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Self-reported sleep and circadian characteristics predict alcohol and cannabis use: A longitudinal analysis of the National Consortium on Alcohol and Neurodevelopment in Adolescence study

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Abstract

BACKGROUND: Growing evidence indicates that sleep characteristics predict future substance use and related problems. However, most prior studies assessed a limited range of sleep characteristics, studied a narrow age span, and included few follow-up assessments. Here, we used six annual assessments from the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) study, which spans adolescence and young adulthood with an accelerated longitudinal design, to examine whether multiple sleep characteristics in any year predict alcohol and cannabis use the following year.

METHODS: The sample included 831 NCANDA participants (423 females; baseline age 12–21 years). Sleep variables included circadian preference, sleep quality, daytime sleepiness, timing of midsleep (weekday/weekend), and sleep duration (weekday/weekend). Using generalized linear mixed models (logistic for cannabis; ordinal for binge severity), we tested whether each repeatedly-measured sleep characteristic (years 0–4) predicted substance use (alcohol binge severity or cannabis use) the following year (years 1–5), covarying for age, sex, race, visit, parental education, and previous year's substance use.

RESULTS: Greater eveningness, more daytime sleepiness, later weekend sleep timing and shorter sleep duration (weekday/weekend) all predicted more severe alcohol bingeing the following year. Only greater eveningness predicted a greater likelihood of any cannabis use the following year. Post-hoc stratified exploratory analyses indicated that some associations (e.g. greater eveningness, shorter weekend sleep duration) predicted binge severity only in female participants, and that middle-high school, versus post-high school, adolescents were more vulnerable to sleep-related risk for cannabis use.

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CONCLUSIONS: Our findings support the relevance of multiple sleep/circadian characteristics in the risk for future alcohol binge severity and cannabis use. Preliminary findings suggest that these risk factors vary based on developmental stage and sex. Results underscore a need for greater attention to sleep/circadian characteristics as potential risk factors for substance use in youth, and may inform new avenues to prevention and intervention.

Keywords

sleep; circadian preference; adolescence; young adulthood; alcohol; cannabis; NCANDA

INTRODUCTION

Growing longitudinal evidence indicates that late childhood and adolescent sleep characteristics predict alcohol and cannabis use and related problems in later adolescence and young adulthood (Hasler and Pedersen, 2020, Winiger et al., 2021). Sleep is widely recognized as a multidimensional construct sometimes referred to as sleep health (Meltzer et al., 2021b, Buysse, 2014), and considering how multiple relevant characteristics relate to substance use outcomes can yield novel insights. Several sleep characteristics have been shown to accelerate alcohol and cannabis use in adolescents, including sleep satisfaction or quality (e.g. perceiving that one's sleep is of poor quality), sleep efficiency (e.g. difficulty falling and/or staying asleep), sleep duration (e.g. obtaining insufficient sleep), alertness (e.g. difficulty staying awake during the day), and sleep timing (e.g. later or variable preferred or actual sleep timing) (Hasler and Clark, 2013, Mike et al., 2016, Hasler et al., 2014, Wong et al., 2015, Haynie et al., 2017, Troxel et al., 2021). The link between sleep characteristics and substance use may involve positive or negative reinforcement pathways. For example, sleep-related risk may increase the likelihood of binge drinking or use of cannabis in the presence of anxiety or other negative emotions (i.e., a negative reinforcement pathway) (Hasler and Pedersen, 2020). A better understanding of prospective sleep-substance use relationships may provide insights pertinent for improving substance use prevention or intervention practices (Fucito et al., 2017).

Many prior studies on relationships between sleep characteristics and alcohol or cannabis use in adolescents have design or measurement limitations. These limitations include the use of sparse and/or unvalidated sleep measures [e.g. (Verkooijen et al., 2018, Hasler et al., 2016)], a narrow age span [e.g., (Cheng et al., 2020, Sivertsen et al., 2015)], a cross-sectional design (Chen et al., 2017, Verkooijen et al., 2018), a case-control approach (Hasler et al., 2014), a short follow-up period (Hasler et al., 2019a), or few follow-up assessments (Hasler et al., 2017). A preference for later sleep-wake timing (a.k.a. eveningness) appears to be an important risk factor for substance use and substance-related problems (Taylor and Hasler, 2018, Hasler et al., 2017, Kivelä et al., 2018). Still, most studies have not included measures of actual sleep timing, which may differ from subjective circadian preference. Studies with adolescents are needed that simultaneously examine multiple relevant sleep characteristics (Meltzer et al., 2021b), including eveningness and actual sleep timing, as well as sleep duration and related disturbances. Marked and consequential weekday-weekend differences in sleep timing and duration during adolescence necessitate distinct weekday and weekend sleep measurement (Crowley et al., 2018).

The National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) study design and assessment protocol (see (Brown et al., 2015) for a summary) enables analyses on multiple sleep characteristics, alcohol use and cannabis use patterns and progression through adolescence and young adulthood that address some of the limitations of prior studies. NCANDA assessed multiple self-reported sleep characteristics, including sleep quality, daytime sleepiness, sleep timing and duration across school and free days, and circadian preference, using reduced versions of validated scales that correlated highly with the full scales (Hasler et al., 2017). These sleep constructs were selected based on prior literature showing associations with substance use and their relevance to adolescent development. In adolescence, tendencies for later sleep/circadian timing are mismatched with early school start times of secondary education, resulting in insufficient sleep on school nights, daytime sleepiness on school days, weekday-weekend differences in sleep timing and duration, and reduced sleep quality (Crowley et al., 2018).

We previously reported NCANDA prospective associations between sleep characteristics at baseline and several substance use metrics with a single one-year follow-up assessment (Hasler et al., 2017). Specifically, greater eveningness preference, lower sleep quality, later weekday and weekend bedtimes, and shorter weekday sleep duration at baseline all predicted more severe binge-drinking, endorsing cannabis use, or both, one year later. Here, we extend our prior findings using the first 6 annual assessments of data from NCANDA to examine whether multiple sleep characteristics in any year predict alcohol or cannabis use the following year. These additional follow-up data captured the onset and progression of substance use across a broader, older age range, providing a more robust examination of prospective sleep-substance use relationships.

We hypothesized that greater eveningness and later sleep timing (weekday and weekend), as well as other sleep characteristics associated with worse overall sleep (more daytime sleepiness, worse sleep quality, and shorter sleep duration across weekdays and weekends), would each predict increased risk for more severe binge-drinking and cannabis use the following year. Because so few prior studies of sleep-substance use relationships have included such a wide range of sleep characteristics, our primary approach was to examine them in separate models to evaluate their marginal contributions. Secondarily, we considered which associations were predominant when multiple sleep characteristics were simultaneously examined. We also explored whether there were developmental differences between sleep-substance use relationships across the middle/high-school timepoints (when school start times systematically constrain participants' sleep schedules, causing a constellation of sleep disturbances (Crowley et al., 2018)) versus post-graduation from high school (when college and/or employment demands may allow more flexible sleep schedules). Finally, given the growing evidence that sleep, substance use, and sleep-substance use relationships may vary by sex (Hasler and Pedersen, 2020, Baker et al., 2020), we explored whether sleep-substance associations differed between male and female participants.

