RISE RESEARCH INNOVATION SCHOLARSHIP ENTREPRENEURSHIP

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Mescaline-Induced Modulation of Fear and Reward Pathways: BOLD phMRI Study in Rats

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Background & Goals

Mescaline is a psychoactive alkaloid found in peyote, acting as a 5-HT2A/2C agonist and inducing hallucinations and euphoria through sensory system effects. Sensory perception, dominated by olfaction in rodents, processes and interprets external stimuli.

The goal of this study was to examine mescaline's effects on responses to olfactory stimuli in awake rats. Mountain lion urine and benzaldehyde were used to activate fear and reward pathways, respectively. This study aimed to address gaps in the current knowledge about mescaline and hallucinogens overall, by offering insight into the neurobiological mechanisms behind its sensory effects.

Conclusion

This study illustrated that rats under the influence of mescaline exhibit a more significant negative BOLD response as compared to vehicle rats. The cerebellum had a separate response as compared to the rest of the cortex, with varying degrees of change in positive and negative BOLD signaling in deep cerebellar nuclei. The functional connectivity of the hippocampus increased, carrying potential implications for memory and learning. Of note, mescaline inhibits a change in BOLD response to rewarding olfactory stimuli. However, the positive and negative BOLD responses are conserved in response to olfactory fear stimuli, which prompts further exploration of mescaline's effects on sensory processing.

Future Directions

Multimodal Sensory Inputs
- Visual Stimuli: flashing lights
- Auditory Stimuli: high frequency tone
- Tactile Stimuli: electrode shock on paw

Behavioral Testing
- Effects on learning and memory: Barnes Maze, Open Field Test, Novel Object Recognition

Comparative Studies
- Other psychedelics including psilocybin, LSD, and 5-MeO-DMT

Acknowledgements

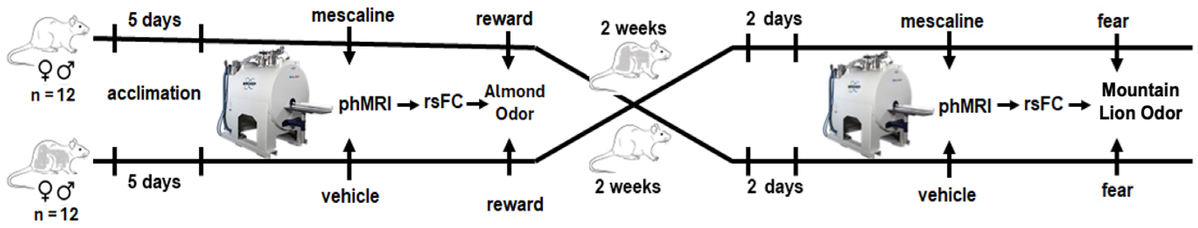
EKAM THE IMAGE OF DRUG DISCOVERY

NIDA Drug Distribution Program

NIDA Advancing Addiction Science for 50 years

Northeastern University Center for Translational Neuro-imaging

Process & Methods



Sprague Dawley rats (12 male, 12 female) were split into 2 cohorts that received either 50 mg/kg Mescaline (Mesc.) or the same volume of vehicle (VEH). All experiments were conducted on reverse L/D cycles to preserve circadian rhythms. Rats were exposed to benzaldehyde during the first image acquisition and were then allowed 2 weeks to wash out. The Mesc/VEH cohorts were then swapped, and the same process was repeated with mountain lion urine.

Significant Findings

Pharmacological fMRI
- Mesc. signficantly decreases positive BOLD signaling in the cerebellum and posterior midbrain regions.
- Mesc. increases negative BOLD signaling in the lateral midbrain and hindbrain.

Resting State Functional Connectivity
- Mesc. increases connectivity between the hippocampus and thalamus, and cerebellar nuclei, respectively.
- Mesc. also increases activity in the hippocampus and olfactory bulb, as well as between the somatosensory cortex and deep cerebellar nuclei.

Fear vs. Reward fMRI
- Mesc. decreases positive and negative BOLD signaling in response to reward stimuli as compared to VEH
- Positive BOLD was similar in Mesc. and VEH groups exposed to fear stimuli
- Negative BOLD response to fear in Mesc. was greater than negative BOLD in VEH