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CIRCADIAN MISALIGNMENT AND WEEKEND ALCOHOL USE IN LATE ADOLESCENT DRINKERS: PRELIMINARY EVIDENCE

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Abstract

Alcohol use accelerates during late adolescence, predicting the development of alcohol use disorders (AUDs) and other negative outcomes. Identifying modifiable risk factors for alcohol use during this time could lead to novel prevention approaches. Burgeoning evidence suggests that sleep and circadian factors are cross-sectionally and longitudinally linked to alcohol use and problems, but more proximal relationships have been understudied. Circadian misalignment, in particular, is hypothesized to increase risk for AUDs, but almost no published studies have included a biological measure of misalignment. In the present study, we aimed to extend existing research by assessing the relationship between adolescent circadian misalignment and alcohol use on a proximal timeframe (over two weeks) and by including three complementary measures of circadian alignment. We studied 36 healthy late (18–22 years old, 22 females) alcohol drinkers (reporting 1, standard drink per week over the past 30 days) over 14 days. Throughout the study, participants reported prior day's alcohol use and prior night's sleep each morning via smartphone and a secure, browser-based interface. Circadian phase was assessed via the dim light melatonin onset (DLMO) in the laboratory on two occasions (Thursday and Sunday nights) in counterbalanced order. The three measures of circadian alignment included (1) DLMO-midsleep interval, (2) "classic" social jet lag (weekday-weekend difference in midsleep), and (3) "objective" social jet lag (weekday-weekend difference in DLMO). Multivariate imputation by chained equations was used to impute missing data, and Poisson regression models were used to assess associations between circadian alignment variables and weekend alcohol use. Covariates included sex, age, Thursday alcohol use, and Thursday sleep characteristics. As predicted, greater misalignment was associated with greater weekend alcohol use for two of the three alignment measures (shorter DLMO-midsleep intervals and larger weekday-weekend differences in midsleep), while larger weekday-weekend differences in DLMO were associated with less alcohol use. Notably, in contrast to expectations, the distribution of weekday-weekend differences in DLMO were nearly equally distributed between individuals advancing over the weekend and those delaying over the weekend. This unexpected finding plausibly reflects the fact that college students are not subject to the same systematically earlier weekday schedules observed in high school students and working adults. These preliminary findings support the need for larger, more

definitive studies investigating the proximal relationships between circadian alignment and alcohol use among late adolescents.

INTRODUCTION

Alcohol use during late adolescence has long-term individual and public health implications. Alcohol use accelerates during this timeframe (age ~18–22) (1, 2), and upsurges in binge-drinking during late adolescence predict the development of alcohol use disorders (AUDs) and other negative outcomes, including worse general health (3, 4). Existing alcohol use prevention programs for late adolescents have limited efficacy (5, 6) suggesting that researchers should consider additional risk factors that could lead to novel prevention approaches.

Burgeoning evidence suggests that adolescents' and young adults' sleep and circadian factors are linked to alcohol use and alcohol problems (7). As such, sleep and circadian factors may be viable, novel targets for alcohol problem prevention. Both cross-sectional and longitudinal data link sleep and circadian rhythms to alcohol use behaviors and the development of alcohol use disorders. Specifically, a number of human studies investigating the link between insomnia-related sleep characteristics and/or sleep loss generally show that insomnia symptoms, shorter sleep duration, and daytime sleepiness are associated with both concurrent and later alcohol use and alcohol problems (e.g. (8–12)). Yet, to our knowledge, no existing adolescent alcohol prevention programs target sleep and circadian factors, likely because further work is needed to delineate which sleep/circadian characteristics are the most appropriate targets for prevention and/or intervention.

One promising prevention target that links sleep and alcohol use in late adolescence is circadian misalignment. Circadian misalignment occurs when people attempt to sleep and wake at times that are incongruent with their internal circadian timing. Adolescents are at risk of circadian misalignment because of post-pubertal sleep changes and typical secondary school schedules. Specifically, the onset of puberty coincides with a progressive shift to later circadian timing and a slower rise in the homeostatic sleep drive (13), both of which cause adolescents to, (1) fall asleep later, and (2) sleep in later than adults (14). This propensity for later sleep times is mismatched with increasingly early secondary school start times (15) that can result in insomnia and sleep loss (especially during school week) (16) as well as large weekday-weekend shifts in sleep timing and duration, also known as “social jet lag” (17). Nighttime use of electronic devices and peer influences to communicate late at night (18–20) may also put adolescents at risk of circadian misalignment.

Most human studies examining associations between sleep/circadian factors and alcohol use have relied on self-report measures that are, at best, proxies for circadian misalignment. These proxies include self-reported evening chronotype (i.e., preference for later sleep and activity schedules (21)) and weekday-weekend differences in sleep timing (i.e., social jet lag (17)). For instance, studies show that adolescents with an evening chronotype or who report later sleep timing are at increased risk for alcohol use (22–28). Studies investigating self-reported weekday-weekend differences in sleep timing, however, show more nuanced results (28–30). For example, in one large survey of high school students, 11th graders' social jet

lag predicted subsequent year alcohol use, and 11th grade chronotype and social jet lag predicted subsequent year binge drinking (28). In another, increased hours of weekday sleep was associated with decreased risk of alcohol use, but increased risk of episodes of drunkenness (30).

Although available studies of circadian misalignment as measured with self-reported proxies provide important, large-scale estimates of its association with alcohol use, they are also limited by threats to validity of participants' self-reported sleep data. Specifically, participant self-report data is subject to bias through participant error such as forgetting and systematic biases toward rounding, momentary influences on reporting (e.g., hot and cold emotions) and intentional misreporting (e.g., social desirability bias) (see discussion in (31)). Biological measures of circadian misalignment can provide more objective assessments. However, to our knowledge, only one published study has examined associations between adolescent alcohol involvement and circadian misalignment using a physiological measure of circadian alignment; specifically, the interval between the dim light melatonin onset (DLMO), which typically occurs 2–3 hours before bedtime (32), and the timing of sleep. In this study of 21 adolescent (33), greater misalignment (shorter DLMO-sleep intervals) was associated with more symptoms of substance use disorders (SUD). This small study was further limited by the nature of the sample—the adolescents had just completed substance abuse treatment programs and had necessarily reduced their substance use, thus obscuring associations between circadian misalignment and naturally occurring substance use. A second limitation of past studies is that they are either cross-sectional studies using global, retrospective measures (e.g., (7, 26)), or longitudinal studies assessing sleep/circadian factors and alcohol use a year or more apart (e.g., (28, 29)). More proximal, real-time assessment could better identify the links among sleep behavior, circadian timing, and alcohol use behavior, thus suggesting more direct connections between these processes and behaviors, which, in turn, would suggest more proximal targets for interventions aimed at altering sleep-circadian timing.

