association between sleep quality and white matter was present after specifically accounting for environmental factors such as stress.

Methods: The study included 240 members of Old Order Amish/Mennonite families [137 female and 103 males, age (37.9 ± 17.9, mean ± s.d.)] from Pennsylvania and Maryland with no major lifetime psychiatric or medical disorders. White matter integrity of 42 tracts was measured by diffusion tensor imaging to obtain fractional anisotropy values using a 3 Tesla Prisma scanner. Current stress was measured with the perceived stress scale and lifetime stress was measured with the lifetime stressor inventory. Sleep quality was determined by the self- reported Pittsburgh Sleep Quality Index (PSQI).

Results: Integrity of several white matter tracts were significantly associated with sleep quality all of which were located at the frontal lobe areas (all $p < 0.05$ after correction for multiple comparisons using the false discovery rate).

In multiple regression analyses to account for stress factors, models showed PSQI remained a significant predictor of white matter integrity in these frontal tracts after accounting for age, sex, current stress and lifetime stress (all $p < 0.01$) while current and lifetime stress were not significant predictors in any of the four models. Meanwhile, current stress was a significant predictor on sleep quality (all $p \leq 0.01$) in a model where both white matter tracts and current stress were predictors, further suggesting that current stress is linked to poorer sleep quality as expected, which was independent of and additional to the effects of these white matter tracts on sleep quality. Life-time stress was not a significant predictor of sleep quality.

Conclusions: Sleep quality was found to be significantly associated with several frontal white matter tracts that connect brain structures important in the regulation of sleep. For example, the anterior internal capsule contains fibers connecting subcortical nuclei and the prefrontal cortex. Similarly, the corona radiata contains ascending fibers that connect the thalamus to the cerebral cortex and descending fibers that connect the frontal cortex to subcortical nuclei where the pons, hypothalamus, thalamus and prefrontal cortex are important structures for the regulation of sleep and wakefulness. Stress may impact sleep and white matter integrity, but despite stress having a strong relationship with sleep, the data showed that stress level is not a significant confounder in this study of white matter integrity and sleep quality.

Furthermore, our findings are from a population with far less environmental heterogeneity than the general population which may indicate that environmental factors known to effect sleep and/or white matter such as technology and education are not major confounding factors when studying the relationship between sleep quality and white matter integrity.

In conclusion better sleep quality is associated with higher white matter integrity in frontal areas of the brain, specifically tracts that connect structures implicated in the physiology of sleep.

Keywords: Sleep, Perceived Stress, Diffusion Tensor Imaging (DTI), White Matter Integrity

Disclosure: Nothing to disclose.

P587. A Longitudinal Assessment of Decision-Making on Problematic Cannabis Use and Polydrug Use Trajectories Among Adolescent Cannabis Users

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Background: Based on recent national estimates, one out of four adult cannabis users will develop a Cannabis Use Disorder (CUD) over their lifetime. Multiple factors have been associated with CUD onset among adolescents. However, most studies have employed cross-sectional designs and few have examined the role of Decision-Making (DM) as a potential risk factor. The current longitudinal study examined the role of DM in predicting the development of problematic cannabis use and escalation in polydrug use among adolescents who use cannabis.

Methods: The study included five bi-annual assessments over two years among 315 adolescents ages 14-17, who reported having used cannabis at baseline. Decision-making (DM) was assessed at odd-numbered timepoints using the Iowa Gambling Task (IGT). Problematic cannabis use was assessed at all timepoints using the reported number of symptoms of abuse and dependence using the Structured Clinical Interview for DSM-IV Cannabis Use Disorder (CUDn) and the Marijuana Problem Scale (MPS) score. Polydrug use was assessed at all timepoints using the Drug Use History Questionnaire, based on the number of Drugs Other Than Cannabis (DOTC). Latent growth curve models were applied to examine bidirectional influences between DM and the outcomes of interest.

