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Effects of a CB1 Receptor Antagonist on Anxiety in Adult Rats Exposed to THC During Development

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Background

- The recreational and medical use of cannabis has become prevalent in the U.S. after at least 24 states have passed laws that legalize its consumption.
- Tetrahydrocannabinol (THC) is a potent cannabinoid contained in the cannabis plant. It produces the euphoric feelings associated with recreational marijuana.
- Increased access for the general public is concerning since little research has been conducted on this drug.
- The Elevated Plus Maze (EPM) has been widely-used in studies to examine anxiety behavior in rats.
- In the EPM, rats have the option to spend time in the closed sections or the open sections of the maze.
- Increased anxiety hinders the rat's natural instinct to explore all parts of the maze.
- AM 251 is a CB1 receptor inverse agonist. We hypothesized that AM 251 would induce anxiety behaviors in rats.
- CB1 receptors are concentrated in the central nervous system and respond to naturally-occurring endocannabinoids. When THC binds to CB1, it suppresses the release of other neurotransmitters.
- Juvenile rats were previously exposed to THC in our lab. We tested these animals in the EPM as adults, following the administration of AM 251 or control vehicle.

Methods

- Groups of rats were exposed to THC throughout the adolescent period (0, 5, or 10 mg/kg/day from postnatal day 22-40).
- The AM 251 dosage was calculated based on the selected rat's body weight. After injection, there was a 30 minute wait period.
- The EPM assessment was recorded for 10 minutes in an isolated room with the lights turned off. Each trial began with a rat placed in a closed arm.
- The initial time the rat entered a new space was recorded as well as the time they exited that space, in order to obtain the total amount of time the rat spent in each space.
- Total entries were determined by the number of time entries for each section of the maze.
- The rat was considered to be in a new arm or the center when all four paws crossed the threshold.
- We also observed behaviors such as head-dips, rearing, and immobility.
- Head-dips were considered when the rat lowered its head over the side of the arm.
- Rearing was observed each time a rat raised its body on their hind legs.
- Immobility was observed when a rat stopped all motion for at least 3 consecutive seconds.

