The Effects of Tetrahydrocannabinol on Circadian Rhythmicity and the Response to Nicotine in Long-Evans Rats

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Background

The marijuana legalization trend promotes the notion that cannabinoids such as tetrahydrocannabinol (THC) can be safe and effective medications for conditions such as insomnia. Unfortunately, exposure to THC during development has been shown to impair cognition and motor behavior in humans and laboratory animals. The current study used VitalView software and cage-top infrared activity monitors to quantify the effects of a range of THC throughout adolescence.

Rats were further administered acute nicotine drug challenges to determine if THC altered the development of the acetylcholine neurotransmitter system. It is hoped that the results of this work in progress can be used to determine if THC presents a risk to adolescent brain development and predisposes an individual to future activity and sleep dysregulation.

Methods

The **VitalView** software system records locomotor activity in the home cage, 24/7, in 5-minute intervals. Motor activity was quantified through beam breaks of a cage top infrared monitor.

Baseline activity data was recorded and analyzed in six female Long-Evans rats before introducing nicotine via **intraperitoneal injection**. They were dosed with either water, 0.2mg/kg, 0.5mg/kg, 1.0mg/kg of nicotine. They then were recorded via VitalView software and analyzed for changes in motor activity.

Figure 4. Arrow pointing to the injection site of nicotine or water.

Figure 5. Pictured is the VitalView cage top monitor fastened on top of a typical rat cage topper.

Results

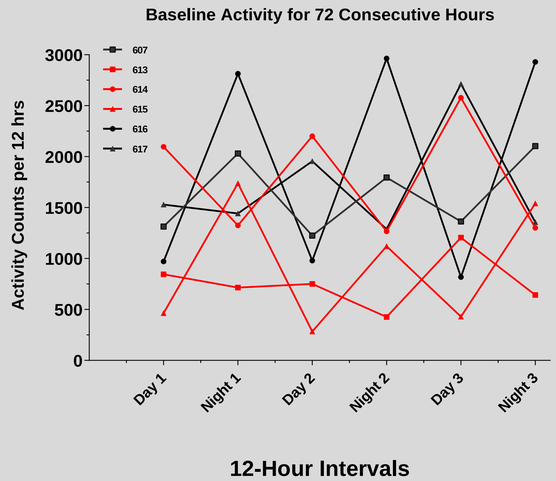

Figure 1. Baseline activity data for six rats over 72 hours. Activity lines in red depict animals who were exposed to 10mg/kg of THC throughout adolescence (day 22-40).

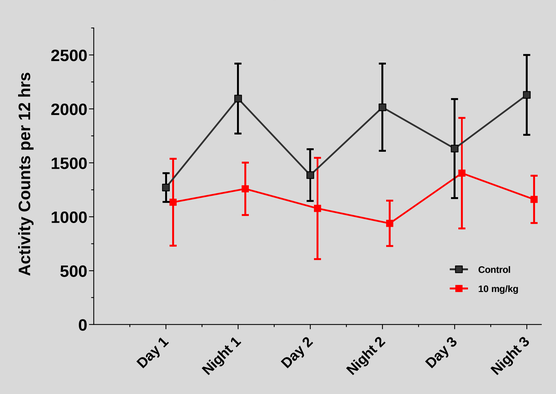

Figure 2. Average of rat activity over 72 hours. Activity lines in red depict animals who were exposed to 10 mg/kg of THC during adolescence.

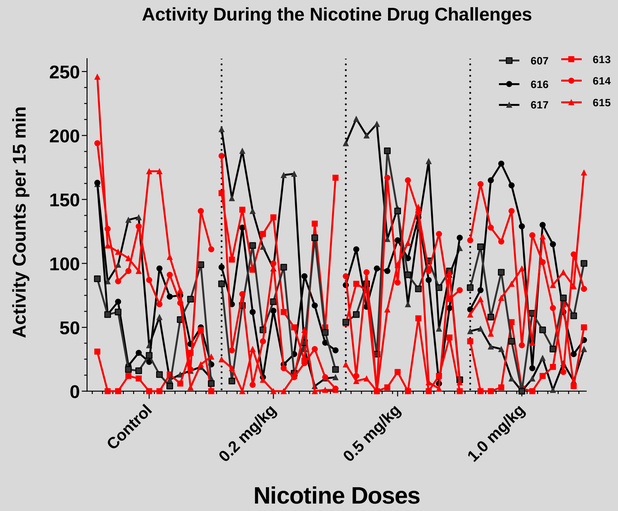

Figure 3. Activity during the nicotine drug challenges.

Discussion

As shown in Figure 1 and 2, rats tend to be more active at night and show decreased activity during the day. This normal circadian behavior is more apparent in the control animals. However, the animals that were exposed to THC show decreased cyclicity and less overall activity during both day and night.

Figure 3 depicts activity levels in 15 min increments for 3 hours following the acute nicotine drug challenges. The high variability suggests that we have not yet found the appropriate nicotine dose range and/or the timecourse of the nicotine effect. One advantage of the VitalView system is that we can easily perform additional micro- and macroanalyses of the nicotine timecourse.

Future Directions

Since this is an ongoing experiment, we plan to increase our sample size by testing additional squads of animals. We are currently assessing the male littermates of the six animals presented here. Eventually, we plan to test animals at different points in the lifespan, as well as pregnant animals, to determine if THC and nicotine produces unique effects in these groups.

One goal of this experiment is to draw meaningful conclusions about the relationship between frequently-used drugs, like nicotine and THC, and how they might affect health by impacting the sleep-wake cycle.

Acknowledgements

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