The purpose of the present study is to extend the existing research on adolescent circadian misalignment and alcohol use and address the aforementioned limitations of current work in three important ways. First, we aim to provide a robust assessment of the relationship between circadian misalignment and alcohol use by operationalizing and measuring circadian misalignment in three complementary ways. [1] *DLMO-Midsleep Interval*: Our first measure is an established, fixed (i.e., single assessment during the study period) measure of the comparison of the timing of sleep (based on sleep diaries) relative to circadian phase (based on salivary Dim Light Melatonin Onset (DLMO)-midsleep difference) (33, 34). [2] *Classic Social Jet Lag*: Our second measure, commonly-termed social jet lag, is an examination of the difference in weekend midsleep and weekday midsleep. Of note, although social jet lag is conceptualized as capturing the misalignment between biological timing and socially-constrained sleep timing, it is not typically measured using biological measures. In our study, midsleep is calculated from sleep-wake times reported in electronic daily diaries in order to improve the data quality by reducing bias and error from retrospective recall. [3] *Objective Social Jet Lag*: Our third measure is a novel, exploratory, and objective measure of social jet lag calculated as the difference between weekday and weekend DLMO. Our second and most important aim is to conduct a

temporally-proximal assessment of circadian misalignment and alcohol use in order to characterize their short-term relationships. Finally, although we expect that all of our measures for circadian misalignment will be related, our third aim is to examine the correspondence among these measures and explore the ways in which they may be differentially related to alcohol use, perhaps by capturing specific aspects of the general circadian misalignment construct.

METHODS

Participants

Participants were 36 healthy late adolescent (18–22 years old, 22 females) alcohol drinkers, consuming a minimum of one standard drink per week over the past 30 days (assessed via a web-or phone-based time line follow back (TLFB)). Participants were recruited via flyers and a research registry. They were required to be right-handed to avoid lateralization issues for a neuroimaging component of the study (not reported here). We recruited adolescents with a range of alcohol use levels, including light ($n=3$; <12 drinks/month, no binges), moderate ($n=21$; 13–28 drinks/month and/or 1–4 binges), and heavy ($n=12$; >28 drinks/month and/or 5+ binges) drinking.

Participants were excluded for past month substance use (other than alcohol, cannabis, or nicotine) as per the screening TLFB, or if they reported significant current medical (e.g., liver disease, cardiovascular disorder, head injury with loss of consciousness), or psychiatric (e.g., major depression, schizophrenia, bipolar disorder) illness. Psychiatric disorders were diagnosed via Structured Clinical Interview for DSM-IV (35). Participants were also excluded for any current sleep disorders other than insomnia, as determined via a locally-developed structured interview for sleep disorders based on DSM-IV and the International Classification of Sleep Disorders, 3rd edition (36). We included individuals with insomnia given that insomnia was expected to be prevalent among our population of greatest interest—those with regular alcohol use and/or circadian misalignment.

Participants with extreme habitual sleep times (bedtimes later than 2:00 am, rise times later than 10:00 am) or habitual sleep durations (longer than 9 hours or shorter than 6 hours) were also excluded due to the practical challenges of studying participants with extreme sleep times (e.g., difficulty staffing the sleep lab) and concern over having extreme outliers in a relatively small sample. Finally, participants were excluded if they used medications that interfere with sleep and/or reward function (e.g., hypnotics, antidepressants, anxiolytics, beta blockers, benzodiazepines, stimulants).

A total of 41 participants were consented for the study and 36 completed the protocol. One participant was ruled ineligible due to past month substance use, one was withdrawn by investigators due to poor adherence to study procedures, one withdrew due to illness, and two withdrew due to schedule conflicts. Written informed consent was obtained for all participants. The study was approved by the Institutional Review Board of the University of Pittsburgh.

Protocol

In vivo assessment.—All participants completed a 14-day ecological momentary assessment (EMA) protocol, which was designed to assess their sleep and alcohol use (along with affect, craving, and other measures not discussed here) throughout the day under naturalistic conditions. The EMA protocol was administered via smartphones; text message prompts were sent six times a day with a link to a secure, browser-based assessment system developed by the Office of Academic Computing in the Department of Psychiatry at the University of Pittsburgh School of Medicine. For the present analyses, we focus on sleep and alcohol use as collected via self-report from the first morning assessment, which was prompted via text at participants' habitual rise time. The response window remained open until noon, and participants were incentivized to complete the morning assessment (completion was required to earn that day's payment).

Laboratory assessment.—Participants came into the sleep laboratory for two pre-weekend (Thu/Fr) and post-weekend (Sun/Mon) overnight visits to assess circadian phase via salivary melatonin (Figure 1). The order of these visits was counter-balanced to address potential task habituation effects during each visit's fMRI scan (not discussed here); participants were randomly assigned to either a Thursday/Friday-Sunday/Monday ('FM') or Sunday/Monday-Thursday/Friday ('MF') order. We included two weekends in the protocol because requiring participants to sleep in the lab during the pre-/post-weekend circadian phase assessments altered their sleep (see below) and necessarily restricted them from any alcohol use. The second weekend was intended to provide unconstrained assessments of pre-/post-weekend sleep and alcohol use.

Measures

Substance use.—During initial screening, the use of alcohol and other drugs over the past 30 days was assessed via Time Line Follow Back (TLFB) (37). Some participants completed the TLFB via a web-based format (38, 39), which included instructions and a calendar covering the past 30 days that allowed entry of relevant events (e.g., parties) and number of drinks for each day. Other participants completed the TLFB via a phone interview with a trained staff member. Following the detailed assessment of alcohol use, participants were also asked "Did you use any drugs other than alcohol in the past 30 days?" with a Yes/No response format. Participants answering "Yes" were asked to list the drugs. Additional lifetime drinking and drug use data are not reported here but are available from the authors upon request.

The morning electronic daily diary assessed alcohol use with the question "How many alcoholic drinks did you have yesterday?" with a drop-down menu allowing responses from 0–29. Our primary outcome variable was weekend alcohol use, calculated as the sum of self-reported alcohol use across the first Friday and Saturday in the protocol (corresponding to Study Days –7 and –6 for protocol scheme FM and Study Days –3 and –2 for protocol scheme MF). We also included weekday alcohol use as a covariate, calculated based on the total alcohol use reported on the Thursday preceding the Friday/Saturday used for weekend alcohol use (corresponding to Study Day –8 and –4 for protocol schemes FM and MF respectively).

Sleep and circadian phase.—Sleep was assessed daily in the electronic diary rise time assessment using a standard sleep diary, which includes items corresponding to sleep timing, continuity, and quality. In this study, we focused on midsleep (midpoint between sleep onset and offset) as a widely-used and parsimonious measure of sleep timing.

Circadian phase was assessed via the salivary DLMO (40) during the Thursday (pre-weekend) and Sunday (post-weekend) overnight laboratory visits. Saliva samples (to assess melatonin) were collected in Salivettes (Sarstedt, Newton, NC) under dim light conditions (<15 lux at any angle of gaze) every half-hour starting 6 hours before, and ending 1 hour after, each participant's habitual bedtime. Dim light conditions were instituted starting 1 hour before collection and were confirmed each visit using a light meter (see model above). The sampling protocol followed standard procedures to control for posture (participants remained seated other than trips to the bathroom) and other possible confounding factors (e.g., no eating/drinking within 10 min of sampling, caffeine, bananas, and chocolate were prohibited throughout the study visit, etc.) (41). Participants were asked to rinse their mouths with water 10 minutes prior to each sample if they had eaten or drank. After collection, saliva samples were frozen at -80°C and shipped overnight on dry ice for radioimmunoassaying by Solid Phase, Inc. (Portland, ME) using commercially available kits (ALPCO, Inc., Salem, NH). The DLMO was calculated as the clock time when levels exceeded the mean of three consecutive baseline samples plus twice the standard deviation of those samples (42); this approach produces DLMO estimates that are closer to the initial rise of melatonin than fixed threshold methods (43).