Results

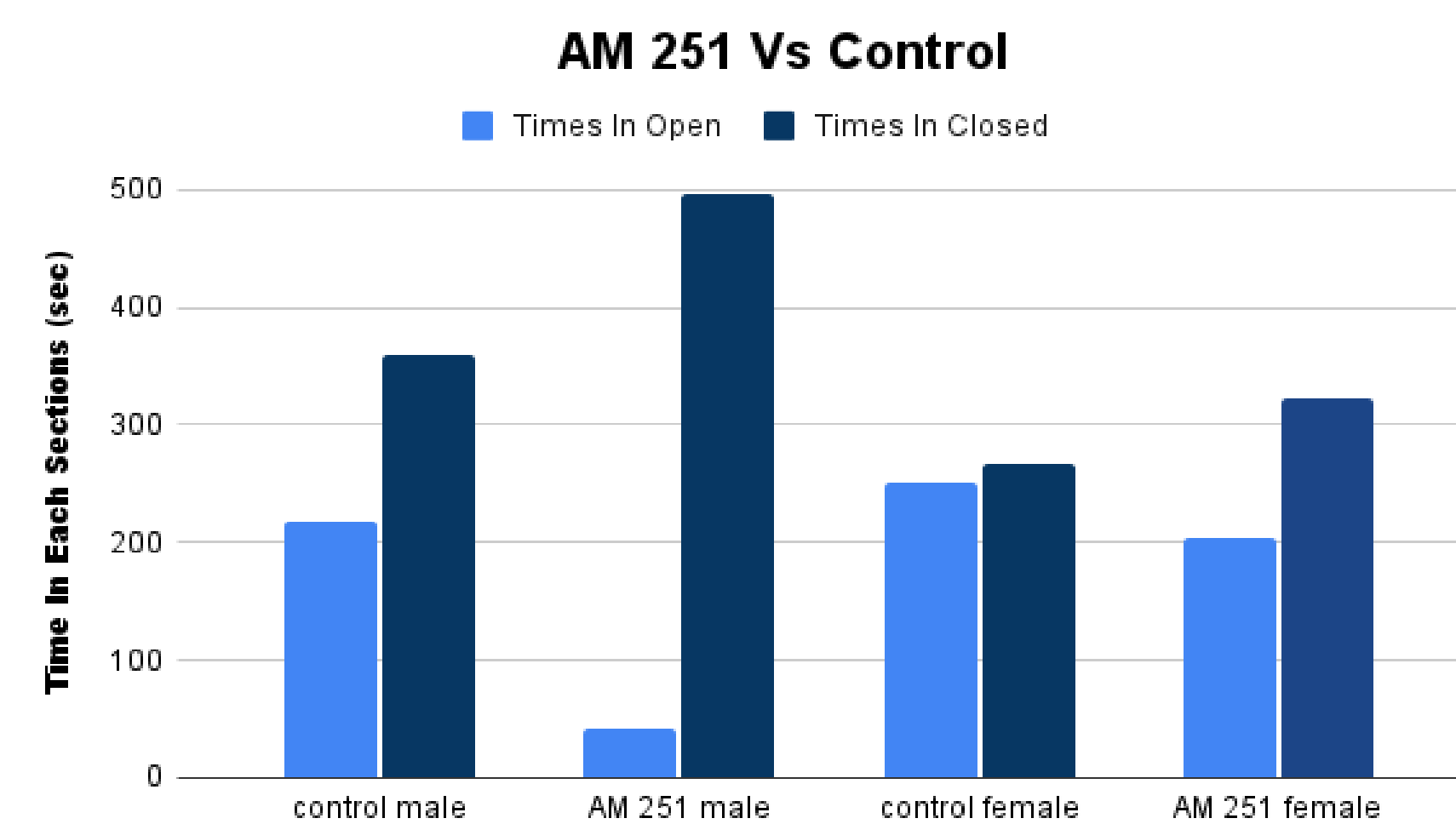


Figure 1. Average time spent in each arm area.

