All Correspondence this week responds to Barbara Sahakian and Sharon Morein-Zamir's Commentary 'Professor's little helper' (Nature **450,** *1157–1159; 2007) and the related discussion at http://network.nature.com/forums/naturenewsandopinion.*

This week, Nature *launches an anonymous online survey to build on the informal questionnaire that the Commentary authors sent academics on the usage of brain-boosting drugs. In aggregate, the survey results will guide future editorial content on this topic. To take part, please visit: http://tinyurl.com/yq7nn3.*

The action of enhancers can lead to addiction

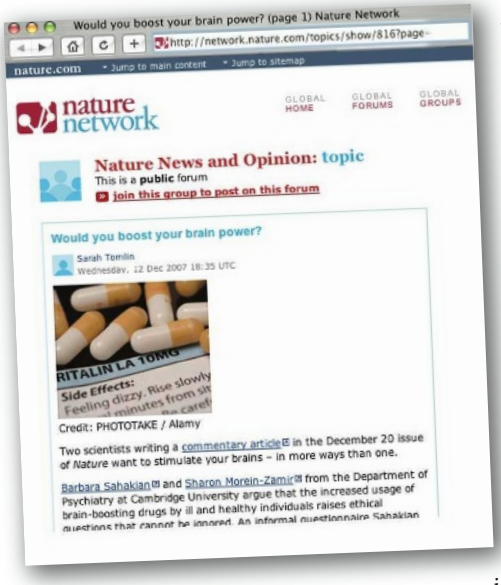
SIR — Sahakian and Morein-Zamir revive questions about the widespread availability and diversion of prescription medications for non-clinical use in healthy individuals (*Nature* **450,** 1157–1159; 2007). Such questions drove legislators to impose controls a few decades ago, when amphetamines and barbiturates were widely available.

Because the diversion of drugs is linked to their availability, the World Health Organization monitors their production and consumption by individual nations. In the United States, production of stimulant drugs has soared during the past two decades, and enough are now produced each year for the daily treatment of at least four million individuals. Even though stimulants and other cognitive enhancers are intended for legitimate clinical use, history predicts that greater availability will lead to an increase in diversion, misuse and abuse. Among high-school students, abuse of prescription medications is second only to cannabis use.

Although access to medications that improve our cognitive performance might be desirable in theory, these may have adverse medical consequences. Some limitations are necesssary, for these medications can be addictive. This is because cognitive enhancers such as the stimulants methylphenidate (Ritalin) and amphetamine amplify the activity of dopamine, a neurotransmitter that increases saliency, making cognitive tasks and everyday activities seem more interesting and rewarding. This learned experience can lead to abuse of the drug and to compulsive use and addiction in vulnerable people.

As we increase our knowledge of how the brain works, we may one day have safe interventions to improve cognition. In the meantime, we need to learn from history and avoid using them unnecessarily.

Nora D. Volkow*, James M. Swanson†
*National Institute on Drug Abuse, 6001 Executive Boulevard, Room 5274, Bethesda, Maryland 20892, USA
†University of California at Irvine, Child Development Center, Irvine, California 92612, USA



Drugs can be used to treat more than disease

SIR — Your fine Commentary draws attention to some important questions (*Nature* **450,** 1157–1159; 2007). I agree with the point made by several commentators, that there is a need for better understanding of the long-term effects of using potential cognitive enhancers in an ecological setting. It is one thing to show a short-term positive effect on some artificial lab task; it is quite another to show that long-term use actually leads to sustainable performance gains on important real-world tasks, such as academic output. The former is easier to demonstrate, but the latter is what ultimately matters.

Unfortunately, progress on developing effective cognitive enhancers, and on understanding their long-term effects, is hampered by a shortage of focused research in this area. In general, the potential of enhancement medicine has yet to be fully appreciated.

Prevailing patterns of medical funding and regulation are organized around the concept of disease. Every pharmaceutical on the market with alleged cognitive-enhancing effects was developed as a treatment for some pathology. Its good effects on healthy adults' brains were discovered as fortuitous side effects. This disease-centred framework impedes the development of safe and effective enhancing medicines and has several consequences.

