Ethical issues in the use of cognitive enhancement

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A recent survey of *Nature* readers, mainly those involved in research and academic medicine, revealed that up to forty percent of those who replied were using prescription drugs commonly used for cognitive enhancement.[1] Of these, fifty percent were being obtained without a prescription for a medical disease. Subsequently, Henry Greely and colleagues have called for the responsible use of enhancement in normal individuals.[2] An article in the *New Yorker* by Margaret Talbot describes the use of enhancing drugs by business executives, computer programmers, poker players, and students, evoking a sense of the seemingly limitless application of cognitive enhancing drugs.[3] The message is that the use of drugs for cognitive enhancement is not merely a philosophical thought experiment, but an actual problem that deserves careful consideration.

Unregulated cognitive enhancement—harm to society

Ethical arguments against the use of drugs for cognitive enhancement can be divided into two categories: issues dealing with the individual use of enhancement, such as maintaining autonomy and authenticity, and those dealing with the larger implications of a society accepting enhancement, including coercion to use enhancement and the creation of inequality. Arguments against the individual use of enhancement can be overcome, provided there is autonomy of choice and accurate information on the costs and benefits of cognitive enhancing drugs. The extent to which enhancement will have negative effects on society depends more on the way that institutions apply these technologies than on the characteristics of the technologies themselves, and these negative effects are the result of decreased autonomy for certain groups of persons. Enhancement is consistent with certain definitions of the role of medicine. Medicine, as an institution, can help to minimize the negative effects of enhancement on society while maximizing its possible benefits to individual patients through rigorous research into the side effects and efficacies of these drugs. Guidelines based on cost-benefit analysis should be developed to aid physicians in the management of cognitive enhancing drugs. Such analyses will require realistic expectations of the effects of these drugs and the specific situations in which enhancement would be beneficial. Ultimately, fulfillment of these conditions could allow for the ethical use of cognitive enhancement.

