eveningness preference ($p$=.15) or global sleep disturbance on the PSQI ($p$=.93; See Table 4). DLMO significantly advanced by 45 minutes on average per 3k ($Z$=−2.43, $p$=.01) and 3 pg/mL thresholds ($Z$=−2.43, $p$=.01; see Figure 1). See Online Resource 3 for sensitivity analyses.

### LT associated with reduced tic severity, anxiety, and disability in adults with TD.

LT was associated with significant reductions in clinician-rated tic outcomes (see Table 4), including YGTSS total ($Z$=−2.92, $p$=.002), YGTSS motor ($Z$=−2.75, $p$=.01), YGTSS vocal tic severity scores ($Z$=−2.57, $p$=.01), and YGTSS impairment ($Z$=−2.26, $p$=.03). Anxiety ($Z$=−2.57, $p$=.01) and disability significantly decreased ($Z$=−1.60, $p$=.11) across LT. There were no significant reductions in depression ($Z$=−1.44, $p$=.19) or stress ($Z$=−1.12, $p$=.27; see Table 4). An advance in DLMO (3k) was correlated with a reduction in YGTSS Impairment ($r$=−.87, $p$=.003). An advance in DLMO (3 pg/mL) was correlated with subjective sleep worsening (i.e., an increase in PSQI Global Score) ($r$=.74, $p$=.01). See Online Resource 6 for relationships among change-in-clinical-measures.

### LT Side Effects, Acceptability, Feasibility, and Adherence

Five of the 14 adults (35.7%) with TD endorsed one or more adverse effects of LT, including headache ($n$=1, 7.1%), dizziness ($n$=1, 7.1%), nausea ($n$=1, 7.1%), eye irritation ($n$=1, 7.1%), blurred vision ($n$=1, 7.1%), perceiving the light as bothersome ($n$=2, 14.3%), or an “other” side effect ($n$=2, 14.3%). No participants endorsed eye redness, restlessness, excessive energy, or irritability. Green light and activity readings per actigraph sensor were used to track LT adherence. Participants wore the device for an average of 12.4 days ($SD$=2.8). On average, 33.6 minutes (SD=23.1) of participant LT wear-time occurred during

the assigned time window. From post-hoc analysis, increased minutes of LT worn within the assigned window was associated with a greater advance in DLMO per 3k ($r$=.79, $p$=.02), but not per 3 pg/mL ($r$=.45, $p$=.14). There were no significant correlations between number of days used and change in DLMO per 3k ($r$ =.33, $p$=.39), or 3 pg/mL ($r$=.16, $p$=.62).

Participants provided a rating of 5.21 ($SD$=1.25) on a scale from 1 (‘very unacceptable’) to 7 (‘very acceptable’) for acceptability of the intervention and 4.79 ($SD$=1.58) on a scale from 1 (‘very uncomfortable’) to 7 (‘very comfortable’) for physical comfort of the device. Some feasibility issues were noted. Participants reported disliking having to rise earlier than typical in order to have enough time to use the device and prepare for their day, especially during the weekends, as it resulted in sleep loss despite the instruction to go to bed earlier if sleepy. Another concern was physical discomfort from wearing the device (e.g., irritation on nose, retraction of the adjustable nosepiece, unsteadiness of the device during certain activities, irritation due to the actigraph we affixed to the device). Additionally, participants expressed concerns regarding being unable to follow their preferred morning routine (e.g., gym, showering, washing face, makeup routine, going straight to work, etc.). One participant with disinhibition-related tics noted that wearing the device triggered tics involving touching the device and face during LT sessions. However, participants also reported favorable changes, including increased sleepiness earlier at night, earlier morning rising, increased morning alertness, increased daytime energy, and feeling calmer.

## Discussion

The present study compared markers of circadian rhythms and sleep in adults with TD and HC, and assessed the effects of wearable, short-wavelength morning LT on circadian and sleep measures, and clinical symptoms. Baseline group comparisons showed that adults with TD displayed significantly greater eveningness preference relative to HC. Additionally, although not statistically significant, adults with TD went to bed and rose later than HC, also suggesting a delay. However, adults with TD did not universally exhibit greater circadian phase delay (i.e., DLMO) relative to HC. Furthermore, we did not find significant group differences in the timing between DLMO and sleep mid time (i.e., the phase angle).

Nevertheless, even without objective circadian delay, the finding of delayed chronotype in TD is consistent with a larger body of literature linking eveningness with psychiatric illness [11]. In particular, mood disorders are commonly associated with eveningness [47], and there is some support for associations between the common comorbidities of ADHD and OCD with eveningness [13,14,12]. Over half of our clinical sample had a history of depression, three had ADHD, and one had OCD. Therefore, it is possible that psychiatric comorbidity contributed to this association in our sample. However, depressive symptoms were not significantly correlated with sleep or circadian measures in this study. Research has identified several mediators of the association between chronotype and psychiatric illness, including sleep disturbance, shared genetic factors, and neural circuitry implicated in emotion regulation and reward responsivity [11]. Among these, we observed significantly increased sleep disturbance per actigraphy and questionnaire among adults with TD.

