Title: Preclinical Imaging of Adolescent Cannabidiol on Brain Structure and Functional Connectivity

PI: Marcelo Febo, PhD

Contact info: febo@ufl.edu

Department: Psychiatry

Funding: NIDA 1R03DA042971-01

Description:
The most recent statistics indicate that one out of 45 children are now diagnosed with an autism spectrum disorder (ASD). ASD individuals express a range of conditions from mild-to-severe intellectual disability, sleep disturbances, anxiety/mood disorders, self-injurious behavior, psychosis, and over 25% suffer from seizures. The complex comorbidities accompanying ASD challenge our ability to identify effective treatments. Cannabidiol (CBD) is considered as a potential medication to alleviate various ASD comorbidities. CBD has been reported to alleviate psychosis, anxiety, facilitate REM sleep, and suppress seizure activity, which are all outcomes that may benefit individuals with an ASD. A long-term objective of the proposed research is to characterize the in vivo effects of chronic CBD treatment in control rats and in an animal model showing well-defined and -characterized ASD-like neurobiological alterations and behavioral symptoms. The main hypothesis to be investigated is that CBD normalizes structural and functional deficits in this animal model. The present proposal will use the rat valproic acid (VPA) model of ASD to explore this hypothesis. Two specific aims are proposed. Specific aim 1 will determine the time-dependent effects of CBD on resting state functional connectivity in control and VPA rats. Studies will be accompanied by behavioral assessments to characterize the pharmacotherapeutic effects of CBD on ultrasonic vocalizations, motor activity, and social interactions. Specific aim 2 will determine the time-dependent effects of CBD on white and grey matter structural integrity, structural connectivity, and regional brain volumes in control and VPA rats. We will focus our investigation on critical brain regions affected in ASD, such as the amygdala, ventral hippocampus, mediodorsal thalamus, and temporal and anterior cingulate cortices. The long-term impact on public health of the proposed experiments will be: (1) a fully characterized relationship between changes in ASD behaviors, neural circuitry changes, and CBD treatment, (2) specific in vivo neurobiological data on the effects of CBD on neuronal connectivity and growth in the ASD brain, and (3) preclinical imaging biomarkers for in-depth magnetic resonance microscopic-level assessment of the effects of CBD treatment on changes in neural pathways in ASD and control brains.