# EFFECTS OF CANNABIS SMOKE EXPOSURE ON WORKING MEMORY PERFORMANCE IN AGED RATS

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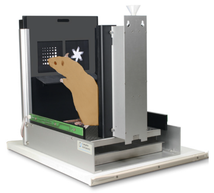
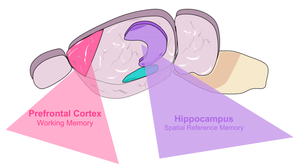
## INTRODUCTION

Cannabis is the most widely used illicit drug in the United States, with individuals over the age of 65 becoming the fastest growing demographic of cannabis consumers. With the population of older adults expected to reach 90 million individuals by the year 2050, it will be imperative to understand the potential cognitive impacts of cannabis consumption in this population. Aging is associated with impairments in cognitive functions mediated by the hippocampus and prefrontal cortex, and studies in both humans and animal models show that acute administration of delta-9-tetrahydrocannabinol (THC, the psychoactive component of cannabis) can impair performance on cognitive tasks dependent on these brain regions. The vast majority of cannabis users consume the drug by smoking, however, rendering it important to understand how this route of administration affects cognition. Hence, the goal of these experiments was to use a rat model to determine how acute exposure to cannabis smoke affects performance of young and aged rats on memory tasks mediated by the prefrontal cortex and the hippocampus.

## METHODS

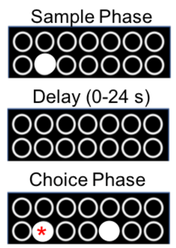





**Subjects.** Young adult (8-10 mo.) and aged (25-28 mo.) male Brown Norway rats were trained in touchscreen operant chambers (left) in a delayed response working memory task or a trial-unique nonmatching-to-location episodic memory task.

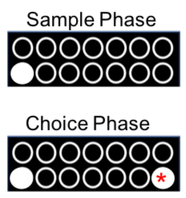
### Delayed Response Working Memory Task

Each trial in the delayed response task is composed of 3 phases. In the *sample phase*, one location is illuminated for the rat to touch. The variable *delay phase* (0-24 s) occurs following the nose poke, and rats must nose-poke at the food magazine. In the *choice phase*, two locations are illuminated, and the rat must touch the same location as in the sample phase to receive a food reward. Rats perform ~ 100 trials/day, and performance is evaluated as the percentage of correct choices at each delay. Red asterisk indicates correct choice.

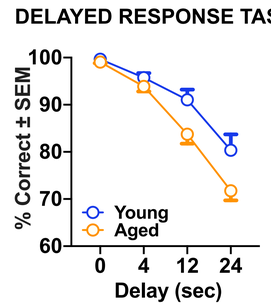



### Trial-Unique Nonmatching-to-Location (TUNL)

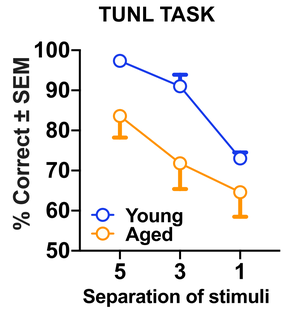
Each trial in the TUNL task is composed of 2 phases. In the *sample phase*, one location is illuminated for the rat to touch. In the *choice phase*, two locations are illuminated (separated by 1, 3, or 5 spaces – see diagram), and the rat must touch the location not illuminated in the sample phase to receive a food reward. Rats perform ~ 100 trials/day, and performance is evaluated as the percentage of correct choices at each separation. Red asterisk indicates correct choice




## AGED RATS ARE IMPAIRED ON BOTH PREFRONTAL CORTEX- AND HIPPOCAMPAL-DEPENDENT TASKS




***Aged rats perform worse than young on the prefrontal cortex-dependent delayed response task.*** All rats performed less accurately as the delay increased, but aged rats performed disproportionally worse than young as the delay increased.

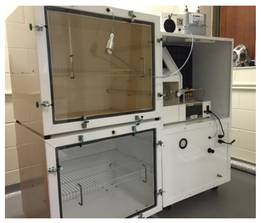



***Aged rats perform worse than young on the hippocampus-dependent TUNL task.*** All rats performed less accurately as the separation between the two locations decreased, but aged rats performed disproportionally worse than young at smaller separations

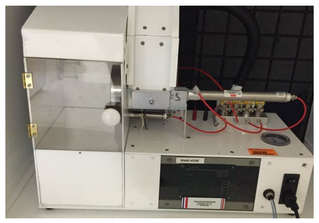
## CANNABIS SMOKE EXPOSURE PROCEDURES

Exposure to cannabis smoke began once rats reached stable performance on the delayed response or TUNL task. For smoke exposure, rats were placed in a ventilated chamber where they were exposed to smoke generated by burning cannabis cigarettes (5.3% THC) in an automated cigarette smoking machine. A within-subjects design was used such that each rat was exposed to smoke from 0, 3, 5, or 10 cigarettes, with at least a 48 h washout period between exposure sessions.

A.