With regard to actigraphy-based sleep outcomes, we noted significantly longer sleep onset latency, poorer sleep efficiency, and greater sleep fragmentation in adults with TD relative to HC. This was corroborated by greater self-reported sleep disturbance in adults with TD. Wrist actigraphy outcomes were generally consistent with those of polysomnography studies in TD, showing delayed sleep onset and reduced sleep efficiency [6]. In contrast to prior objective studies [48–50], we did not find an increased number of awakenings in adults with TD.

Two weeks of wearable, short-wavelength morning LT were associated with a significant circadian phase advance of approximately 45 minutes. The intervention was also associated with significant improvements in daytime sleepiness and anxiety. However, there were no significant improvements in sleep disturbance by actigraphy or self-report. Interestingly, an advance in DLMO was associated with subjective sleep worsening. Our findings are in accordance with a two-week pilot of LT in adults with ADHD that resulted in a significant circadian phase advance per DLMO, but no significant change in sleep [51]. It is possible that the lack of improvement in sleep found in the present study was partially attributed to the need for many participants to rise earlier to wear the device for an hour, resulting in sleep loss. Per our analysis of actigraphy, bedtime did not appear to shift early enough to account for the greater advance in rise time. Stronger guidance to ensure sleep duration is not shortened during LT may be needed. It is also possible that longer LT duration may be needed to effect changes in sleep. A meta-analysis showed that LT does positively impact several sleep variables, with large effects noted for insomnia, and moderate effects observed for sleep quality, fatigue, sleep onset latency, and sleepiness [52]. However, most if not all of the studies reviewed utilized bright light as opposed to the target wavelengths used in the present study. Number of treatment days did not moderate effects in this meta-analysis; however, other study design elements (e.g., light intensity, daily treatment duration) covaried with number of treatment days [52]. Still, we predicted that LT would significantly boost mood. Surprisingly, we found no significant improvements in depression following LT. Given the direct and indirect effects of light on mood [53,54] and the preponderance of depression history in the sample, this finding countered expectations. However, it should be noted that measures of mood and anxiety at baseline indicated mild depression and minimal anxiety on average within our sample. Nevertheless, we did observe significant reductions in anxiety. Research examining the effects of LT on anxiety symptoms is limited and outcomes have been mixed [55–57].

Following LT, there were significant reductions in clinician-rated tic severity and impairment. Additionally, a greater advance in DLMO was associated with a greater reduction in impairment. Although statistically significant, these reductions were small and may not represent clinically significant changes. Given the single-group design, and fluctuating nature of tics, we cannot attribute these changes to the intervention. However, the reductions in anxiety and daytime sleepiness provide some possible means by which tics could have been influenced. We feel that this improvement in tic severity is an important area to follow up on with future work.

Finally, LT was completed with minimal side effects and good adherence. Greater LT adherence was associated with a greater advance in DLMO, highlighting the importance

of appropriate use of LT within the assigned time window. The LT device was generally rated as acceptable and comfortable. However, participants did report feasibility concerns (i.e., early rising, disruption to morning routine, some physical discomfort). This disinterest in rising earlier is an important consideration in LT, as desire and commitment to change have been implicated in LT adherence [58]. More research is needed to examine the role of motivation and readiness to change in LT. A number of participants also reported positive experiences, including greater alertness, energy and sense of calm in the day, increased sleepiness at night, and earlier rising in the morning.

This study has several limitations worth noting. First and foremost, the sample size is small, reducing generalizability of findings. Second, eligibility criteria allowed for comorbidities in the Tourette's disorder group, but not the control group. Although this increased the ecological validity of the Tourette's disorder group, the use of well controls may have introduced bias [59]. Third, some participants were taking psychotropic medications, known to influence sleep and circadian rhythms. Fourth, we did not apply a fixed sleep-wake schedule during the baseline monitoring period, and instead sleep timing was stabilized during the light treatment, which may have influenced the results. Fifth, we utilized a single-group, pre-test, post-test design to evaluate LT, which reduces the ability to link outcomes to LT. Other aspects of the protocol may have influenced changes in DLMO, including the need for some to rise earlier in the morning than their baseline average rise time to wear the device. Further, protocol instructions to go to bed earlier if sleepy, refrain from sleeping in on the weekends, and alter time of potential caffeine consumption and naps may have influenced treatment expectations regarding sleepiness and impacted exposure to evening light. Sixth, LT was limited to a brief two-week course. Although LT sessions generally produce immediate mood-boosting effects [60] and can shift circadian phase within days, a longer duration may be needed to observe substantial change in other clinical dimensions. Moreover, adults with TD were heterogeneous with respect to eveningness. As such, participants ranged in their potential need for morning LT.