Results: Baseline DM ($b = .06$, $p = .635$) and the rate of change of DM ($b = .26$, $p = .08$) did not predict escalation in CUDn. Similarly, baseline DM ($b = .16$, $p = .189$) and rate of change of DM ($b = .14$, $p = .501$) failed to predict escalation in MPS scores. Neither baseline DM, nor its rate of growth were associated with escalation in the number of DOTC used. Results from post-hoc exploratory analyses revealed that a one-unit increase in the number of DOTC overtime was associated with increases in problematic cannabis use based on the DSM-IV Cannabis Use Disorder and the MPS score.

Conclusions: Results do not support a role for DM (as assessed by the IGT) as a risk factor for problematic cannabis use or polydrug use among adolescents who use cannabis. Future studies examining fine-grained aspects of DM or assessing the association under study among particular population subgroups may help to clarify our findings.

Keywords: Cannabis Use, Cannabis Use Disorder, Decision-Making, Polydrug Use, Adolescent

Disclosure: Nothing to disclose.

P588. Emotional Facial Expression During Impulsive Choice in Opioid Users Experiencing Craving

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Background: Drug craving often leads to reuse and relapse events. Craving can amplify the value of specific goods resulting in the decision to seek and consume them. Similarly, emotional states influence decision-making, and craving is often preceded or presents in conjunction with negative affective states. While much has been investigated about the neurobiology of craving and emotion, we still lack understanding about how craving relates to emotion and how these may influence decision-making so as to become a barrier to recovery, even for highly committed treatment seekers. In this study, we evaluated how different levels of craving affect emotional expression during a delay discounting task (a measure of impulsivity). Our approach involved electromyographic (EMG) analysis of muscles specifically involved in positive valence emotional expression (zygomaticus muscle) and in negative valence emotional expression (corrugator muscle). We chose facial EMG because it allows for continuous measurement of emotional expression rather than discrete self-reported measures of emotional state.

Methods: 31 Individuals with Opioid Use Disorder (OUD) who endorsed recent craving for heroin or other opioids were recruited from a methadone treatment program to participate in 2 sessions: one prior to the participant receiving methadone, and the other after, i.e., at "trough" and at "peak" methadone levels. The order of the two sessions was randomized across subjects. We employed validated instruments to assess craving, subjective withdrawal symptom severity, and current levels of anxiety. Participants then completed a 12-minute delay discounting task. We estimated a discount rate parameter for each session. Corrugator (necessary for frowning) and zygomatic (necessary for smiling) surface electromyography (EMG) were measured during the task. The resulting EMG signal was filtered (30-400 Hz) and rectified. Muscle activity was calculated as the Root Mean Square (RMS) across the session or across specific epochs within each trial.

Results: Participants reported higher craving for opioids in the session before methadone administration, than in the session after ($t = 3.66$, $P = 0.001$). In the post-medication session, the discount rate across participants was negatively correlated with zygomaticus activity (positive valence) and positively correlated with corrugator activity (negative valence). Interestingly, these relationships were inverted in the pre-medication session, such that negative valence now was inversely related to the discount rate.

Conclusions: Taken together, these preliminary results indicate that opioid users' facial emotional expression during impulsive choice is not invariant to context. In high craving states, more impulsive individuals show less negative valence expression, suggesting that craving may dampen the emotional response to decisions about immediate versus delayed rewards. Further elucidation of the physiological relationship between craving, emotion and decision-making could help understand, predict, and prevent relapse in OUD.

Keywords: Facial Emotion Processing, Opioid Addiction, Impulsivity, Craving

Disclosure: Nothing to disclose.

P589. Neurobiological and Behavioral Consequences of Repeated THC or Nicotine E-Cigarette Vapor Inhalation

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Background: The use of electronic nicotine delivery systems (ENDS) or e-cigarettes continues to be a popular method of drug delivery. Recent preclinical models of vapor inhalation have shown that exposure to vaporized Δ9-tetrahydrocannabinol (THC) may produce lasting behavioral and neurobiological changes. Further, investigations have confirmed that e-cigarette aerosols, with and without nicotine, pose a considerable risk to the developing nervous system. Understanding the lasting effects of repeated e-cigarette exposure will be critical for assessing harms and for identifying mechanisms for potential therapeutic targets.