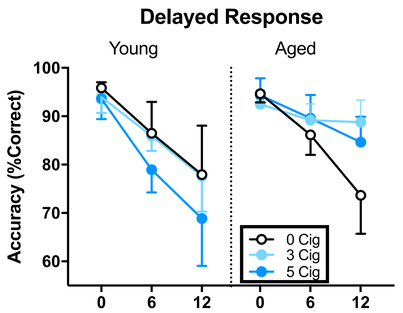


B.

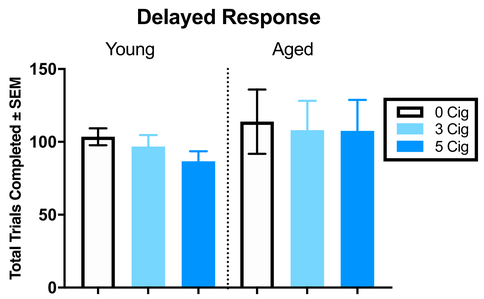


***Smoke exposure apparatus.*** Rats were placed in standard home cages, which were placed into the upper chamber of the exposure apparatus (brown-tinged chamber in A.). Cigarettes were burned sequentially using an automated smoking machine (B.) from which the smoke was pumped into the exposure chamber.

## EFFECTS OF ACUTE CANNABIS SMOKE ON DELAYED RESPONSE

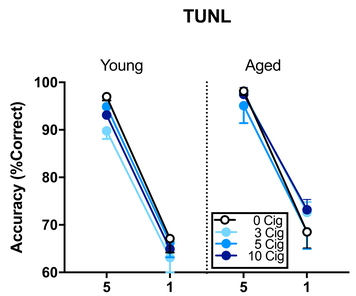



**Cannabis smoke exposure had differential effects on task accuracy in young and aged rats.** Cannabis smoke exposure had contrasting effects on a prefrontal cortex-dependent task, with young rats showing impaired accuracy and aged rats showing enhanced accuracy. (Young: F(2,10)=4.72, p=.04; Aged: F(4,28)=3.04, p=.03).

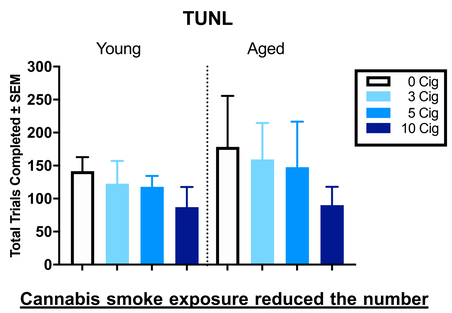



**Cannabis smoke exposure reduced the number of trials completed in aged rats.** Cannabis smoke exposure did not affect the number of trials completed in young rats, but reduced the number of trials completed in aged rats. (Young: F(2,10)=2.14, p=.17; Aged: F(4,28)=4.09, p=.04)

## EFFECTS OF ACUTE CANNABIS SMOKE ON TUNL

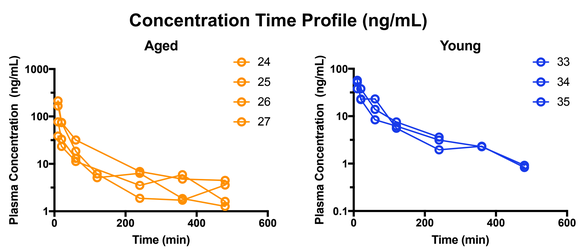



**No effects of cannabis smoke on performance accuracy.** Acute cannabis smoke exposure did not affect performance accuracy on a hippocampal dependent task in either young or aged rats.

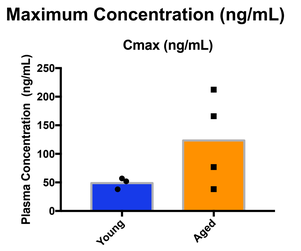



**Cannabis smoke exposure reduced the number of trials completed in aged rats.** Cannabis smoke exposure did not affect the number of trials completed in young rats, but reduced the number of trials completed in aged rats (Young: F(3,9)=3.25, p=.07; Aged: F(3,9)=10.19, p=.003)

## THC PHARMACOKINETICS




***Greater variability in the aged rats.*** Aged rats exhibited a greater variability in their THC concentration time profiles compared to the young rats after a 5-cigarette exposure condition (each line represents data from a single rat).




***Aged rats achieved greater Cmax.*** The aged rats achieved a greater maximum plasma THC concentration compared to the young rats.

## SUMMARY & CONCLUSIONS

- Aged rats are impaired relative to young on both a prefrontal cortex-dependent delayed response working memory task and a hippocampus-dependent TUNL task.
- In the delayed response task, acute exposure to cannabis smoke impaired performance accuracy in young rats, but enhanced accuracy in aged rats.
- In the TUNL task, acute exposure to cannabis smoke, even at a high dose (10 cigarettes) did not affect accuracy in either aged or young rats.
- Cannabis smoke exposure reduced the number of trials completed in aged rats in both tasks; however, the fact that this reduction was evident irrespective of effects on task accuracy suggests that the effects in the delayed response task were not dependent on changes in the number of trials completed.
- Considered together, this pattern of results suggests that in aged rats, which exhibit impaired cognitive performance, cannabis smoke can enhance prefrontal cortex-dependent cognition, but has no effect on hippocampus-dependent cognition

## Acknowledgments & References

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