

conditions. Consider iodine: What makes it the case that it is not a CED? It raises intelligence in children whose diet includes it, compared to those who do not, but iodine deficiency usually results in IQs that, while lower than they would otherwise have been, are within the normal range (UNICEF 2003).

An effectively risk-free enhancer that targets general-purpose capacities should be no more controversial than the teaching of logic or general reasoning skills. Most people believe it is appropriate to require parents to meet minimum standards of general-purpose education for their children; there seems no reason why that shouldn't include cognitive enhancement using CEDs, assuming the costs and benefits weigh decisively in favor of their use. After all, the minimum standards to which parents are held have risen historically; we no longer believe that bare literacy is sufficient. The standards have risen because people need more education, and better thinking skills, to meet minimum standards for employability and to live meaningful lives in societies that make heavy use of text and technology. For the same kinds of reasons that the standards have risen in the past, we may expect them to rise in the future, in part because

of the availability of safe and effective CEDs. When, and if, this occurs, it may be appropriate to require parents to enhance their children. ■

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# Some First Steps Toward Responsible Use of Cognitive-Enhancing Drugs by the Healthy

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In December 2008 Barbara Sahakian, John Harris, Ronald C. Kessler, Michael Gazzaniga, Philip Campbell, Martha J. Farah, and I published a commentary in *Nature* entitled "Towards Responsible Use of Cognitive-Enhancing Drugs by the Healthy" (Greely et al. 2008). As the first-listed author, I received a lot of correspondence about this commentary, far more than on any other piece I've written. About one-third were thoughtful discussions of the issues raised by cognitive enhancement, often by people who had used it, and roughly evenly divided between advocates and opponents. Another one-third asked, "How much money did Big Pharma pay you to write that?" And the final third asked, more or less, "How much crack were you smoking when you wrote that?"<sup>1</sup>

It was an interesting experience, but in the longer run the results have been a bit frustrating. I thought our main points were that cognitive-enhancing drugs needed to be evaluated on the evidence of their risks and benefits and that careful policies needed to be crafted concerning their

use. Although many reacted to our piece, few seemed to act on it. Until now. Veljko Dubljević's target article (2013) both provides a careful assessment of the costs of benefits on two cognitive-enhancing drugs and suggests some policy structures to govern the availability of one of them, and this is just one of several recent or forthcoming articles by the very ("unnaturally"?) productive Dr. Dubljević on these questions. I am both pleased and grateful to have our challenge taken up—though not so grateful as to avoid a few suggestions and criticisms, both about his assessment of amphetamine and methylphenidate and about his policy recommendations.

"We call for an evidence-based approach to the evaluation of the risks and benefits of cognitive enhancement" (Greely et al. 2008, 703).

Dubljević nicely summarizes research on the safety and efficacy of Ritalin and Adderall, the commercially available preparations of methylphenidate (Ritalin) and of certain mixed amphetamine salts (Adderall). Particularly

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1. Alas, no one asked me, "How much crack did Big Pharma give you to write that?"

important is his analysis of the differences between the extended-release form of Ritalin, on the one hand, and, on the other hand, the instant-release form of Ritalin and both the instant-release and extended-release forms of Adderall. It is not just that drugs differ in their risks and benefits, but different preparations of the same drugs can differ.

"We call for a programme of research into the use and impacts of cognitive-enhancing drugs by healthy individuals" (Greely et al. 2008, 704).

It would have been useful, though, for Dubljević to go beyond summarizing the existing research to pointing out what further research would be useful. We know very little about the effects of long-term use, either regular or sporadic, of these drugs on healthy adults. This is true not only of safety, but of efficacy. The balance of the two is important in making decisions about drug use (whether those decisions are made by a regulatory agency or by an individual). It would really be useful to see results of a randomized, double-blind placebo trial of long-acting Ritalin on the school performance of healthy university students over the course of, say, two years, as well as any health effects. The studies we have are not necessarily studies of the drugs being used as they would be used if they were more freely available. And, of course, it would also be nice if we had more trials that were funded by someone other than the drugs' manufacturers.

Even more valuable would have been some discussion of mechanisms to assure that unbiased scientists would produce relevant research on various cognitive-enhancing drugs. Real *programs* of research, instead of the occasional one-off study, would be invaluable in providing a more accurate assessment of Ritalin and Adderall—and Provigil, Aricept, and other drugs (as well as cognitive-enhancing devices, such as transcranial direct current stimulation, which seems to be in the middle of at least a media boom). I would have been very interested in Dubljević's thoughts on how to encourage, or require, the kind of systematic research needed to weigh the safety and efficacy of enhancements.

"We call for careful and limited legislative action to channel cognitive-enhancement technologies into useful paths" (Greely et al. 2008, 705).

Dubljević's discussion avoids the false tyranny of polar choices in legislative action. The alternatives, as he points, are not just *laissez-faire* legalization and strict criminal prohibition—many other options exist in the multidimensional spaces between those policy points. He lays out four such options in some detail: the tobacco model, the coffee shop model, the Regulatory Authority for Cognitive Enhancement (RACE) model, and the author's own Economic Disincentives Model.