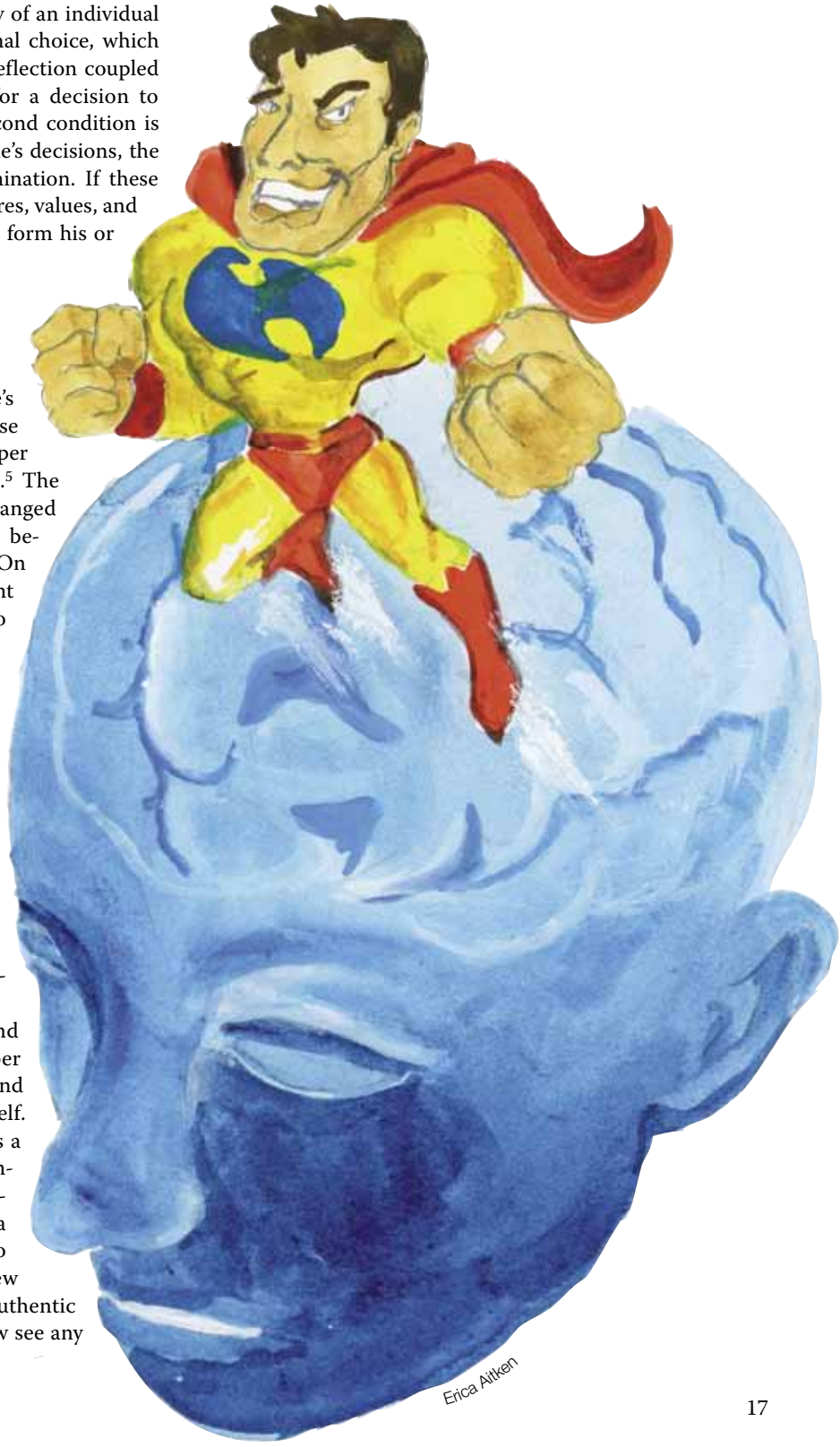
The authenticity of enhanced persons is a key moral argument of both both supporters and critics of enhancement. While authenticity relies on autonomous choice, the two

words are not synonymous. Gerald Dworkin defines autonomy as the "capacity of a person to critically reflect upon, and then attempt to accept or change, his or her preferences, desires, values, and ideals."[4p48] Autonomy thus rests on two underlying conditions. The first is the ability of an individual to critically reflect on an important, personal choice, which requires the cognitive capacity for critical reflection coupled with the accurate information necessary for a decision to reflect one's individual preferences. The second condition is what Dworkin refers to as authority over one's decisions, the freedom to change one's beliefs after examination. If these two conditions are met, the preferences, desires, values, and ideals established by an autonomous person form his or her authentic self.

Will enhancement help evolve the authentic self?

Whether enhancement compromises one's authentic self is an important question because this is the main objection to its use in a paper from the Presidential Council on Bioethics.[5] The authors argue that enhanced selves are changed selves, and that such change is inauthentic because it does not represent the "true" self. On the other hand, proponents of enhancement argue that these technologies allow one to create a truly authentic self, and that enhancement thus facilitates authenticity. Erik Parens describes these two points of view as the gratitude argument and the creativity argument.[6] The gratitude argument is based on accepting and appreciating the authentic self as a gift, while the creativity argument posits that one's self must be modified and developed before it is completely authentic. Parens argues that both sides are justified, and that, since both stem from a belief in the importance of authenticity, they represent an ideological common ground between supporters and opponents of enhancement.