First, it makes funding hard to come by; it also makes it difficult to obtain regulatory approval for enhancement drugs. The result is that those who wish to research cognitive enhancement must often mask their work under the guise of addressing some 'respectable' disease.

Second, in order to gain access to the benefits of a cognitive enhancer, the user must first be classified as sick. This leads to the expansion of diagnostic categories and the invention of new pathological conditions — sometimes to cover cases that in earlier times would have been regarded as within normal human variation.

Third, it contributes to inequity in access. The main obstacle for someone who might be interested in trying modafinil or a related drug is not cost (which is similar to that of a large cup of coffee) but information: knowing that the drug exists and how to obtain it. This discriminates against people with little access to information.

With the cockcrow of enhancement medicine, we need to retool our regulatory paradigm. It is not only special occupations such as military commandos and air-traffic controllers that would benefit from good enhancement drugs. Other jobs are just as important and intellectually taxing — including the jobs of many scientists and academics. Anything that can help our brains deal better with the complex challenges of the twenty-first century is to be not only welcomed but actively sought. But it will require substantial investment to develop interventions that are both safe and effective in long-term use.

Nick Bostrom
Future of Humanity Institute, James Martin 21st Century School, University of Oxford, Littlegate House, 16/17 St Ebbe's Street, Oxford OX1 1PT, UK

Low dose of alertness drug counters 'family fatigue'

SIR — I have been taking 50 mg of modafinil almost daily for over a year. For most of my 74 years, I have struggled with fatigue and markedly reduced brain function every afternoon. This is part of my family history: my father and grandfather both structured afternoon naps into their schedules. I have found that caffeine and nicotine are either ineffective or cause a jittery nerviness. The side effects of the antidepressants I tried — desipramine, Paxil and Wellbutrin — were not worth the minimal benefits.

At first, I used modafinil only when I desired an extended high level of attention. Previously, I could work competently on the fracture-mechanics of high-silica stone (while replicating ancient tool-flaking techniques) for about an hour. With modafinil, I could continue for almost three hours. It did not make me 'smarter', but extended the length of concentrated focus.

When I used it on a three-day cross-country drive, I was not only more alert but found the journey more enjoyable and less tiring than previously.

I have not seen any data suggesting that modafinil is either habit-forming or easily abused (I have not looked for studies in

children). A 50-mg dose is quite low, but 100 mg does not increase the level or length of focus, for me at least, and can result in nervousness. As no 'high' is achieved, anyone taking too high a dose would soon cut down.

Competitive advantage is not a public-health issue at all, but a personal ethical and philosophical question. Today I will give my seven-year-old granddaughter a piano lesson, lead her in a chemistry experiment, listen to her sums and encourage her to enter any new words of her vocabulary into her personal dictionary. Am I trying to nurture her towards a 'competitive advantage'? You bet!

Charles Eaton
Corrales, New Mexico 87048, USA

Drugging unruly children is a method of social control

SIR — Sahakian and Morein-Zamir's reference to attention-deficit hyperactivity disorder (ADHD) as heritable and affecting 4–10% of children worldwide is contentious (*Nature* **450,** 1157–1159; 2007). The claimed incidence of ADHD varies strikingly over time: less than 0.1% in the United Kingdom before 1990, and now generally claimed to be between 1% and 5%. This variation is equally dramatic by country: highest in the United States, followed by Australia and Iceland, but low in Italy, for instance.

The diagnosis is in many cases questionable, and evidence for its heritability is shaky except in highly selected groups. The marked increase in the number of prescriptions of methylphenidate (Ritalin) — from 2,000 a year in 1991 to more than 300,000 in the United Kingdom today — says more about fashions in the diagnosis and treatment of naughty, inattentive or badly parented children than it does about a genuinely heritable 'disease.'

In the United States, the Federal Drug Administration has called attention to the 'epidemic' of schoolyard Ritalin use. As Sahakian and Morein-Zamir note, there is disturbing evidence of long-term, adverse sequelae associated with the use of such amphetamine-like drugs, especially on young and developing brains.

The assumption behind the cognitive-enhancer debate is that users are essentially making free choices about whether or not to take risks. But children being prescribed Ritalin are being drugged as a method of social control.

