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REWARD

A separate sweet circuit

Ingestion of sugar activates taste and nutrition-sensing pathways, but it is not known whether these pathways have shared or distinct neural circuits. Tellez *et al.* now show that, in mice, the dorsal and ventral regions of the striatum convey the nutritional and hedonic values of sugar, respectively.

To separate these values, the authors used a paradigm in which mice had to lick a spout to consume a solution containing a non-nutritive sweetener, and this licking triggered intra-gastric administration of either sugar (D-glucose) or the non-nutritive sweetener. Dopamine levels, measured by microdialysis, increased in the ventral striatum (VS) following licking and intra-gastric release of either sugar or the non-nutritive sweetener; however, these levels only increased in the dorsal striatum (DS) if licking was coupled with intra-gastric D-glucose release. Reducing the hedonic value of the licked solution, by including a bitter-tasting compound with the non-nutritive sweetener (and accompanying this solution with intra-gastric release of D-glucose), blocked the lick-induced increase in dopamine levels in the VS but not in the DS.

In a separate experiment, matching a non-nutritive sweetener at the spout to intra-gastric administration of a non-metabolizable form of glucose prevented a licking-induced increase in dopamine release in the DS but not in the VS. Thus, in the VS the licking-induced increase in dopamine release depends on hedonic value of the spout solution, but in the DS it depends on nutritional value of the accompanying intra-gastric solution.

Dopamine D1 receptor (D1R)-expressing neurons (D1R neurons) in the striatum show an increase in excitability in response to dopamine release. Here, the authors selectively ablated D1R neurons in either the VS or DS, and then coupled licking of a spout containing a bitter solution to the intra-gastric administration of D-glucose solutions of different concentrations. Mice with VS depletion of D1R neurons made fewer licks of the bitter solution when it was paired with intra-gastric infusion of low-glucose solutions than did mice with DS depletion of D1R neurons in the same paradigm. However, when the intra-gastric glucose concentration was increased, mice with VS depletion of D1R neurons made more licks of the bitter spout solution, at a level similar to that observed in non-ablated control mice, whereas mice with DS depletion of D1R neurons did not. This suggests that DS D1R neurons are required for the nutrient-driven consumption of unpalatable solutions.

The authors next selectively expressed channelrhodopsin 2 in D1R neurons in mice. These mice were trained to lick a spout that contained a non-nutritive sweetener, which triggered light pulses to DS- or VS-region neurons, rather than delivering an intra-gastric infusion of glucose. Licking-induced optogenetic stimulation of DS D1R neurons increased the rate of licking of the sweetener, and also suppressed the inhibitory effect on licking rate of including the bitter taste in the solution. By contrast, although licking-induced stimulation of D1R-neurons in VS also increased the licking rate of the non-nutritive sweetener solution, activation of these neurons was insufficient to overcome the decrease in the licking rate induced by including the bitter tastant. Thus, activation of DS D1R-neurons mimicked the detection of nutritional value that would occur in the presence of sugar, but activation of VS D1R neurons did not.

Together, these findings show that, in mice, there are separate striatal circuits for the encoding of the taste and nutritional value of sugar, which may have implications for developing strategies to reduce sugar intake in humans.

Fiona Carr

> “DS D1R neurons are required for the nutrient-driven consumption of unpalatable solutions”

ORIGINAL ARTICLE Tellez, L.A. *et al.* Separate circuitries encode the hedonic and nutritional values of sugar. *Nat. Neurosci.* http://dx.doi.org/10.1038/nn.4224 (2016)

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