subjectively hard-to-control episodes in which one eats "an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances." The cumulative lifetime risk of BED in the US is only 3.9%; even when combined with subthreshold BED and "any binge eating," this only rises to 11%, about one-third of the current prevalence of adult obesity (body mass index ≥ 30), 34%. Among adults with BED, the point prevalence of obesity is 42%, which is only about 8% higher than that seen in the general population[13]. BED is also distinct from obesity in terms of prognosis (BED is associated with a lower quality of life than obesity) and treatment response (BED responds to antidepressants, but obesity generally does not).

Of course, food addiction could be defined more broadly as frequent heavy consumption of energy-dense foods without frank bingeing. In that case, its overlap with obesity is surely much greater (although there are probably no reliable statistics to quantify the extent of the overlap), but there are still reasons to avoid drawing an easy equivalence. For example, it has been argued that the effects of behavior on weight could be subverted by metabolic defense of a 'set point'[14]. A high set point could result from overeating, but could also be established pre/perinatally and could be influenced by environmental factors that do not even involve food[15]. There is vigorous debate about the interactions of genetic, environmental and behavioral causes of obesity, but it is best to be leery of any account that overwhelmingly attributes obesity to the behavior of the obese.

The second caveat is that, in the realm of behavioral causes of obesity, if we invoke the concept of addiction, we need to remember what we have learned from the study of other addictions: addiction does not obliterate the capacity for choice. Even addiction to intravenous heroin and crack cocaine can be highly responsive to consequences when the consequences (for example, money) are sufficiently large and predictable. Despite Johnson and Kenny's findings[2] of changes in BSR sensitivity, human addicts are not always hyporesponsive to alternative rewards, even in studies that have been interpreted as evidence that they are. This caveat is important because it underlies behaviorally based treatments for addiction. And if the kinds of alternative-reinforcer treatments that are effective in drug addiction can reduce regular overindulgence in energy-dense food (with or without frank bingeing), health benefits are likely to accrue regardless of whether appreciable weight loss occurs.

To restate the two caveats, whatever entity we call food addiction should not be seen as an excuse for unhealthy eating and the unhealthy eating associated with food addiction should not be equated with obesity. Johnson and Kenny's rat data[2] suggest something interesting but not something that reduces to an enticing headline or sound bite. We would be mistrustful of any summary simpler than this: given enough access to cheesecake and bacon, rats display patterns of eating that resemble those that account to some unknown degree for human obesity and these patterns seem behaviorally similar to, and share some neurophysiological substrates with, patterns of drug self-administration and withdrawal symptoms that resemble those seen in drug addiction.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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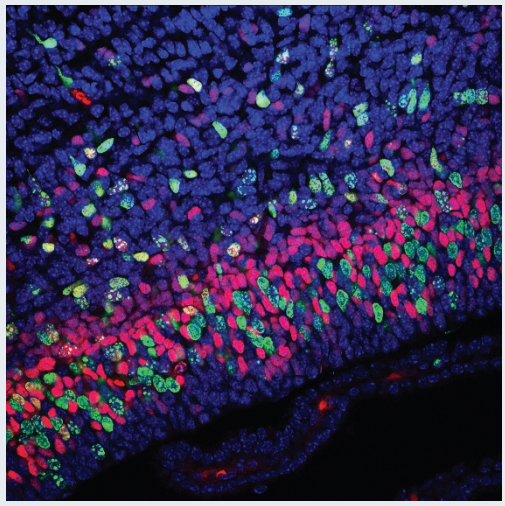
Regulating brain size



In this issue on page 551, Silver and colleagues report a surprising regulator of neural stem cell mitosis and brain size in mice and investigate how its disruption might lead to microcephaly.

In a previous mutagenesis screen, the authors had isolated a mutant mouse with a small body size, hypopigmentation and a reduced brain size. Here they identify *Magoh* as a candidate gene responsible for the microcephalic phenotype. The *Magoh* gene, which is completely conserved between mice and humans, encodes a component of the RNA-binding exon junction complex (EJC). Mice homozygous for the *Magoh* loss-of-function mutation died prenatally, whereas the brains of adult mice heterozygous for the mutation showed disordered cortical layering and fewer neurons as compared with wild-type mice. The figure shows wild-type embryonic day 16.5 (E16.5) cortex, with Tbr2 (red) labeling intermediate progenitors, BrdU (green) indicating proliferating cells and DAPI (blue) staining all nuclei. Dividing intermediate progenitors appear yellow. In the *Magoh* mutant cortex, the number of dividing intermediate progenitors was reduced from E12.5 onwards, whereas the numbers of cells expressing immature neuron markers were increased. The prematurely born neurons, however, did not survive by E18.5.

How does an EJC component maintain the intermediate progenitor pool and prevent precocious neurogenesis? Dividing cells in the *Magoh* mutants had altered mitotic spindle orientations and aberrant chromosome numbers, a phenotype similar to that of *Lis1* mutant mice. *Lis1* encodes a microtubule-associated protein that is critical for mitotic spindle integrity; in humans, altered *LIS1* dosages have been associated with microcephaly syndromes. Lis1 protein levels were decreased in the *Magoh* mutant cortex. Critically, Silver *et al.* rescued the *Magoh* microcephaly phenotype with *Lis1* expression. By finding that *Magoh* controls neural stem cell division by regulating levels of Lis1 protein, Silver and colleagues have identified a new role for the EJC in determining brain size. ***Kathleen A Dave***