That, it seems to me, is a real ethical issue. If we don't recognize the real-world situation in which drugs are bought, prescribed and used, then the ethical debate is vacuous.

Steven Rose
Department of Life Sciences,
The Open University,
Milton Keynes MK7 6AA, UK

Humans have always tried to improve their condition

SIR — The Commentary 'Professor's little helper' (*Nature* **450,** 1157–1159; 2007) entreats us to consider how the non-medical use of cognitive-enhancing drugs such as modafinil and Ritalin might influence society as a whole. They note concerns that a 'better, faster, stronger' mentality might coerce individuals into taking these drugs so that they can give themselves an edge.

Science and technology will continue to generate all sorts of new enhancers, and the quest for enhancement is not necessarily unfair or unethical. We humans are inveterate enhancers, striving to increase our intelligence and to improve our memory and powers of perception.

Consider spectacles: before they became commonplace, those who had good eyesight enjoyed an advantage over those who did not. Later, those who could afford spectacles joined those with naturally good eyesight — increasing (or decreasing?) natural unfairness. Enhancing technologies that improve eyesight are now widely available; we do not conclude that they are unethical because they are not globally accessible.

Before the invention of lamps or candles, most people went to bed at dusk; these inventions, and then electricity, enabled social life and work to continue into the night. Night owls can steal a march on their lazier or saner competitors, raising the bar and creating pressure for longer working hours. But such enhancement technologies are not considered unethical.

The same is and will continue to be true of cognitive enhancers. We must press for wider and more equitable access, turning our backs neither on technology nor on improving the human condition.

John Harris, Muireann Quigley
Institute for Science, Ethics, and Innovation,
School of Law, University of Manchester,
Oxford Road, Manchester M13 9PL, UK

Policy must recognize drug impact on different sectors

SIR — Sahakian and Morein-Zamir encourage us to explore a range of new issues raised by their reflections (*Nature* **450,** 1157–1159; 2007). In particular, we need to develop legal and social policies to guide the setting of parameters and milestones for integrating new enhancing technologies into healthcare for treatment — and into society for non-therapeutic application.

Policy-making is complex. It becomes even more so when the priorities of different healthcare systems come into play, which are inevitably influenced by the commercial interests of big-business pharmaceutical companies. One-size-fits-all policies will not work because of the range of multicultural factors that also need to be taken into consideration. For example, blanket regulation of cognitive enhancers will not play out evenly where socioeconomic status determines ease of access.

Sahakian and Morein-Zamir call for better drugs. Our call is for next-generation research and translation that is focused on regulatory policies. Those policies should recognize the differential impact of drugs on different segments of society. They should protect people from impulsive quick fixes and against vulnerabilities arising from short-sighted solutions.

Robin Pierce, Judy Illes
National Core for Neuroethics,
Department of Medicine, Division of Neurology,
The University of British Columbia, 2211
Wesbrook Mall, Koerner 5124, Vancouver,
British Columbia V6T 2B5, Canada

Rationality is a better basis for ethics than repugnance

SIR — Sahakian and Morein-Zamir's Commentary 'Professor's little helper' (*Nature* **450,** 1157–1159; 2007) makes an important contribution to the neuroethics of enhancement, as much for what it doesn't say as for what it does.

Much of the debate over neurocognitive enhancement has been guided by the so-called 'wisdom of repugnance'. We are encouraged to focus on our gut reaction to perfectly healthy individuals drugging themselves (or worse, their healthy children) for the sake of satisfying oversized ambitions. This highlights issues such as the need to earn one's success and self-esteem, and respect for our natural limitations.

Shouldn't we attempt a more rational analysis of the different contexts, methods and motives for neurocognitive enhancement and their likely outcomes, including the likely impact on society and human values?

Sahakian and Morein-Zamir provide a cautious yet open-minded assessment of risks and benefits, without any obeisance to the wisdom of repugnance. They have done us a service in framing the issues in this way.

Martha J. Farah
Center for Cognitive Neuroscience,
University of Pennsylvania, 3720 Walnut Street,
Philadelphia, Pennsylvania 19104, USA