

# **Inactivation of the Interoceptive Insula Disrupts Drug Craving and Malaise Induced by Lithium**

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## **Abstract**

Addiction profoundly alters motivational circuits so that drugs become powerful reinforcers of behavior. The interoceptive system continuously updates homeostatic and emotional information that are important elements in motivational decisions. We tested the idea that interoceptive information is essential in drug craving and in the behavioral signs of malaise. We inactivated the primary interoceptive cortex in amphetamine-experienced rats, which prevented the urge to seek amphetamine in a place preference task. Interoceptive insula inactivation also blunted the signs of malaise induced by acute lithium administration. Drug-seeking and malaise both induced Fos expression, a marker of neuronal activation, in the insula. We conclude that the insular cortex is a key structure in the perception of bodily needs that provides direction to motivated behaviors.