METHODS

Participants

The NCANDA sample (Brown et al., 2015) included 831 participants, aged 12.0 to 21.9 years at baseline, who were recruited at five NCANDA data collection sites (i.e., University of California San Diego, SRI International, Duke University, Oregon Health & Science University, University of Pittsburgh). The Institutional Review Board at each site approved the study. At recruitment, adult participants provided written informed consent. For child participants, a parent/legal guardian of children provided written informed consent along with written assent from the child participant. At the baseline assessment, 83% had limited or no history of alcohol or other drug use and 17% exceeded NIAAA-defined age-specific low-risk alcohol use thresholds. Socioeconomic status (SES) was estimated using parental education (years of education attained), with 20% of parents reporting education below a college degree. The study used an accelerated longitudinal design for recruitment, recruiting participants age 12–21 years at baseline and following them with annual evaluations. Years 0–5 are the focus of the present analyses (a total of 6 annual assessments). Additional details are available in (Brown et al., 2015) and updated information and recent publications at www.ncanda.org.

The present analyses included 801 participants with complete baseline data on circadian preference, sleep, alcohol and cannabis use, and the relevant covariates, including age, sex, race, and parental SES.

Measures

The primary measures used in these analyses closely paralleled those of our previous NCANDA sleep analyses (Hasler et al., 2017).

Substance use.—Past year alcohol and cannabis use was determined by the Customary Drinking and Drug Use Record (CDDR: (Brown et al., 1998), with items including use frequency in the past year and the maximum number of drinks in a drinking episode. *Binge Drinking Severity:* Using responses to CDDR #36 [i.e., largest amount consumed in one time period], binge alcohol use was defined by age-specific thresholds of estimated blood alcohol concentrations (eBACs: (Donovan, 2009)) as follows: ages ≤13 years: ≥3 drinks; 14 or 15 years: ≥4 for male, ≥3 for female participants; 16 or 17 years: ≥5 for male, ≥3 for female participants. For ≥18 years: ≥5 for male, ≥4 for female participants. Heavy binge levels were defined as double and and extreme binge levels triple the initial age-based binge levels, respectively (Patrick, 2016) as previously applied in an adolescent sample (Creswell et al., 2020). *Cannabis Use* frequency was determined by reported past year days of cannabis use.

Sleep.—Sleep characteristics assessed included circadian preference, sleep quality, daytime sleepiness, and habitual sleep timing and duration as follows. *Circadian Preference.* Circadian preference was assessed with an abbreviated 4-item version (CSM-4) of the Composite Scale of Morningness (CSM; (Smith et al., 1989)). These items were selected to evaluate three important dimensions: (1) preferred rise and bedtimes (CSM items #1 and 2);

(2) difficulty rising in the morning (CSM#3); and (3) self-identification of morning versus evening type (CSM#9). The CSM-4 score ranges from 4 to 18, with higher scores indicating greater morningness. The baseline CSM-4 strongly correlated with the full CSM (Hasler et al., 2017). *Sleep Quality.* Sleep quality was assessed with item #6 from the Pittsburgh Sleep Quality Index (i.e., based on the past month, rate your sleep quality overall: 1: very good; 2: fairly good; 3: fairly bad; 4: very bad) ((PSQI; (Buysse et al., 1989)). At baseline, responses on this item strongly correlated with the full PSQI score (Hasler et al., 2017). *Daytime Sleepiness.* Daytime sleepiness was assessed with an abbreviated 5-item version (CASQ-5) of the Cleveland Adolescent Sleepiness Questionnaire (CASQ; (Spilsbury et al., 2007)). The items determine whether participants ever fall asleep during different parts of the school day (e.g., morning classes, afternoon classes; CASQ items #1, #3, #6, #15) or feel tired during the school day (CASQ#2) during a "usual week". The baseline CASQ-5 strongly correlated with the full CASQ (Hasler et al., 2017). *Sleep Timing and Duration.* Habitual sleep timing (i.e., bedtime and rise time) and sleep duration were assessed separately for weekdays and weekends. The Sleep Timing Questionnaire (Monk et al., 2003) asks participants about when they "normally" sleep, assessing "Good Night Time" (i.e., the time when they are finally in bed and trying to fall asleep) and "Good Morning Time" (i.e., the time at which they finally get out of bed and start their day) on "school or work days" and "days off (e.g., weekends)." Sleep midpoint was calculated as the halfway point between Good Night Time and Good Morning Time, as was used as an indicator of sleep timing. Sleep duration was the difference between good nighttime and good morning time.

Data Analyses

Our selection of substance use and sleep measures were informed by our prior findings (Hasler et al., 2017), and were streamlined based on parsimony and multicollinearity considerations (see Supplement for further details).

For binge drinking severity, we used generalized linear mixed effects models with a logit link function to accommodate the ordinal outcome (R package "ordinal"). For cannabis use, our primary outcome was "any days of cannabis use" modeled with a generalized mixed effects model with a logit link (R package "stats"), and our secondary outcome was the number of days of use modeled with a zero-inflated negative binomial (ZINB) mixed effects model (R package "GLMMadaptive"). The latter outcome was considered secondary because we anticipated being under-powered to detect meaningful effect sizes for the ZINB models, especially given the larger proportion of participants with zero days of cannabis use (Channouf et al., 2021). We regressed each substance use outcome (measured repeatedly across years 1–5) on each sleep variable measured the prior year (i.e., circadian preference, sleep quality, daytime sleepiness, weekend/weekday sleep duration and timing [midpoint] in years 0–4), covarying for scaled age, $(\text{scaled age})^2$, sex, race (Asian, Black, Other, White), parental years of education, and substance use measured the prior year. The "Other" category was comprised of individuals reporting racial backgrounds that were unspecified (participant declined to respond), ambiguous with regards to how to assign to the standard race categories (e.g., a geopolitical term like Middle-Eastern), or with too low of frequency to justify a separate category (e.g., Caucasian/Native American). The $(\text{scaled age})^2$ term was included to allow for a quadratic association between age and substance use (i.e., a

unit increase in age confers a stronger risk of substance use in older ages). The primary analytic strategy was to test each sleep variable in a separate model to robustly establish the contribution of each selected sleep characteristic. Secondarily, we also fit models with all sleep characteristics included simultaneously ("full models") to identify which effects are most prominent after accounting for intercorrelations. All models included a random participant effect.