His discussion of these models, both in general in the first part of the article and briefly as applied to extended-release methylphenidate near the end of the article, is useful, but is also the area I would have most liked to see expanded.

For example, the tobacco model is one of over-the-counter availability, but in a context that discourages use, through taxes, advertising restrictions, and graphic warnings. In the case of extended-release methylphenidate,

though, why should the state want to discourage use? Dubljević makes a case that it is safe and effective—certainly much safer than tobacco. If so, although the tobacco model is a more restrictive alternative to *laissez-faire*, why is it appropriate?

Similarly, the coffee shop model is a way of controlling, though not necessarily discouraging, various aspects of the drug's use: location, products, quantities, users, and so on. As Dubljević notes, the coffee shop model may not be appropriate for a drug people use to help them work, but other ways exist for asserting some of the same kinds of control, from "behind-the-counter" regulations to prescription requirements. But what problems with extended-release methylphenidate would either the coffee shop or the behind-the-counter models seek to cure?

Dubljević almost completely ignores the RACE model. He dismisses it largely by noting that creating a new statutory regulatory body is difficult and expensive, and that it might not conform to the Convention on Psychotropic Substances. Yet the first of those flaws might be overcome, particularly through the use of an existing agency, similar to the Food and Drug Administration in the United States (Greely 2011). And such a regulatory body might be well placed to make comparisons—for example, to decide that the existence of the safer extended-release version of methylphenidate as an option is a strong argument against allowing broad access to immediate release methylphenidate or any form of Adderall.

Dubljević pushes his own, oddly named, Economic Disincentives Model, which uses existing regulatory agencies to license firms to sell cognitive enhancing drugs more broadly. Under this scheme, the drug users would have to be licensed to use the drug after taking a course and passing a test, would have to carry medical insurance, and would have to undergo annual medical tests. (Note that some of this seems similar to a version of a prescription requirement, which he summarily rejected.) But given the apparent safety of extended-release methylphenidate, why are all of these limitations necessary for this drug? Furthermore, the prices would be regulated to limit profits, and the companies making the drugs would both be subject to additional taxes and be required to invest in orphan drugs. Why should profits be limited specifically for this kind of product? Why should these companies be forced, presumably against their wishes, into the orphan drug development business? What does this have to do with problems raised, specifically, by extended-release methylphenidate?

In this article at least, Dubljević does not do much either to specify the problems to which intermediate regulatory models would respond, let alone examine, carefully, the match between those problems and his solutions. Our 2008 article listed some specific problems (along with safety) that we thought cognitive-enhancing drugs could raise, notably fairness and coercion; it would be good to see Dubljević examine solutions in light of those problems, or any other specific problems.

Another question about his analysis goes to the appropriate role of this kind of academic policy

recommendation. Although Dubljević nods occasionally to the realities of policymaking, as in his discussion of “capture” through tax revenues, he writes largely about appropriate policies, not about feasible politics. But might cognitive enhancing drugs be taxed, not to discourage their use, but to encourage cash-strapped governments to allow their broader use? Should physicians be given a gatekeeper role in part to encourage them to support wider use of such drugs? How important to a country, as a practical matter, is compliance with the 1971 United Nations Convention on Psychotropic Substances? Any more detailed presentation of policy recommendations should discuss, in more detail, foreseeable ways in which political and other nonpolicy considerations may affect the recommendations’ fate.

It may be unfair to seek careful, thoroughly justified policy recommendations in this article. This is one piece, subject to tight space limitations, and Dubljević recently has published three other articles on the subject. Here or elsewhere, more needs to be said—but I need to say, here, that

this is an excellent start. Dubljević calls his article a “limited ‘case analysis’” that is an invitation to further discussion, by experts, governments, and the public. By digging into two specific drugs, he has provided a valuable example that there can be a path forward to truly responsible use of cognitive enhancing drugs. ■

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# How Research on Stakeholder Perspectives Can Inform Policy on Cognitive Enhancement

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In his analysis, Dubljević (2013) argues for a moderately liberal public policy on cognitive enhancement that is based on the evidence regarding harm profiles of substances. Based on his analysis of relevant characteristics of methylphenidate and amphetamine, the author suggests that extended-release forms of methylphenidate may be acceptable. In contrast, amphetamine and instant-release forms of methylphenidate should be prohibited given the “the danger of abuse, and especially the threats of addiction, increased aggression, and erratic and violent behavior [that] make their use a potential danger to others” (31). While we agree with the case-by-case approach, we argue that public policies on cognitive enhancement should not only be based on an assessment of benefits and harms of the substances but also be informed by evidence on the

perceptions and views of the groups that are affected by cognitive enhancement (i.e., stakeholders). Our approach is based on socioempirical work that 1) supports the role of stakeholders in developing and evaluating public policies, 2) examines the perspectives of stakeholders regarding cognitive enhancement, and 3) helps integrate the complexity of values in policymaking consistent with a moderate liberal approach.

## STAKEHOLDERS’ INPUT IN THE DEVELOPMENT AND EVALUATION OF POLICY

Evidence on benefits and harms is key information for policymakers, both public and professional, but the analysis and synthesis of data on benefits and harm are not a

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