Effects of Prenatal Cannabis Vapor Exposure on Cognitive Flexibility

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Abstract
Cannabis is the most commonly used illicit substance among pregnant women, yet the effects of prenatal cannabis exposure on cognitive wellbeing remain largely unknown. With recreational cannabis laws now in effect in 8 states and counting, there is growing concern that prenatal cannabis exposure could increase dramatically in the coming years. Thus, there is an urgent need to better understand the impact of maternal cannabis exposure on cognition. We investigated whether chronic exposure to vaporized cannabis during pregnancy alters cognitive flexibility in male and female offspring. Female dams were passively exposed to vaporized cannabis extract (50 or 400mg/mL; 1 puff every 2 min for 1 hr, twice daily) or vehicle vapor throughout mating and gestation. Beginning at postnatal day 50, offspring were trained to press a lever that was paired with delivery of a cue light to receive a food reward. Next, rats had to disregard the previously learned strategy in favor of an egocentric spatial strategy (i.e., ignore the cue and always press the left, or right, lever). Finally, rats were tested in a reversal task that required them to press the lever opposite of the previous task. The number of trials to criterion and errors, along with error type (perseverative, regressive, or never reinforced) and spatial reference of distractor (i.e., toward or away from cue) were tabulated and compared across groups. Preliminary results indicate that prenatal cannabis exposure repeatedly affected the visual cue discrimination strategy learning or reversal learning, but impaired strategy shifting. Moreover, cannabis-exposed offspring made more never reinforced and regressive errors, which indicates an inability to obtain and maintain the new optimal strategy. These data indicate that prenatal cannabis exposure may lead to deficits in cognitive flexibility in adulthood.

Background
- Cannabis is the most commonly used illicit substance among pregnant women, but the effects of cannabis exposure during pregnancy on cognitive abilities of offspring has yet to be fully explained.
- Human longitudinal studies (OPPS & MHPCD) show a negative relationship between maternal cannabis use and performance on tests involving higher-order cognitive functions such as abstract and visual reasoning (Fried & Smith 2001).
- The primary objective of this study was to investigate whether maternal exposure to vaporized cannabis during pregnancy alters cognitive flexibility in offspring.

Methods
- Female dams were passively exposed to vaporized cannabis extract (50 or 400mg/mL; 1 puff every 2 min for 1 hr, twice daily) or vehicle vapor throughout mating and gestation.
- Beginning PND 50, offspring [n=6-9/treatment/sex] were trained to press levers for food reward and tested for cognitive flexibility in an automated attentional set-shifting task.
- Data collected: Trials to Criterion, Type of Error (Perseverative — inability to abandon old strategy; Regressive — inability to maintain new strategy; Never Reinforced — inability to obtain new strategy), Number of Errors

Cognitive Flexibility
- Set-Shifting Task
- THERE IS A PLOT SHOWING THE NUMBER OF ERRORS MADE ACROSS DIFFERENT GROUPS (VEHICLE, CANNABIS 50, CANNABIS 400) FOR MALE AND FEMALE RATS.
- Perseverative Errors
- Regressive Errors
- Never Reinforced Errors
- The number of errors in the reversal task is significantly higher in the cannabis-exposed groups compared to the vehicle groups.

Conclusions
- Results from cognitive flexibility testing show no significant effect of cannabis exposure on acquisition of the visual cue discrimination strategy or reversal learning, however an impairment in shifting to an egocentric spatial strategy was observed.
- We also observed an increase in never reinforced-type and regressive-type errors compared to vehicle and control groups, which suggests a difficulty in maintaining a new optimal strategy.

Future Directions
- Changes in receptor and enzyme expression within medial prefrontal cortex and nucleus accumbens core
- Dopamine receptor type 2, FAAH, NAPE-PBD
- Epigenetic changes (i.e. gene methylation)

References