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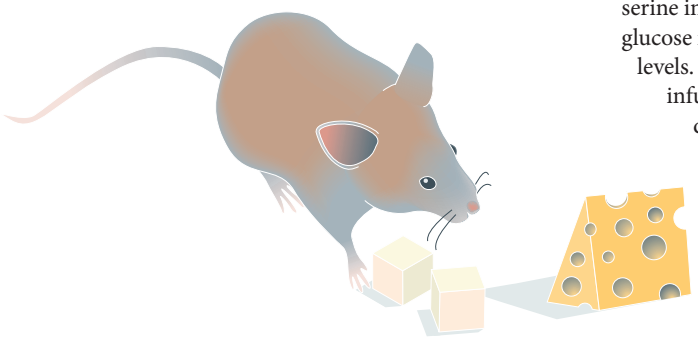
CHEMOSENSATION

Tasteless mice prefer sugar

As our expanding waistlines testify, many humans (and other animals) prefer carbohydrates over proteins and amino acids. Ren *et al*. now show that glucose oxidation regulates this preference independently of the taste and caloric value of a nutrient.

The authors used wild-type mice and mice that lack the transient receptor potential channel (TRP) M5 (*Trpm5*$^{-/-}$ mice), an ion channel that is required for sweet, bitter and L-amino acid taste signalling. Unlike wild-type mice, *Trpm5*$^{-/-}$ mice showed no immediate preference for a glucose solution over an isocaloric solution of serine. However, they did develop such a preference over time, which suggests that post-ingestive factors might regulate this taste-independent development of glucose preference.



What might these factors be? Both wild-type and *Trpm5*$^{-/-}$ mice had a higher respiratory quotient (a measure of glucose oxidation) during glucose consumption than during serine consumption. Blood glucose and liver glycogen levels also increased after glucose but not serine consumption. Interestingly, only respiratory quotient values were significantly correlated with glucose intake. This suggests that the ability of glucose to increase glucose oxidation — rather than its ability to raise blood glucose levels per se — determines its reinforcing value, and that this reinforcing value is independent of taste.

On investigation of whether taste-independent glucose preference is reflected in the reward system, the authors found that compared with serine infusions, gastric infusions of glucose increased striatal dopamine levels. Specifically, gastric glucose infusions increased extracellular dopamine levels in the dorsal striatum, whereas serine infusions decreased them in the ventral striatum. To determine whether glucose oxidation triggers these nutrient-specific changes in dopamine levels, the authors infused wild-type mice systemically with 2-deoxyglucose, which inhibits glucose metabolism without decreasing blood glucose levels. The 2-deoxyglucose infusion decreased striatal dopamine levels within 1 hour and this decrease was quickly reversed by a subsequent glucose infusion. In addition, *Trpm5*$^{-/-}$ mice consumed more glucose after an injection with 2-deoxyglucose than after a vehicle injection. Together, these data indicate that reinstating glucose oxidation levels — by consuming glucose after 2-deoxyglucose injections — increases the reward value of glucose independently of its sweetness.

These findings show that glucose oxidation levels rather than the taste or the caloric value of a nutrient can regulate carbohydrate preference, and support the hypothesis that dopamine regulates food intake through metabolic rather than gustatory pathways.

Leonie Welberg

ORIGINAL RESEARCH PAPER Ren, X. *et al.* Nutrient selection in the absence of taste receptor signaling. *J. Neurosci.* **30**, 8012–8023 (2010)