Because NCANDA is an accelerated longitudinal design study, the age range of the sample across follow-up assessments is relatively large (ages 12 to 27). We conducted exploratory analyses to investigate developmental effects on the association between sleep and substance use, particularly during middle/high school, when adolescents' sleep patterns are constrained by early school start times (Crowley et al., 2018, Watson et al., 2017). We stratified the above models into two groups: (a) pre-high school graduation age and; (b) post-high school graduation age. Pre-high school graduation observations were defined as observations in which participants were <19 years old and the visit occurred before August (n=681); all later observations were defined as post-high school graduation observations (n=637). Some participants contributed data in both age windows, and therefore are included in both age cohorts (n=487 in both; n=194 in the pre-high school graduation sample only; and n=150 in the post-high school graduation sample only). See Supplement (Figure S1) for additional details. We also conducted exploratory analyses in which we stratified the samples by sex.

The Benjamini Hochburg false discovery rate procedure (Benjamini and Hochberg, 1995) was used to adjust for multiple comparisons. We calculated adjusted p-values (BH-adjusted p-values) for the seven sleep measures (i.e., chronotype, sleep quality, daytime sleepiness, weekend/weekday duration and midpoint) across each outcome (cannabis use and binge severity) and each model type (individual and full) separately.

RESULTS

Sample description (Table 1)

Table 1 shows sample demographics, sleep characteristics, and substance use at baseline assessment. Supplemental Table S1 and Figures S2 and S3 show how these same characteristics changed as participants aged in our sample. As expected, both alcohol and cannabis use increased with age. Some sleep characteristics showed more complex patterns, with sleep timing and circadian preference showing more curvilinear trajectories, peaking in tendencies towards late timing and eveningness around age 20, similar to prior studies (Fischer et al., 2017, Randler, 2011). Sleep duration generally decreased with age.

Primary analyses: Sleep as a predictor of next year's substance use in the full sample

Binge drinking severity—Individual models of binge severity (Figure 1, Table S2) showed that greater eveningness (OR=1.25, 95% CI[1.10, 1.41] p=0.001), greater daytime sleepiness (OR=1.13, 95% CI[1.01, 1.26], p=0.029), shorter weekday sleep duration (OR=1.22, 95% CI[1.10, 1.35), p<0.001), later weekend sleep midpoint (OR=1.25, 95% CI[1.11, 1.42], p < 0.001) and shorter weekend sleep duration (OR=1.20, 95% CI[1.08, 1.35], p=0.002) were all associated with higher odds of being in a more severe binge

category the next year. That is, for each measure, an approximately one standard deviation increase in each of these sleep measures was associated with approximately 1.20–1.25 times the odds of being in a more severe binge category the next year. All of these associations passed multiple comparison corrections.

The full model including all seven sleep characteristics simultaneously (Figure 1, Table S3) showed that shorter weekend sleep duration was associated with higher odds of progressing to a more severe binge category than the previous year (OR=1.19, 95% CI[1.05, 1.35], p=0.004). No other associations passed multiple comparisons corrections. We also observed that shorter weekday sleep duration (OR=1.14, 95% CI[1.00, 1.27], p=0.044) was associated with increased binge severity. The direction and magnitude of this effect was similar to when this same variable was tested individually. However, this result did not pass multiple comparison corrections.

Cannabis Use—Individual logistic models of cannabis use (Figure 2, Table S4) showed that greater eveningness was associated with increased odds of cannabis use in the subsequent year (OR=1.25, 95% CI[1.06, 1.45], p=0.005; passed multiple comparison corrections). No associations in the full model (Table S5) that included all sleep variables simultaneously passed multiple comparison corrections. However, greater eveningness (OR=1.20, 95% CI[1.00, 1.45], p=0.050) and shorter weekend sleep duration (OR=1.20, 95% CI[1.03, 1.39], P=0.018) showed similar directions and magnitudes of effects in the full models to those in the individual models in predicting of risk of cannabis use in the next year.

Using the ZINB model, no associations between sleep variables and the number of days of cannabis use reported for the next year passed multiple comparison corrections in the individual or full models. However, without adjusting for multiple comparisons, we observed that greater eveningness (RR=1.15, 95% CI[1.01, 1.28)], p=0.028) and shorter weekday sleep duration (RR=1.11, 95% CI[1.01, 1.20), p=0.025) were each individually associated with an increased risk of more days of cannabis use the following year. In the full model, shorter weekday sleep duration was associated with an increased risk of more days of cannabis use the following year (RR=1.14, 95% CI[1.02, 1.25], p=0.016) without adjusting for multiple comparisons.

Exploratory analyses: Sleep-substance use relationships by developmental stage (middle/high school age vs post-high school age)

Binge drinking severity.—Figure 3 (Table S6) shows the findings of exploratory analyses performed in samples stratified by developmental stage (i.e., middle/high school age versus post-high school age). In the middle/high school age sample, greater daytime sleepiness (OR=1.21, 95% CI[1.04, 1.41], p=0.011), shorter weekend sleep duration (OR=1.23, 95% CI[1.05, 1.45], p=0.011), and shorter weekday sleep duration (OR=1.22, 95% CI[1.04, 1.43], p=0.013) were individually associated with greater odds of being in a more severe binge category the next year. These findings passed multiple comparison corrections.

Conversely, in the post-high school age sample, there were distinct effects of greater eveningness (OR=1.30, 95% CI[1.08, 1.54], p=0.005) and later weekend midpoint (OR=1.32, 95% CI[1.12, 1.56], p=0.001) for more severe binge category the subsequent year. Formal tests of interactions showed that the effect of weekday midpoint on next year's binge drinking severity was significantly different based on developmental stage (OR=1.46, 95% CI[1.11, 1.91], p=0.006), such that having a later weekday midpoint in middle/high-school is associated with ~1.5 times higher odds of having higher binge severity next year compared to those post-high school age or with earlier weekday midpoints. These findings from the individual models passed multiple comparison corrections. However, in full models that examined all sleep measures simultaneously within the stratified samples, there were no significant findings after adjusting for multiple comparisons.

Cannabis use.—Figure 4 (Table S7) shows exploratory findings of the association of sleep and next year's cannabis use, stratified by developmental stage. In the middle/high school sample, greater eveningness (OR=1.32, 95% CI[1.06, 1.67], p=0.014), later weekday (OR=1.27, 95% CI[1.04, 1.54], p=0.018) and weekend midpoints (OR=1.29, 95% CI[1.06, 1.57], p=0.012), and shorter weekend sleep duration (OR=1.25, 95% CI[1.04, 1.52], p=0.019) are all individually associated with increased odds of using cannabis in the next year. However, there was no significant association between individual sleep variables and cannabis use in participants in the post-high school age range. Formal tests of interactions did not show statistically significant interaction effects of sex and sleep on next year's cannabis use.

Full models including all sleep variables simultaneously that were stratified by developmental period showed no significant findings after adjusting for multiple comparisons.

