Brain activation in relation to specific dietary components: what does fMRI measure and how should one interpret cravings for certain foods?1,2

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In this issue of the Journal, Lennerz et al (1) used fMRI to identify areas of the brain that appear to be differentially activated by foods with a high or low glycemic index (GI). Overweight and obese men were studied 4 h after consuming 1 of 2 meals with predicted GIs of 84% and 37%. Unfortunately, the blood glucose measurements made in the study do not allow reliable comparison of the glycemic response to be made, because antecubital venous sampling was used. The fMRI assessments were also not performed fasted so there is no information of the change in brain “activation” as a consequence of either meal, just a comparison of the 2 meals 4 h after ingestion. This analysis showed that the higher-GI meal led to greater brain activity centered in the right nucleus accumbens, other areas of the right striatum, and the olfactory area. These observations add to a growing literature on the effect of different foods and food ingredients on brain activation and are linked to a possible neuro-psychological basis to food cravings. They may also be interpreted by some as providing possible links to dopaminergic systems in the brain, which in other contexts are linked to addictive behavior. However, before such studies are used in a wider context, it is important to address several features in more detail.

Glucose is the primary metabolic fuel used by the central nervous system to support its energy needs. The human adult requires ~6 g glucose/h (2), and only after prolonged fasting can some of this be replaced by alternative fuels such as ketones. Thus, it is essential that dietary carbohydrate content is sufficient to deliver glucose to the brain and to enable liver glycogen storage to be maximized to support brain requirements between meals. It is not surprising that increased availability of glucose is associated with activation of the brain, although a substantial amount of additional work is needed to conclude that this is harmful rather than a normal physiologic drive to consume carbohydrate to support brain function.

Brain imaging is a powerful technique that is enhancing neuroscience research. fMRI is widely used to map brain activity. However, rather than detecting neuronal activity directly, fMRI exploits the local increase in blood flow and hence blood volume and blood oxygenation that occur to support the resulting increase in metabolic demand (3, 4). Most conventional fMRI studies are based on the BOLD effect (5), which is the term used to describe the increase in MRI signal due to the change in blood oxygenation and blood volume secondary to the increase in blood flow.

The rapid and widespread uptake of fMRI over the past 2 decades is due to the high sensitivity and spatial resolution of BOLD compared with alternative techniques (nuclear medicine and electrophysiology). For instance, BOLD fMRI has been used to map the primary cortical representation of taste and odor in humans (6) and to study response to pleasant and aversive stimuli (7). However, BOLD is a relative measure and as such it can only be used to detect changes relative to baseline, so experiments have to be carefully designed to produce short perturbations in brain activity. This is particularly limiting when studying the hedonic and homeostatic responses to food because these often occur over a longer time scale. Some experiments have been designed to tackle this problem; for instance, BOLD fMRI has been used to assess the cortical response to the infusion of gut hormones (8) or glucose administration (9). Alternatively, arterial spin labeling MRI can directly measure the increase in blood flow (10). This is less sensitive and more technically challenging than BOLD, but it does allow direct comparison of brain activity between different physiologic states—for instance, the early postprandial changes in hypothalamic and insula activity after the intake of fat (11) and changes in response to GI, as shown in the current study by Lennerz et al. Furthermore, to more fully understand the fMRI responses, future studies should include concurrent behavioral measures of craving, food preference, and intake.

More generally, future studies would benefit by including a broader consideration of the functions of the mesolimbic dopaminergic system. It is often assumed that dopamine plays a central role in hedonics, craving, and reward; however, this is most likely an oversimplification. A body of evidence instead supports a role for dopamine in nonhedonic components of motivation and instrumental learning. Specifically, interference with nucleus accumbens dopamine transmission has a negligible effect on food intake in animals (12). Human tyrosine depletion studies

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provide little evidence that dopamine mediates subjective craving for drug stimuli (13). Similarly, a recent study found that tyrosine depletion reduced subjective hunger ratings (14). This is contrary to the notion that people overeat to compensate for low dopaminergic activity. Future studies could investigate the potential role of dopamine in brain activation after high- and low-GI meals by using dopamine depletion or antagonism.

The article also raises questions as to whether certain foods might be “addictive,” in a similar way to drugs of abuse. It has been shown recently that the clinical overlap between drug addiction and overeating is partial at best (15). The authors rightfully acknowledge that food is essential for survival, meaning that the parallels with substance abuse are less clear-cut. We agree that additional mechanistically oriented studies are needed. Specifically, much insight can be gained by understanding overeating within a psychological framework. In an important article, Rogers and Smit (16) argued that ambivalence about certain foods leads to attempts to resist eating them; however, restriction is often futile because it elicits a strong desire for the food. Critically, however, experiencing this desire or “craving” does not mean that the food in question is addictive. Rather, it could be that certain foods are labeled as “addictive” as an explanation for why they are so difficult to resist. Future studies should aim to further unravel the psychological processes that govern eating and overconsumption.

Combining neuroimaging, metabolic, and behavioral approaches is clearly of major importance to help improve our understanding of the factors that influence food intake and potential differences in relation to different carbohydrate foods. Whether any differences are of significance in relation to overeating and obesity, or whether these are simply responses linked to the essential requirements of the brain for glucose as a fuel, remains to be determined by future studies.

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REFERENCES