Parens's description of the gratitude and creativity arguments reveals an even deeper fundamental difference in how proponents and critics of enhancement define authentic self. The gratitude view sees the authentic self as a gift to be revered as is, a necessarily static entity. In contrast, the creative view sees the authentic self as something that is created over a lifetime. It is no surprise, then, that those who are most comfortable with the creative view see enhancement as a path towards the authentic self, while those espousing the gratitude view see any



Erica Aitken

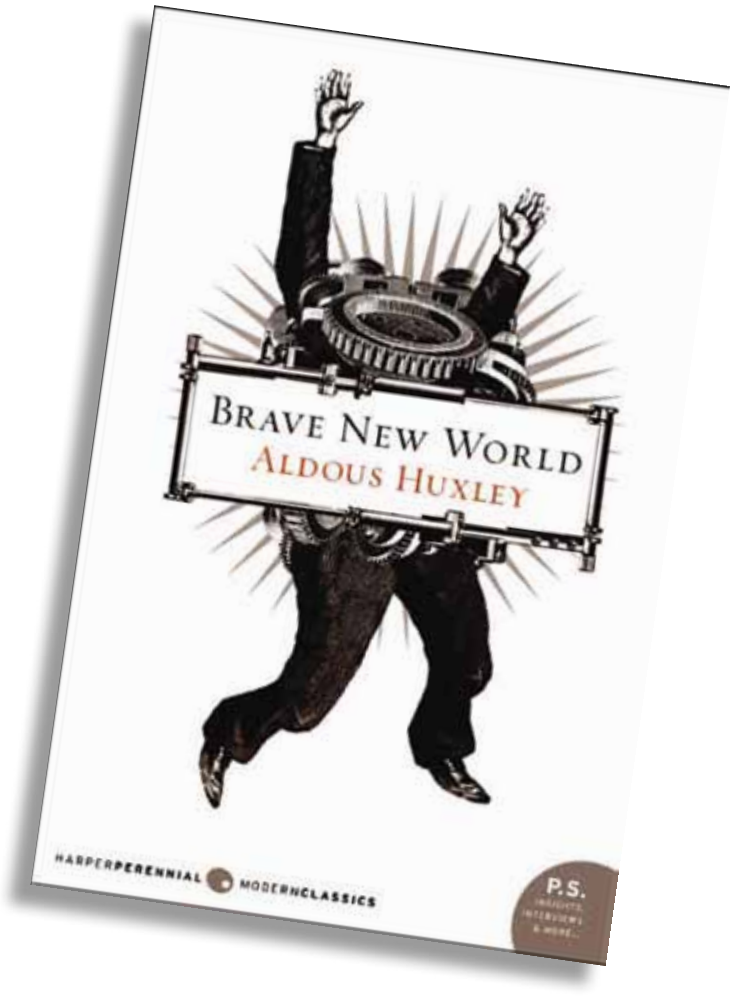
change to the authentic self, such as by the use of cognitive enhancing drugs, as resulting in a less authentic self. While opponents of enhancement may object to the classification of the authentic self as static, they might nevertheless concede that development of the authentic self should be limited to such conventional means as insight, introspection, and intense examination of one's life. Proponents of the creative authentic self, or those who support enhancement, probably would not object to such methods, and may feel that they are essential to creating the authentic self. However, they might further argue that enhancement can not only assist in this introspection by increasing concentration and other cognitive abilities, but might also help in the implementation of the goals of an authentic self after introspection has taken place. For these reasons, while Parens correctly argues that opposing sides in the enhancement debate use different definitions of authenticity, which he refers to as the gratitude view versus the creativity view, it is not clear that this insight reconciles these differing viewpoints.

