Acute Effects of Psilocybin on Anxiety-Related Behaviors in Non-human Primates

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Background
Psilocybin is a 5HT2A receptor agonist that has rapid-acting antidepressant effects in humans1. Recently, the effectiveness of psilocybin to treat other psychiatric illnesses including anxiety disorders has been explored2,3,4. The mechanisms behind its therapeutic effects remain unknown and are of considerable interest. Most of the preclinical studies on psilocybin have been done in rodent models. However, non-human primate (NHP) models are critical to bridge the translational research gap between rodents and humans. The Kalin Lab has a well-established NHP model of pathological anxiety5, which is ideally suited to investigate psilocybin’s effects on threat-related behaviors in NHPs and translate these findings to humans.

Study Design
Five rhesus macaques (2M, 3F) were administered vehicle, 0.3, and 1.0 mg/kg of psilocybin intramuscularly in a within-subjects, counterbalanced, crossover design. There were approximately 2 weeks in between treatments.

Study Timeline
Immediately after treatment, animals were placed in the test cage for a modified version of the Human Intruder Paradigm. A human intruder stared at the animal for approximately 3 minutes straight at 15, 30, 60, 90, 120, and 180 minutes after psilocybin injection. The animal was alone in the test cage with access to water at all other times. Behavioral observations lasted approximately 183 minutes long.

Behavioral Conditions
Two trained observers scored the 3 minute stare conditions as well as the 5 minutes of behavior preceding the stare conditions.

Conclusions
We found that psilocybin significantly decreased locomotion (F(1,56.19) = 9.55, p = 0.021) in a dose-dependent manner. There were also significant interactions between dose and context (stare vs alone) on hypervigilance (F(1,163.00) = 9.19, p = 0.0028), stereolocomotion (F(1,163.00) = 4.21, p = 0.042) and vocalizations (F(1,163.00) = 26.08, p = 9.0e-7). These data indicate acute psilocybin-induced anxiety as reflected in a decrease in locomotion and vocalizations along with an increase in hypervigilance. Some studies in rodents are consistent with the acute anxiogenic effects of psilocybin observed here, and anxiety has been reported as an “adverse effect” of acutely administered psilocybin in humans. Going forward, we plan to select a dose of psilocybin to test its effects on anxiety-related behaviors 24 hours later to match the timeline of when therapeutic effects are observed.

References

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