Findings have implications for the clinical management of TD. As eveningness and sleep disturbance are associated with poor mental and physical health outcomes [11,61], their increased presence in adults with TD highlights the need for assessment and monitoring of sleep and chronotype in clinical care. Additionally, as group differences in sleep onset latency were particularly robust, this may suggest this is a prominent sleep problem among adults with TD. Further, as daytime sleepiness decreased following LT, it is possible that this intervention could boost alertness in individuals experiencing sedation as a side effect of tic medication. As there were complaints about early rising during LT, it is important to consider lower-effort alternatives. For example, exogenous melatonin is a circadian phase shifting agent and can advance circadian phase if administered approximately five hours prior to bedtime, or serve as a soporific agent when administered closer to bedtime [43]. Moreover, as sleep did not improve over the course of LT, a more gradual approach, whereby the patient times sessions according to their typical weekend rise time, and successively advances rise time by 15- to- 30-minute increments may be more acceptable to participants and more likely to preserve or improve sleep. In sum, although these preliminary findings are promising, future empirical investigations including a more comparable control group,

and sham-control condition (e.g., dimmed light or light at the incorrect wavelength) are needed to discern the benefits of LT in adults with TD.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Funding:

The research reported in this publication was supported by Tourette Association of America and NIMH K23MH113884 grants to Dr. Ricketts, and NIMH T32MH073517 support to Drs. Ricketts and McGuire. This manuscript reflects the views of the authors and may not reflect the opinions or views of the Tourette Association of America or NIH.

### Conflicts of Interest:

Dr. Ricketts has received honoraria and research funding from the Tourette Association of America (TAA), and serves on the TAA Diversity Committee. Dr. Burgess serves on the scientific advisory boards for Natrol, LLC, and Moving Mindz, Pty, Ltd. Dr. McGuire has received support from the Tourette Association of America, American Academy of Neurology, the Brain Research Foundation, American Psychological Foundation, the Hilda and Preston Davis Family Foundation, and Johns Hopkins Discovery Fund Program Challenge Award. He also receives book royalties from Elsevier and an honorarium for editorial responsibilities from Springer. Dr. McGuire has served as a consultant for Signant Health, Syneos Health, and Luminopia. Dr. McCracken has received research or grant support from National Institutes of Health, Seaside Therapeutics, Roche, and Otsuka. He has served as a consultant to BioMarin and PharmaNet. Dr. Piacentini has received grant or research support from the National Institute of Mental Health, Pfizer Pharmaceuticals through the Duke University Clinical Research Institute CAPTN Network, Psyadon Pharmaceuticals, and the Tourette Association of America. He has received financial support from the Petit Family Foundation and the Tourette Syndrome Association Center of Excellence Gift Fund. He has received royalties from Guilford Press and Oxford University Press. He has served on the speakers' bureau of the TAA, the International Obsessive-Compulsive Disorder Foundation (IOCDF), and the TLC Foundation for Body-Focused Repetitive Behaviors. Dr. Colwell serves as an unpaid consultant for Real Sleep™. All other authors declare no conflicts of interest.

## References

1. American Psychiatric Association (2013) Diagnostic and Statistical Manual of Mental Disorders. 5th edn. American Psychiatric Association Publishing, Washington, D
2. Sheppard DM, Bradshaw JL, Purcell R, Pantelis C (1999) Tourette's and comorbid syndromes: Obsessive compulsive and attention deficit hyperactivity disorder. a common etiology? Clinical Psychology Review 19 (5):531–552. doi:10.1016/S0272-7358(98)00059-2 [PubMed: 10467490]
3. Bloch MH, Leckman JF (2009) Clinical course of Tourette syndrome. J Psychosom Res 67 (6):497–501. doi:10.1016/j.jpsychores.2009.09.002 [PubMed: 19913654]
4. Groth C, Mol Debes N, Rask CU, Lange T, Skov L (2017) Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study. J Am Acad Child Adolesc Psychiatry 56 (4):304–312. doi:10.1016/j.jaac.2017.01.010 [PubMed: 28335874]
5. Freeman RD (2007) Tic disorders and ADHD: answers from a world-wide clinical dataset on Tourette syndrome. Eur Child Adolesc Psychiatry 16 Suppl 1:15–23. doi:10.1007/s00787-007-1003-7
6. Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, Agúndez JAG (2020) Sleep disorders in tourette syndrome. Sleep Med Rev 53:101335. doi:10.1016/j.smrv.2020.101335 [PubMed: 32554211]
7. Kirov R, Becker A, Rothenberger A (2014) Sleep in Tourette Syndrome. Current Developmental Disorders Reports 1 (4):252–259. doi:10.1007/s40474-014-0028-0
8. Sollars PJ, Pickard GE (2015) The Neurobiology of Circadian Rhythms. Psychiatr Clin North Am 38 (4):645–665. doi:10.1016/j.psc.2015.07.003 [PubMed: 26600101]
9. Jones SG, Benca RM (2015) Circadian Disruption in Psychiatric Disorders. Sleep Med Clin 10 (4):481–493. doi:10.1016/j.jsmc.2015.07.004 [PubMed: 26568124]