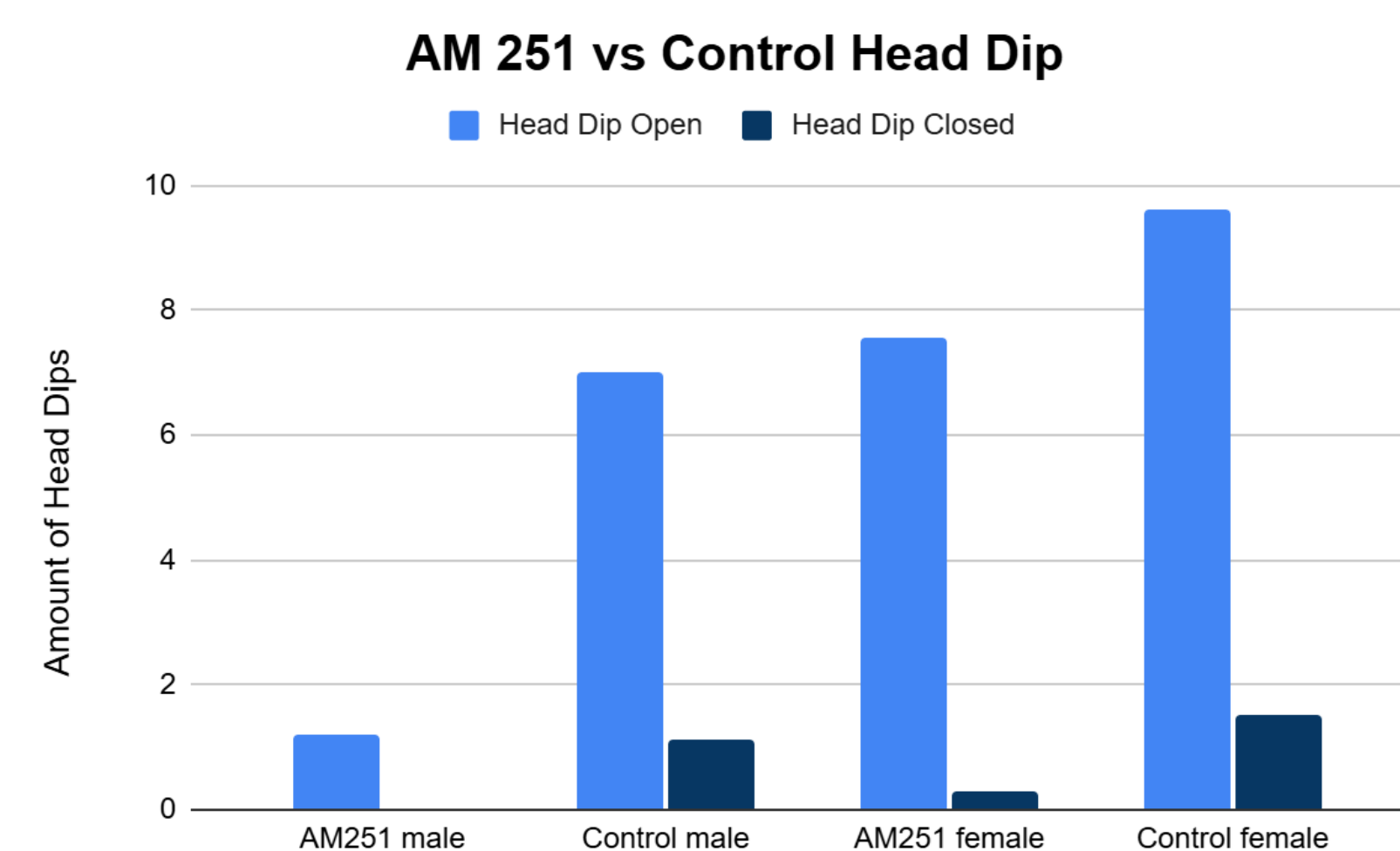


Figure 2. Average head dips performed in each arm.

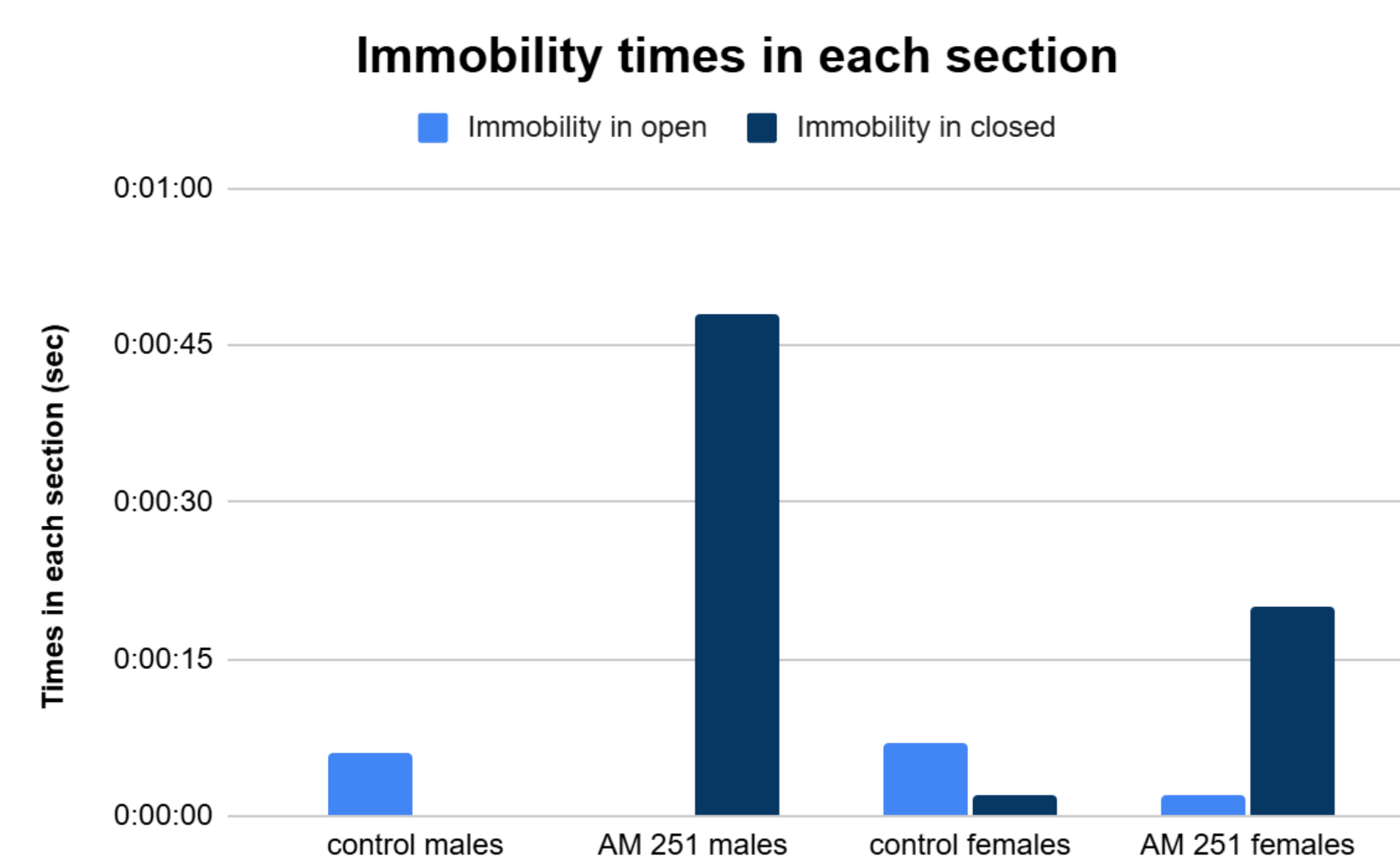


Figure 3. Time duration of immobility.

