Yummy Food Is Made From Fat and Sugar

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Over the past several decades, postmortem studies have provided novel insights on coronary atherosclerosis, and investigators have established the relationship between cardiovascular risk factors and the extension of atherosclerosis. They have concluded that the fundamental cause of coronary events is plaque vulnerability and the subsequent rupture or erosion of plaques. Following acknowledgment of their pleiotropic effects, statins have been widely used for healing vulnerable coronary plaques as well as lowering lipid levels. Nevertheless, residual risks remain, even after treatment with strong statins, and thus we should focus on the next target for further risk reduction.

Recent innovations in intravascular imaging modalities have greatly contributed to the precise pathophysiological diagnosis of coronary artery disease, as well as to decision making on coronary intervention procedures. For assessing coronary plaque morphology, optical coherence tomography (OCT) provides superior spatial resolution. With a resolution 10-fold higher than that of intravascular ultrasound imaging, OCT technology provides precise information about thrombi, spotty calcifications, and fibrous caps, and therefore, its images provide an “in vivo histology.”

In this issue of the Journal, De Rosa et al. assess the relationship between coronary plaque characteristics and cardiovascular risk factors using their own OCT observations. In their results, diabetes, prediabetes, and obesity were the only independent predictors of thin-cap fibroatheroma, and diabetes and prediabetes were the only independent predictors of plaque erosion. Although patients enrolled in their study were not aggressively treated with statins, their lipid profiles had favorable values. This may be the reason why comorbidity with dyslipidemia did not contribute to OCT-observed plaque vulnerability in the multivariate analysis of their study. Therefore, this study indicates that we need to focus on glucose metabolism and obesity, independently of lipid profiles. The novelty of this study was its use of OCT images for the in vivo histological analysis of plaque morphology.

After the 1940’s Pacific war, the Japanese lifestyle underwent a “sea change” under the American occupation. School lunches were introduced to prevent childhood hunger, and the food preferences of the Japanese population were changed. Since the opening of the first McDonald’s fast food restaurant in Tokyo in the 1970s, the prevalence of fast food has facilitated a high-fat and/or high-sugar diet among Japanese children. This has led to increased morbidity from diabetes, obesity, and related cardiovascular events. Obesity is accompanied by other risk factors, such as diabetes, hypertension, and dyslipidemia, in which adipocytokines secreted from adipose tissues increase insulin sensitivity, resulting in increased plaque burden and plaque vulnerability. This “large clinical trial” demonstrates that a Western diet in childhood is associated with increased risk of cardiovascular diseases in the Japanese population.

A high-fat diet is associated with endoplasmic reticulum stress in the hypothalamus, which activates the reward system in the brain. The reward system consists of a group of neural structures, responsible for motivational salience, in which dopaminergic neurons project from the mesencephalic ventral tegmental area (VTA) to the cerebral cortex. In animal and human brains, the satisfaction of wants or desires stimulates the reward system, which recognizes these stimuli as a positive emotion or delection. It is an essential system for the survival of individuals and their offspring because it is associated with instinctive behaviors, such as eating, sexual intercourse, and breastfeeding. Eating acts as a reward stimulus and activates dopaminergic neurons in the VTA. Recently, the similarity between food addiction and drug dependency has garnered a lot of attention. Drug dependency raises the reward system threshold with each dose. Obesity, similar to cocaine dependency, decreases the activity of dopaminergic receptors in the dorsal striatum of the basal ganglia, leading to a decrease in reward stimuli. Mice fed a high-fat diet develop...
a preference for that diet and repeat their intake of high-fat foods. Another experimental study revealed that sugar or a sweeter also led to a preference more deeply established than cocaine. Therefore, a high-fat or high-sugar diet may be chosen in the pursuit of delectation (Figure 1). On the other hand, leptin, an adipocytokine secreted from adipocytes, signals the hypothalamus to modulate appetite and maintain body weight. Because leptin is secreted from adipocytes, the total amount of leptin is directly related to the amount of an individual's body fat. Therefore, obesity increases serum leptin levels. Leptin also suppresses dopaminergic activity in the VTA. An uninterrupted intake of a high-fat diet amplifies endoplasmic reticulum stress in the hypothalamus and causes leptin resistance. Therefore, control of appetite is lost, even if serum leptin levels increase. As a result, the threshold for activation of the reward system increases, inducing “binge eating” and/or “food addiction”. Moreover, the number and size of adipocytes vary between obese and non-obese children. Recent data suggests that the overconsumption of fat and carbohydrates during the gestational period may influence the development of taste preferences and increase the risk of obesity in the offspring (Figure 2). Hence, diabetes and obesity should be recognized as hurdles to be overcome, similar to or more important than lipid metabolism, in improving cardiovascular morbidity and mortality, particularly in children. We need to educate people to avoid a high-fat and high-sugar diet from early childhood.

References