health through disrupted rest-activity rhythm (RAR) in the mother and child. We also explore whether mothers' benevolent childhood experiences (BCEs) are protective against disrupted RAR.

Methods: We conducted a cross-sectional pilot study of maternal-child dyads with preschool-age children. Mothers reported history of childhood adversity (ACEs Scale, Childhood Trauma Questionnaire) and protective factors (BCE Scale). Dyads wore wrist actigraphs for 8-10 days and mothers completed daily electronic diaries. Nonparametric measures of RAR (e.g. interdaily stability [IS], intradaily variability [IV]) were calculated. We used linear regression to examine associations between mothers' childhood history and maternal and child RAR measures, controlling for household size and maternal employment.

Results: Maternal-child dyads (N=20) identified as white (75%), Black (15%), and Hispanic/Latina (10%). Mean child age was 4.2 years (40% female). Average household size was 4.5 ±.1.1 and 65% of mothers were employed. Forty-two percent of mothers reported 1-2 ACEs and 25% reported 3 or more ACEs. Maternal childhood history was not associated with mothers' RAR. However, maternal ACEs and CTQ total score were associated with decreased child IS (ACEs: β= -0.47, SE=0.01, p=.02; CTQ total: β= -0.53, SE=.01, p=.001) and increased child IV (ACEs: β=0.29, SE=.01, p=.051; CTQ total: β=0.38, SE+.00, p=.03). CTQ subscales revealed maternal childhood physical abuse (β= -0.54, SE=.01, p<.0001), emotional abuse (β= -0.42, SE=.00, p=.002), and sexual abuse (β= -.73, SE=.00, p<.0001) were associated with decreased child IS, while maternal childhood emotional neglect was associated with increased child IV (β= 0.39, SE=.01, p=.04). Maternal BCEs were associated with decreased child IV (β= -0.44, SE=.01, p=.03).

Conclusion: Maternal ACE history may influence child health through effects on children's circadian rhythm (i.e. decreased synchronization, increased fragmentation), while maternal BCEs may protect against rhythm fragmentation. Additional research is needed to support these novel preliminary findings.

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0208

DAYTIME ALERTNESS QUANTIFICATION AND MODELLING: RESULTS FROM A LARGE OBSERVATIONAL STUDY

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Introduction: Subjective alertness variations throughout the day can be characterized using the two-process model (TPM) of sleep regulation, which combines sleep homeostasis and the circadian rhythm to derive a theoretical daytime alertness curve. The TPM has been adopted to model the effect of sleep deprivation on memory, circadian misalignment, temperature regulation, and brain function; however, despite its broad influence, evidence supporting the TPM-derived alertness comes largely from small-scale, controlled studies. Here, we show that a similar three-parameter alertness measure can scale to a large study sample under real-world conditions.

Methods: Subjective alertness was voluntarily rated on a scale from 1 to 10 by Sleep Number smart bed users (N=22 499) through the SleepIQ app. Three age groups (18–40, 41–65, and 66–90 years) were analyzed. A 3-parameter version of the TPM-derived alertness curve was fit to the self-rated alertness responses using nonlinear least-squares fitting.

Results: A total of 65 528 sleep sessions were gathered over 95 days and analyzed. Overall, subjective alertness followed a similar trend to that reported in published literature: mean hourly alertness increased in the morning, dipped slightly in the afternoon, increased during the evening, and dropped again during the night. In contrast to previous studies, mean alertness ratings only changed by approximately 1 unit from low to high, and a greater increase in alertness occurred from afternoon to evening. Age-group analyses found that youngest sleepers' mean daily alertness was more stable throughout the day, and the amplitude of alertness variation decreased with age. These experimental results showed high agreement with model prediction (R^2=0.96, P<0.001).

Conclusion: Overall, our results were similar to previous reports, with the exception of a small absolute change over the course of the day (about 1 unit) and an evening peak in alertness that was more pronounced in our data. These results show that the TPM-derived alertness can effectively predict daily alertness trends in a large sample under real-world conditions.