We calculated three measures of circadian alignment. [1] DLMO-Midsleep Interval: Our primary, and most direct, measure of circadian alignment was based on the interval between DLMO (from the Thursday lab visit) and midsleep (from the prior Thursday night). Specifically, DLMO was assessed on Study Days -1 and 3 for protocol schemes FM and MF, respectively, while midsleep came from Study Days -8 and -4 for protocol schemes FM and MF, respectively. We used midsleep from the prior Thursday as a more naturalistic assessment of sleep timing; sleep timing of the DLMO assessment night was impacted by DLMO collection procedures that kept participants up an hour later and potentially any other factors typically associated with sleeping in a laboratory environment. Our two secondary measures of circadian misalignment were indicators of social jet lag. [2] Classic Social Jet Lag: The first (weekday-weekend differences in midsleep, aka "classic" social jet lag) was calculated by subtracting Thursday midsleep from the mean midsleep across the subsequent Friday and Saturday, all prior to the first DLMO assessment. Thus, the weekday-weekend difference in midsleep was calculated by subtracting midsleep from Study Day -8 from the mean midsleep from Study Days -7 and -6 in protocol scheme FM, and by subtracting midsleep from Study Day -4 from the mean midsleep from Study Days -3 and -2 in protocol scheme MF. [3] Objective Social Jet Lag: The second (weekday-weekend differences in DLMO, aka "objective" social jet lag) was calculated by subtracting the Thursday DLMO from the Sunday DLMO, corresponding to Study Days -1 and 2 in protocol scheme FM, and to Study Days 3 and -1 in protocol scheme MF.

Data analysis

Incomplete data imputation.—While the majority of morning assessments for the 36 participants across the 14-day protocol were fully completed (89.9%), some assessments were skipped or only partially completed. Additionally, DLMO assessments for 5 of the 36 participants showed no clear onset of melatonin secretion, resulting in incomplete DLMO information. To reduce possible bias due to data incompleteness arising from these situations, we used multivariate imputation by chained equations (MICE) (44, 45) to generate multiple imputed data sets to be used for analysis. MICE is a principled method for dealing with complex missing data problems (46) which uses observed values in the data to impute missing values and has been successfully applied across many different fields (47). Also, multiple imputation (48, 49) takes into account uncertainty in the imputations and yields accurate standard errors. For our data analysis, 100 imputed data sets were generated and analyzed.

Modeling circadian alignment and alcohol use.—We only considered sleep timing and alcohol use data reported prior to the first lab visit, which better represents participants' natural sleep timing and alcohol use patterns independent of any sleep disruptions associated with sleeping in the lab. This includes Thursday, Friday, and Saturday corresponding to Study Days −8, −7, −6 and −4, −3, −2 for protocol scheme FM and MF respectively (see Figure 1). We assessed the relationship between circadian alignment, as measured by the three alignment variables (DLMO-midsleep interval, “classic” social jet lag, and “objective” social jet lag), and weekend alcohol use, as measured by the total number of drinks consumed on Friday and Saturday nights, while controlling for other covariates that may influence weekend alcohol use, such as sex, age, Thursday alcohol use, and Thursday sleep characteristics (total sleep time, midsleep, DLMO).

Since the response variable (weekend alcohol use) is integer-valued, we used a Poisson regression model to estimate the impact of circadian alignment on the expected number of drinks consumed over the weekend through a log-linear relationship. However, we hypothesized that circadian alignment deviations from a ‘central’ or ‘usual’ value, or range of values, could be associated with alcohol use, so we needed to operationalize our alignment measures appropriately in order to test for this specific kind of relationship. To accomplish this, we created two separate variables for each alignment measure that captured deviations in either direction from a central value. Specifically, for DLMO-midsleep interval, we considered deviations above and below the median interval in our dataset (6.8 hours), and for the social jet lag measures, we considered ‘advance’ and ‘delay’ variables associated with positive and negative weekday-weekend differences respectively. Since we also expect small deviations from the ‘central’ or ‘usual’ value to have little effect on weekend alcohol use, while large deviations may significantly impact weekend alcohol use, we analyzed squared deviations, rather than absolute deviations. Squaring deviations will shrink the effect sizes of small deviations (close to zero) such that all small deviations will have similar effect sizes. Additionally, the effect sizes of larger deviations will be greater than the effect sizes using absolute deviations. Taking these two characteristics together, the squared transformation of deviations more closely aligns with our hypothesized effect of alignment deviations on weekend alcohol use.

Bringing all of these elements together, we specifically consider the following log-linear Poisson regression models:

$$\begin{aligned}\log(\lambda) &= \beta_0 + \beta_1 \text{ThursdayAU} + \beta_2 \text{FemaleInd} + \beta_3 \text{Age} + \beta_4 \text{ThursdayTST} \\ &\quad + \beta_5 (\text{DLMO} - \text{Midsleep Dev})^2 - + \beta_6 (\text{DLMO} - \text{Midsleep Dev})^2 + \\ \log(\lambda) &= \beta_0 + \beta_1 \text{ThursdayAU} + \beta_2 \text{FemaleInd} + \beta_3 \text{Age} + \beta_4 \text{ThursdayTST} \\ &\quad + \beta_5 \text{ThursdayDLMO} \\ &\quad + \beta_6 (\text{Midsleep Diff})^2 - + \beta_7 (\text{Midsleep Diff})^2 + \\ \log(\lambda) &= \beta_0 + \beta_1 \text{ThursdayAU} + \beta_2 \text{FemaleInd} + \beta_3 \text{Age} + \beta_4 \text{ThursdayTST} \\ &\quad + \beta_5 \text{ThursdayMidsleep} \\ &\quad + \beta_6 (\text{DLMO Diff})^2 - + \beta_7 (\text{DLMO Diff})^2 +\end{aligned}$$

where λ is expected weekend alcohol use, *ThursdayAU* is Thursday alcohol use, *FemaleInd* is an indicator variable (1=female, 0=male), *Age* is as named, *ThursdayTST* is total sleep time from Thursday night, *ThursdayMidsleep* is midsleep from Thursday night, *ThursdayDLMO* is DLMO assessed on Thursday night, $(\text{DLMO} - \text{Midsleep Dev})^2 -$ is the squared deviation of DLMO-midsleep interval from median when interval *is below* the median (and 0 otherwise), $(\text{DLMO} - \text{Midsleep Dev})^2 +$ is the squared deviation of DLMO-midsleep interval from median when interval *exceeds* the median (and 0 otherwise), $(\text{MidsleepDiff})^2 -$ is the squared midsleep difference when mean weekend midsleep *is earlier than* Thursday midsleep (and 0 otherwise), $(\text{MidsleepDiff})^2 +$ is the squared midsleep difference when mean weekend midsleep *is later than* Thursday midsleep (and 0 otherwise), $(\text{DLMODiff})^2 -$ is the squared DLMO difference when Sunday DLMO *is earlier than* Thursday DLMO (and 0 otherwise), and $(\text{DLMODiff})^2 +$ is the squared DLMO difference when Sunday DLMO *is later than* Thursday DLMO (and 0 otherwise). It is important to note that this model structure allows for different effect sizes for DLMO-midsleep interval, midsleep difference, and DLMO difference deviations in either direction.

