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Human drug addiction behaviors tied to specific impairments in six brain networks

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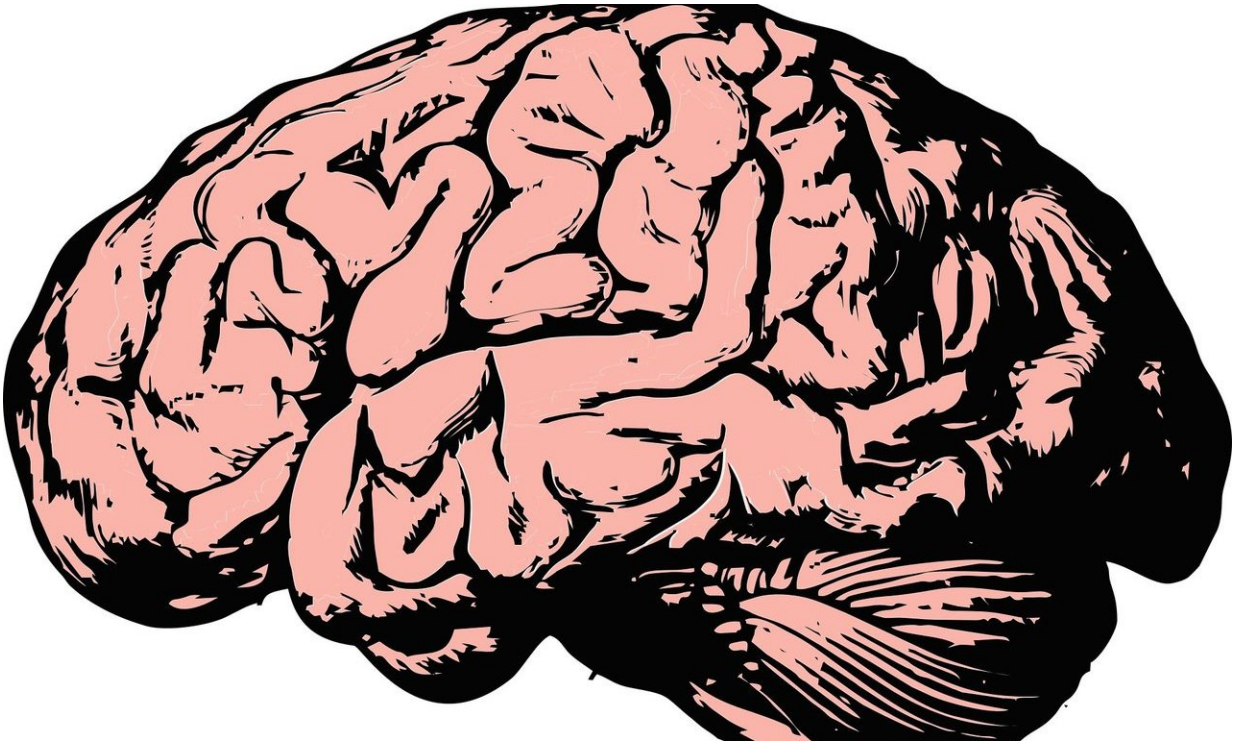

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Specific impairments within six large-scale brain networks during drug cue exposure, decision-making, inhibitory control, and social-emotional processing are associated with drug addiction behaviors, according to a systematic review of more than 100 published neuroimaging studies by experts at the Icahn School of Medicine at Mount Sinai and published

Wednesday, June 6 in the journal *Neuron*.

Drug addiction is a disorder that encompasses not only excessive drug-seeking and taking, but also fundamental changes in cognition and emotional processing. It comprises core clinical symptoms and behavioral manifestations including a chronically relapsing cycle of intoxication, bingeing, withdrawal, and craving that propels uncontrollable drug use despite adverse consequences and a reduction in the pleasure derived from the drug. While much of the early research on drug addiction focused on understanding the rewarding properties of the drug, recent research has made it increasingly clear that cognitive and emotional impairments support the initiation, escalation, and maintenance of the cycle of addiction. A better understanding of the underlying impaired neural mechanisms in human drug addiction is critical to paving the way for the development of more targeted, evidence-based treatment interventions and timely prevention approaches.

The Impaired Response Inhibition and Salience Attribution (iRISA) model, first published in 2002 by Rita Goldstein, Ph.D., Professor of Psychiatry and Neuroscience and Director of the Neuropsychoimaging of Addiction and Related Conditions research program at the Icahn School of Medicine at Mount Sinai, and Nora Volkow, Director of NIDA, proposed that impairments of two broad neuropsychological functions—response inhibition (a cognitive process that permits individuals to inhibit their impulses) and salience attribution (the property of tagging something as valuable or important)—and their underlying neural substrates contribute to the cycle of addiction across a broad range of substances of abuse. The iRISA model uses multiple neuroimaging modalities including magnetic resonance imaging, electroencephalogram (EEG) and derived event-related potentials, positron emission tomography, and neuropsychological testing to explore the underlying neurobiology of human drug addiction and the shift to

excessive salience attributed to the drug and drug-related cues at the expense of other salient reinforcers as associated with impaired self-control (especially in a drug related context) and increased drug taking in drug addicted individuals.

"We conducted the current review to update the iRISA model with the most recent evidence from the neuroimaging literature by systematically reviewing 105 task-related neuroimaging studies published since 2010," says Dr. Goldstein, last and senior author of the paper. "We found consistent impairments in brain function in six large-scale brain networks during performance of different tasks. While the involvement of these specific brain networks was task-specific, we generally observed that in a drug-related context (e.g., during exposure to drug cues) drug addicted individuals had increased engagement of the brain networks underlying decision making, inhibitory control, and social-emotional processing, but a blunted response during non-drug related tasks, as predicted by the iRISA model."

Specifically, the Mount Sinai study team assessed brain function in drug addiction across a number of brain networks, including findings from whole-brain analyses of significant group differences. They organized the results across six large-scale brain networks that showed impairment of brain function in addiction, encompassing the "reward network," which includes subcortical and cortical brain regions activated during the appraisal of subjective value; the striatal "habit network," which underlies learning of automated behavior; the "salience network," regions involved in (re)directing attentional resources toward salient stimuli; and the "executive network," which supports the selection of possible behavioral responses (often also named the inhibitory control network).

Two additional networks, which were not discussed in prior reviews of the iRISA model, were found to be relevant to brain function in drug

addiction: the "self-directed network," which is activated during self-directed/referential cognitive processes, and the "memory network," involved in flexible, multi-cue learning and memory.

"Our review is the first systematic approach to integrate what we know about the function of each of these networks into a comprehensive model underlying drug addiction symptomatology across the addiction cycle," says Anna Zilverstand, Ph.D., Assistant Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai and first author of the paper. "We demonstrated common deficits underlying drug addiction independent of the primary drug of choice, which are associated with measures of daily, real-life, drug use and which predict onset, escalation, and relapse into drug use. Our work could inform the development of treatments specifically targeted to alleviate these brain-behavioral deficits."

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