Enhancing Autism Therapeutics: The Influence of Acute Cannabidiol Treatment and the Estrous Cycle on Social Behavior and Hormone Changes in Adult Male and Female Mice

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by persistent social interaction deficits and repetitive behaviors. Current FDA-approved drugs reduce irritability and aggression but fail to effectively address core symptoms. Additionally, limited research on sex-based differences and hormonal changes complicates treatment in females. Therefore, this study aims to enhance pharmaceutical options that alleviate core ASD symptoms while investigating sex-specific treatment complexities. Cannabidiol (CBD), a non-intoxicating constituent of Cannabis sativa, has shown promise in alleviating ASD social deficits. The estrous cycle, a four-stage reproductive cycle in female mice, causes hormonal fluctuations that introduce behavioral complexities. We hypothesized that an acute 15 mg/kg CBD dose improves social behavior in adult BTBR and C57BL/6 mice, and that hormone changes during the estrous cycle influence social behavior. CBD's impacts on autism-relevant behaviors were evaluated using social interaction sniffing, social novelty sniffing, marble burying, and a social dominance tube test. Additionally, fecal boli were counted to assess anxiety. Macroscopic and microscopic analyses were performed to determine estrous cycle stages, and hormone assays quantified estradiol and progesterone concentrations in blood samples. Significant behavioral effects were observed in marble burying, number of fecal boli, tube test wins, and tube test duration. In female mice, higher estradiol levels correlated with increased social novelty, and higher progesterone levels correlated with reduced repetitive behavior. These findings demonstrate that CBD has potential to improve ASD core symptoms and that reproductive hormone fluctuations influence behavioral outcomes.

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