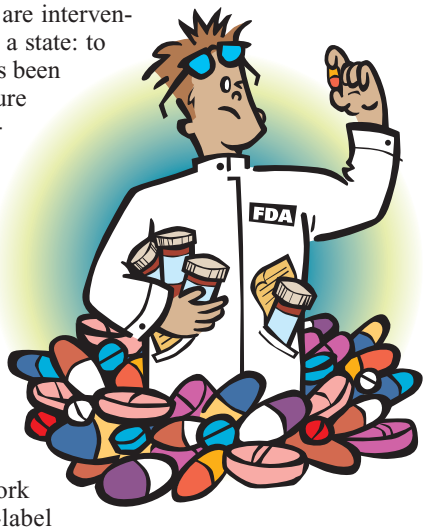
Just Treat, or Enhance?

In this issue (p. 34), *Science's* News Focus looks into remembering and forgetting—a topic of increasing interest, not only to my cohort but also to the young as they cram for the next exam. What we've learned from a recent flurry of exciting neuropharmacology is that there are some promising drug targets out there. What we already knew is that here in the United States, people have been making use of approved drugs labeled for other indications to assist mental concentration and executive functions or to improve memory retention. Moreover, they are taking increasing advantage of dietary supplements that advertise memory enhancement but that Congress has exempted from regulation by the U.S. Food and Drug Administration (FDA).

All this raises some interesting questions. Some are ethical issues, involving the line that distinguishes treatment from enhancement. Others are challenges for public policy: Have we adopted enough protections against "off-label" uses of prescription drugs, and have we given the FDA enough tools to protect consumers against the claims made regarding many dietary supplements?

With respect to treatment and enhancement, the ethical terrain is particularly uneven. Those of us who have some interest in athletic performance are troubled by the enhancement issue, and Congress, which probably has better things to do, is now absorbed with the matter of steroid use among baseball players. That has to do with the ritual of competition and the need for a level playing field. But what about the student who takes Ritalin (methylphenidate), without having been diagnosed with attention deficit hyperactivity disorder (ADHD), to improve her ability to focus when preparing for a College Board exam? Some might disapprove, but would they be equally critical of her fellow student who prepared instead by taking the Kaplan course? Perhaps there are just too many ways to tilt this playing field.

A different argument has been advanced by Francis Fukuyama and by Leon Kass, chair of the President's Council on Bioethics; both suggest that procognitive therapy interferes with something they perceive as "our nature." But it is difficult to distinguish between this and other interventions in neurotransmitter biochemistry, such as the use of antidepressants. Moreover, there is a naïve nativism in the view that when we modify any behavioral state, we are intervening in some "natural" state of being. How far back do we go to find such a state: to the earliest hominids? to the last hunter-gatherers? The human narrative has been marked for most of its history by an accelerating interaction between culture and brain evolution. For eons, we have been changing human nature, whatever that is, by alloying natural selection with cultural innovation.



There are also issues of safety, which should overshadow other concerns about the enhancement issue. The human nervous system is so sensitive and so labile compared with other parts of our physiology that interventions in brain function should demand an extra dose of caution. Our experience with Ritalin, even as it is appropriately prescribed for cases of ADHD, began relatively recently. As users of that drug enter the ranks of seniors, we might anticipate some unpleasant surprises. It is good news that distinguished biomedical scientists are developing potential drug targets from their basic research findings. But the FDA will have to look carefully at the possibility of adverse effects from chronic use of the new memory boosters if and when they appear. After all, who will want to stop taking them?

More serious are the holes that already exist in the regulatory framework for neurocognitive enhancers. The first is a chronic FDA problem: off-label prescriptions. It has become increasingly clear that prescriptions for methylphenidate are given in numbers far greater than the number of ADHD people. College health service personnel recognize that many students are preparing for exams with that kind of help. That will remind old FDA hands of the late 1970s, when the high rate of off-label prescriptions was for amphetamines, often destined for a similar use. The second is the virtually unregulated domain of dietary supplements. The Federal Trade Commission has some control over the way in which alleged memory enhancers are advertised, but it's permeable; if you doubt this, read your spam e-mail. Worse, there is no control whatever over efficacy or safety. Congress has long resisted equipping the FDA to deal with this exploding area, and it's past time for them to get over it.

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