Exploratory analyses: Sleep-substance use relationships within female and male samples

Binge drinking severity.—Exploratory analyses investigating the relationship between individual sleep variables and substance use within male and female participants separately (Figure 5, Table S8) revealed that in female participants greater eveningness (OR=1.39, 95% CI[1.15, 1.67], p=0.001), greater daytime sleepiness (OR=1.19, 95% CI [1.02, 1.39], p=0.026), shorter weekday duration (OR=1.18, 95% CI[1.01, 1.35], p=0.035), later weekend midpoint (OR=1.27, 95% CI[1.07,1.50], p=0.005), and shorter weekend duration (OR=1.19, 95% CI[1.02, 1.41], p=0.025] were individually associated with greater odds of being in a more severe binge category the subsequent year. Findings for greater eveningness and later weekend midpoint passed multiple comparisons correction. However, in males, only shorter weekday duration (OR=1.28, 95% CI[1.10, 1.49], p=0.001) and shorter weekend duration (OR=1.22, 95% CI[1.04, 1.45], p=0.016) were individually associated with more severe binge category the next year. Findings for shorter weekday duration passed multiple comparisons correction. Formal tests of interactions did not show statistically significant interaction effects of sex on sleep and next year's binge severity. Full models including all sleep variables simultaneously that were stratified by sex showed no significant findings after adjusting for multiple comparisons.

Cannabis use.—Figure S4 and Table S9 show findings of exploratory analyses effects of sleep on cannabis use by sex. In female participants, shorter weekend duration (OR=1.20, 95% CI[1.01, 1.43], p=0.034) was individually associated with increased odds of using cannabis in the next year. In male participants, greater eveningness (OR=1.35, 95% CI[1.08, 1.69], p=0.015) and later weekend midpoint (OR=1.30, 95% CI[1.04, 1.62], p=0.022) were associated with using cannabis the following year. However, none of these findings survived multiple comparisons correction. Formal tests of interactions did not show statistically significant interaction effects of sex on sleep and next year's cannabis use. Full models including all sleep variables simultaneously that were stratified by sex showed no significant findings after adjusting for multiple comparisons.

DISCUSSION

These findings across a 5-year follow-up period show the importance of sleep and circadian characteristics as predictors of subsequent substance use in adolescence and young adulthood. When tested individually, greater eveningness, greater daytime sleepiness, shorter sleep duration on weekdays and weekends, and later weekend sleep timing were associated with binge severity the following year. When considering all sleep measures in context of one another in the full sample, shorter sleep duration on weekends emerged as the predominant sleep predictor of future binge severity, with one hour less sleep on weekends translating to a 19% increased risk for more severe bingeing the following year. Concerning sleep predictors of future cannabis use, only greater eveningness predicted a greater likelihood of cannabis use, and only when tested individually. Further, our novel exploratory analyses suggested distinct patterns of sleep-substance use relationships by developmental stage and by sex. Compared to findings in the post-high school subsample, the middle/high school subsample was characterized by stronger associations between sleep characteristics and next year's binge severity and cannabis use.

Our current findings mostly support our prior NCANDA analyses with a single one-year follow-up, with greater eveningness, later sleep timing on weekends, and shorter sleep duration on weekdays predicting the next year's binge alcohol use severity. A key finding that emerged with the additional follow-up data was that greater daytime sleepiness and shorter sleep duration on weekends predicted more severe binge alcohol use. It is noteworthy that shorter sleep duration on weekends was the predominating sleep characteristic when all sleep variables were included in the model. While sleep characteristics are interrelated, short weekend sleep duration may be particularly indicative of an overall pattern of sleep problems. For example, eveningness tends to increase the mismatch with early academic schedules, leading to insufficient sleep on weekdays and, in turn, increasing the need for catch-up sleep on the weekends (Wittmann et al., 2006, Crowley et al., 2018)). Thus, the present finding may indicate that this pattern of poor sleep—epitomized by the failure to achieve sufficient catch-up sleep on weekends—is associated with elevated risk for binge alcohol use. Another interpretation (not mutually exclusive with the former interpretation) is that individuals who regularly prioritize other weekend activities over getting sufficient sleep may be the same individuals who engage in risky drinking, perhaps due to a tendency towards sensation seeking. Alternatively, other social or environmental barriers to sleep

(e.g., lack of parental supervision, noise in the house or neighborhood) could be important contributors that should be examined in future studies.

Although our finding on shorter sleep duration on weekends may imply interventions focused solely on this sleep characteristic, other studies have indicated that obtaining weekend catch-up sleep is often not sufficient to fully mitigate the health consequences of insufficient weekday sleep (Depner et al., 2019, LeMay-Russell et al., 2019). Meaningfully improving overall sleep health likely requires a comprehensive approach, simultaneously targeting multiple predictive sleep characteristics (i.e., eveningness, later sleep timing on weekends, shorter sleep duration on weekdays and weekends, and greater daytime sleepiness) (Harvey and Buysse, 2017, Meltzer et al., 2021b). However, experimental study designs that inform causal relationships will be required to ascertain this possibility.

With regard to cannabis use, in our prior NCANDA analysis (Hasler et al., 2017), baseline sleep characteristics including greater eveningness, worse sleep quality, shorter weekday sleep duration, and later weekend bedtimes were predictive of subsequent cannabis use. With the additional follow-up data used here, only greater eveningness was predictive of future cannabis use, and no sleep characteristics passed multiple comparison correction in the full model. We speculate that the larger inclusion of data from older ages may have diluted the effects seen in the prior paper. This speculation is buttressed by the relatively greater number of sleep characteristics predicting binge severity in the middle/high school age sample (as discussed further below).

The present findings complement other recent longitudinal studies on youth sleep and substance use. For example, Troxel and colleagues (2021) examined multiple sleep characteristics in a sample of 3,265 youth aged 16–22 years over 6 waves. Using parallel process latent growth models, increased alcohol use was predicted by relatively persistent social jetlag (weekday-weekend difference in midsleep), later shifts in bedtime on weekdays and weekends, and increases in trouble sleeping. Similarly, increased cannabis use was predicted by increases in time in bed on weekdays, decreases in time in bed on weekends, and later shifts in bedtime on weekdays and weekends. Ho and colleagues (2020) examined the cumulative impact of poor sleep during adolescence (5 waves of data collection from age 13 through age 20) on substance use at age 21, reporting that social jet lag (weekday-weekend difference in bedtime) predicted greater alcohol and cigarette use, and sleep disturbance (based on a 3-item scale) predicted cigarette, but not alcohol, use. They also reported a counterintuitive finding that accumulated waves of short sleep were associated with *lower* cigarette use at age 21 years, and only the shortest sleep duration (<6 hours) accumulating over time predicted increased alcohol use at age 21 years.

Taken together, the literature suggests that there may be differential relationships between specific sleep and circadian characteristics and specific substance use outcomes. Our exploratory analyses suggest that these relationships are influenced by sex and developmental stage. For example, in age-stratified analyses we observed that greater daytime sleepiness and shorter sleep duration on both weekdays and weekends predicted binge severity during middle/high school. In contrast, in the post-high school ages, greater eveningness and later sleep timing on the weekend predicted binge severity. Concerning

cannabis use, only the middle/high school aged-sample showed any sleep-related risk, with greater eveningness, later sleep timing on weekdays and weekends, and shorter sleep duration on weekends predicting cannabis use. We speculate that younger adolescents (middle/high school ages) may be relatively more vulnerable to sleep-related risk for substance use, and that the pattern of predictive sleep characteristics (particularly for binge severity) may reflect circadian misalignment imposed by environmental contingencies such as early school start times.

