Obesity: Increasing Awareness of Novel Environmental Factors

Kevin D. Niswender[1,2] and Bettina M. Beech[3]

Over the past 20 years, the molecular underpinnings of energy homeostasis have come to light (1–4) at a rate strikingly similar to that of the rising prevalence of obesity (5, 6). The fact that one is statistically more likely to be overweight or obese in the U.S. today has profound ramifications for basic scientific research, translational research, public policy, and our health care economy.

Homeostatic regulation of feeding. Current obesity statistics generate a striking contrast to abundant experimental evidence indicating that body adiposity is (or can be) a remarkably tightly regulated physiological variable (7–9), much like blood glucose concentration. Studies in rodent models, many of which have been confirmed in humans, have identified a plethora of humoral signals, neuropeptides, brain nuclei, and metabolic pathways involved in the precise physiological mechanism termed energy homeostasis (10). Primitive brain structures involved, such as the hypothalamus and hindbrain, are capable of sensing the status of body energy stores and initiating the appropriate homeostatic responses to maintain optimal body adiposity. Unfortunately, this rapidly expanding body of basic science in energy homeostasis has yet to be translated into efficacious therapies or prevention strategies for human obesity. Similarly, the limited translational research experience in obesity, which has focused on increasing physical activity, changing patterns of dietary practices, and modifying the built environment in communities, has yet to yield significant effectiveness.

Human feeding behavior and nonhomeostatic mechanisms. Humans are not mice and, in current times, do not appear to feed in response to an evolutionary drive to preserve dwindling energy reserves. Rather, human feeding behavior is highly complex, involving social cues; olfactory, visual, and auditory stimuli; learned behaviors; and the response to reward stimuli, among others (10). All of these nonhomeostatic feeding signals are integrated in higher order structures such as the cortico-limbic system that, in turn, are known to influence hypothalamic and brainstem function. Casting an even wider net over nonhomeostatic influences on feeding, Dr. Cohen (11) speculates on the existence of an array of additional neural mechanisms that may explain susceptibility to obesity in an energy-dense, multimedia, sophisticated marketing environment. That our newest class of obesity drugs, not yet approved in the U.S., targets the endocannabinoid system (12), which is closely allied to food reward, provides proof of principle of the complexity of the motivation for feeding in humans.

"Wanting" and "liking" in feeding: efficacy of stealth food marketing. Common sense suggests that children do not need to consume carbonated beverages containing 240 calories and 65 g of high-fructose corn syrup at school in order to maintain a survival advantage, or even adequate adipose stores. Numerous forces clearly play into current nutritional trends, such as palatability, marketing, advertising, socioeconomic, and other pressures. In the accompanying article, Dr. Cohen speculates on the existence of neurophysiological pathways that generate susceptibility to subconscious food choices, resulting in the overconsumption of potently obesogenic foodstuffs. These pathways are hypothesized to be targeted by clever marketing forces to reflexively promote consumption of processed and obesogenic foods. Common to several mechanisms proposed is the dopaminergic system (13), in which increasingly solid evidence indicates that brain nuclei (such as ventral tegmental area, nucleus accumbens, and others) and pathways that influence susceptibility to drugs of addiction (14) also influence macronutrient preference (15), sensitivity to adiposity negative feedback signals (16), and, as speculated in her article, susceptibility to stealth food marketing campaigns. Given advances in functional brain imaging, it will now be possible to confirm and extend preliminary data cited by Dr. Cohen. Of the systems discussed, dopamine neurobiology appears to hold significant promise in unraveling the complexity of human feeding behaviors, and recent data have tied this system even more closely to metabolic disorders (17).

Other proposed mechanisms include mimicking behavior via mirror neurons, stereotypic behavior, limited cognitive capacity to choose healthy foods, and subliminal advertising or "priming." These ideas are thought provoking, but, at this stage, lack significantly convincing data both for specific underlying neurobiological mechanisms and for involvement in the obesity epidemic. Lack of nutritional knowledge, reduced accessibility and availability of affordable healthy foods (18), and poor numeracy skills (19) have all been associated with obesity, but it has not been suggested that these factors are inherently neurobiological. Of course, motivation within the food industry clearly exists to enhance the financial bottom line, as

From the [1]Department of Veterans Affairs Tennessee Valley Healthcare System, Nashville, Tennessee; the [2]Department of Medicine, Division of Diabetes, Endocrinology and Metabolism, Vanderbilt University School of Medicine, Nashville, Tennessee; and the [3]Department of Medicine, Division of General Internal Medicine and Public Health, Vanderbilt University School of Medicine, Nashville, Tennessee.
Corresponding author: Kevin Niswender, kevin.niswender@vanderbilt.edu.
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would exist in any for-profit enterprise and, thus, the industry probably does target such vulnerabilities with marketing. Whether the array of proposed neurobiological pathways contributes to consumption of obesogenic foods in response to strategic advertising remains to be proven. In a different light, this area may represent significant opportunity if industry resources can be marshaled toward profitable outcomes that reduce obesity burden.

Another concern is the assertion that "people were designed to over-consume and store excess calories to survive times when food may be scarce." This concept has its basis in "the thrifty genotype hypothesis" (20), a useful concept in context but one that, as discussed, ignores abundant evidence in favor of the existence of systems designed to control caloric intake and excess adiposity. The argument presented leads one to move away from attempts to understand how energy homeostasis becomes disrupted toward an exoneration of individual responsibility and global condemnation of the food industry. Whether warranted or not, this is unlikely to represent an approach that leads to successful interventions for obesity. Rather, we hypothesize that success in the fight against obesity will arise from integration of findings from both homeostatic and nonhomeostatic feeding models, from translational and educational work in communities, and, perhaps, from partnerships with industry.

Below awareness—but moving forward. As the burden of obesity grows, careful consideration should be given to novel concepts in pathogenesis, such as the provocative ideas presented by Dr. Cohen. Generation of rigorous experimental findings indicating a neurobiological basis for our subconscious interaction with our "food environment," such as is occurring in the dopamine research arena, may yield significant opportunity for intervention. If these pathways are as potent as suggested and can be targeted with sound nutritional and lifestyle messages, we may be able to reverse our poor track record of obesity intervention and prevention.

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