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0209

THE EFFECT OF TIME OF DAY OF COVID-19 VACCINATION AND OTHER COVARIATES ON SIDE EFFECTS

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Introduction: Circadian rhythms have critical roles in human health. We quantified the effect of time-of-day of COVID-19 vaccination and other covariates on self-reported side effects post vaccination.

Methods: The dataset was created from MassGeneralBrigham (MGB) electronic health records and REDCap survey that collected self-reported symptoms for 1-3 days after each immunization. Variables are demographics (age, sex, race, and ethnicity), vaccine manufacturer, clock time of vaccine administration/appointment, any COVID-19 diagnosis/positive test prior to vaccination, any history of allergy, and any note of epinephrine self-injection (e.g., EpiPen) medication. Time of day groupings were morning (6 am–10 am), midday (10 am–2 pm), late afternoon (2 pm–6 pm) or evening (6 pm–10 pm). Side effects were classified as Allergic (Rash; Hives; Swollen lips, tongue, eyes, or face; Wheezing) and Non-Allergic (New Headache, New Fatigue, Arthralgias, Myalgias, Fever) symptoms. The study was approved by the MGB IRB.Machine learning (ML) techniques (e.g., extreme gradient boosting) were applied to the variables to predict the occurrence of side effects. Stratified k-fold cross validation was used to validate the performance of the ML models. Shapley Additive Explanation values were computed to explain the contribution of each of the variables to the prediction of the occurrence of side effects.

Results: Data were from 54,844 individuals. On day 1 after the first vaccination, (i) females, people who received the Moderna vaccine, and those with any allergy history were more likely to report Allergic side effects; and (ii) females, people who received the Janssen vaccine, those who had prior COVID-19 diagnosis ,and those who received their vaccine in the morning or midday and were more likely to report

Non-Allergic symptoms. Older persons had fewer side effects of any type.
Conclusion: ML techniques identified demographic and time-of-day-of-vaccination effects on side effects reported on the first day after the first dose of a COVID-19 vaccination. We will use these techniques to test for changes on days 2 and 3 after the first dose, and the first 3 days after the second dose and for the influence of recent night or shiftwork. Future work should target underlying physiological reasons.
Support (If Any):

0210

SOCIAL RHYTHM REGULARITY: ASSOCIATIONS WITH SLEEP, CIRCADIAN, MENTAL HEALTH, AND ALCOHOL USE OUTCOMES IN ADOLESCENTS

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Introduction: Circadian rhythms and sleep regularity relate to a range of negative health outcomes, such as mental illness and substance abuse including binge drinking. According to the social zeitgeber hypothesis, the timing of key modifiable daily behaviors serves as time cues that entrain circadian rhythms, ostensibly stabilizing them and thereby improving health. The cross-day stability in timing of these behaviors (i.e., social rhythm regularity) is measured by SRM5; however, studies have not tested whether SRM5 correlates with circadian rhythm regularity based on physiological measures, such as dim light melatonin onset (DLMO). The current study examined whether SRM5 was associated with: (1) the regularity of circadian rhythms and/or sleep regularity metrics, and (2) sleep quality, depression, and binge drinking.
Methods: Late adolescents aged 18 to 22 years old who drink alcohol (n = 36; 61.1% female, Mage = 21.26) completed a self-reported sleep diary (including SRM5 items for first contact, start work, and dinner time), wore a wrist actigraph for 14 days, and completed 2 overnight visits to assess DLMO. We used the self-reported data to calculate SRM5 and standard deviation (StDev); actigraphy data to calculate composite phase deviation (CPD), social jet lag (SJL), and interdaily stability (IS); and DLMO data to calculate the stability of the circadian phase (Sunday minus Thursday). Participants also completed surveys that assessed global sleep quality, depressive symptoms, and frequency of binge drinking. Correlational analysis and hierarchical linear regression modeling were used.
Results: Higher SRM5 scores (i.e., higher social rhythm regularity) were associated with higher regularities of mid-sleep timing ($r = –.48$, $p < .001$) and total sleep duration ($r = –.41$, $p = .01$) based on StDev metrics but were not associated with IS ($r = 13$, $p = .45$), CPD ($r = –.19$, $p = .28$), SJL ($r = –.07$, $p = .68$), and stability of DLMO ($r = –.003$, $p = .99$). A post-hoc analysis found that higher stability of the "out of bed" item of SRM5 was related to higher stability of DLMO ($b = –.11$, $se = .05$, $p = .03$, $r2 = .33$). Higher SRM5 scores were associated with better sleep quality ($b = –.73$, $se = .30$, $p = .02$, $r2 = .21$), but were not with depressive symptoms or binge drinking
Conclusion: In contrast with the social zeitgeber hypothesis, SRM5 was not associated with circadian rhythm regularity measured by DLMO. However, social rhythm regularity is an important factor in predicting better sleep quality. This study provides a foundation for future research with better power to determine the extent to which social rhythms influence circadian stability and to better understand why social rhythm regularity relates to sleep quality.
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0211

