reflects ipRGC functioning and may be a physiological vulnerability for disrupted photoentrainment. Understanding how retinal responsivity relates to sleep and circadian timing may inform who might most benefit from sleep and circadian interventions.
Methods: 64 participants (85 observations) ages 20-66 years old were recruited during winter (n=35) and summer months (n=50), and included individuals with seasonal depression (n=33) and nonseasonal, never depressed controls (n=31). The post-illumination pupil response (PIPR) to red and blue light was used to measure the responsivity of ipRGCs (average 1:30pm; 10am-7pm). Circadian phase was assessed using Dim Light Melatonin Onset (DLMO), collected every 30-minutes on Friday evenings. Midsleep timing was measured using actigraphy (average number nights=4), and circadian alignment was calculated as the DLMO-midsleep phase angle. We performed a multilevel regression to determine the relationship between PIPR and markers of sleep and circadian timing, accounting for repeated seasonal assessments with a random intercept of participant. Covariates included age, gender, diagnostic group, and circadian time of PIPR assessments. We ran sensitivity analyses including photoperiod length on the day of PIPR assessment to account for potential light exposure on the PIPR.
Results: Greater retinal responsivity was associated with later DLMO (b=4.45; partially standardized b=0.28; SE=1.84; p=0.03), and shorter DLMO-midsleep phase angle (b= -7.33; partially standardized b= -0.32; SE=2.51; p=0.004), but not midsleep (b= -3.44; partially standardized b= -0.14; SE=2.35; p>0.05). Individuals with later DLMO had PIPR assessments at earlier circadian times (b= -0.12; SE=0.04; p=0.01). Older participants (b= -0.04; SE=0.02; p=0.04) and controls (b= -0.95; SE=0.44; p=0.04) had earlier sleep midpoints, but covariates were not associated with circadian markers. The association between circadian timing and PIPR became nonsignificant (b=4.15; partially standardized b=0.26; SE=1.88; p=0.06) when including photoperiod.
Conclusion: Retinal responsivity was associated with circadian but not behavioral sleep timing, suggesting ipRGC functioning may have downstream effects on circadian entrainment. Assessing circadian variation of retinal responsivity remains a crucial next step prior to testing whether retinal responsivity impacts response to circadian-focused interventions.
Support (If Any): NIMH K.A.R.MH103303

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INCREASED BRAIN KYNURENIC ACID ELICITS SEX-DEPENDENT ABNORMALITIES IN NREM SLEEP SPINDLE DYNAMICS

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Introduction: Sleep spindles are thalamocortical oscillations which occur during non-rapid eye movement (NREM) sleep. NREM sleep spindle aberrations are a consistent clinical sleep deficiency associated with psychotic disorders and exacerbation of cognitive symptoms. Kynurenic acid (KYNA), a tryptophan metabolite synthesized from kynurenine via kynurenine aminotransferases (KATs) and modulator of glutamatergic and cholinergic neurotransmission, is elevated in the brain of patients with psychotic disorders, including schizophrenia and bipolar disorder. Currently, we sought to understand the neurodevelopmental and transient impacts of brain KYNA elevation on sleep spindle dynamics.
Methods: In Experiment #1, sleep spindles were evaluated in adult offspring, postnatal day (PD) 56 from embryonic kynurenine (EKyn) treated rat dams (Rentschler et al., 2021 Sz Bull) (N=7-9 per group). EKyn KYNA male, but not female, offspring have elevated KYNA during the light phase (Wright et al., 2021 Frontiers in Psychiatry). In Experiment #2, sleep spindles were evaluated in adult rats injected with kynurenine (100 mg/kg; i.p.) to acutely elevate brain KYNA levels at zeitgeber time 0 (N=8-12 per group). Polysomnography was recorded via EEG/EMG telemetry. Sleep spindles were evaluated using a custom-made manual scoring system during the first 4 hr of the light cycle.
Results: Male EKyn, but not female, exhibited a decrease in spindle density compared to ECon (2-wayANOVA: ***P<0.001). FFT spectral power for peak spindle frequency (10-15 Hz) was reduced for all EKyn offspring (3-way ANOVA; frequency x treatment interaction: ****P<0.0001; treatment: *P<0.05). Kynurenine challenge reduced spindle density for both sexes (2-way ANOVA: ***P<0.001; M: **P<0.01; F: *P<0.05). Frequency x treatment interaction for males (2-way ANOVA: ***P<0.001) was observed with lower FFT spectral power for 10-10.5 Hz (*P<0.05) and greater power for 14-14.5 Hz (*P<0.05).
Conclusion: We determined conspicuous sex differences in spindle dynamics in the EKyn paradigm that may be related to brain KYNA levels; only males exhibited a decrease in spindle density, however all EKyn offspring had reduced FFT spectral power. Kynurenine challenge reduced spindle density in both sexes, however only males had changes in FFT spectral power. Future work will consider the efficacy of KYNA synthesis inhibition to prevent NREM sleep spindle abnormalities induced by KYNA elevation.
Support (If Any): Funding Source: National Institute of Health Grants: NIH RO1 NS102209 & P50 MH103222.