Circadian alignment and circadian timing.—It should be noted that most prior publications reporting links between sleep/circadian timing and alcohol use have employed absolute timing measures (i.e. chronotype, sleep timing, DLMO) rather than the relative measures employed here. For comparison, we also considered an alternative model specifications in which midsleep and DLMO were considered as independent variables rather than the alignment variables introduced in this section. This will allow for a comparison of the effect sizes to determine whether circadian alignment or circadian timing carries a larger impact on expected weekend alcohol consumption in our study data.

RESULTS

Demographics, clinical characteristics, and sleep (Tables 1 and 2)

Participant characteristics are in Tables 1 and 2. On average, participants were regular drinkers but otherwise healthy. They were not depressed (mean IDS<14), excessively sleepy during the day (mean ESS< 10), or exhibiting poor sleep quality (mean PSQI< 6). Participants were intermediate chronotypes (versus early/morning or late/evening types) on

average. However, they had a mean DLMO-midsleep interval that was ~0.8 h longer than the ~6 h reported in other samples (e.g., (34, 50)), suggesting that the average participant was sleeping at a relatively later biological time than expected. With respect to the social jet lag measures (weekday-weekend differences), mean midsleep and DLMO were 41.4 and 7.8 minutes later on the weekend, respectively, but both had wide ranges, with a portion of the sample exhibiting *earlier* midsleep and DLMO times on the weekend.

Does pre-weekend circadian alignment relate to weekend alcohol use? (Table 3, Figure 2)

Table 3 contains the estimates for the regression coefficients in the first model where DLMO-midsleep interval is the explanatory variable of interest, and Figure 2 displays the estimated relationship between DLMO-midsleep interval and expected weekend alcohol use while holding all other variables constant at their mean values.

As hypothesized, smaller DLMO-midsleep intervals (relative to the median interval) on Thursday were associated with greater than expected weekend alcohol use (p-value <0.001). In other words, sleeping at an earlier time relative to one's circadian timing on weekdays was associated with higher than expected weekend alcohol use. In terms of the effect size, shortening the median DLMO-midsleep interval by one hour was associated with a 27.5% increase in expected weekend alcohol use. Additionally, the effect size increased as DLMO-midsleep intervals became shorter (e.g. a one-hour decrease in DLMO-midsleep interval from 6.5 hours to 5.5 hours was associated with a 44.1% increase in expected weekend alcohol use). On the other hand, larger DLMO-midsleep intervals (relative to the median interval) were not significantly associated with alcohol use (see Figure 2).

For a comparable alternative model specification, absolute timing of DLMO and midsleep was used rather than DLMO-midsleep interval after accounting for the same covariates as above. Later Thursday DLMO was significantly associated with increased expected weekend alcohol use (p-value=0.011) while Thursday midsleep was not significantly associated with expected weekend alcohol use (p-value=0.105). In terms of the effect size, a one-hour later DLMO was associated with a 20.8% increase in expected weekend alcohol use. Comparing the effect size of later DLMO with that of shorter DLMO-midsleep interval reveals that changes in circadian alignment are associated with larger impacts on expected weekend alcohol use compared to circadian timing changes alone.

Does greater social jet lag relate to weekend alcohol use? (Tables 4 and 5; Figures 3–5)

Tables 4 and 5 contain the estimates for the regression coefficients in the additional two models where social jet lag variables are of primary interest and Figures 3 and 4 display the estimated relationship between midsleep difference/DLMO difference and expected weekend alcohol use while holding all other variables constant at their mean values.

As hypothesized, later average weekend midsleep relative to Thursday night midsleep was associated with greater expected weekend alcohol use (p-value 0.004). On the other hand, earlier average weekend midsleep relative to Thursday night midsleep was not significantly associated with alcohol use. Unexpectedly, both advances and delays in DLMO were moderately associated with less weekend alcohol use (p-values 0.033 and 0.042). Since later DLMO was previously found to be associated with increased expected weekend alcohol use,

we also explored the relationship between Thursday DLMO, Sunday DLMO, and DLMO advances/delays to determine if later Thursday and Sunday DLMO were associated with smaller DLMO advances/delays (i.e., persistently later DLMO), which may explain the unexpected finding. While both later Thursday DLMO and later Sunday DLMO were significantly associated with increased expected weekend alcohol use (Thursday DLMO p -value=0.011, Sunday DLMO p -value=0.005), neither were significantly correlated with absolute DLMO differences (Thursday DLMO p -value=0.129, Sunday DLMO p -value=0.627). However, the distribution of DLMO differences have a roughly equal number of advances and delays, which was also quite unexpected and may contribute to these unexpected findings (see Figure 5).

Are circadian alignment variables correlated? (Figure 6)

The sample Pearson correlation coefficients among the three alignment variables are reported in Figure 6 along with p -values to determine if there exists any linear relationships among these alignment variables. Note that all the sample correlation coefficients are close to zero with large p -values, indicating no evidence of a linear relationship among any two of these three alignment variables. Figure 6 also provides the scatterplot matrix of the pairwise associations among these three alignment variables. Upon visual inspection of these scatterplots, there does not appear to be any strong linear or non-linear relationship between any two of these three alignment variables.

DISCUSSION

We examined the proximal associations between circadian alignment and alcohol use via three different measures: a direct assessment of circadian alignment via the interval between DLMO and midsleep, and two proxies for circadian misalignment based on the weekday-weekend differences in midsleep (i.e., “classic” social jet lag) and DLMO (i.e., “objective” social jet lag). As predicted, shorter pre-weekend DLMO-midsleep intervals (later circadian timing relative to sleep timing) and greater “classic” social jet lag (later weekend midsleep relative to weekday midsleep) were both associated with greater weekend alcohol use. The exploratory attempt to look a novel measure of objective social jet lag (weekday-weekend differences in DLMO) resulted in unexpected findings—that shifts in either direction were associated with less weekend alcohol use. Overall, however, these novel findings offer preliminary evidence that previously-reported associations between circadian alignment and alcohol use also exist on a proximal timeframe, which has implications for understanding the mechanisms linking circadian alignment to alcohol use, and may inform prevention and/or intervention approaches.

The observed association between our most direct measure of circadian alignment (DLMO-midsleep) is consistent with multiple prior reports suggesting that altered circadian timing is common within samples characterized by alcohol use and/or abuse (e.g., (51, 52)). Typically, circadian timing appears relatively delayed (shifted later) in association with heavy alcohol use, and in several small studies of alcohol-dependent patients, appeared to be fully “inverted” (melatonin levels going up during daytime rather than nighttime hours) (53–55). However, most of these prior studies have not reported circadian timing relative to sleep

timing, thereby obscuring alignment, as later circadian timing should theoretically not be problematic if one is able to shift sleep timing later accordingly. Specifically, we found that smaller weekday DLMO-midsleep intervals were associated with greater weekend alcohol use, suggests that sleeping at too early relative to a biological time may be relevant to alcohol use, and extending prior work showing that similar circadian misalignment (again, smaller DLMO-midsleep intervals) was associated with greater symptoms of substance abuse (33). Alcohol was the most commonly-used substance in that somewhat younger adolescent sample (age 14–19 years). In both the prior (33) and current studies, we found that later absolute circadian timing (DLMO) was associated with greater substance involvement. Importantly, however, in both studies it was the relative measure of circadian misalignment rather than the absolute measure of circadian phase that exhibited a stronger association with the substance involvement measures. This supports the contention that misalignment confers risk above and beyond late phase alone.