Our exploratory analyses also support the value of considering sex differences when examining sleep-substance use relationships. Greater eveningness, daytime sleepiness, later weekend sleep timing, and shorter weekend sleep duration were predictive of binge severity only in the female participants, whereas shorter weekday sleep duration was predictive of binge severity in both male and female participants. Noting that female, compared with male, adolescents and young adults trend towards early sleep/circadian timing (e.g., (Fischer et al., 2017)), our findings suggest that later sleep/circadian timing may be at odds with their natural tendencies and thus put them at greater risk of mental health problems. This hypothesis is consistent with other recent findings linking later sleep/circadian timing in women to elevated risk for depression (Kim et al., 2020, Morita et al., 2015). In contrast, males may be relatively more vulnerable to short sleep. In a cross-sectional study in high school students (14–18 y/o: Kwon et al., 2020), both sex/gender and age were relevant moderators. Insufficient sleep (operationalized as <8 hours) was associated with higher likelihood of alcohol and cannabis use (but not cigarettes or nicotine vaping), with the sleep-cannabis use association being stronger in male (vs. female) and younger (vs. older) students (Kwon et al., 2020).

While the present analyses were not intended to test the mechanisms linking sleep and substance use. there are plausible mechanisms consistent with these findings that are worth further investigation. Sleep/circadian characteristics may influence positive or negative reward pathways, potentially moderated by impulsivity (Hasler and Pedersen, 2020). Eveningness, circadian misalignment, and sleep loss have all been linked to altered reward function (e.g., (Hasler et al., 2021). Alcohol or cannabis may be sedating or anxiolytic and consequently these substances may be used as sleep aids, particularly by individuals with tendencies towards eveningness or poor sleep quality (Lam et al., 2018). Eveningness, circadian misalignment, and sleep loss are also associated with increased impulsivity (e.g., (Russo et al., 2012, Song et al., 2019, Hasler et al., 2022), which may interact with positive or negative reinforcement pathways. For example, impaired inhibition may increase substance use in the presence of negative emotions (i.e., negative urgency) (Parra et al., 2005, McCabe et al., 2021). We cautiously interpret the present findings as reflecting circadian misalignment and sleep restriction that may cumulatively lead to increased risk for substance use through multiple and likely related pathways, including positive and negative reinforcement moderated by impulsivity. Experimental designs may reduce confounding variables to illuminate sleep-related brain mechanisms and sleep-alcohol relationships. Efforts to identify and disentangle putative mechanisms will also require comprehensive and multidimensional assessment in both human studies and translational animal models (Logan et al., 2018). Finally, new technologies measuring real-time blood alcohol levels may

add precision to the examination of sequential and synergistic relationships between alcohol exposure and sleep changes.

Limitations

NCANDA has several limitations for examining sleep and substance use relationships. The baseline NCANDA sample consisted of 692 participants (83%) with histories of little or no alcohol or cannabis use. For participants exceeding the “non/low drinker” threshold (n=139: 17%), the “exceeds” threshold was relatively low by clinical standards (e.g., maximum drinks on one occasion: age 20–21.9 years: male: >5, females >3 drinks on one or more occasions) and individuals with substance dependence were excluded. At the assessment ages included here, some participants had not yet reached the peak ages of binge alcohol and cannabis use, dampening our ability to detect relationships with more severe alcohol and cannabis outcomes. We anticipate additional participants with clinically significant alcohol or cannabis use will be observed in subsequent assessments of this ongoing project. Nevertheless, these findings indicating a significant relationship between sleep characteristics and alcohol or cannabis outcomes suggest that these are robust relationships observed in non-clinical populations. For the main NCANDA study assessment of sleep characteristics, reliance on self-report measures, rather than behavioral (e.g., actigraphy) or physiological (e.g., melatonin) indicators of sleep and circadian rhythms, limits our ability to determine whether subjective bias in reporting sleep characteristics may be present. The study also used abbreviated versions of validated measures which, while they appear to correlate strongly with the full standard (Hasler et al., 2017), may be less psychometrically robust. A thorough assessment of caffeine use patterns may also have informed these relationships, as evening-type adolescents tend to report more caffeine use (Cole, 2015), caffeine use can disturb sleep and circadian rhythms (Clark and Landolt, 2017, Burke et al., 2015), and early caffeine use may be a risk factor for alcohol and other substance use (Kristjansson et al., 2018). Finally, the present analyses focused on developmental stage (middle/high school versus post-high school age) and sex as potential moderators of sleep-substance use associations but it will be important to consider race/ethnicity as a moderator moving forward (Hasler and Pedersen, 2020). For example, prior work indicates increased morningness (Malone et al., 2017) among Black adults, but also worse sleep among Black adolescents and young adults (Johnson et al., 2019). However, another preliminary finding suggested that Black, compared to White, drinkers were spared from an association between later sleep timing and greater stimulation in response to alcohol (Hasler et al., 2019b). Finally, understanding environmental contingencies (e.g., actual school start time) may further the understanding of mechanisms influencing this relationship.

Conclusion

These findings extend a growing literature supporting the relevance of sleep/circadian characteristics to risk for alcohol and cannabis use. Overall, our findings illustrate that multiple sleep characteristics are relevant to risk for engaging problematic drinking patterns and cannabis use. Although weekend sleep duration emerged as the predominant predictor of binge drinking severity in the full analytic model, it is important to remember the interrelationships among weekday and weekend sleep characteristics. Our most novel finding was that middle/high school age adolescents may be most vulnerable to sleep-related

