New insights into brain's reward circuitry could aid addiction treatment

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Clustering of snRNA-seq data. Single nucleus RNA sequencing was performed on nucleus accumbens samples from male, drug-naïve Brown Norway rats and data were clustered based on transcriptomic profile. Credit: Scientific Reports (2024). DOI: 10.1038/s41598-024-69255-0

A research team—co-led by Penn Nursing—has made a significant breakthrough in understanding the complex neural circuitry underlying reward and addiction by identifying 34 distinct subtypes of medium spiny neurons (MSNs) in the nucleus accumbens (NAc), a key brain region involved in pleasure and motivation. The findings, published in
the journal *Scientific Reports*, offer insights into the diversity of these neurons and their potential roles in substance use disorders.

MSNs are the primary type of neuron in the NAc and have long been classified based on their expression of dopamine receptors. However, this new research reveals a far more intricate picture of MSN diversity. By analyzing a massive dataset of single-nucleus RNA sequencing data from rat brains, the researchers identified 34 distinct MSN subtypes, each with its own unique genetic profile.

"Our study challenges the traditional view of MSNs as a homogenous population," said co-lead author Heath D. Schmidt, Ph.D., Professor in Penn Nursing's Department of Biobehavioral Health Sciences. "By uncovering this level of diversity, we can begin to understand how specific MSN subtypes contribute to different aspects of reward processing and addiction."

The researchers also found that these MSN subtypes are conserved across species, suggesting that the findings may have broad implications for human brain function and behavior. Additionally, by analyzing genetic data linked to substance use disorders, the team identified potential differences in the roles of specific MSN subtypes in these conditions.

This research provides a foundation for future studies aimed at developing targeted therapies for addiction and other brain disorders. By understanding the specific functions of different MSN subtypes, scientists can develop treatments that precisely target these cells, potentially leading to more effective and less harmful interventions.

**More information:** Benjamin C. Reiner et al, A single-nucleus transcriptomic atlas of medium spiny neurons in the rat nucleus accumbens, *Scientific Reports* (2024). DOI:
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