Stimulation of the endocannabinoid system in a mouse model of ASD
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Introduction
Autism Spectrum Disorder (ASD) is a developmental disability characterized by deficits in social communication, and repetitive/restricted behaviors. ASD is diagnosed through clinical behavioral assessments, as there is no biomarker. The occurrence of ASD is 1 in 54 children. The endocannabinoid system (ECS) is a neuromodulatory cell-signaling system that has been implicated in the pathology of ASD. The ECS consists of two main components: the cannabinoid receptors type 1 (CB1) and type 2 (CB2), and the endogenous molecules anandamide (AEA) and 2-arachidonoylglycerol (2-AG). The majority of the CB1 receptors are found in the brain, and expression is the highest in the hippocampus, basal ganglia and cerebellum, while moderate levels are seen in the amygdala and hypothalamus. The ECS regulates sleep, appetite, memory and mood.

Objectives
The effects of JZL-184 and CP-55940 will be tested on social communication, social behaviors, and learning and memory using the following behavioral tests: Social Approach, Direct Social Interaction and Contextual Fear Conditioning. Our hypothesis is that the ECS is understimulated or less active in people with ASD, and stimulating it through either direct agonism (CP-55940) or by blocking the enzymatic degradation of 2-AG (JZL-184) will lead to improvements in the behaviors related to ASD.

Methods
Treatment: The vehicle for both drugs was a solution of 10% ethanol, 10% kolliphor and 80% saline, sterile filtered. JZL-184 was administered in a 15 mg/kg dose and CP-55940 in a 0.2 mg/kg dose. All drugs were administered 1 hour prior to the experiments via intraperitoneal injection in a 10 ml/kg volume.

Subjects: Female and male BTBR and C57BL/6J mice ages 2-8 months.

Conclusion
Overall, despite the hypothesis that both CP-55940 and JZL-184 will improve social behaviors and learning and memory, only slight to moderate effects were seen with these drugs. CP led to a decrease in the total distance traveled by the C57BL/6J and BTBR mice, suggesting a sedative-like effect that interfered with the behavioral analysis. In the final analysis, the endocannabinoids only expressed modest effects on behaviors in the ASD mouse model which could be a result of the doses used in these experiments. Future research utilizing these drugs should more closely monitor the effects of CP with a few different doses to determine its sedative like effect.

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References