risk for substance use, although it'll be important to replicate these findings. Sleep is a modifiable behavior in adolescents (e.g., (Griggs et al., 2020) and, consequently, adolescent sleep may be a viable target for reducing substance use risk through, for example, policy-level changes delaying school start times (Meltzer et al., 2021a).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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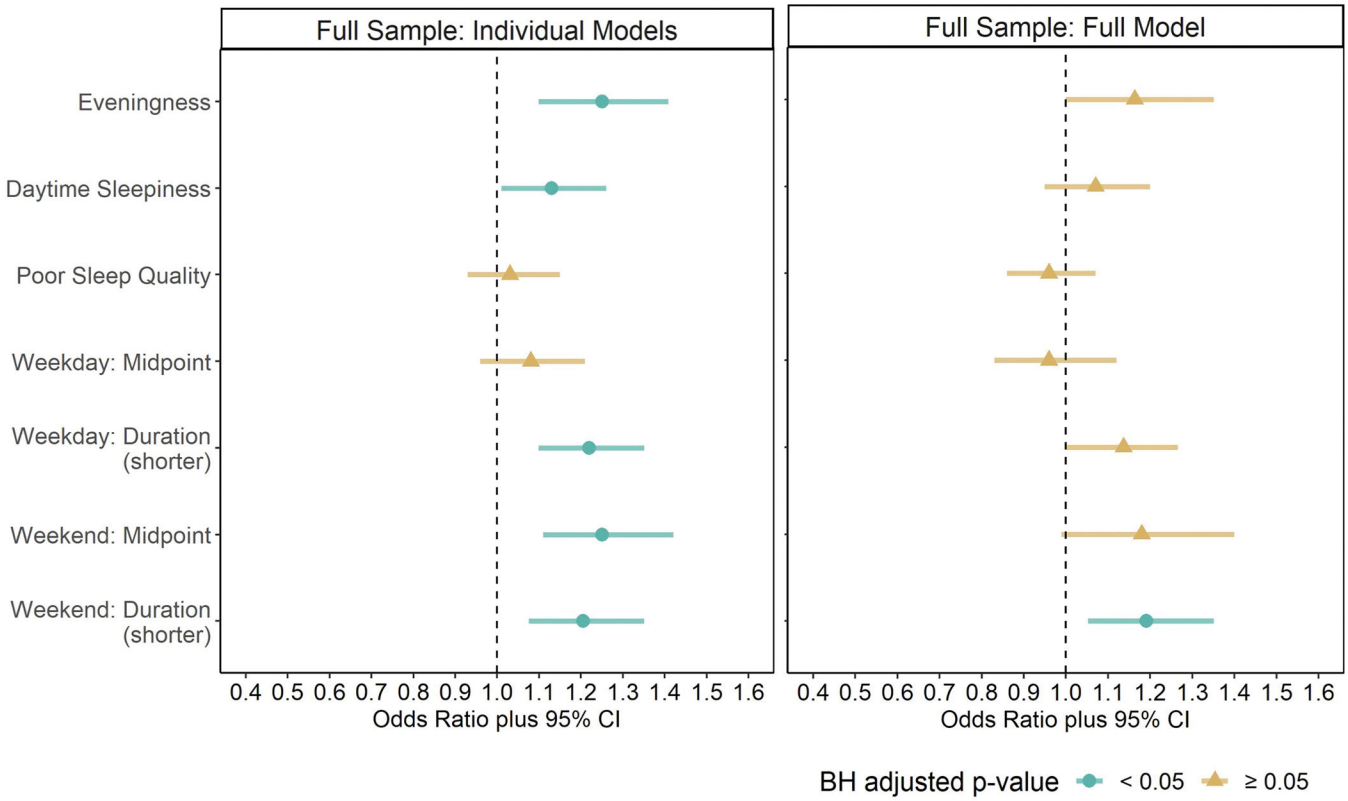

Figure 1.

Sleep characteristics predicting next year's alcohol binge severity in the NCANDA cohort (full sample) for individual models and the full model (7 items combined in one model)

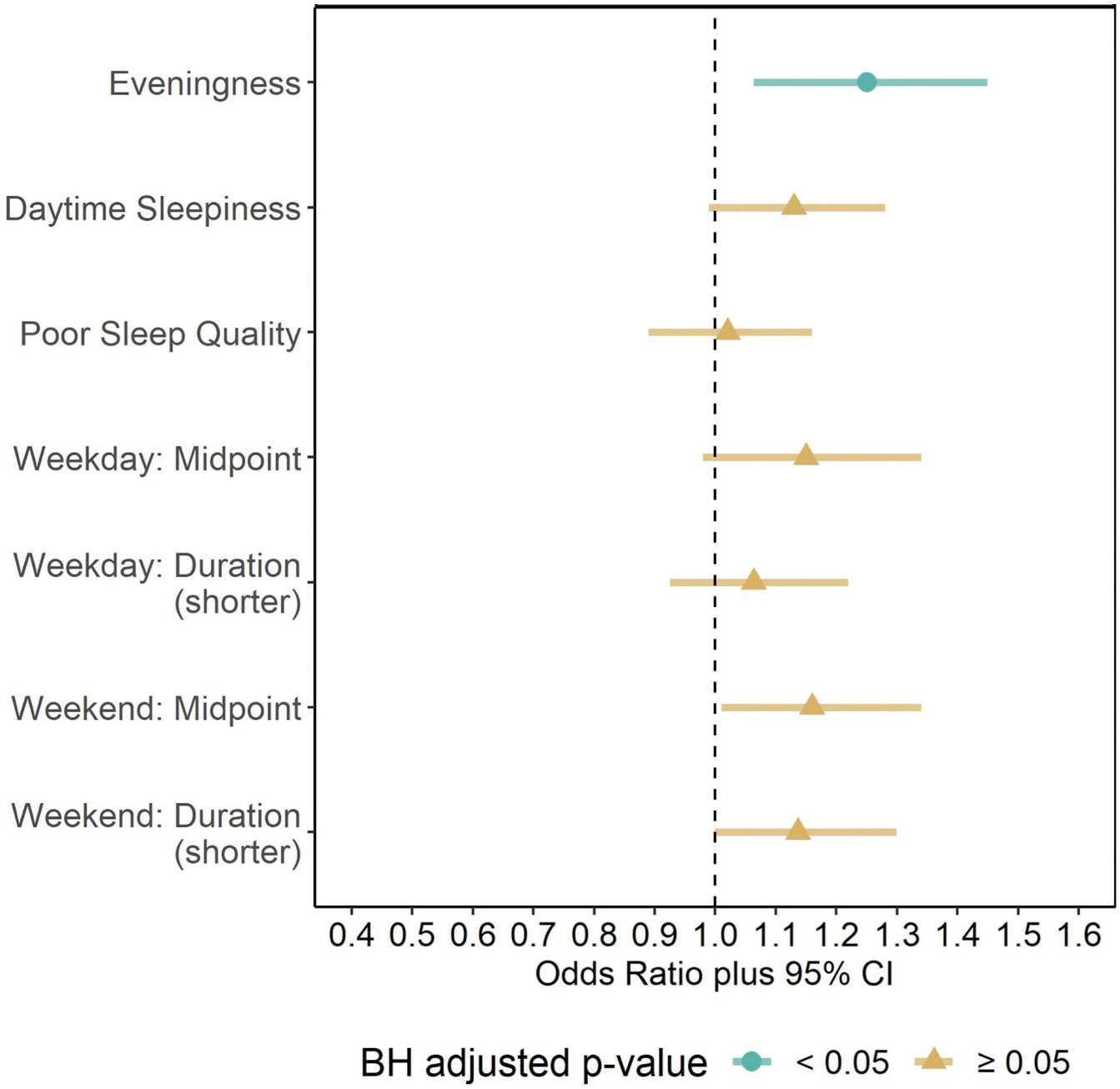

Figure 2.
Sleep characteristics predicting next year's cannabis use (yes/no) in the NCANDA cohort (full sample) for individual models only