Circadian misalignment has been linked to an increasing list of negative health outcomes (21, 34), which is understandable given the realization that the circadian system is an “orchestra” of tissue-specific rhythms, with the molecular clock in essentially every cell of the body, that must be properly synchronized for proper functioning (56). Given increasing evidence that the circadian system modulates reward circuitry (57–60), we speculate that the circadian misalignment’s association with elevated alcohol use may be due in part to altered reward functioning. Preliminary evidence suggests that evening chronotypes, who tend to suffer more circadian misalignment, exhibit altered neural responses to reward that is associated in turn with their alcohol involvement (22, 60). Alternatively, greater misalignment could lead to impaired impulse control, which has well-documented links to a range of alcohol use outcomes (61, 62). Evening chronotypes appear to endorse greater impulsivity as well (63, 64). Alternatively, greater alcohol use could contribute to circadian misalignment; animal studies indicate that alcohol disrupts circadian timing via interfering with the effects of light and other non-photoc cues (65–69), although an initial attempt to demonstrate this in humans found no effect of alcohol on circadian shifts (70).

We also found that “classic” social jet lag, as measured via later weekend sleep timing relative to weekday sleep timing, was associated with greater weekend alcohol use. Based on the original social jet lag model (17), later sleep times on the weekend reflect a mismatch between sleep timing preferences and imposed early schedules on weekdays, thereby implying circadian misalignment. Social jet lag has also been linked to a range of negative health outcomes (71–73), although findings have been mixed from other cross-sectional and longitudinal studies of substance use, with some (28–30) but not all (27) reporting that weekday-weekend differences in sleep timing are associated with an increased risk of substance use. Our finding suggests that these associations exist at a proximal level, a novel and potentially important finding. Furthermore, this is consistent with other research that has failed to demonstrate relationships between affect and behavior when examined retrospectively, instead of prospectively and through real-time assessment, which affords a closer lens (e.g., (74)). Interestingly, we did not find an association between weekday-weekend differences in sleep timing in the opposite direction (earlier timing on the weekend), which could reflect fewer consequences of advancing, rather than delaying timing over two days. Alternatively, the association between less weekend drinking and earlier

sleep timing on the weekend could simply reflect that participants were not staying up to drink. We also note that a substantial portion of participants shifted earlier over the weekend, which likely reflects the fact that undergraduates have more control over their school and sleep schedules, and thus are not subjected to the same systematic schedule pressures as are younger teens in high school.

The association between DLMO shifts in either direction and less weekend drinking is both unexpected and difficult to reconcile with our other findings. The more chaotic schedule changes of the undergraduate milieu are almost certainly at play in the nearly equal distribution of advances and delays in DLMO timing from Thursday to Sunday. However, one would expect that the patterns of weekday-weekend changes in sleep and weekday-weekend changes in DLMO would be highly similar, given that circadian timing shifts in response to the varying light exposure dictated by the sleep-wake schedule, and in turn, the ability to sleep at particular times is influenced by circadian timing. In this study, we selected different weekday and weekend nights to capture the sleep and DLMO-based measures in order to best capture naturalistic sleep-alcohol associations unperturbed by laboratory visits. This plausibly reduces the degree of concordance between the sleep/circadian timing being captured by each measure, and indeed, the Pearson's correlations between the three measures were relatively low (Figure 6). The low correlations across the three measures of circadian misalignment raises a larger point; although social jet lag-type measures are conceptually reflecting circadian misalignment, they are inherently capturing a different construct than that measured by the interval between sleep and DLMO timing. Finally, the distribution and magnitude of weekday-weekend DLMO changes suggests that studies of undergraduate populations should be cautious about interpreting single DLMO assessments as indicative of "trait-like" circadian phase.

Our primary limitation was that DLMO was assessed on the following Thursday from the sleep and alcohol use assessments. While this has the advantage of assessing sleep and alcohol use unconfounded by lab visits and saliva collection, it precludes determination of temporal precedence between weekday circadian alignment and weekend alcohol use. Another limitation was that sleep was based on self-report and is thus subject to biases, although we mitigated bias from recall and rounding errors by using date and time-stamped, daily data collection techniques. Notably, we also assessed participants' sleep via an objective measure (wrist actigraphy), but it was not included in the present project due to a large amount of missing data for Thursday night used in the analyses. We did not assess whether school/work obligations influenced sleep schedules, which would be valuable moving forward in order to unpack the factors underlying social jet lag. Our sample in this preliminary study was small, with light drinkers less well represented, and thus may be less generalizable to late adolescents as a whole. Finally, the missing data and need for imputation was a limitation (although we note that results considering only participants without missing data produced similar findings and are available from the authors upon request).

The study also has several strengths. This is the first study to include two objective assessments of circadian timing (DLMO) at systematic times (Thursday and Sunday), in conjunction with naturalistic, in vivo assessment of self-reported sleep and alcohol use.

Furthermore, our novel study design allowed for more proximal examination of the relationship between sleep and circadian characteristics and alcohol use, shedding further light on an under-examined set of potential risk factors for the development of problem alcohol use. Our data provide further evidence that circadian misalignment is associated with alcohol use, and the first replication of our prior finding (33) that a measure of alignment based on objective circadian timing (DLMO) relative to sleep timing is associated to substance involvement. Although our sleep-based measure of social jet lag was associated with alcohol use in the expected direction, the DLMO-based measure of social jet lag showed an unexpected association with alcohol use that is difficult to reconcile. These findings, along with the unexpected distribution of DLMO shifts, suggest that further work is needed to understand the construct of social jet lag across different populations, particularly those where sleep-wake schedules are less systematically influenced than those during high school. Indeed, in addition to the relevance to alcohol use, our social jet lag findings provide new information about the potential instability of sleep/circadian characteristics in late adolescents. In conclusion, these preliminary findings suggest that larger, more definitive studies investigating the proximal relationships between circadian alignment and alcohol use among late adolescents are needed. We speculate that alcohol prevention and treatment programs may be enhanced by the inclusion of sleep/circadian-focused approaches, a position underscored by emerging evidence that late adolescents may be more open to sleep-based approaches than traditional alcohol-focused programs (75).