10. Wulff K, Gatti S, Wettstein JG, Foster RG (2010) Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. Nat Rev Neurosci 11 (8):589–599. doi:10.1038/nrn2868 [PubMed: 20631712]
11. Taylor BJ, Hasler BP (2018) Chronotype and Mental Health: Recent Advances. Curr Psychiatry Rep 20 (8):59. doi:10.1007/s11920-018-0925-8 [PubMed: 30039327]
12. Coles ME, Schubert J, Stewart E, Sharkey KM, Deak M (2020) Sleep duration and timing in obsessive-compulsive disorder (OCD): evidence for circadian phase delay. Sleep Medicine 72:111–117. doi:10.1016/j.sleep.2020.03.021 [PubMed: 32575000]
13. Coogan AN, McGowan NM (2017) A systematic review of circadian function, chronotype and chronotherapy in attention deficit hyperactivity disorder. Atten Defic Hyperact Disord 9 (3):129–147. doi:10.1007/s12402-016-0214-5 [PubMed: 28064405]
14. Cox RC, Olatunji BO (2019) Circadian Rhythms in Obsessive-Compulsive Disorder: Recent Findings and Recommendations for Future Research. Curr Psychiatry Rep 21 (7):54. doi:10.1007/s11920-019-1033-0 [PubMed: 31165330]
15. Dodson ER, Zee PC (2010) Therapeutics for Circadian Rhythm Sleep Disorders. Sleep Med Clin 5 (4):701–715. doi:10.1016/j.jsmc.2010.08.001 [PubMed: 21243069]
16. Blume C, Garbazza C, Spitschan M (2019) Effects of light on human circadian rhythms, sleep and mood. Somnologie (Berl) 23 (3):147–156. doi:10.1007/s11818-019-00215-x [PubMed: 31534436]
17. Terman M, Terman JS (2013) Chronotherapeutics: Light Therapy, wake therapy, and melatonin. In: Mann PJM JJ, Roose SP () Clinical handbook for the management of mood disorders. Cambridge University Press, Cambridge, UK, 332–344
18. Burgess HJ, Emens JS (2016) Circadian-Based Therapies for Circadian Rhythm Sleep-Wake Disorders. Curr Sleep Med Rep 2 (3):158–165 [PubMed: 27990327]
19. Warman VL, Dijk DJ, Warman GR, Arendt J, Skene DJ (2003) Phase advancing human circadian rhythms with short wavelength light. Neurosci Lett 342 (1–2):37–40. doi:10.1016/s0304-3940(03)00223-4 [PubMed: 12727312]
20. Wright HR, Lack LC, Kennaway DJ (2004) Differential effects of light wavelength in phase advancing the melatonin rhythm. J Pineal Res 36 (2):140–144 [PubMed: 14962066]
21. Lau T, Lovato N, Lack L (2018) Evaluation of a portable light device for phase advancing the circadian rhythm in the home environment. Sleep and Biological Rhythms 16 (4):405–411. doi:10.1007/s41105-018-0167-5
22. Zalta AK, Bravo K, Valdespino-Hayden Z, Pollack MH, Burgess HJ (2019) A placebo-controlled pilot study of a wearable morning bright light treatment for probable PTSD. Depress Anxiety 36 (7):617–624. doi:10.1002/da.22897 [PubMed: 30995350]
23. Niederhofer H (2009) Bright light therapy may be a therapeutic option for Tourette's syndrome. Acta Neuropsychologica 7:283–285
24. Coles ME, Strauss GP (2015) Shedding light on tics. Psychiatry Res 225 (3):743. doi:10.1016/j.psychres.2014.12.024 [PubMed: 25571772]
25. Leckman JF, Riddle MA, Hardin MT, Ort SI, Swartz KL, Stevenson J, Cohen DJ (1989) The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry 28 (4):566–573. doi:10.1097/00004583-198907000-00015 [PubMed: 2768151]
26. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 59 Suppl 20:22–33;quiz 34–57
27. Merikangas KR, Zhang J, Emsellem H, Swanson SA, Vgontzas A, Belouad F, Blank MM, Chen W, Einen M, He JP, Heaton L, Nakamura E, Rooholamini S, Mignot E (2014) The structured diagnostic interview for sleep patterns and disorders: rationale and initial evaluation. Sleep Med 15 (5):530–535. doi:10.1016/j.sleep.2013.10.011 [PubMed: 24780136]
28. Wechsler D (2011) Wechsler Abbreviated Scale of Intelligence, Second Edition. Pearson, San Antonio, TX

29. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 28 (2):193–213. doi:10.1016/0165-1781(89)90047-4 [PubMed: 2748771]
30. Terman BJ, Terman JS (2010) Light Therapy. In: Kryger WCD MH () Principles and practice of sleep medicine. 5th ed. edn. Elsevier/Saunders, St. Louis, MO, 1682–1695
31. Lovibond PF, Lovibond SH (1995) The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 33 (3):335–343. doi:10.1016/0005-7967(94)00075-u [PubMed: 7726811]
32. Sheehan DV (1983) The Sheehan Disability Scales. In: The Anxiety Disease Charles Scribner and Sons, New York, p 151
33. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14 (6):540–545. doi:10.1093/sleep/14.6.540 [PubMed: 1798888]
34. Lovato N, Lack L (2016) Circadian phase delay using the newly developed re-timer portable light device. Sleep and Biological Rhythms 14 (2):157–164. doi:10.1007/s41105-015-0034-6
35. Piacentini J, Woods DW, Scahill L, Wilhelm S, Peterson AL, Chang S, Ginsburg GS, Deckersbach T, Dziura J, Levi-Pearl S, Walkup JT (2010) Behavior therapy for children with Tourette disorder: a randomized controlled trial. Jama 303 (19):1929–1937. doi:10.1001/jama.2010.607 [PubMed: 20483969]
36. Patel SR, Weng J, Rueschman M, Dudley KA, Loredo JS, Mossavar-Rahmani Y, Ramirez M, Ramos AR, Reid K, Seiger AN, Sotres-Alvarez D, Zee PC, Wang R (2015) Reproducibility of a Standardized Actigraphy Scoring Algorithm for Sleep in a US Hispanic/Latino Population. Sleep 38 (9):1497–1503. doi:10.5665/sleep.4998 [PubMed: 25845697]
37. Kantermann T, Burgess HJ (2017) Average mid-sleep time as a proxy for circadian phase. Psych J 6 (4):290–291. doi:10.1002/pchj.182 [PubMed: 29035008]
38. Ricardo AC, Knutson K, Chen J, Appel LJ, Bazzano L, Carmona-Powell E, Cohan J, Kurella Tamura M, Steigerwalt S, Thornton JD, Weir M, Turek NF, Rahman M, Van Cauter E, Lash JP (2017) The Association of Sleep Duration and Quality with CKD Progression. J Am Soc Nephrol 28 (12):3708–3715. doi:10.1681/asn.2016121288 [PubMed: 28912373]
39. Lichstein KL, Stone KC, Donaldson J, Nau SD, Soeffing JP, Murray D, Lester KW, Aguillard RN (2006) Actigraphy validation with insomnia. Sleep 29 (2):232–239 [PubMed: 16494091]
40. Marino M, Li Y, Rueschman MN, Winkelman JW, Ellenbogen JM, Solet JM, Dulin H, Berkman LF, Buxton OM (2013) Measuring sleep: accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. Sleep 36 (11):1747–1755. doi:10.5665/sleep.3142 [PubMed: 24179309]
41. Klerman EB, Gershengorn HB, Duffy JF, Kronauer RE (2002) Comparisons of the variability of three markers of the human circadian pacemaker. J Biol Rhythms 17 (2):181–193. doi:10.1177/074873002129002474 [PubMed: 12002165]
42. Lewy AJ, Sack RL (1989) The dim light melatonin onset as a marker for circadian phase position. Chronobiol Int 6 (1):93–102. doi:10.3109/07420528909059144 [PubMed: 2706705]
43. Burgess HJ, Revell VL, Molina TA, Eastman CI (2010) Human phase response curves to three days of daily melatonin: 0.5 mg versus 3.0 mg. J Clin Endocrinol Metab 95 (7):3325–3331. doi:10.1210/jc.2009-2590 [PubMed: 20410229]
44. Eastman CI, Young MA, Fogg LF, Liu L, Meaden PM (1998) Bright light treatment of winter depression: a placebo-controlled trial. Arch Gen Psychiatry 55 (10):883–889. doi:10.1001/archpsyc.55.10.883 [PubMed: 9783558]
45. Smith PF (2012) A note on the advantages of using linear mixed model analysis with maximal likelihood estimation over repeated measures ANOVAs in psychopharmacology: comment on Clark et al. (2012). J Psychopharmacol 26 (12):1605–1607. doi:10.1177/0269881112463471 [PubMed: 23192250]
46. Brammer RJ (2003) Modelling covariance structure in ascending dose studies of isolated tissues and organs. Pharmaceutical Statistics 2:103–112
47. Au J, Reece J (2017) The relationship between chronotype and depressive symptoms: A meta-analysis. J Affect Disord 218:93–104. doi:10.1016/j.jad.2017.04.021 [PubMed: 28463712]

