Neural Processing of a Cocaine-Associated Odor Cue Revealed by Functional MRI in Awake Rats

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Introduction

Drug-paired stimuli, or cues, can elicit relapse to cocaine seeking and can act as an incentive in the absence of the drug. Previously neutral stimuli repeatedly associated with self-administered cocaine can provoke heightened levels of drug seeking, even after periods of abstinence from drug use. Febo *et al*. [1] used pharmacological MRI in awake rats to investigate areas of the brain showing increased blood oxygen level dependent (BOLD) signal in response to cocaine. The present study used methods similar to those cited above for awake rats in order to investigate the neural processing of a cocaine-associated odor cue.

Experimental

Using an olfactory conditioning procedure, brain stimulation reward threshold measurements, and functional magnetic resonance imaging (fMRI), we investigated brain stimulation reward threshold change and fMRI neural activation in response to a cocaine-associated odor cue. In the first brain stimulation experiment, over 10 days of rate-frequency curve-shift testing, rats were administered intravenous cocaine (1.0mg/kg) paired with a contextual cue of peppermint odor previously placed in the operant chamber or they were given vehicle treatment (no cocaine) in the presence of no olfactory cue. Following a 14-day drug-free rest period, rats were again given the rate-frequency curve-shift threshold test with or without the odor cue. In a second experiment, rats were similarly conditioned with a peppermint odor but with intraperitoneally delivered cocaine (10 mg/kg). After a 14-day rest period, rats were imaged for their blood oxygen level dependent (BOLD) in response to the cocaine-paired peppermint odor versus an unpaired neutral lemon odor.

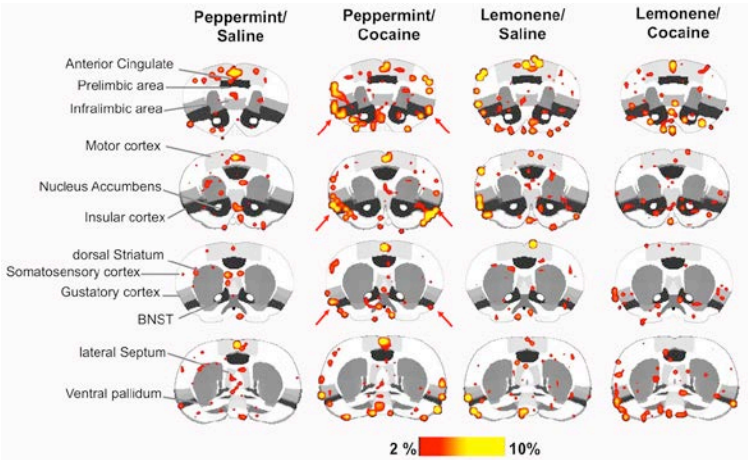

Figure Caption: Composite functional magnetic resonance activation maps in rats treated with saline or cocaine in the presence of an olfactory stimulus. Scale bar hue indicates percent change value of voxels. These correspond to % changes but also to p value < 0.05, FDR corrected.

Results and Discussion

In the brain stimulation experiment, expected significant reward threshold shifts were produced by cocaine and, importantly, about half that level of shift was produced by the paired contextual olfactory cue. In the fMRI experiment, the insular cortex showed a significantly greater BOLD activation in cocaine-treated versus saline-treated animals to the olfactory cue, but not with the unpaired lemon scent.

Conclusions

These data are in agreement with previous studies suggesting a role of the insular cortex in attributing reward value (positive or negative) to conditioned odor stimuli.

Acknowledgements

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References

[1] Febo M., *et al,* Neuropsychopharmacology 36:936-43 (2005).
[2] Johnson *et al*, Neuroscience Letters *in press* (2013).