REFERENCES CITED

1. Tucker JS, Ellickson PL, Orlando M, Martino SC, Klein DJ. Substance use trajectories from early adolescence to emerging adulthood: A comparison of smoking, binge drinking, and marijuana use. *Journal of Drug Issues*. 2005;35(2):307–32.
2. White HR, McMorris B, Catalano RF, Fleming CB, Haggerty KP, Abbott RW. Increases in alcohol and marijuana use during the transition out of high school into emerging adulthood: The effects of transitions and protective factors. *Journal of Studies on Alcohol*. 2006;67:810–22. [PubMed: 17060997]
3. Hill KG, White HR, Chung JJ, Hawkins JD, Catalano RF. Early adult outcomes of adolescent binge drinking: person- and variable-centered analyses of binge drinking trajectories. *Alcoholism: Clinical and Experimental Research*. 2000;24(6):892–901.
4. Okoro CA, Brewer RD, Naimi TS, Moriarty DG, Giles WH, Mokdad AH. Binge drinking and health-related quality of life: do popular perceptions match reality? *American Journal of Preventive Medicine*. 2004;26(3):230–3. [PubMed: 15026103]
5. Foxcroft DR, Coombes L, Wood S, Allen D, Santimano NMA. Motivational interviewing for alcohol misuse in young adults. *Cochrane Database of Systematic Reviews*. 2014(8).
6. Stockings E, Hall WD, Lynskey M, Morley KI, Reavley N, Strang J, et al. Prevention, early intervention, harm reduction, and treatment of substance use in young people. *The Lancet Psychiatry*. 2016;3(3):280–96. [PubMed: 26905481]
7. Hasler BP, Clark DB. Circadian misalignment, reward-related brain function, and adolescent alcohol involvement. *Alcoholism: Clinical and Experimental Research*. 2013;37(4):558–65.
8. Hasler BP, Martin CS, Wood DS, Rosario B, Clark DB. A longitudinal study of insomnia and other sleep complaints in adolescents with and without alcohol use disorders. *Alcoholism: Clinical and Experimental Research*. 2014;38(8):2225–33.
9. Hasler BP, Kirisci L, Clark DB. Restless sleep and variable sleep timing during late childhood accelerate the onset of alcohol and drug involvement. *Journal of Studies on Alcohol and Drugs*. 2016;77(4):649–55. [PubMed: 27340970]

10. Wong MM, Robertson GC, Dyson RB. Prospective relationship between poor sleep and substance-related problems in a national sample of adolescents. *Alcoholism, clinical and experimental research*. 2015;39(2):355–62.
11. Miller MB, Janssen T, Jackson KM. The prospective association between sleep and initiation of substance use in young adolescents. *Journal of Adolescent Health*. 2017;60(2):154–60. [PubMed: 27769761]
12. Pieters S, Burk WJ, Van der Vorst H, Dahl RE, Wiers RW, Engels RC. Prospective relationships between sleep problems and substance use, internalizing and externalizing problems. *J Youth Adolesc*. 2015;44(2):379–88. [PubMed: 25385390]
13. Hagenauer MH, Perryman JI, Lee TM, Carskadon MA. Adolescent changes in the homeostatic and circadian regulation of sleep. *Developmental Neuroscience*. 2009;31(4):276–84. [PubMed: 19546564]
14. Borbély AA, Daan S, Wirz-Justice A, Deboer T. The two-process model of sleep regulation: a reappraisal. *Journal of sleep research*. 2016;25(2):131–43. [PubMed: 26762182]
15. Crowley SJ, Acebo C, Carskadon MA. Sleep, circadian rhythms, and delayed phase in adolescence. *Sleep Medicine*. 2007;8(6):602–12. [PubMed: 17383934]
16. Hansen M, Janssen I, Schiff A, Zee PC, Dubocovich ML. The impact of school daily schedule on adolescent sleep. *Pediatrics*. 2005;115(6):1555–61. [PubMed: 15930216]
17. Wittmann M, Dinich J, Mellow M, Roenneberg T. Social jetlag: Misalignment of biological and social time. *Chronobiology International*. 2006;23(1&2):497–509. [PubMed: 16687322]
18. Cain N, Gradisar M. Electronic media use and sleep in school-aged children and adolescents: A review. *Sleep Medicine*. 2010;11(8):735–42. [PubMed: 20673649]
19. Hysing M, Pallesen S, Stormark KM, Jakobsen R, Lundervold AJ, Sivertsen B. Sleep and use of electronic devices in adolescence: results from a large population-based study. *BMJ open*. 2015;5(1):e006748.
20. Troxel WM, Hunter G, Scharf D. Say “GDNT”: frequency of adolescent texting at night. *Sleep health*. 2015;1(4):300–3. [PubMed: 26981583]
21. Baron KG, Reid KJ. Circadian misalignment and health. *International Review of Psychiatry*. 2014;26(2):139–54. [PubMed: 24892891]
22. Hasler BP, Casement MD, Sitnick SL, Shaw DS, Forbes EE. Eveningness among late adolescent males predicts neural reactivity to reward and alcohol dependence two years later. *Behavioural Brain Research*. 2017.
23. Hasler BP, Franzen PL, de Zambotti M, Prouty D, Brown SA, Tapert SF, et al. Eveningness and Later Sleep Timing Are Associated with Greater Risk for Alcohol and Marijuana Use in Adolescence: Initial Findings from the National Consortium on Alcohol and Neurodevelopment in Adolescence Study. *Alcohol Clin Exp Res*. 2017;41(6):1154–65. [PubMed: 28421617]
24. Hasler BP, Sitnick SL, Shaw DS, Forbes EE. An altered neural response to reward may contribute to alcohol problems among late adolescents with an evening chronotype. *Psychiatry Res*. 2013;214(3):357–64. [PubMed: 24144507]
25. Watson NF, Buchwald D, Harden KP. A twin study of genetic influences on diurnal preference and risk for alcohol use outcomes. *J Clin Sleep Med*. 2013;9(12):1333–9. [PubMed: 24340296]
26. Prat G, Adan A. Influence of circadian typology on drug consumption, hazardous alcohol use, and hangover symptoms. *Chronobiology international*. 2011;28(3):248–57. [PubMed: 21452920]
27. Tavernier R, Munroe M, Willoughby T. Perceived morningness–eveningness predicts academic adjustment and substance use across university, but social jetlag is not to blame. *Chronobiology international*. 2015;32(9):1233–45. [PubMed: 26507124]
28. Haynie DL, Lewin D, Luk JW, Lipsky LM, O’Brien F, Iannotti RJ, et al. Beyond sleep duration: Bidirectional associations between chronotype, social jetlag, and drinking behaviors in a longitudinal sample of US high school students. *Sleep*. 2017.
29. Hasler BP, Franzen PL, de Zambotti M, Prouty D, Brown SA, Tapert SF, et al. Eveningness and later sleep timing are associated with greater risk for alcohol and marijuana use in adolescence: Initial findings from the National Consortium on Alcohol and Neurodevelopment in Adolescence. *Alcoholism: Clinical and Experimental Research*. 2017;41(6):1154–65.

