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Low-dose psilocybin enhances novel object recognition but not inhibitory avoidance in adult rats

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Presenter Information

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Introduction

The use of psychedelic substances to treat various psychological disorders is a growing area of interest for researchers. Among the substances being considered, psilocybin has drawn a great deal of attention due to its agonistic effects on the serotonergic system[1], a system that has been repeatedly associated with psychological illness[2]. Previous studies using psilocybin, or similar 5-HT_{2A} agonists, have concluded that administration of the drug can enhance fear learning and novel object recognition (NOR), as well as increase the extinction of conditioned fear[3]. If work with psilocybin or similar psychedelics shows that psilocybin can influence memory strength, it could indicate a potential therapeutic opportunity to treat mental conditions such as phobias or post-traumatic stress disorder (PTSD), which both seemingly result from abnormal fear learning or the inability to extinguished conditioned fear[4]. In the present study, we examined the impact of psilocybin on learning and memory in male and female Sprague-Dawley rats.

Method

Experiment 1: Psilocybin and NOR

Day 1: Acclimation in the open field apparatus for 5 min

Day 2: Rats injected intraperitoneally with vehicle (0.9% saline) or 0.1 mg/kg psilocybin 10 min prior to training

- During training, rats were exposed to two identical objects for 3 min; time spent exploring the objects was measured

Day 3: One object was replaced with a novel object

- Rats were given 5 min to explore the objects; time spent exploring each of the object replicas was measured

Experiment 2: Psilocybin and IA Conditioning

Day 1: Rats underwent IA fear conditioning with a 0.45, 0.65, or 1.0 mA scrambled footshock

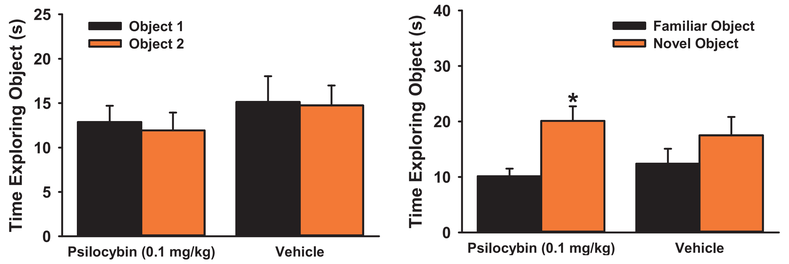
- Immediately after IA training, rats were intraperitoneally injected with vehicle (0.9% saline) or 1 mg/kg psilocybin

Day 3: Rats underwent IA testing to observe their fear memory, during which their initial crossing latency was measured

Results

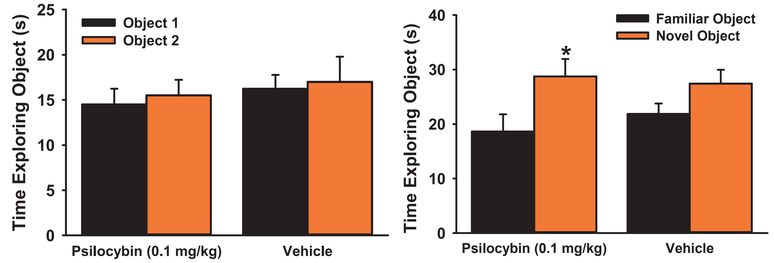
Novel Object Recognition (data are means ± SEM)

Males



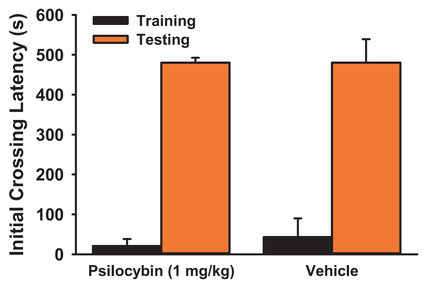
Male rats were injected with psilocybin (0.1 mg/kg) or vehicle 10 min prior to novel object training on Day 1. During training, male rats spent a comparable amount of time exploring both objects, regardless of drug condition. During testing 24 hr later, male rats treated with psilocybin spent significantly more time exploring the novel object than they spent exploring the familiar object, t_7 = 3.991, p = 0.005. Male rats treated with vehicle exhibited no such object preference, t_7 = 1.96, p = 0.091. n = 8 rats / group; * p < 0.01 relative to familiar object.

Females

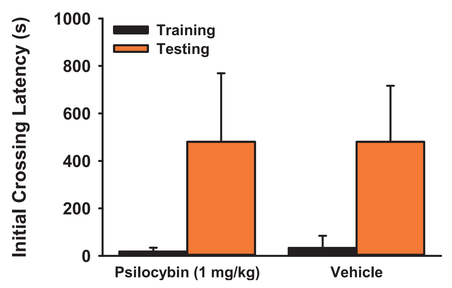


Female rats were injected with psilocybin (0.1 mg/kg) or vehicle 10 min prior to novel object training on Day 1. During training, the rats spent a comparable amount of time exploring both objects, regardless of drug condition. During testing 24 hr later, female rats treated with psilocybin spent significantly more time exploring the novel object than they spent exploring the familiar object, t_7 = 2.553, p = 0.038. Female rats treated with vehicle exhibited no such object preference, t_7 = 1.65, p = 0.15. n = 8 rats / group; * p < 0.05 relative to familiar object.

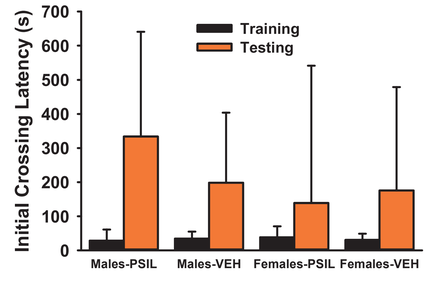
Inhibitory Avoidance (data are medians ± interquartile range)



Male rats were exposed to step-through inhibitory avoidance training with 1.0 mA footshock; the rats were injected with psilocybin (1 mg/kg) or vehicle immediately after training. Although the rats demonstrated successful fear learning, no group differences were observed for training or testing. n = 11-12 rats / group.



Female rats were exposed to step-through inhibitory avoidance training with 0.65 mA footshock; the rats were injected with psilocybin (1 mg/kg) or vehicle immediately after training. Although the rats demonstrated successful fear learning, no group differences were observed for training or testing. n = 11-12 rats / group.



Male and female rats were exposed to step-through inhibitory avoidance training with 0.45 mA footshock; the rats were injected with psilocybin (1 mg/kg) or vehicle immediately after training. No group differences were observed for training or testing. n = 6-9 rats / group.

Conclusions

Experiment 1: Psilocybin and NOR - In both male and female rats, psilocybin-treated animals spent significantly more time exploring the novel object than the familiar object. Such a difference was not observed in vehicle-treated animals, suggesting that psilocybin did enhance novel object recognition memory.

Experiment 2: Psilocybin and IA Conditioning - There was no significant impact of psilocybin on IA conditioning. It could be that the specific dose utilized or the timing of injection prevented psilocybin from exerting a significant effect on fear memory.

Overall Conclusions - Differences in observed effects could be due to dose/timing differences or differential effects of psilocybin on different types of learning.

References

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