Social implications of enhancement: Coercion as depicted in literature

In his comparison of the utopian and dystopian views on the use of psychopharmacology in Aldous Huxley's novels, *Brave New World* and *Island*, M. H. N. Schermer posits that the portrayal of pharmacological enhancement in a positive or negative light is dependent on the degree of governmental coercion.[7] These novels offer insight into the fears and promise of enhancement. *Brave New World* is the quintessential example of coerced enhancement. In the novel, the drug soma provides an artificial state of happiness and pleasure, and is used in various contexts as a method of social control. It is given to lower class workers after their shifts to keep them satisfied with their menial, tedious jobs. Even for members of higher castes, soma is an everyday part of life, used to prevent dissent, stress, and conflict, which have been programmed into the minds of the citizens to be bad things. It is used to stimulate sexual promiscuity, consumption, and limited social intimacy, which have been programmed into the minds of citizens to be good things. The drug thus reinforces the goals of the government, not those of the authentic self. As such, Schermer states that "In *Brave New World*, soma stands for alienation, de-humanization, and mind-numbing pleasure. This image is reflected in many present day ethical commentaries that fear the dehumanizing and identity- and authenticity-corrupting effcts of psychopharmacology."[7p119]

In contrast to the use of soma in *Brave New World*, in Huxley's novel *Island*, "the *moksha*-medicine used on the Island of Pala stands for revelation, authentic self-experience, mind-expansion and true human flourishing."[7p120] In the very different society of *Island*, psychopharmacology is not used to dehumanize its citizens, but to aid them in their own pursuits at understanding their true selves, values, and desires. It evokes understanding, not ignorance. And, perhaps most importantly, it is used not to increase control of the state over the individual, but to foster the abilities of the individual to better control the formation of an authentic self. Thus, while *Brave New World* reinforces the fears associated with enhancement—the control of superficially happy and submissive persons by a powerful governmental regime—moksha-medicine from *Island* shows instead the promise of enhancement, such as deeper understanding of self, the formation of more meaningful personal relationships, and above all, the capacity for personal growth that might be difficult to obtain without such aid.

Which scenario is more likely to occur? As Schermer points out, and as Huxley clearly understood, the plausibility of utopian or dystopian outcomes depends not on the technology itself, but on the social landscape into which it is introduced. While psychopharmacology might prove to be manipulative and inauthentic under a totalitarian regime, it could instead be beneficial and transcendent in a liberal, pluralistic democracy. Schermer states that the outcome "will depend for a great part on social factors, not on the drug or substance itself. Critique on psychopharmacological



enhancement is therefore better understood as a critique on the existing culture, trends and popular values, than as a critique on these substances 'as such.'" [7p126]

The competitive edge produced by enhancement

Coercion as a result of competition is a widely feared consequence of the widespread universal acceptance of enhancement. If coworkers are taking these drugs and are thus more productive, the argument goes, others might feel pressured to keep up. If most high school seniors take cognitive enhancing drugs to prepare for the SAT, resulting in higher scores, those who do not might be viewed as relatively less qualified in reviews by college admissions staff. Companies could have hiring preferences for employees willing to take enhancements to become more productive, a form of direct coercion, or consumers could demand pilots or physicians who use enhancements, a form of indirect coercion.[8]

These fears, though perhaps justified, are not criticisms of enhancement itself, but of the extant culture and value systems. It is these that decrease the authority of persons to make autonomous decisions leading to authentic selves. Competition is the basis for many of our life projects. While one could argue that these enhancements offer value independent of their competitive edge, such as learning for the sake of knowledge, or the ability to understand and appreciate art and poetry, the competitive benefits will be the main driving force for their use.[9] Since enhancement is only one arena in which competition becomes coercive, the real problem is the culture that promotes this competition, not the technology itself.

Although cognitive enhancement could be used to gain more control over our lives, this is nothing new. Every technology brings with it the potential for both good and sinister uses. The Internet, for example, has helped to spread information to the masses, but this information can be inaccurate or, worse, misused when placed in the wrong hands. Most would admit, however, that the Internet has brought with it more good than harm. Regulation is clearly necessary, but to ban enhancement because of the potential harms of its widespread use seems akin to banning the Internet.