0198

REMOTE SALIVA SAMPLE COLLECTION FOR DIM LIGHT MELATONIN ONSET (DLMO) MEASUREMENT IN URBAN CHILDREN WITH ASTHMA DURING THE COVID-19 PANDEMIC

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Introduction: The COVID-19 pandemic has challenged researchers to use remote data collection. Our project includes determining DLMO phase, requiring a family-friendly without face-to-face interaction. We describe here our protocol, experiences, lessons learned, and findings from the first 15 participants.
Methods: Fifteen urban-dwelling children with moderate to severe persistent asthma [7 girls, ages 7 (n=1) to 10 years; and 8 boys, 8 or 9 years] and caregiver (CG) participated. CG tracked bedtimes and risetimes in daily diaries for 10-14 days; average bedtimes from 5 nights preceding saliva collection were used to determine timing for 10 half-hourly samples. CG and child were oriented and then watched a demo video. A "spit-kit" was delivered to the home the afternoon of the study. Kits included a small cooler bag with bottle of water, 10 numbered and 5 spare Salivette tubes (Starstedt, Germany), plastic bag, dark wraparound glasses with securing strap, and log sheet. Data collection began with a zoom call with staff, CG, and child to reiterate the instructions, answer questions, and observe the first sample. Thereafter, a staff member telephoned the caregiver every 30 minutes to prompt the next sample and query whether glasses had been kept on. CG placed kit outside the home for morning pick up. Samples were centrifuged and frozen (-20°) until sending to the assay lab (SolidPhase, Portland, ME) for melatonin radioimmunoassay (Alpco, Windham, NH).

Results: DLMO phase was determined with a 4pg/ml threshold for 11 children. DLMO phases (mtime=21:46±68 min) and average bedtimes (mtime=20:40±88min) were positively correlated (r=.87). Challenges identified for missed DLMOs included: one child supervised by a teenaged sibling (not CG); one child/CG identified as potentially uncooperative. The other two "misses" likely arose from low saliva quantity, inconsistencies with staff training, and inadequate description of requirements for wearing glasses. Procedure modifications included strategies tailored to families' needs, experiences, and home environment that can challenge adherence to protocol, greater emphasis on wearing glasses, and cartoon reminder card and scales added to kit. Subsequent samples were successful.
Conclusion: Our approach was effective for determining DLMO phase in children using a remote approach with careful application of methods.
Support (If Any): R01HL142058, P20GM139743

0199

IRIS COLOR PREDICTS MELANOPSIN-DRIVEN RETINAL RESPONSES IN OLDER BUT NOT YOUNGER INDIVIDUALS

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Introduction: The retina contains melanopsin-containing retinal ganglion cells, which underlie non-image forming responses to light. The Post-Illumination Pupil Response (PIPR) can assess melanopsin cell responsivity, with applications for sleep disorders, mood disorders, and circadian entrainment. Lighter pigmented irises allow more light to pass through the retina. The present study tested an association between the PIPR and iris pigmentation.
Methods: Participants (N=49) included seasonal depression (n=26) and never-depressed controls (n=23). Photos of participants' irises were rated using both the Franssen (2008) scale, a set of 24 standardized iris photos, and the Mackey (2011) scale, a 9-category rating system. Red and blue stimuli 13.5 log photons/cm2/s were presented, and infrared pupillometry measured pupil diameter for 40 seconds. We used multilevel regression with a random intercept of participant to predict the PIPR from each iris rating system separately, controlling for age, gender, and circadian time of testing determined from Dim Light Melatonin Onset.
Results: Agreement between raters, calculated using Cohen's κ, was moderate for both scales (Franssen, κ=0.57, 95% CI: 0.42 to 0.71, p<0.001; Mackey, κ=0.67, 95% CI: 0.53 to 0.81, p<0.001). Bivariate correlations showed age was inversely associated with iris color: older individuals had lighter iris pigmentation. Analyses were therefore stratified by age (older >=31 years: n=24; younger <31 years, n=25). Greater retinal responsivity was associated with lighter iris pigmentation in the older sample (Mackey: unstandardized b=-0.016; SE=0.005; p=0.002; Franssen: unstandardized b=-0.006; SE=0.002, p=0.002), but not the younger sample (Mackey: unstandardized b=-0.0008; SE=0.003; p=0.770; Franssen: unstandardized b=-0.0009; SE=0.002, p=0.619). There was no effect of iris color on PIPR in the whole sample (p's >0.13).
Conclusion: Iris color explained ~8% of variance in the PIPR, indicating that PIPR studies should recruit samples with similar distributions of iris pigmentation across conditions and ages, as this finding was only seen in the older sample with more individuals with lighter iris pigmentation. Future studies will test iris pigmentation by light exposure interactions on the PIPR. Light stimuli focused to a point on the pupil (i.e., Maxwellian) would eliminate variation in the amount of light incident on the retina due to iris pigmentation.
Support (If Any): NIMH K.A.R. MH103303