Methods: Male Wistar rats were repeatedly exposed to vaporized Δ9-tetrahydrocannabinol (THC; 200 mg/mL), nicotine (30 mg/mL), or propylene glycol (PG) vehicle twice daily for up to 2 weeks. Rat brain tissues (hippocampus and frontal cortex) were collected for immunohistochemical and Western blot analyses. Tissues were immmunostained for cannabinoid receptor 1 (CB1), glial fibrillary acidic protein (GFAP) and ionized calcium binding adapter molecule 1 (IBA1). Western blot analyses of CB1, GFAP, IBA1, peroxisome proliferator-activated receptor-alpha (PPAR-α), and C3 compliment protein were performed using tissue from the frontal cortex. In a separate study, pregnant Wistar rats were repeatedly exposed to THC (100 mg/mL) or PG vapor for up to 2 weeks. The offspring were tested for anxiety-like behavior using the elevated plus maze procedure.

Results: Repeated THC vapor inhalation significantly reduced CB1 receptor expression in the hippocampus ($P < 0.05$). In addition, repeated exposure to PG vehicle vapor increased GFAP + cells ($P < 0.05$) and IBA1 + cells ($P = 0.06$), whereas repeated exposure to THC or nicotine resulted in differential effects. Western blot analyses confirmed partial changes in GFAP and IBA1, but only a modest change in PPAR-α or C3. Lastly, rats born to mothers exposed to repeated THC vapor exhibited decreased time spent in the open-arms compared to rats born to mothers exposed to PG vehicle, confirming the effects of prenatal e-cigarette exposure.

Conclusions: Overall, this study confirms that repeated THC vapor inhalation via e-cigarettes downregulates CB1 receptor density in rats, consistent with tolerance effects, and may produce lasting age-dependent effects on behavior. These data also suggest that repeated exposure to e-cigarette vapor inhalation may selectively modulate microgliosis and astrogliosis in rat brains.

Keywords: Electronic Cigarette (e-cigarette), delta9-tetrahydrocannabinol, THC, Nicotine

Disclosure: Nothing to disclose.

P590. Pharmacokinetic Assessment of High Affinity D4R-Selective Ligands to Attenuate Cocaine Self-Administration

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Background: Dopamine receptors (D1-like (D1R, D5R) and D2-like (D2R, D3R, D4R)) are G-protein coupled receptor proteins that regulate physiological functions such as movement, emotion, and cognition. The D4R is enriched in the prefrontal cortex where it plays important roles in cognition, attention, decision making and executive function. Studies have indicated D4R-selective ligands as a promising medication development to treat neuropsychiatric conditions, including Alzheimer's disease, ADHD and cocaine use disorders (CUD). D4R ligands have been shown to alter cognition and behavior in animal models of drug addiction and variations in the DRD4 gene are associated with novelty-seeking and risk behavior, as well as ADHD. A better understanding of D4R-mediated signaling is essential to understanding and treating D4R-associated disorders, including substance abuse disorders. Despite its clinical importance, there are currently no FDA approved medications that target the D4R and CUD treatment. The present study focuses on the design of D4R ligands based on the parental phenylpiperazine scaffold with pharmacokinetic analysis in rat and human liver microsomes, followed by preliminary in vivo behavioral analysis.

Methods: Based on the 4-phenylpiperazine scaffold, a series of high affinity and selective D4R ligands were designed by using computational modelling. Final compounds were purified and analytically characterized followed by CHN combustion elemental analysis. Their in vitro receptor affinities were determined using HEK293 cells expressing dopamine D2-like receptors (D2R, D3R, D4R). These binding studies were coupled with functional studies using β-arrestin recruitment and cAMP inhibition assays. For several D4R-selective ligands, we calculated in silico brain penetration using central nervous system multiparameter optimization of chemical features (CNS MPO) and performed Caco-2 membrane permeability tests. For selected compounds, we