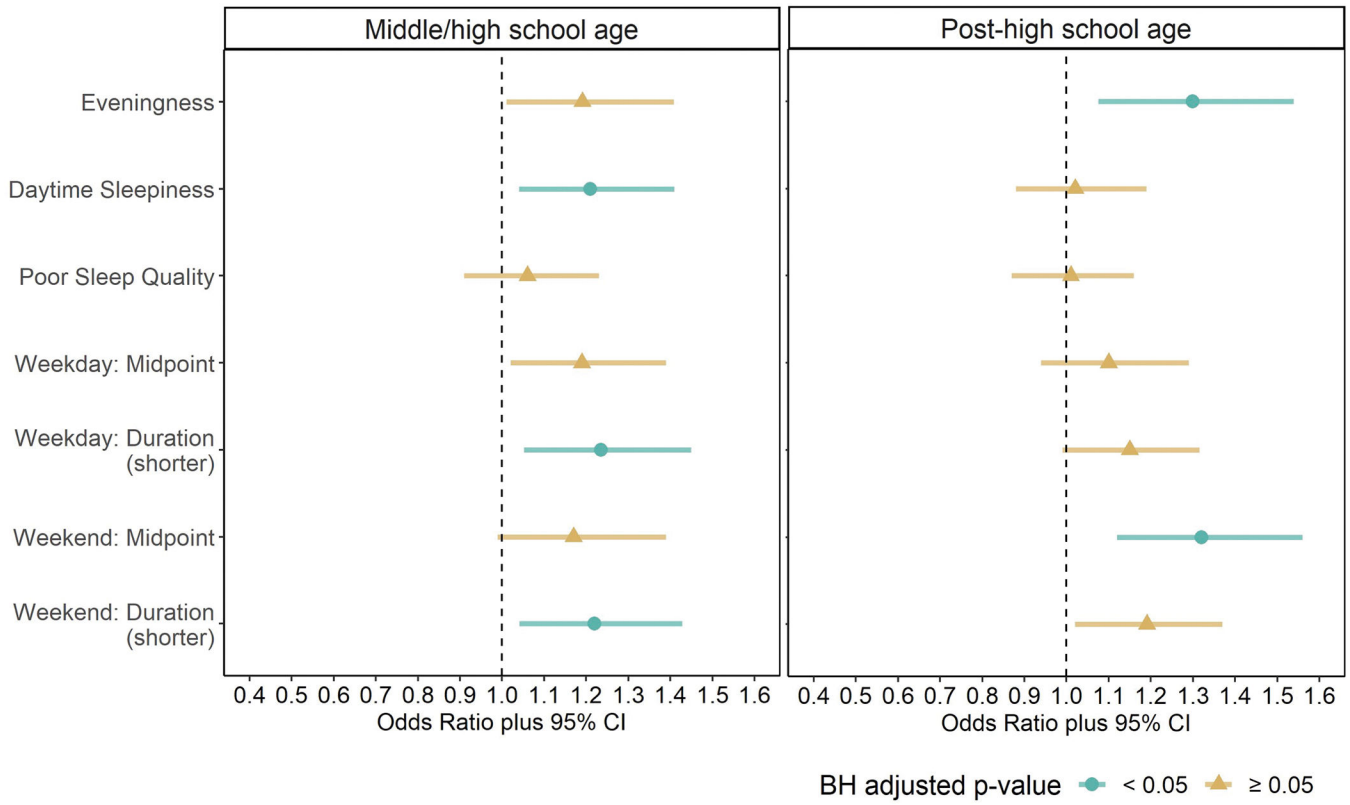

Figure 3.

Differentiation in sleep characteristics predicting next year's binge severity between middle/high school age and post-high school age in the NCANDA cohort (sleep characteristics run in individual models)

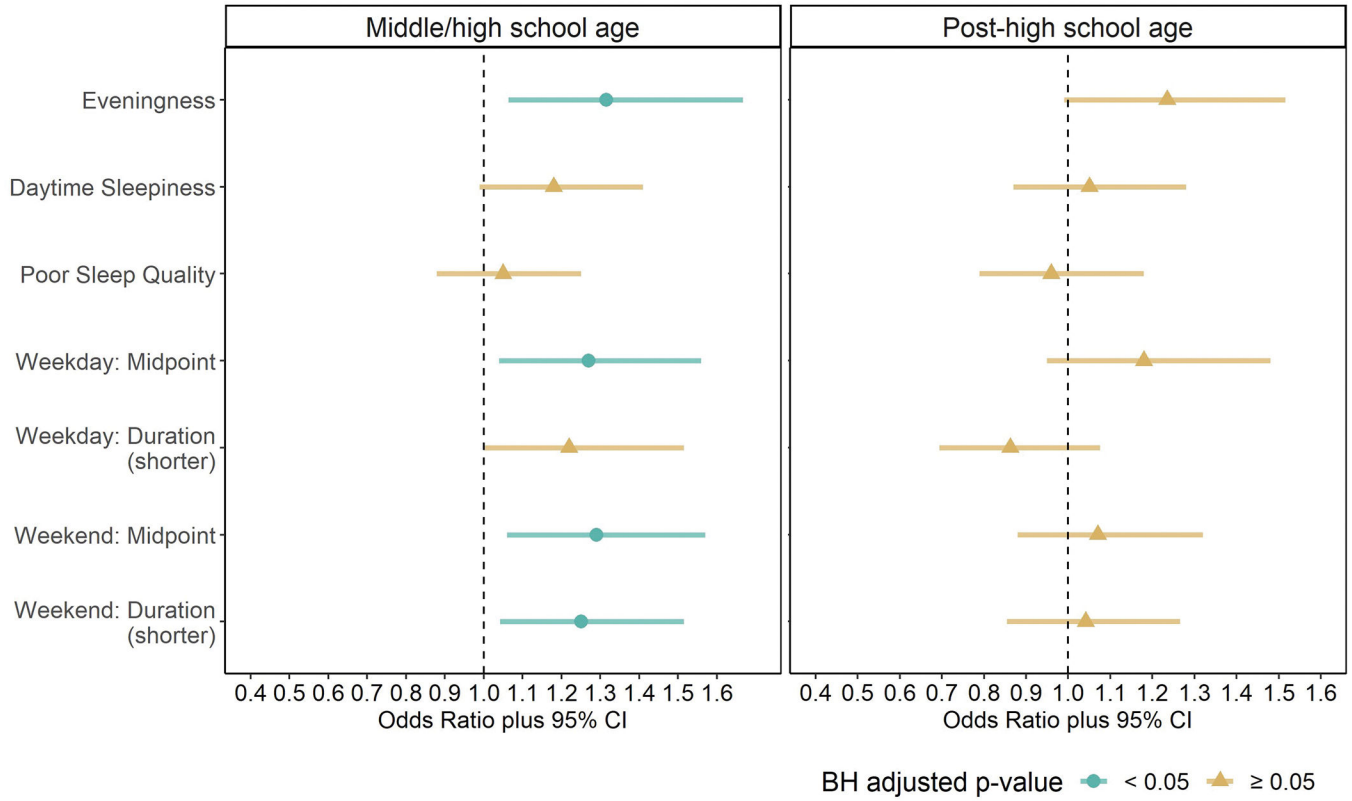

Figure 4.

