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Fat and free will

Since the identification of leptin in 1994, great progress has been made in unraveling the pathways that regulate fat accumulation in mammals. On the one hand, this offers the hope of new treatments for obesity, a large and growing health problem in most western countries. On the other hand, however, it raises some hard questions about the biological basis of human behavior; how these scientific advances are applied reflects our fundamental philosophical beliefs about the role of biology in human nature.

There are two schools of thought as to why people become obese. One view is that they gain weight because they succumb to the temptation to eat more and exercise less—in other words, because they are gluttonous and idle. The alternative view is that obesity is a biological problem, a disorder of the regulatory system that controls food intake and energy balance.

The latter view has gained force recently, as the relevant regulatory systems have been identified. Maintenance of body weight requires a very precise balance between energy intake and expenditure, and given enough time, even slight discrepancies can have large effects. The key insight into how this balance is achieved came with the discovery of leptin, a circulating hormone produced by fat cells that acts on neurons of the hypothalamus to inhibit eating behavior (as well as producing many other physiological effects). Leptin thus provides a negative feedback loop that restricts feeding when fat reserves are high, and promotes feeding when they are low. In addition to this long-term feedback (which establishes energy balance over a time scale of several days), there is a short-term loop, involving gastric feedback pathways to the brainstem, that acts within minutes to signal satiety and thus limit the amount of food consumed during a single meal. Intermediate between these systems is thought to be a 'hunger trigger' that controls when feeding is initiated, but this is much less well understood, and the underlying molecules and circuitry are not known.

Most of these regulatory pathways were first discovered in mice, but the main features have proved to be highly conserved in humans. Mutations in the leptin gene, or in downstream targets of leptin signaling such as the melanocortin system, cause overeating and obesity in both mice and humans. These single-gene mutations account for only a small proportion of human obesity (perhaps 5%), but obesity in the population as a whole is highly heritable, and it seems clear that many other genes are also involved. Most have yet to be identified, but it seems likely that at least some of them will be discovered in the near future, given the increasing power of whole-genome scans to identify loci for complex traits. It also seems likely that many of these genes will turn out to affect eating behavior, given that differences in food intake, rather than in basal metabolism, appear to be the most important determinant of who becomes obese.

As biological mechanisms of appetite regulation are discovered, it is easy to lose sight of the point that obesity depends primarily on voluntary behavior. Most industrialized countries have seen dramatic increases in obesity in recent years (in the US, about 20% of the population is now considered obese), not because of any change in gene pool, but because people are increasingly exposed to (or creating for themselves) an environment in which food is readily available and physical exertion is largely unnecessary. Genes are clearly involved in determining susceptibility to these environmental effects, but the final common pathway of all these influences is a series of volitional acts, primarily decisions about when, what and how much to eat.

The traditional dichotomy between determinism and free will seems inadequate to describe this situation; decisions may appear to be individually free, yet in the aggregate they are unquestionably subject to regulation, sometimes overwhelmingly strong, by biological factors. The intensity of the desire to overeat clearly varies between individuals, in ways that we are now just beginning to understand. Perhaps biological factors also influence our ability to resist temptation; indeed, given the complexity of human eating habits, one can imagine any number of ways in which genes might affect the probability that a person will gain weight.

The relevance of these arguments goes beyond eating behavior. Obesity happens to be well studied, partly because it is relatively easy to quantify, and partly because of its health implications and economic importance. But there is no reason to think that eating is unique, and it seems likely that other human actions, including aggression, sexual behavior, drug abuse, and many other behaviors that have traditional connotations of vice and virtue, will be subject to similar biological influences, which may some day be discovered. The biomedical community has been very willing to embrace the idea that obesity is a failure not of willpower but of regulatory circuits within the brain, and that the best way to tackle it is by developing drugs that act on the brain to change behaviors that people cannot or will not change voluntarily. This approach might be uncontroversial for psychiatric illness, but nobody suggests that the overweight are mentally ill. Using mechanistic knowledge of brain function to design drugs that affect our natural impulses is a serious step toward the 'medicalization' of human behavior, which should be taken only with considerable caution.