The role of medicine—education and regulation

Medicine is one institution that could ensure that decisions regarding enhancement are autonomous and conducive to the development of authentic selves. While the use of enhancement technologies is and will continue to be widespread, medicine should play an integral role in use and regulation of enhancement to assure that safety and responsible use are top priorities. The medical profession would educate the public about the possible uses and limitations of cognitive enhancement.[2]

Because enhancement affects our most cherished capacities, safety and regulation of both development and administration of use are of the utmost importance. Medicine already has the infrastructure to accomplish these tasks. The FDA oversees the development of new drugs, and expanding its authority to regulating drugs used for enhancement is entirely possible. Doctors administer and monitor treatment to optimize the health of their patients; this function could encompass the administration of enhancement technology. Furthermore, physicians possess the knowledge necessary to administer these cognitive enhancing drugs in a safe, effective manner using evidence-based medicine and other methods of monitoring their effects. In this way, enhancement might be implemented in a responsible manner rather than in unregulated, illegal, and unsafe settings, as is currently the case.

Some of the views on the clinical scope of medicine and its underlying goals include the use of enhancement.[8] The most restrictive definitions of medicine allow only the power to treat disease. Such definitions make assumptions about what health is and, more specifically, what normal health is. Such views categorize impairments as those that constitute disease and those that do not because they are within the normal range of human variation. To treat these outlier states is to "medicalize" them, to consider them as somehow wrong. This could also lead to homogenizing the population and decreasing the diversity of human abilities and capacities. Enhancement could thus similarly result in the medicalization of the human condition, pushing patients toward a more generic, though increased, set of capacities, resulting in decreased diversity and individuality. The problem, of course, is that defining "normal" and treating diseases that take people away from this value results in the same effects, except that the population is selected towards the normal as opposed to the enhanced state. Moreover, while we have preconceived notions of normal, or

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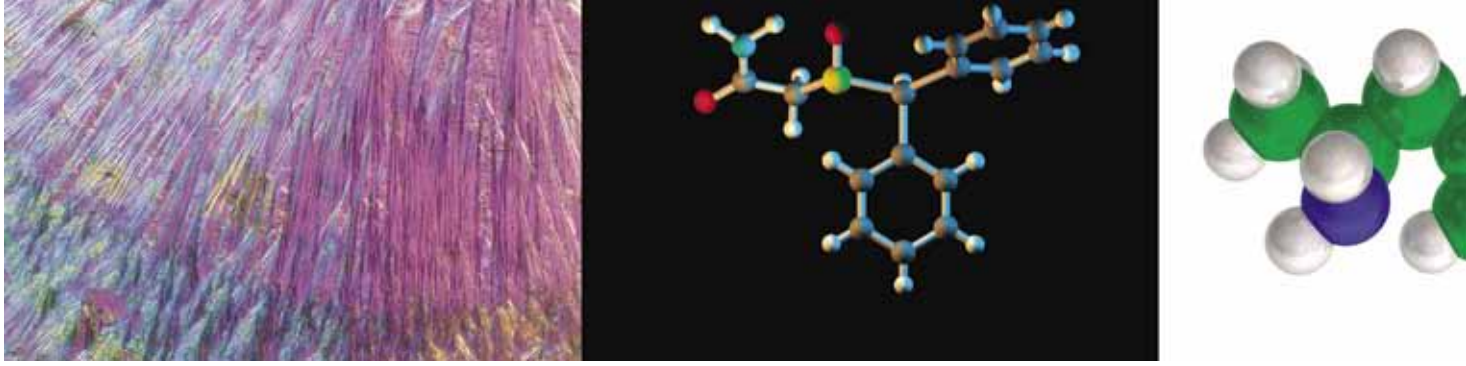
Since college, I have been fascinated by the brain, not only the science of how it works, but the implications this knowledge has to how we define ourselves. I also became interested in ethics after taking course work in this as an undergraduate at Princeton. I am looking forward to beginning my clinical years in medical school, to apply some of what I have learned to help individual patients. When I am not trying to be a doctor or contemplating the meaning of life, I enjoy swimming, comedy movies, and capturing the moments in life with my friends.



adequate, health, these notions constantly change with medical advances, so that an acceptable level of health is higher now than it was years ago. "Normal" health thus depends on the state of medical technology. Medicine therefore always progresses towards the enhanced state, so that the claim that an enhanced state does not qualify as normal is both arbitrary and unfounded. Current medical technologies such as preventive medicine do not qualify as disease treatment. If we allow that the goals of medicine go beyond the treatment of disease, medicalization is no longer a negative outcome of enhancement, but part of the profession's natural progression.