48. Cohrs S, Rasch T, Altmeyer S, Kinkelbur J, Kostanecka T, Rothenberger A, Rüther E, Hajak G (2001) Decreased sleep quality and increased sleep related movements in patients with Tourette's syndrome. J Neurol Neurosurg Psychiatry 70 (2):192–197. doi:10.1136/jnnp.70.2.192 [PubMed: 11160467]
49. Drake ME Jr., Hietter SA, Bogner JE, Andrews JM (1992) Cassette EEG sleep recordings in Gilles de la Tourette syndrome. Clin Electroencephalogr 23 (3):142–146. doi:10.1177/155005949202300309 [PubMed: 1628407]
50. Glaze DG, Frost JD, Jankovic J (1983) Sleep in Gilles de la Tourette's syndrome. Neurology 33 (5):586. doi:10.1212/WNL.33.5.586 [PubMed: 6573576]
51. Fargason RE, Fobian AD, Hablitz LM, Paul JR, White BA, Cropsey KL, Gamble KL (2017) Correcting delayed circadian phase with bright light therapy predicts improvement in ADHD symptoms: A pilot study. J Psychiatr Res 91:105–110. doi:10.1016/j.jpsychires.2017.03.004 [PubMed: 28327443]
52. van Maanen A, Meijer AM, van der Heijden KB, Oort FJ (2016) The effects of light therapy on sleep problems: A systematic review and meta-analysis. Sleep Med Rev 29:52–62. doi:10.1016/j.smrv.2015.08.009 [PubMed: 26606319]
53. Fisk AS, Tam SKE, Brown LA, Vyazovskiy VV, Bannerman DM, Peirson SN (2018) Light and Cognition: Roles for Circadian Rhythms, Sleep, and Arousal. Front Neurol 9:56. doi:10.3389/fneur.2018.00056 [PubMed: 29479335]
54. LeGates TA, Fernandez DC, Hattar S (2014) Light as a central modulator of circadian rhythms, sleep and affect. Nat Rev Neurosci 15 (7):443–454. doi:10.1038/nrn3743 [PubMed: 24917305]
55. Baxendale S, O'Sullivan J, Heaney D (2013) Bright light therapy for symptoms of anxiety and depression in focal epilepsy: randomised controlled trial. Br J Psychiatry 202 (5):352–356. doi:10.1192/bjp.bp.112.122119 [PubMed: 23520221]
56. Raymackers JM, Andrade M, Baey E, Vanneste M, Evrard F (2019) Bright light therapy with a head-mounted device for anxiety, depression, sleepiness and fatigue in patients with Parkinson's disease. Acta Neurol Belg 119 (4):607–613. doi:10.1007/s13760-019-01214-3 [PubMed: 31571135]
57. Youngstedt SD, Kline CE, Ginsberg JP, Zielinski MR, Hardin JW (2011) Bright light treatment for high-anxious young adults: a randomized controlled pilot study. Depress Anxiety 28 (4):324–332. doi:10.1002/da.20784 [PubMed: 21254315]
58. Micic G, Richardson C, Cain N, Reynolds C, Bartel K, Maddock B, Gradisar M (2019) Readiness to change and commitment as predictors of therapy compliance in adolescents with Delayed Sleep-Wake Phase Disorder. Sleep Med 55:48–55 [PubMed: 30763869]
59. Schwartz S, Susser E (2011) The use of well controls: an unhealthy practice in psychiatric research. Psychological Medicine 41 (6):1127–1131. doi:10.1017/S0033291710001595 [PubMed: 20810003]
60. Stephenson KM, Schroder CM, Bertschy G, Bourgin P (2012) Complex interaction of circadian and non-circadian effects of light on mood: shedding new light on an old story. Sleep Med Rev 16 (5):445–454. doi:10.1016/j.smrv.2011.09.002 [PubMed: 22244990]
61. Partonen T (2015) Chronotype and Health Outcomes. Current Sleep Medicine Reports 1. doi:10.1007/s40675-015-0022-z

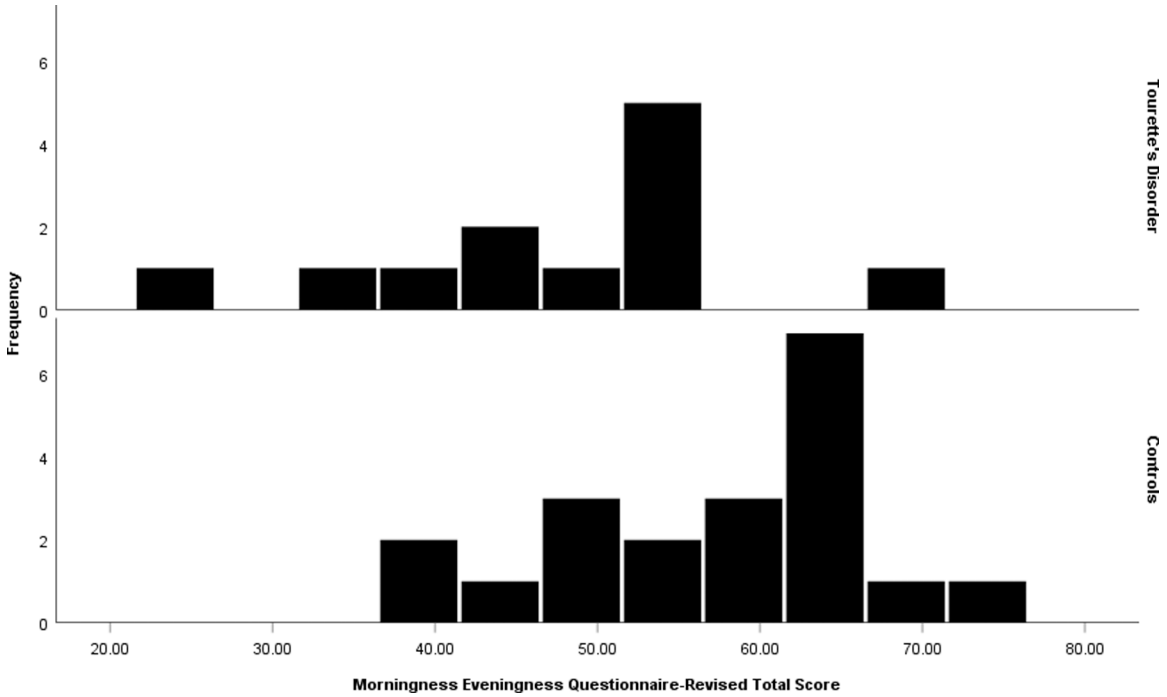


**Fig. 1. Histogram of Distribution of Morningness-Eveningness Questionnaire-Revised Total Score in Adults with Tourette's disorder and Healthy Controls**

*Note.* Morningness-Eveningness Questionnaire-Revised Total scores range from 16 to 86. Lower scores indicate greater eveningness and higher scores indicate greater morningness [30].