30. Pasch KE, Laska MN, Lytle LA, Moe SG. Adolescent sleep, risk behaviors, and depressive symptoms: are they linked? *American Journal of Health Behavior*. 2010;34(2):237–48. [PubMed: 19814603]
31. Shiffman S Ecological momentary assessment (EMA) in studies of substance use. *Psychological assessment*. 2009;21(4):486. [PubMed: 19947783]
32. Burgess HJ, Fogg LF. Individual differences in the amount and timing of salivary melatonin secretion. *PloS one*. 2008;3(8):e3055. [PubMed: 18725972]
33. Hasler BP, Bootzin RR, Cousins JC, Fridel K, Wenk GL. Circadian phase in sleep-disturbed adolescents with a history of substance abuse: A pilot study. *Behavioral Sleep Medicine*. 2008;6(1):55–73. [PubMed: 18412037]
34. Emens J, Lewy A, Kinzie JM, Arntz D, Rough J. Circadian misalignment in major depressive disorder. *Psychiatry Research*. 2009;168(3):259–61. [PubMed: 19524304]
35. First MB, Spitzer RC, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Edition*. New York: Biometrics Research, New York State Psychiatric Institute; 2002.
36. Medicine AAoS. *International classification of sleep disorders—third edition (ICSD-3)*. Darien, IL: American Academy of Sleep Medicine 2014.
37. Sobell LC, Sobell MB. *Timeline Follow-Back Measuring Alcohol Consumption*: Springer; 1992 p. 41–72.
38. Rueger SY, Trela CJ, Palmeri M, King AC. Self-administered web-based timeline followback procedure for drinking and smoking behaviors in young adults. *Journal of Studies on Alcohol and Drugs*. 2012;73(5):829–33. [PubMed: 22846247]
39. Sobell LC, Brown J, Leo GI, Sobell MB. The reliability of the Alcohol Timeline Followback when administered by telephone and by computer. *Drug and Alcohol Dependence*. 1996;42(1):49–54. [PubMed: 8889403]
40. Benloucif S, Burgess HJ, Klerman EB, Lewy AJ, Middleton B, Murphy PJ, et al. Measuring melatonin in humans. *Journal of Clinical Sleep Medicine*. 2008;4(1):66–9. [PubMed: 18350967]
41. Burgess HJ. Partial sleep deprivation reduces phase advances to light in humans. *Journal of biological rhythms*. 2010;25(6):460–8. [PubMed: 21135162]
42. Voultsios A, Kennaway DJ, Dawson D. Salivary melatonin as a circadian phase marker: validation and comparison to plasma melatonin. *Journal of biological rhythms*. 1997;12(5):457–66. [PubMed: 9376644]
43. Molina TA, Burgess HJ. Calculating the dim light melatonin onset: the impact of threshold and sampling rate. *Chronobiology international*. 2011;28(8):714–8. [PubMed: 21823817]
44. Van Buuren S, Brand JP, Groothuis-Oudshoorn CG, Rubin DB. Fully conditional specification in multivariate imputation. *Journal of statistical computation and simulation*. 2006;76(12):1049–64.
45. Van Buuren S Multiple imputation of discrete and continuous data by fully conditional specification. *Statistical methods in medical research*. 2007;16(3):219–42. [PubMed: 17621469]
46. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? *International journal of methods in psychiatric research*. 2011;20(1):40–9. [PubMed: 21499542]
47. Sv Buuren, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in R. *Journal of statistical software*. 2010:1–68.
48. Rubin DB. *Multiple imputation for nonresponse in surveys*: John Wiley & Sons; 2004.
49. Rubin DB. Multiple imputation after 18+ years. *Journal of the American statistical Association*. 1996;91(434):473–89.
50. Lewy AJ, Bauer VK, Cutler NL, Sack RL, Ahmed S, Thomas KH, et al. Morning vs evening light treatment of patients with winter depression. *Archives of general psychiatry*. 1998;55(10):890–6. [PubMed: 9783559]
51. Hasler BP, Smith LJ, Cousins JC, Bootzin RR. Circadian rhythms, sleep, and substance abuse. *Sleep Medicine Reviews*. 2012;16(1):67–81. [PubMed: 21620743]

52. Conroy DA, Hairston IS, Arnedt JT, Hoffmann RF, Armitage R, Brower KJ. Dim light melatonin onset in alcohol-dependent men and women compared with healthy controls. *Chronobiology International*. 2012;29(1):35–42. [PubMed: 22217099]
53. Murialdo G, Filippi U, Costelli P, Fonzi S, Bo P, Polleri A, et al. Urine melatonin in alcoholic patients: a marker of alcohol abuse? *Journal of Endocrinological Investigation*. 1991;14(6):503–7. [PubMed: 1774447]
54. Majumdar SK, Miles A. Disturbed melatonin secretion in chronic alcoholism and withdrawal. *Clinical Chemistry*. 1987;33(7):1291.
55. Danel T, Cottencin O, Tisserand L, Touitou Y. Inversion of melatonin circadian rhythm in chronic alcoholic patients during withdrawal: preliminary study on seven patients. *Alcohol & Alcoholism*. 2009;44(1):42–5. [PubMed: 19029096]
56. Dibner C, Schibler U, Albrecht U. The mammalian circadian timing system: organization and coordination of central and peripheral clocks. *Annual review of physiology*. 2010;72:517–49.
57. Murray G, Nicholas CL, Kleiman J, Dwyer R, Carrington MJ, Allen NB, et al. Nature's clocks and human mood: the circadian system modulates reward motivation. *Emotion*. 2009;9(5):705–16. [PubMed: 19803592]
58. Logan RW, Williams WP, McClung CA. Circadian rhythms and addiction: Mechanistic insights and future directions. *Behavioral neuroscience*. 2014.
59. Forbes EE, Dahl RE, Almeida JR, Ferrell RE, Nimgaonkar VL, Mansour H, et al. PER2 rs2304672 polymorphism moderates circadian-relevant reward circuitry activity in adolescents. *Biological Psychiatry*. 2012;71(5):451–7. [PubMed: 22137505]
60. Hasler BP, Sitnick SL, Shaw DS, Forbes EE. An altered neural response to reward may contribute to alcohol problems among late adolescents with an evening chronotype. *Psychiatry Research: Neuroimaging*. 2013;214(3):357–64.
61. Henges AL, Marcinski CA. Impulsivity and alcohol consumption in young social drinkers. *Addictive Behaviors*. 2012;37(2):217–20. [PubMed: 21981824]
62. Coskunpinar A, Dir AL, Cyders MA. Multidimensionality in impulsivity and alcohol Use: a meta-analysis using the UPPS model of impulsivity. *Alcoholism: Clinical and Experimental Research*. 2013;37(9):1441–50.
63. Kang JJ, Park CI, Sohn SY, Kim HW, Namkoong K, Kim SJ. Circadian preference and trait impulsivity, sensation-seeking and response inhibition in healthy young adults. *Chronobiol Int*. 2015;32(2):235–41. [PubMed: 25286137]
64. Adan A, Natale V, Caci H, Prat G. Relationship between circadian typology and functional and dysfunctional impulsivity. *Chronobiology International*. 2010;27(3):606–19. [PubMed: 20524804]
65. Seggio JA, Logan RW, Rosenwasser AM. Chronic ethanol intake modulates photic and non-photic circadian phase responses in the Syrian hamster. *Pharmacology Biochemistry & Behavior*. 2007;87(3):297–305.
66. Seggio JA, Fixaris MC, Reed JD, Logan RW, Rosenwasser AM. Chronic ethanol intake alters circadian phase shifting and free-running period in mice. *Journal of Biological Rhythms*. 2009;24(4):304–12. [PubMed: 19625732]
67. Ruby CL, Prosser RA, DePaul MA, Roberts RJ, Glass JD. Acute ethanol impairs photic and nonphotic circadian phase resetting in the Syrian hamster. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*. 2009;296(2):R411–8.
68. Ruby CL, Brager AJ, DePaul MA, Prosser RA, Glass JD. Chronic ethanol attenuates circadian photic phase resetting and alters nocturnal activity patterns in the hamster. *Am J Physiol Regul Integr Comp Physiol*. 2009;297(3):R729–37. [PubMed: 19553498]
69. Brager AJ, Ruby CL, Prosser RA, Glass JD. Chronic ethanol disrupts circadian photic entrainment and daily locomotor activity in the mouse. *Alcoholism: Clinical and Experimental Research*. 2010;34(7):1266–73.
70. Burgess HJ, Rizvydeen M, Fogg LF, Keshavarzian A. A single dose of alcohol does not meaningfully alter circadian phase advances and phase delays to light in humans. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 2016;310(8):R759–R65.