Goals of medicine—improving quality of life . . . is this enhancement?

A more consistent definition of the goals of medicine is the use of knowledge of the human body to improve the quality and length of human life. Such a definition encompasses not only therapeutic and preventive medicine, but also enhancement, in that enhancement could increase the quality of life as well as its duration for many people.

Enhancement might exacerbate existing inequalities in health care coverage. While it has great potential for individuals, it may also widen the gap between the rich and poor. Drug companies today may charge large amounts for their products; many are not covered by insurance, and others are only partially covered. Technology available only to the very wealthy limits the autonomy of the poor. If, on the other hand, such technologies are available to all, inequalities of access and resources are reduced, and the poor become empowered to make autonomous choices. Will enhancement technologies be widespread and inexpensive, or reserved for the elite? Will they create a two-tiered society, or a more equalized society?

The key issue is opportunity. Giving the poor equal opportunity to participate in enhancement creates a level playing field. The question, then, is how to make this a reality. James Hughes, for example, argues for the democratic use of enhancements, to make their benefits available to all, in a manner that will decrease inequality.[10] This depends on both extending coverage to the uninsured and including enhancement in this coverage. Hughes's justification for this inclusion is that the benefits of cognitive enhancing drugs, in regards to quality of life, should be judged in comparison to similar measures from other interventions so that interventions with the greatest potential to improve human life are where the limited resources would be spent.

Testing . . . the objective measure of enhancement

While cognitive enhancing drugs are often discussed as a group, they in fact represent a heterogeneous mix of components that ultimately result in increased cognition. Because cognition is a nebulous term, it is important that the effects and side effects of each drug be clearly understood so that responsible choices can be made for their use.

A rational, practical approach is necessary in testing the efficacies of cognitive enhancing drugs, involving both task-specific measurements and "real-world" tests that determine the applicability of such measures to situations patients will encounter. Task-specific measurements are important in determining what specific aspects of cognition are improved by these drugs. These tests are necessarily different from tests aimed at detecting improvement in the diseases for which these drugs were developed and approved. It is important that the tasks used to measure such efficacies are difficult enough to prevent a "ceiling effect" in which performance at higher levels could not accurately be measured. These tasks should test narrow domains within cognition, such as attention, alertness, and various forms of working memory to pinpoint the behavioral effects of these drugs. These results should be correlated, where possible, to neurological changes in brain function. Basic cellular, molecular, and genetic neuroscience research in human and appropriate animal models will elucidate the neuronal targets of these drugs, and spur development of new agents for specific targets.

More practical, "real world" measures of efficacy are also needed. These are important for assessing cognitive enhancing drugs, because they are ultimately the outcomes of most importance. Several approaches could be used to designing such measures. Individual groups of professionals might use their own unique, objective measurements of performance to judge the efficacy of various interventions. Pilots might be judged on flight simulations, while doctors might use simulated patient/surgical exercises. Standardized tests such as the IQ or SAT could also be used as a measure of efficacy, as well as of general applicability. Testing of real world tasks is complementary to task-specific tests. The combination is necessary to show that improvements in one facet of cognition are not overpowered by other effects. Knowledge from both types of studies would allow physicians and patients to make informed, accurate decisions regarding the use of cognitive enhancing drugs.