**Table 1**

Demographic and Clinical Characteristics in Full Sample, Adults with Tourette's Disorder, and Controls

| Characteristic | Full Sample (n=34) | Tourette's Disorder (n=14) | Controls (n=20) | Statistic | *p* |
|---|---|---|---|---|---|
| Male | 67.60% | 71.40% | 65.00% | --- | >.99[a] |
| Age (M, SD) | 30.15 (7.48) | 27.86 (5.20) | 31.75 (8.49) | 1.52 | .11[b] |
| Race (% Minority) | 44.10% | 21.40% | 60.00% | 3.53 | .06[c] |
| Highest Education (% Some college or higher) | 100.00% | 100.0% | 100.00% | --- | ---[d] |
| Marital Status (% Single/Never married) | 82.40% | 71.40% | 90.00% | --- | .20[a] |
| Living Situation (% Living alone) | 23.50% | 14.30% | 30.00% | --- | .42[a] |
| Employment Status (% Employed) | 55.90% | 71.40% | 45.00% | 1.38 | .24[c] |
| Student (% Yes) | 38.20% | 21.40% | 50.00% | 1.77 | .18[c] |

Note.

[a] = Fisher's exact test;

[b] = *t* statistic;

[c] = Chi-squared statistic;

[d] = no statistics computed because highest education is a constant.

**Table 2**

Psychiatric and Sleep Diagnoses in Adults with Tourette's Disorder

| **Diagnosis** | **(n=14) n (%)** |
|---|---|
| Tourette's Disorder | 12 (85.7%) |
| Persistent Motor Tic Disorder | 2 (14.3%) |
| Attention-Deficit Hyperactivity Disorder | 3 (21.4%) |
| Major Depressive Disorder | 8 (57.1%) |
| Social Phobia | 1 (7.1%) |
| Obsessive-compulsive disorder | 1 (7.1%) |
| Binge Eating Disorder | 1 (7.1%) |
| Alcohol Use Disorder, Past 12 months | 1 (7.1%) |
| Substance Use Disorder, Past 12 months | 1 (7.1%) |
| Delayed Sleep-Wake Phase Disorder | 1 (7.1%) |
| Insomnia | 3 (21.4%) |
| Bruxism | 1 (7.1%) |
| Medication | n (%) |
| On tic medication | 4 (28.6%) |
| On other psychotropic medication | 5 (35.7%) |
| Severity | |
| YGTSS Total M (SD)[1] | 26.57 (8.75) |
| CGI-S M (SD) | 4.64 (0.84) |
| Moderately ill n (%) | 8 (57.1%) |
| Markedly ill n (%) | 3 (21.4%) |
| Severely ill n (%) | 3 (21.4%) |

Note. M = mean; SD = standard deviation; YGTSS = Yale Global Tic Severity Scale;

[1]YGTSS total tic severity scores ranged from 14 to 44.

**Table 3**

Mann-Whitney U Test Comparing Baseline Circadian, Sleep, and Clinical Measures in Adults with Tourette's Disorder and Controls

| Measure | Mean (SD) | Mean (SD) | Median (IQR) | Median (IQR) | *U* | $p$ [a] | $\eta^2$ |
|---|---|---|---|---|---|---|---|
| | Tourette's Disorder | Controls | Tourette's Disorder | Controls | | | |
| *Subjective Sleep Measure* | | | | | | | |
| Pittsburgh Sleep Quality Index Global Score | 7.00 (2.92) | 2.55 (1.36) | 6.00 (1.75) | 3.00 (1.75) | 8.50 | <.001 | .62 |
| *Actigraphy Variables* [b] | | | | | | | |
| Sleep Time (HH:MM) | 00:24 (01:00) | 00:08 (01:23) | 00:11 (01:30) | 00:06 (01:59) | 117.00 | .58 | .01 |
| Mid Time (HH:MM) | 04:03 (00:39) | 03:44 (01:20) | 04:14 (01:00) | 03:30 (02:12) | 108.00 | .38 | .03 |
| Wake Time (HH:MM) | 07:34 (00:55) | 07:19 (01:22) | 07:23 (01:23) | 07:02 (02:05) | 111.00 | .44 | .02 |
| Sleep Onset Latency (Minutes) | 33.66 (14.01) | 14.25 (9.94) | 32.14 (22.36) | 11.57 (10.14) | 29.00 | <.001 | .45 |
| Wake After Sleep Onset (Minutes) | 42.33 (22.07) | 36.64 (16.27) | 38.52 (41.20) | 34.86 (23.29) | 126.00 | .82 | .002 |
| Number of Wake Bouts | 35.88 (18.11) | 31.69 (9.55) | 31.79 (21.39) | 32.33 (14.29) | 124.50 | .77 | .003 |
| Total Sleep Time (Minutes) | 386.20 (68.35) | 393.72 (41.61) | 385.32 (121.98) | 389.93 (61.57) | 127.00 | .84 | .001 |
| Sleep Efficiency (%) | 78.52 (6.72) | 84.99 (5.10) | 77.74 (11.67) | 85.38 (4.09) | 65.00 | .01 | .19 |
| Fragmentation Index | 19.87 (6.16) | 15.02 (6.15) | 18.34 (10.19) | 13.58 (6.42) | 78.00 | .046 | .13 |
| *Circadian Measures* | | | | | | | |
| Morningness-Eveningness Questionnaire | 47.03 (10.82) | 57.55 (9.76) | 49.50 (11.25) | 59.00 (17.75) | 57.50 | .01 | .19 |
| DLMO 3k | 21:00 (01:09) | 20:41 (01:59) | 20:32 (01:53) | 20:25 (02:40) | 73.00 | .56 | .01 |
| DLMO 3 pg/mL | 21:09 (01:14) | 21:35 (02:02) | 21:02 (00:53) | 21:19 (02:16) | 91.00 | .57 | .01 |
| Phase Angle: DLMO 3k to Sleep Mid Time | 07:00 (00:58) | 06:56 (01:08) | 07:10 (01:59) | 06:15 (01:01) | 69.00 | .56 | .01 |
| Phase Angle: DLMO 3 pg/mL to Sleep Mid Time | 06:50 (01:01) | 06:08 (01:15) | 06:50 (01:33) | 07:04 (01:12) | 67.00 | .11 | .09 |

