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 (8-10 mo.) and aged (25-28 mo.) male Fischer 344 x Brown Norway F1 hybrid rats of both sexes were trained in touchscreen operant chambers (left) in a delayed response working memory task and 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 nose poke. 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 nose-poke in same location as in the sample phase to receive a food reward. Performance is evaluated as the percentage of correct choices at each delay.

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 nose poke. In the choice phase, two locations are illuminated (separated by 1, 3, or 5 locations – see diagram), and the rat must nose-poke the location not illuminated in the sample phase to receive a food reward. Performance is evaluated as the percentage of correct choices at each separation.

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 for 1 h in a ventilated chamber in which 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, or 5 cigarettes, with at least a 48 h washout period between exposure sessions.

EFFECTS OF ACUTE CANNABIS SMOKE ON DELAYED RESPONSE

Effects of cannabis smoke on accuracy in the delayed response working memory task in young and aged rats of both sexes. In male rats (n=7 young, n=7 aged) a three-factor ANOVA (Age x Cigarettes x Delay) revealed a significant interaction between Age and Cigarettes (F(2,24)=3.79, p=0.04), such that the effects of cannabis smoke exposure differed as a function of age (improving in young and enhancing in aged). In female rats (n=5 young, n=6 aged), the same analysis revealed no significant main effects or interactions involving Cigarettes.

EFFECTS OF ACUTE CANNABIS SMOKE ON TUNL

Effects of cannabis smoke on accuracy in the TUNL task in young and aged rats of both sexes, in male rats (n=7 young, n=7 aged) a three-factor ANOVA (Age x Cigarettes x Separation) revealed a significant main effect of Cigarettes (F(2,24)=4.98, p=0.02), such that the effects of cannabis smoke exposure differed as a function of age (improving in young and enhancing in aged).

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 in males had differential effects in young and aged rats, with a tendency to impair accuracy in young and enhance accuracy in aged; in contrast there were no effects of cannabis smoke in females.
- In the TUNL task, acute exposure to cannabis smoke had no effects in males; in contrast, exposure in female had differential effects in young and aged rats, with a tendency to impair accuracy in young and enhance accuracy in aged.
- Considered together, this pattern of results suggests that the cognitive consequences of acute cannabis exposure differs as a function of age, but that these differences are moderated by both sex and the particular form of cognition evaluated.