Differentiation in sleep characteristics predicting next year's cannabis use (yes/no) between middle/high school age and post-high school age in the NCANDA cohort (sleep characteristics run in individual models)

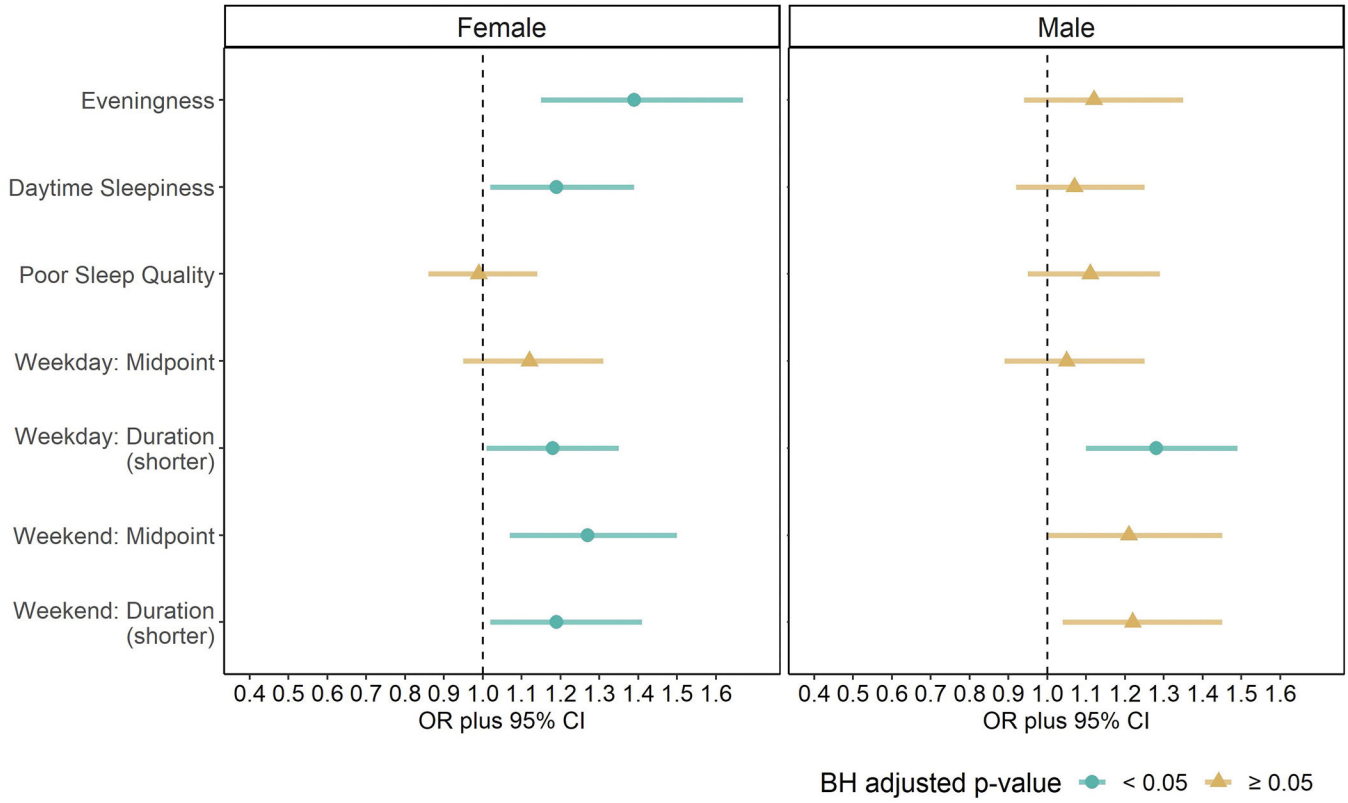

Figure 5.

Differentiation in sleep characteristics predicting next year's binge severity between male and female participants in the NCANDA cohort (sleep characteristics run in individual models)

Table 1.

Cohort characteristics at baseline

		Full Sample (N = 831)	
		Mean ± SD	**Median [Min, max]**
Demographics	Age	16.2 ± 2.5	16.0 [12.0, 22.0]
	Sex, n (%)	423 (50.9%) female	
	Race, n (%)		
	Asian	62 (7.5%)	
	Black	99 (11.9%)	
	Other[a]	75 (9.0%)	
	White	595 (71.6%)	
	Hispanic, n (%)	97 (11.6%) yes	
Sleep Characteristics	Sleep quality[b]	1.8 ± 0.7	2.0 [1.0, 4.0]
	Circadian preference[c]	11.2 ± 2.4	11.0 [5.0, 19.0]
	Daytime sleepiness[d]	8.6 ± 3.0	8.0 [5.0, 23.0]
Weekday	Midpoint (24-h clock time)	2:42 + 1:00	2:30 [0:30, 7:00]
	Duration (hours)	8.2 ± 1.3	8.0 [4.0, 13.0]
Weekend	Midpoint (24-h clock time)	4:42 + 01:18	4:30 [1:30, 9:30]
	Duration (hours)	9.6 ± 1.5	9.50 [4.5, 14.0]
Alcohol Use	Have you ever drunk alcohol? n (%)	263 (31.6%) yes	
	Have you had alcohol in the last year? n (%)	248 (29.8%) yes	
	Frequency of alcohol use (days in last year)	4.5 ± 15.9	0.0 [0.0, 144.0]
	Largest amount of alcohol (number of drinks)	1.6 ± 3.4	0.0 [0.0, 25.0]
	Age- and sex-adjusted binge severity, n (%)		
	No alcohol	557 (67.0%)	
	Alcohol but no binge	118 (14.2%)	
	Binge	82 (9.9%)	
	Heavy	32 (3.9%)	
	Extreme	19 (2.3%)	
Marijuana Use	Have you ever had marijuana?	156 (18.8%) yes	
	Have you had marijuana in the last year? n (%)	127 (15.3%) yes	
	Frequency of marijuana use (days in last year)	3.0 ± 24.2	0.0 [0.0, 365.0]

Notes:

[a]The “Other” category was comprised of individuals reporting racial backgrounds (e.g., Middle-Eastern, Caucasian/Native American) that were unspecified, ambiguous, or with too low of frequency to justify a separate category.

[b]Sleep quality is based on item #6 from the PSQI, with higher scores indicating worse sleep quality.

[c]Circadian preference is based on a 4-item abbreviated version of the CSM, with lower scores indicating greater eveningness.

[d]Daytime sleepiness is based on a 5-item version of the CASQ, with higher scores indicating greater daytime sleepiness.