Note. SD = standard deviation; IQR = interquartile range; HH:MM = hours and minutes; DLMO = dim light melatonin onset;

[a] Exact 2-tailed significance *p*-value corrected for ties;

[b] = sleep time, mid time, wake time, and other variables were derived from actigraphy and averaged across seven nights at baseline.

**Table 4**

Wilcoxon Signed Rank Test Comparing Baseline and Post-light Therapy Sleep, Circadian, and Clinical Outcomes in Adults with Tourette's Disorder

| Measure | Mean (SD) | Mean (SD) | Median (IQR) | Median (IQR) | *Z* | *p* | $\eta^2$ |
|---|---|---|---|---|---|---|---|
| | Baseline | Post | Baseline | Post | | | |
| *Sleep and Circadian Outcomes* | | | | | | | |
| Pittsburgh Sleep Quality Index Global Score | 6.54 (3.40) | 7.69 (3.68) | 6.00 (1.75) | 6.00 (5.50) | −0.12 | .93 | .001 |
| Epworth Sleepiness Scale | 9.21 (4.26) | 7.93 (5.73) | 7.50 (5.50) | 7.50 (6.25) | −2.06 | .04 | .30 |
| Morningness-Eveningness Questionnaire | 49.18 (8.41) | 50.64 (5.70) | 49.50 (11.25) | 53.00 (12.50) | −1.48 | .15 | .20 |
| Dim light melatonin onset (3k) | 21:16 (01:06) | 20:31 (00:47) | 20:32 (01:53) | 20:02 (01:11) | −2.43 | .01 | .66 |
| Dim light melatonin onset (3 pg/mL) | 20:44 (01:15) | 19:59 (00:56) | 21:08 (00:59) | 20:25 (01:18) | −2.43 | .01 | .49 |
| *Tic-related Outcomes* | | | | | | | |
| Yale Global Tic Severity Scale Total | 27.00 (8.30) | 24.79 (8.87) | 26.00 (11.50) | 23.50 (9.75) | −2.92 | .002 | .61 |
| Yale Global Tic Severity Scale Motor | 17.29 (3.27) | 16.00 (3.96) | 16.50 (6.25) | 15.50 (5.75) | −2.75 | .01 | .54 |
| Yale Global Tic Severity Scale Vocal | 9.71 (7.38) | 8.79 (7.12) | 11.00 (14.25) | 9.50 (13.00) | −2.57 | .01 | .47 |
| Yale Global Tic Severity Scale Impairment | 30.15 (10.25) | 27.57 (12.53) | 32.5 (11.00) | 30.00 (17.25) | −2.26 | .03 | .37 |
| *Co-occurring Symptoms and Functioning* | | | | | | | |
| DASS Depression | 12.62 (12.07) | 9.85 (10.63) | 8.00 (22.00) | 8.00 (15.50) | −1.44 | .19 | .16 |
| DASS Anxiety | 6.92 (5.20) | 4.31 (3.45) | 6.00 (6.00) | 4.00 (8.00) | −2.57 | .01 | .51 |
| DASS Stress | 14.92 (12.53) | 12.31 (9.05) | 18.00 (23.00) | 15.00 (17.50) | −1.12 | .27 | .10 |
| Sheehan Disability Scale Total | 12.67 (6.81) | 10.83 (7.37) | 14.50 (11.75) | 12.50 (16.00) | −1.60 | .11 | .21 |

Note. SD = standard deviation; IQR = interquartile range; DASS = Depression Anxiety Stress Scale; exact significance (two-tailed).