VICTORIA SHIFFLETT, West Virginia University, Morgantown, WV 26505. Characterization of sleep regulation and cognitive processing in schizophrenia mouse model

Excitatory and inhibitory (E/I) ratio imbalance is a robust biomarker for many psychiatric disorders, including schizophrenia (SCZ). The E/I ratio is imperative to proper cortical function, including regulation of sensory processing. Previous data from our lab has shown that sleep regulates E/I over the 24h day. This study showed phase-shift dysregulation of the E/I ratio in BTBR, a SCZ-relevant mouse model due to the spontaneous deletion of the disruption in schizophrenia 1 (disc1) gene. Subchronic phencyclidine (PCP), an NMDA receptor antagonist, is a widely used model for schizophrenia-like phenotypes of positive and negative behavioral symptoms in rodents. We hypothesize that subchronic PCP administration will impair sleep regulation, working memory, and auditory processing, and that Clozapine (CLZ), an atypical antipsychotic, will reverse these effects. To test this hypothesis, we administered PCP via an osmotic minipump followed by electroencephalogram/electromyogram (EEG/EMG) recordings (to characterize sleep/wake states) and behavioral assays. Following initial testing, we administered CLZ followed by EEG/EMG recordings and behavioral assays to investigate its reversal effects. Our findings, that sleep architecture remains unaltered while there are deficits in spatial working memory, aim to assess the deficits caused by subchronic PCP administration and the effects of pharmacological modulation. Future experiments will aim to evaluate the effects of subchronic PCP on the E/I ratio, specifically looking at altered sleep quality and endocannabinoid signaling. These findings will provide insights into mechanisms of cannabinoid-dependent signaling and treatments for SCZ and related disorders.