A 10-WEEK OBSERVATIONAL RESEARCH STUDY IN INDIVIDUALS WITH DELAYED SLEEP-WAKE PHASE DISORDER (DSWPD) SYMPTOMS

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Introduction: We conducted an observational research study in suspected delayed sleep-wake phase disorder (DSWPD) participants. The objective was to measure sleep-wake patterns and to conduct exploratory genetic analyses to delineate the landscape of DSWPD.
Methods: We measured the sleep-wake patterns of participants by daily post-sleep diaries for 10 weeks. Participants also completed questionnaires on demographics, medical/surgical history, sleep history, and concomitant medications. Altogether, 119 participants were consented and 76 participants provided samples for whole genome sequencing.
Results: Sleep diary analysis confirmed delayed sleeping patterns in the study population. Midpoint of sleep was 4:50 AM (SD = 2:06) versus 3:06 AM (SD = 0:59) in controls, a statistically significant difference ($t (df) = 6.57 (72.063)$; $p \leq 0.0001$). Mean total sleep time (TST) was 6.88 h (SD = 1.35) versus 7.79 h (SD = 0.56) in controls, a statistically significant difference ($t (df) = -5.38 (70.863)$; $p \leq 0.0001$). This effect was driven by shorter participant-reported TST on work nights (6.33 h) versus free nights (7.22 h). Sleep latency was significantly later on work nights than free nights. Altogether 17% of participants reported at least one psychiatric condition.We observed an enrichment of the minisatellite 54bp (1: 7829913-7829966 (GRCh38)) variable number of tandem repeat (VNTR) PER3 rs57875989 4 allele. Significantly higher frequencies of the 4/4 and 4/5 variants were observed when compared to controls (n = 1937; recessive: OR 3.3, CI 2.1177 to 5.4304, $p < 0.0001$).We analyzed the putative loss-of-function and missense variants. We report on presence of cases with PER3 rs144178755 (NM_001289862:p.T1049), PER3 rs228696 (NM_001289861:p.L835P), and PER2 rs76355956 (NM_022817:p.V197M), among other rare nonsynonymous variants. We observed higher frequency of missense variants in core clock genes when compared to controls.
Conclusion: Sleep diary data confirmed significantly delayed sleep patterns, with more pronounced results during work nights and larger SDs across all sleep parameters, suggesting more variable sleep patterns. Genetic analysis confirmed these individuals are more likely to harbor variants within their core clock genes with enrichment of the VNTR variant, potentially leading to a pronounced delay in sleep period.
Support (If Any): Vanda Pharmaceuticals Inc.

0212

HABITUAL HEAVY ALCOHOL DRINKING IN HEALTHY ADULTS IS ASSOCIATED WITH REDUCED CIRCADIAN PHOTORECEPTOR RESPONSIVITY TO LIGHT

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Introduction: Habitual alcohol consumption and circadian timing are interconnected. Numerous studies have reported that heavy alcohol use is associated with eveningness. Only two studies have assessed the dim light melatonin onset (DLMO) in the context of habitual alcohol use, and both reported a shorter DLMO-midsleep