David Ortiz Sanchez

Best Undergraduate Poster Presentation Award

Program: Biological Psychology/Biology-Premed

College: College of Social and Behavioral Sciences

Type: Poster

Title: Role of NPY on Cannabinoid-Induced Anxiety-Like Behavior

Abstract: Increased cannabis accessibility and use has resulted from recent changes in state laws. These laws were adopted based on our understanding of cannabis effects from research conducted twenty to thirty years ago. Unfortunately, the cannabis now being sold for recreationally and medical purposes contains a greater Δ9-tetrahydrocannabinol (THC) content and much lower cannabidiol (CBD) content than cannabis available in the past. Because THC is the primary psychoactive agent in cannabis and is responsible for its rewarding and addicting properties, it is very possible that the cannabis presently being sold will have a much greater effect on neuronal functioning. Moreover, the lower content of CBD which acts as an indirect antagonist of THC also adds to the greater psychoactive effects of cannabis. These changes in cannabis are particularly concerning as high school students in the United States now report smoking cannabis more often than nicotine products. One particular effect of cannabis that will likely be enhanced by these changes in the chemical makeup of the drug, is its effect on affective behavior. Specifically, THC is believed to be anxiety-inducing while CBD is anxiolytic suggesting that using high THC/low CBD cannabis will lead to greater anxiety. Therefore, the present study will assess the effect of repeated and chronic exposure during adolescence to the cannabinoid receptor agonist CP-55,940 (a synthetic analog of THC) and/or CBD on anxiety-like behavior in young adult rats. To this end, we measured anxiety-like behavior using both an elevated plus maze and the light/dark box.

Effects of adolescent cannabinoid administration on anxiety-like behaviors in adulthood.

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INTRODUCTION

Medical use of cannabinoids by adults has grown in popularity as changes in state laws have increased legal access. As a result, children and adolescents are now being treated with medical cannabis, which usually involves a combination of Tetrahydrocannabinol (THC) the primary psychoactive component of cannabis and the non-psychoactive cannabinoid, cannabidiol (CBD). This combination is thought to allow the medicinal benefits of CBD while protecting against THC-induced psychopathology (i.e., anxiety).

While many states' laws have increased cannabinoid accessibility to the general public, federal law has continuously restricted accessibility to the scientific community. Instead, synthetic analogs of THC (i.e., CP-55,940) are used to assess effects of use, whether on its own or in combination with another compound such as CBD. Although previous literature describes CBD as being anxiolytic in adults, the effects of CBD exposure in adolescents are unknown. Moreover, there is little available data on the combined effects of CBD and THC on affective behavior in adolescents.

Thus, the goal of the present study was to investigate whether acute or chronic cannabinoid agonist exposure beginning in early adolescence would affect anxiety-like behaviors in young adult rats.

METHODS

Subjects

Subjects consisted of 204 male and female Sprague Dawley rats (Charles River Laboratories, Hollister, CA). All procedures were conducted according to the National Institutes of Health (NIH) Guide for the Care and Use of Laboratory Animals and approved by the Institutional Animal Care and Use Committee (IACUC) at California State University San Bernardino.

In Vivo Drug Treatment

Beginning on PD 31, rats were injected daily (sc) with cannabidiol (CBD; 10 mg/kg), CP-55,940 (10 µg/kg), a combination, or vehicle. Rats were injected for an acute period (PD31-PD40), with no drug administered after the 10th day, or for a chronic period (PD31–PD65), with drug administered 1 h prior to behavioral testing.

* (sc) - Subcutaneous

Light Dark Box (LDB) Procedure

On PD60, animals were placed in the light compartment of the box and allowed to roam freely for 5 minutes while tracking software analyzed behavior. Time spent in each compartment of the LDB was measured, along with the frequency of transitions into the light compartment.

Elevated Plus Maze (EPM) Procedure

On PD65, animals were placed in the center of the EPM facing an open arm and allowed to roam freely for 5 minutes. Time spent in the arms of the maze (open or closed) and number of entries into each zone (open or closed) were analyzed.

Data Analysis

Data from LDB and EPM was analyzed in a 4 x 2 x 2 (drug x sex x condition) between-subjects ANOVA. Tukey or Dunnett tests were used to make post hoc comparisons ($p < .05$).

RESULTS

Acute Treatment

No differences in behavior were observed in any of the drug conditions following 10 days of administration.

Chronic Treatment

Animals treated with solely CBD, displayed an overall anxiogenic profile, having spent significantly more time in both the dark compartment of the LDB and closed arms of the EPM. When subjects were exposed to CBD in combination with CP-55,940, a decrease in anxiety was observed when compared to the treatment group that only received CBD. However, anxiety-like behaviors were still observed in the treatment group receiving both drugs in combination when compared to the vehicle-treated group.

Acute Light Dark Box

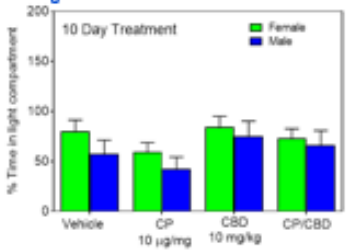

Fig. 1. Time in light compartment of LDB (first 5 min) for all acute 10 day treatment groups. Main effect of Sex.

Acute Elevated Plus Maze

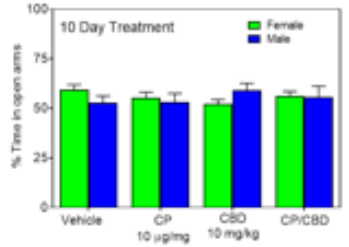

Fig. 2. Time in open arms of EPM for all acute 10 day treatment groups. No significant differences.

Chronic Light Dark Box

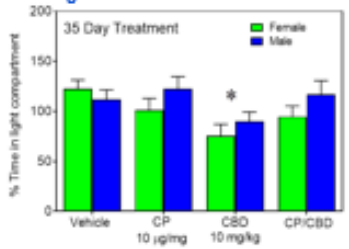

Fig. 3. Time in light compartment of LDB (first 5 min) for all chronic 35 day treatment groups. *Main effect of drug; CBD was significantly different from Vehicle, CP-55,940.

Chronic Elevated Plus Maze

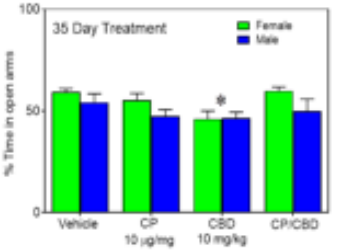

Fig. 4. Time in open arms of EPM for all chronic 35 day treatment groups. *Main effect of sex, Main effect of treatment condition; CBD was significantly different from vehicle, CP/CBD.

DISCUSSION

The results found suggest that chronic cannabinoid treatment during adolescence may produce adult-atypical results. More specifically, long-term exposure to CBD may produce anxiogenic effects when use begins in adolescence. This deviates from previous literature, which has often described CBD as having anxiolytic properties. This is also in contrast to many companies that market CBD as an alternative anti-anxiety treatment. While cannabis use is currently recommended for children and adolescents suffering from a variety of treatment-resistant disorders (i.e., tumors, wasting disorders, epilepsy), the effects on anxiety in adulthood have not yet been clearly elucidated. For that reason, additional research is necessary not only for the scientific community, but also for caretakers of children and adolescents who have not responded to previous treatments.

ACKNOWLEDGEMENTS

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