Processed foods and food reward

Processed foods compromise the fidelity of gut-brain signaling of food reinforcement

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Signals that convey nutritional information from the gut to the brain regulate food reinforcement and food choice (1–4). Specifically, although central neural computations execute choice, the gut nervous system communicates information about the nutritional outcomes of choices to the brain so that representation of food values can be updated. Here, we discuss recent findings that suggest the fidelity of gut-brain signaling and the resulting representation of food value is compromised by processed foods (3, 4). Understanding this axis could inform about feeding behavior involving processed foods and obesity.

In 1947, experiments in which rodents were fed isocaloric diets that varied in volume revealed that rodents accurately titrate the volume of food consumed to maintain constant caloric intake across days, indicating that “rats eat for calories” (5). This implied that a signal must be generated to communicate the energetic value of food to the brain to guide intake. Later, others confirmed that these “post-ingestive” signals can be reinforcing by showing that animals are able to form preferences for flavors consumed with calories compared with those consumed without—a form of learning called flavor-nutrient conditioning (FNC) (6). Importantly, FNC occurs even in the absence of concomitant oral sensory stimulation, which isolates post-ingestive signals as the key reinforcer (7). For example, animals that lack the neurobiological machinery to transduce sweet taste nevertheless form preferences for water containing sucrose compared with water alone, and this behavior is accompanied by rises in extracellular dopamine in the striatum, a brain region that is necessary for motivation and learning. Critically, however, infusion of the antimetabolic agent 2-deoxyglucose, which blocks the ability of cells to use glucose as fuel, attenuates extracellular dopamine and preference formation (8). These signals are likely neural rather than endocrine (that is, hormonal) because the rise in extracellular dopamine is rapid after intragastric infusion of glucose (8). Furthermore, infusion of glucose but not nonmetabolizable glucose at the portal vein increases extracellular dopamine (8). Collectively, this suggests that in animals, the unconditioned stimulus that drives sugar (carbohydrate) reinforcement is a metabolic signal produced when cells use glucose for fuel; this signal is then sensed by a mechanism in the portal vein and subsequently conveyed to the brain to regulate dopamine signaling (see the figure). The exact nature of the metabolic signal, its sensor, and how it is transmitted to the brain are unknown.

There is evidence that a similar mechanism operates in humans. Neuroimaging studies have established that food cues, which are predictive of calories, activate the striatum in humans and that the magnitude of these responses is regulated by metabolic signals (9). Specifically, increases in blood plasma glucose after consumption of a carbohydrate-containing beverage predicted the magnitude of conditioned striatal response to the sight and taste of the beverage. Because glucose must be present to be used as a fuel, this suggests that in humans, as in animals, carbohydrate reinforcement depends on a metabolic signal associated with the presence of glucose. Additionally, observations in humans suggest that brain representation of the metabolic signals is independent from conscious perceptions, such as food-like. The same striatal responses to the calorie-predictive flavor cue that were so tightly coupled to changes in plasma glucose were unrelated to the rated liking of the drinks by participants. This is consistent with additional neuroimaging studies that find that the actual energy density, and not the estimated energy density or rated liking of food pictures, predicts willingness to pay for foods and striatal reward circuit responses (3, 10). These observations suggest that neural representation of these reinforcing nutritional signals is independent of conscious perceptions about food. An intriguing possibility is that the metabolic signals are important generators of incentive salience (how cues become motivationally meaningful) and that the distinct pathways initiated by these signals map onto food-wanting versus food-like neural circuits (11).

Lipids are another important source of energy that are metabolized differently from carbohydrates. Accordingly, the pathway by which the energetic value of fat is communicated to the brain differs. Blocking oxidation of fat increases fat appetite, and blocking glucolysis of fats increases sugar appetite. However, vagotomy (surgery to sever the vagus nerve) in mice only disrupts the increased appetite for fat, leaving glucose appetite unaffected (12). Consistently, like glucose, direct infusion of lipids into the gut produces an immediate rise in extracellular striatal dopamine. However, this occurs through a peroxisome proliferator–activated receptor α (PPARα)–specific mechanism (2). PPARα is expressed by duodenal and jejunal enterocytes in the small intestine and signals to the vagus nerve through as-yet-unknown mechanisms. Like striatal dopamine release by glucose, the rise in dopamine is rapid, which is consistent with neural rather than endocrine signaling. In addition, activation of these vagal sensory neurons in the upper intestine that project to the right nodose ganglion, hindbrain, substantia nigra, and dorsal striatum is sufficient to support reward learning (place preference) and to release striatal dopamine in mice (13). Whether this pathway exists in humans is unclear, and whether such metabolic neural afferent (MNA) pathways exist for other lipids and nutrients is being investigated.

The discovery that the unconditioned stimulus supporting food reinforcement is an MNA signal—that is at least sometimes independent from sensory pleasure—is surprising. However, deeper reflection reveals the elegance of this solution. All organisms must procure energy to survive, and most lack higher-order brain functions that support consciousness. Thus, the mechanism likely reflects a conserved system designed to relay the nutritive properties of food to central circuits in the brain that regulate feeding independently of consciousness, so food is as reinforcing as it is a useful source of energy. Accordingly, a high-fidelity transfer of nutritional information from the gut to the brain is critical for an accurate estimation of value.

Although it is clear that the modern food environment promotes obesity and diabetes, controversy surrounds the precise mechanisms by which this happens. Modern processed foods tend to be energy dense, are engineered to be as irresistible as possible, and provide nutrients in doses and combinations not encountered before. Because energetic signals drive reinforcement, increased doses may increase the reinforcing and hence...
“addictive” potential of processed foods. However, these may not be the only factors to contribute to increased diabetes and obesity.

To increase palatability, non-nutritive sweeteners (substances with no caloric content) are frequently added to foods and beverages that also contain nutritive sugars and starches. For example, sugar-sweetened beverages contain the nutritive sugars glucose and fructose, as well as non-nutritive sweeteners sucralose and acesulfame K. Yogurts often contain nutritive sugars and non-nutritive sweeteners such as stevia leaf extract. A brief perusal of food labels at a grocery store will reveal many examples of foods and beverages that contain both nutritive sugars and non-nutritive sweeteners.

Reinforcing metabolic signals to the brain

In this proposed model for reinforcing metabolic neural afferent (MNA) signals, the signal for fat depends on PPARα-mediated activation of vagal sensory afferents that project to the right nodose ganglion, hindbrain, substantia nigra, and dorsal striatum. The signal for carbohydrate is generated during glucose oxidation and activates an unknown portal vein sensor, which induces a signal that activates midbrain dopamine neurons projecting to the striatum. An independent cortical network integrates MNA signals with conscious value.

Subjective value

Cortical

Nutritive value

Striatal dopamine
Substantia nigra
Hindbrain

Right nodose ganglion
Vagus nerve

Neural afferent signal

PPARα activation

Metabolic signal generation

Carbohydrate
Other macro- and micronutrients

Glucose oxidation

Unknown afferent pathway

Portal vein sensor

REFERENCES AND NOTES


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