Discussion

- The male rats that received AM 251 spent significantly more time in the closed arms than the control rats. This change in behavior can be interpreted as a sign of increased anxiety as a result of CB1 receptor blockade.
- There was also an increase in anxiety-related behavior such as immobility in the rats that received the AM 251 treatment, mirroring findings found in other previous research.
- There was a significant decrease in head dip after the rats received AM 251. Males injected with AM 251 depicted lower amounts of head dips.

Limitations

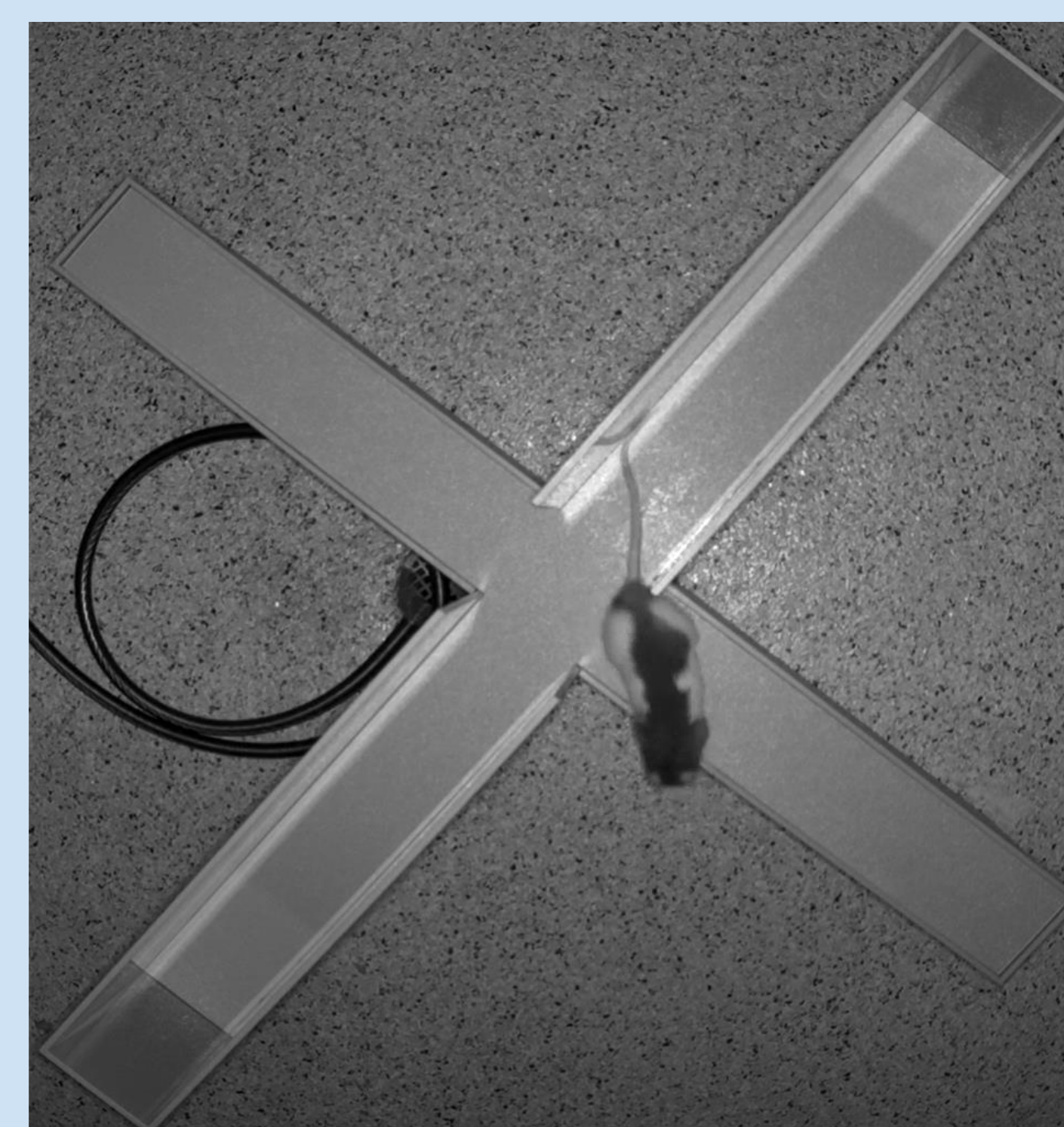
- This experiment was conducted within a brief timeframe of six weeks; however, achieving more precise results would require a longer duration.
- All of our animals were exposed to THC during their juvenile stage. Examining how control animals respond to AM 251 would be informative.
- A larger sample size is needed to provide a more precise estimate of the general population.