The goal: increase the efficacy:side effect ratio of enhancers

Safety monitoring will be vital to the ethical administration of cognitive enhancing drugs. Although adverse effects of many of these drugs may already be known by following use in patients with disease, further long-term monitoring is clearly necessary. Because use of these drugs would be aimed at improving normal function rather than at correcting disease, the acceptable level of adverse events must be very low. The biggest concern about the safety of these drugs, however, is the potential for abuse. Many of these drugs can cause euphoria and addiction at levels above those of their therapeutic benefit for cognition, so careful consideration must be given to administering enhancement in a way that limits the likelihood of this occurring. One mechanism is by drug design itself. Many newer psychostimulants are extended release or pro-drugs, which limit the amount of active drug available at any one time. A complementary approach is to formulate smaller doses to use for enhancement than those formulated for therapy. The correct dose would ensure efficacy because drug levels that are too high may actually impair cognition, and would decrease the risk of abuse. Finally, limiting the number of pills prescribed will limit patients' ability to take too much of the drug at any given time, another safeguard against the development of addiction.

It will be important to evaluate the patient as well as the drug when administering cognitive enhancing drugs. This requires not only an analysis of the patient's given capacities, but also a judgment on the patient's need for cognitive enhancement. The decision to use cognitive enhancing drugs may be appropriate when patient baseline capacities are low, or if the patient is engaged in cognitively demanding tasks. Those with lower baseline cognitive levels, such as patients with ADD, may require longer term therapy, and relatively higher doses. Patients in a state of relative cognitive impairment, such as those suffering from sleep deprivation, may also benefit from enhancement. An additional consideration is the cognitive difficulty of the tasks the patient is performing.

For patients with neither low baseline levels of cognitive capacity nor highly demanding tasks requiring much cognitive energy, the benefits of enhancement may not be clear. While enhancement might lead to better personal decisions in economic matters, moral dilemmas, or even relationships in such persons, it is equally possible that enhancement in these people would show no real benefit, and instead only have the potential for abuse.

By any name . . . these are enhancers of cognition

Several classes of drugs are used today for cognitive enhancement. The psychostimulants include Adderall, a mixed amphetamine salt, Ritalin (methylphenidate), and Vyvanse, a pro-drug form of D-amphetamine. These drugs increase dopamine and norepinephrine levels in the brain, contributing to their ability to improve attention. They are used in the treatment of ADHD, but have not been tested in the setting of enhancement. Psychostimulants are potentially addicting because of their ability to raise dopamine levels in the nucleus accumbens. This risk can be mitigated by using extended release formulations, which are available for both Adderall and Ritalin, as well as through the development of pro-drugs such as Vyvanse.

There are several other drugs that may have cognitive enhancing effects with a relatively low risk of addiction. In addition to having a low risk of abuse, these drugs have also been proven to be effective for enhancement.

Provigil (modafinil) is approved for the treatment of narcolepsy and night-shift sleep disorder. The mechanism of action of modafinil remains elusive; it has been proposed to have effects on norepinephrine, dopamine, GABA, glutamate, serotonin, orexin, and histamine systems in the brain.[11] The effects of modafinil in sleep-deprived pilots were investigated in two separate studies by John Caldwell and his colleagues. In the study published in 2000, they examined the effects of

200 mg of modafinil on sleep-deprived pilots in a helicopter simulation.[12] A subsequent study published in 2004 examined the effects of a smaller dose of modafinil on sleep-deprived fighter pilots.[13] Modafinil administration, compared to placebo, significantly reduced impairment, almost up to baseline levels.

Acetylcholinesterase inhibitors such as donepezil, used in the treatment of dementias such as Alzheimer's, block the degradation of ACh in the synapse, an effect that is believed to improve memory. Jerome Yesavage and colleagues investigated the enhancing properties of AchE inhibitors. Subjects were trained on a flight simulator, and were then given a course of either thirty days of donepezil (5 mg) or placebo; on the thirtieth day they returned for two more sessions of the flight simulator to derive the post-treatment score. Those in the donepezil group performed significantly better than those in the placebo group.[14]

While modafinil and donepezil improve various aspects of working memory and attention, caffeine is the "gold standard" against which newer enhancement drugs must be judged. Comparative studies are needed to determine which drugs are more effective, what safety issues arise, and whether increased enhancement justifies higher prices.