71. Levandovski R, Dantas G, Fernandes LC, Caumo W, Torres I, Roenneberg T, et al. Depression scores associate with chronotype and social jetlag in a rural population. *Chronobiology International*. 2011;28(9):771–8. [PubMed: 21895489]
72. Roenneberg T, Allebrandt KV, Merrow M, Vetter C. Social jetlag and obesity. *Current Biology*. 2012;22(10):939–43. [PubMed: 22578422]
73. Wong PM, Hasler BP, Kamarck TW, Muldoon MF, Manuck SB. Social jetlag, chronotype, and cardiometabolic risk. *The Journal of Clinical Endocrinology & Metabolism*. 2015;100(12):4612–20. [PubMed: 26580236]
74. Shiffman S, Waters AJ. Negative affect and smoking lapses: a prospective analysis. *Journal of consulting and clinical psychology*. 2004;72(2):192. [PubMed: 15065954]
75. Fucito LM, DeMartini KS, Hanrahan TH, Whittemore R, Yaggi HK, Redeker NS. Perceptions of heavy-drinking college students about a sleep and alcohol health intervention. *Behavioral sleep medicine*. 2015;13(5):395–411. [PubMed: 24924956]

Protocol scheme	Study Day											
	-8	-7	-6	-5	-4	-3	-2	-1	0	1	2	3
FM	Thu	Fri	Sat	Sun	Mon	Tue	Wed	Thu	Fri	Sat	Sun	Mon
MF					Thu	Fri	Sat	Sun	Mon	Tue	Wed	Thu
						midsleep		alcohol		DLMO		

Figure 1.

Study design. Data in this paper are drawn from a larger protocol. This figure shows the temporal relationships of the data included in the present analyses.

Figure 2.

DLMO-midsleep interval vs. expected weekend alcohol use (black line represents estimated mean weekend alcohol use from the regression model; dark gray shading bounded by dashed lines represents the 95% pointwise confidence intervals) holding other variables constant at mean values. Consistent with previous findings, shorter DLMO-midsleep intervals are associated with greater than expected weekend alcohol use. No association between longer DLMO-midsleep intervals and alcohol use was observed.

Figure 3.

Midsleep difference vs. expected weekend alcohol use (black line represents estimated mean weekend alcohol use from the regression model; dark gray shading bounded by dashed lines represents the 95% pointwise confidence intervals) holding other variables constant at mean values. Later weekend sleep timing relative to weekday sleep timing was associated with increased alcohol use.

Figure 4.

DLMO difference vs. expected weekend alcohol use (black line represents estimated mean weekend alcohol use from the regression model; dark gray shading bounded by dashed lines represents the 95% pointwise confidence intervals) holding other variables constant at mean values. Both earlier and later DLMO-based circadian timing were associated with less alcohol use.

Figure 5.

Distribution of Thursday-Sunday shifts in DLMO. Individual participants are displayed, along with the mean Thursday-Sunday shift ($M \pm SD = 0.13 \pm 0.83$ hours), which is illustrated by the thicker black line with large circular anchors. There is a roughly equal distribution of advances and delays in DLMO, in contrast to the typical social jet lag pattern in which weekday timing is systematically earlier.

Figure 6.

Scatterplot matrix containing the scatterplots and sample Pearson correlation coefficients for each pairwise comparison (off-diagonal) along with the estimated distribution for each alignment variable (diagonal). Upon visual inspection of these scatterplots, there does not appear to be any strong linear or non-linear relationship between any two of these three alignment variables (p-values for sample Pearson correlation coefficients are all greater than 0.25).

Table 1.

Demographics and clinical characteristics.

	Mean $\pm$ SD	Range
Age	21.3 $\pm$ 1.1	18 – 22
Gender	14 males / 22 females	
Race/ethnicity	25 White, 4 African-American, 4 Asian-American, 3 biracial / 2 Hispanic	
Alcohol use (past 30 days)	31.7 $\pm$ 29.3	7 – 136
Binges (5+/4+ drinks; past month)	3.3 $\pm$ 3.5	0 – 15
Depressive symptomatology (IDS)	5.4 $\pm$ 6.2	0 – 33

Table 2.

Sleep and circadian characteristics.

	Mean $\pm$ SD	Range
Epworth Sleepiness Scale (ESS)	4.5 $\pm$ 2.8	0 – 12
Pittsburgh Sleep Quality Index (PSQI)	3.3 $\pm$ 2.0	1 – 8
Composite Scale of Morningness (CSM)	34.1 $\pm$ 5.9	15 – 45
Diary - midsleep	5:02 $\pm$ 0:50	3:27 – 7:17
Diary - TST	7.2 $\pm$ 0.7	5.7 – 8.6
Diary – sleep efficiency (%)	87.3 $\pm$ 0.1	71 – 96
DLMO – Thursday (<i>n</i> =31)	22:03 $\pm$ 1:29	18:40 – 1:44
DLMO – Sunday (<i>n</i> =32)	22:11 $\pm$ 1:24	18:53 – 1:59
DLMO-midsleep interval	6.77 $\pm$ 1.30	4.04 – 9.29
Social jet lag-midsleep (Fri/Sat-Thu)	0.69 $\pm$ 1.25	–1.77 – 3.40
Social jet lag-DLMO (Sun-Thu)	0.13 $\pm$ 0.83	–1.40 – 1.79

Table 3.

Model 1: DLMO-midsleep interval on expected weekend alcohol use (estimated using m=100 imputed datasets)

	Estimate	P-value
Intercept	4.035	0.019
Thursday Alcohol Use (no. of drinks)	0.120	<0.001
Sex indicator (0=male, 1=female)	-0.086	0.612
Age	-0.075	0.297
Diary - TST	-0.153	0.047
Squared DLMO-midsleep alignment deviation (≤ 6.8 hrs, 0 otherwise)	0.203	<0.001
Squared DLMO-midsleep alignment deviation (>6.8 hrs, 0 otherwise)	0.053	0.332

Table 4.

Model 2: Social jet lag - midsleep on expected weekend alcohol use (estimated using m=100 imputed datasets)

	Estimate	P-value
Intercept	-0.325	0.890
Thursday Alcohol Use (no. of drinks)	0.101	<0.001
Sex indicator (0=male, 1=female)	-0.062	0.726
Age	-0.083	0.238
Diary - TST	-0.087	0.240
Thursday DLMO	0.187	0.006
Squared social jet lag-midsleep alignment deviation (0 hrs, 0 otherwise)	-0.133	0.355
Squared social jet lag-midsleep alignment deviation (>0 hrs, 0 otherwise)	0.072	0.004

Table 5.

Model 3: Social jet lag - DLMO on expected weekend alcohol use (estimated using m=100 imputed datasets)

	Estimate	P-value
Intercept	5.742	<0.001
Thursday Alcohol Use (no. of drinks)	0.113	<0.001
Sex indicator (0=male, 1=female)	-0.032	0.856
Age	-0.143	0.040
Diary - TST	-0.101	0.198
Diary - midsleep	-0.048	0.472
Squared social jet lag-DLMO alignment deviation (0 hrs, 0 otherwise)	-0.485	0.042
Squared social jet lag-DLMO alignment deviation (>0 hrs, 0 otherwise)	-0.349	0.033