RESEARCH HIGHLIGHTS



Consumption control

The consumption of food is regulated not only by metabolic demands but also by external factors, such as the threat of predation, which can quickly inhibit feeding. Inhibitory projections from the medial nucleus accumbens shell (NAcSh) to the lateral hypothalamus (LH) have been proposed to convey signals about such external stimuli; however, the underlying circuit has not been resolved. Now, Lüscher and colleagues show that NAcSh dopamine D1 receptor-expressing medium spiny neurons (D1R-MSNs) that project to the LH are key drivers of this circuit and regulate feeding behaviour.

NEURAL CIRCUITS

To identify which NAcSh neurons project to the LH, the authors injected a retrograde tracer into the LH of transgenic mice in which D1R-MSNs or D2R-MSNs were fluorescently labelled. In both types of mice, the tracer labelled many neurons in the medial NAcSh. Whereas ~90% of the NAcSh-LH projections were found to be DR1-MSNs in the D1R-MSN-transgenic mice, only ~5% of the NAcSh-LH projections were identified to be D2R-MSNs in the D2R-MSN-transgenic animals. Thus, most neurons that project from the NAcSh to the LH are DR1-MSNs.

Next, the authors expressed channelrhodopsin 2 (ChR2) in NAcSh D1R-MSNs or D2R-MSNs in mice. In brain slices taken from these animals, they recorded from LH cells while stimulating ChR2-expressing MSNs with blue light. 56% of LH neurons exhibited inhibitory postsynaptic currents following light stimulation of D1R-MSNs, whereas only 17% of LH neurons exhibited such currents with light activation of D2R-MSNs. This suggests that D1R-MSNs provide most of the inhibition in the LH that comes from the NAcSh.

To assess the role of NAcSh D1R-MSNs in food consumption, the authors recorded from these cells in freely feeding mice. These neurons showed a reduction and an increase in activity at the beginning and the end of feeding bouts, respectively. Moreover, optogenetic inhibition of NAcSh D1R-MSNs promoted feeding in satiated mice and mitigated the ability of distracting auditory or visual stimuli to rapidly stop the mice feeding, suggesting that reductions in the activity of NAcSh D1R-MSNs permit feeding behaviour. Furthermore, activation of the terminals of ChR2-expressing NAcSh D1R-MSNs in the LH with blue light suppressed food consumption even in hungry

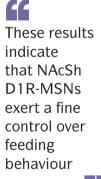
mice and, indeed, could rapidly stop ongoing feeding. These results indicate that NAcSh D1R-MSNs exert a fine control over feeding behaviour.

Previous studies had implicated LH GABAergic neurons in the control of feeding. To examine whether these neurons are the targets of NAcSh D1R-MSNs, the authors generated mice in which NAcSh D1R-MSNs were fluorescently labelled and LH GABAergic neurons could be selectively targeted in retrograde-tracing experiments. Indeed, such experiments revealed monosynaptic connections between D1R-MSNs and LH GABAergic neurons. Furthermore, the authors found that direct optogenetic inhibition of LH GABAergic neuron activity suppressed feeding behaviour.

Together, these data suggest that NAcSh D1R-MSNs via their projections onto LH GABAergic neurons allow tight control over feeding behaviour in response to external stimuli.

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ORIGINAL RESEARCH PAPER O'Connor, E. C. et al. Accumbal D1R neurons projecting to lateral hypothalamus authorize feeding. *Neuron* 88, 553–564 (2015)



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