Future Directions

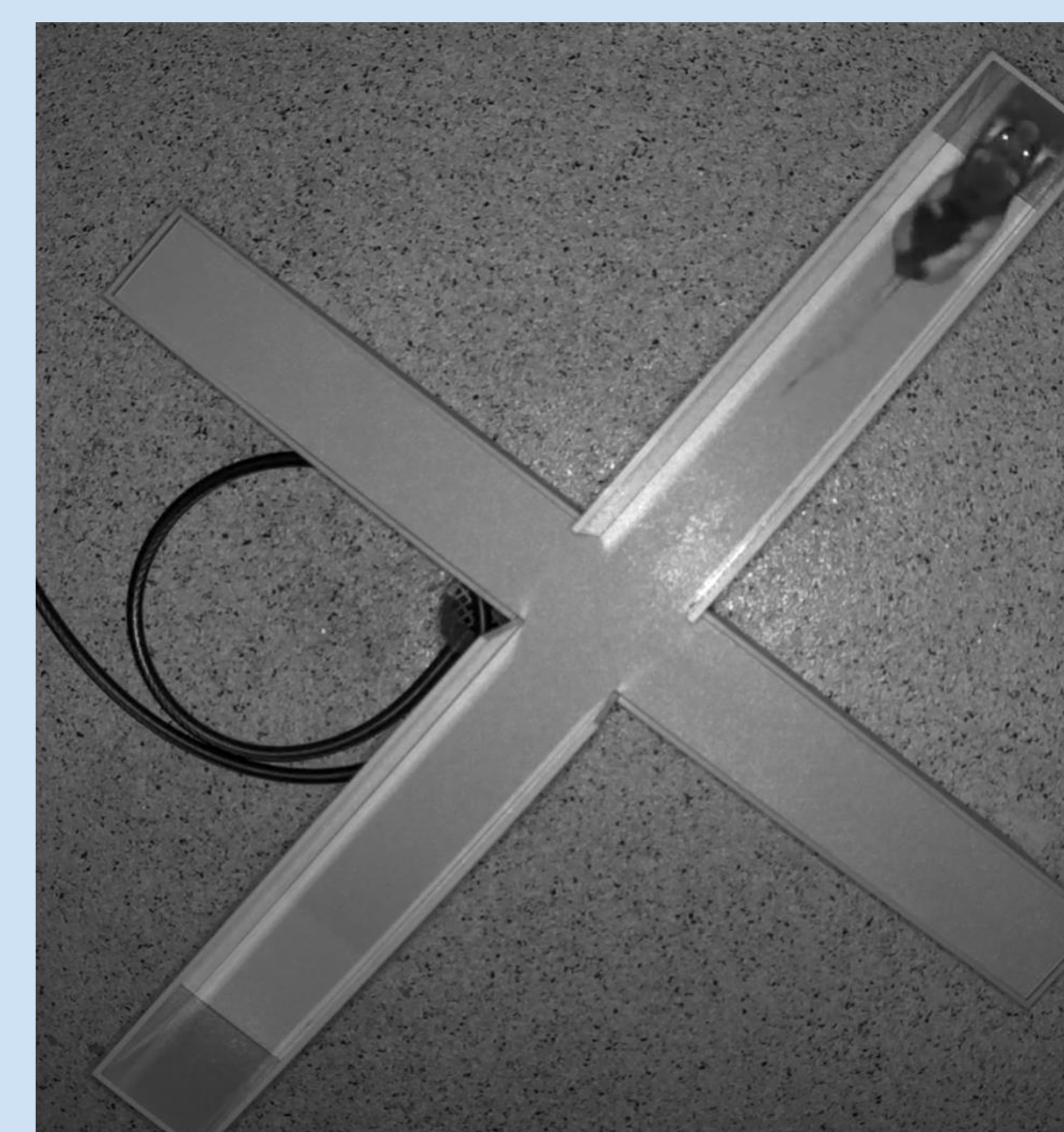
- A control group consisting of non-THC exposed rats would provide a more suitable baseline comparison.
- Previous research noted the effects the THC had on male and female rats, future research needs to directly observe how the THC impacts the behavior of the sexes.
- Animal age should be examined as an additional variable.
- A wider dose range of AM 251 should be examined.

Acknowledgements

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Picture 1: Rat exhibiting head dip behavior



Picture 2: Rat exhibiting rearing behavior