Top priority for medicine: assure autonomy for individuals and society

The moral debate about the use of enhancement centers on whether its use is the result of free, autonomous choice. As long as the conditions of autonomy are met for a given person, there is no bar to the use of enhancement. Issues relating to society's acceptance of enhancement, however, are more problematic, because the availability of enhancement may actually decrease autonomy for certain groups of people. Increased inequality and coercion to use such technologies are serious issues that must be overcome before the widespread use of enhancement is endorsed.

Medicine is the most practical institution to test and administer cognitive enhnacements in a responsible manner. The next step is to create the societal and institutional conditions allowing for the ethical use of enhancement. Discussions and dialog among physicians and ethicists will lead to guidelines for the ethical administration of cognitive enhancing drugs.

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References

1. Maher B. Poll Results: Look who's doping. Nature 2008; 452: 674–75.

2. Greely H, Sahakian B, Harris J, et al. Towards responsible use of cognitive-enhancing drugs by the healthy. Nature 2008; 456: 702–05.

3. Talbot M. Brain gain: The underground world of "neuroenhancing" drugs. New Yorker 2009 Apr 27: 32–43.

4. Dworkin G. The Theory and Practice of Autonomy. New York: Cambridge University Press; 1988: 48–61.

5. The President's Council of Bioethics. Beyond Therapy: Biotechnology and the Pursuit of Happiness. Washington (DC): National Bioethics Advisory Commission; 2003.

6. Parens E. Authenticity and ambivalence: Toward understanding the enhancement debate. Hastings Cent Rep 2005; 35: 34–41.

7. Schermer MHN. Brave New World versus Island—Utopian and dystopian views on psychopharmacology. Med Health Care Philos 2007; 10: 119–28.

8. Chaterjee A. Cosmetic neurology: The controversy over enhancing movement, mentation, and mood. Neurology 2004; 63: 968–74.

9. Parens E. Is better always good? The Enhancement Project. Hastings Cent Rep 1998; 28: S1–S17.

10. Hughes J. Citizen Cyborg: Why Democratic Societies Must Respond to the Redesigned Human of the Future. New York: Westview Press; 2004.

11. Lanni C, Lenzken SC, Pascale A, et al. Cognition enhancers between treating and doping the mind. Pharmacol Res 2008; 57: 196–213.

12. Caldwell JA Jr, Caldwell JL, Smythe NK III, Hall KK. A double-blind, placebo-controlled investigation of the efficacy of modafinil for sustaining the alertness and performance of aviators: A helicopter simulator study. Psychopharmacology 2000; 150: 272–82.

13. Caldwell JA, Caldwell JL, Smith JK, Brown DL. Modafinil's effects on simulator performance and mood in pilots during 37 h without sleep. Aviat Space Environ Med 2004; 75: 777–84.

14. Yesavage JA, Mumenthaler MS, Taylor JL, et al. Donepezil and flight simulator performance: Effects on retention of complex skills. Neurology 2002; 59: 123–25.

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P. 18: Cover of *Brave New World*. Reprinted courtesy of HarperCollins Publishers.

Pages 20 and 21, left to right:

Modafinil molecule. Credit Andre/Photo Researchers, Inc.

Adderall. Credit: Chris Gallagher/Photo Researchers, Inc.

Polarized light micrograph of amphetamine drug crystals. Credit: Astrid & Hanns-Frieder Michler/Photo Researchers, Inc.

Caffeine, 10x magnification. Credit: Michael W. Davidson/Photo Researchers, Inc.

A computer-generated space-filling molecular model of amphetamine. Credit: Scott Camazine/Photo Researchers, Inc.