SCIENCE AND SOCIETY

Neurocognitive enhancement: what can we do and what should we do?

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Our growing ability to alter brain function can be used to enhance the mental processes of normal individuals as well as to treat mental dysfunction in people who are ill. The prospect of neurocognitive enhancement raises many issues about what is safe, fair and otherwise morally acceptable. This article resulted from a meeting on neurocognitive enhancement that was held by the authors. Our goal is to review the state of the art in neurocognitive enhancement, its attendant social and ethical problems, and the ways in which society can address these problems.

Many are predicting that the twenty-first century will be the century of neuroscience. Humanity's ability to alter its own brain function might well shape history as powerfully as the development of metallurgy in the Iron Age, mechanization in the Industrial Revolution or genetics in the second half of the twentieth century. This possibility calls for an examination of the benefits and dangers of neuroscience-based technology, or 'neurotechnology', and consideration of whether, when and how society might intervene to limit its uses.

At the turn of the century, neurotechnology spans a wide range of methods and stages of development. Brain–machine interfaces that allow direct two-way interaction between neural tissue and electronic transducers remain in the 'proof of concept' stage, but show substantial promise[1]. Neurosurgery is increasingly considered as a treatment for mental illnesses and an array of new procedures are under development, including the implantation of devices and tissue[2]. Non-invasive transcranial magnetic stimulation (TMS) of targeted brain areas is the basis of promising new treatments for depression and other psychopathology[3].

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On the leading edge of neurotechnology is psychopharmacology. Our ability to achieve specific psychological changes by targeted neurochemical interventions, which began through a process of serendipity and trial and error in the mid-twentieth century, is evolving into the science of rational drug design. The psychopharmacopia of the early twenty-first century encompasses both familiar, and in some cases highly effective, drugs, and a new generation of more selective drugs that target the specific molecular events that underlie cognition and emotion[4]. For the most part, these drugs are used to treat neurological and psychiatric illnesses, and there is relatively little controversy surrounding this use. However, psychopharmacology is also increasingly used for 'enhancement' — that is, for improving the psychological function of individuals who are not ill.

The enhancement of normal neurocognitive function by pharmacological means is already a fact of life for many people in our society, from elementary school children to ageing baby boomers. In some school districts in the United States the proportion of boys taking methylphenidate exceeds the highest estimates of the prevalence of attention deficit–hyperactivity disorder (ADHD)[5], implying that normal childhood boisterousness and distractibility are being targeted for pharmacological intervention. The use of prescription stimulants (such as methylphenidate and dextroamphetamine) as study aids by high school and college students who do not have ADHD has recently drawn attention, and might include as many as 16% of the students on some campuses[6]. Sales of nutritional supplements that promise improved memory in middle age and beyond have reached a billion dollars annually in the United States alone[7], despite mixed evidence of effectiveness[8]. In contrast to the other neurotechnologies mentioned earlier, whose potential use for enhancement is still hypothetical, pharmacological enhancement has already begun.

What can we do?

Many aspects of psychological function are potential targets for pharmacological enhancement, including memory, executive function, mood, appetite, libido and sleep[9,10]. We will use the first two of these, memory and executive function, as examples to show the state of the art in psychopharmaceutical enhancement, the ethical issues raised by such enhancement and the policy implications of these ethical issues. A brief review of the state of the art in neurocognitive enhancement is offered here; additional

information is freely available to readers of this article at www.nyas.org/ebrief/neuroethics and in recent articles by Rose[11], Lynch[12] and Hall[7].

Memory enhancement. Memory enhancement is of interest primarily to older adults. The ability to encode new memories declines measurably from the third decade of life onwards, and by the fourth decade the decline can become noticeable and bothersome to normal healthy individuals[13]. Memory difficulties in middle or old age are not necessarily a harbinger of future dementia but can be part of the normal pattern of cognitive ageing, which does not make it any less inconvenient when we misplace our glasses or forget the name of a recent acquaintance. What can current and imminent neurotechnologies offer us by way of help?

The changes that underlie normal age-related declines in memory probably differ from those that underlie Alzheimer's disease, indicating that the optimal pharmacological approaches to therapy and enhancement might also differ. Although donepezil, a cholinesterase inhibitor that is used to treat Alzheimer's disease, did enhance performance in one study of healthy middle-aged pilots after flight simulator training[14], drug companies are looking elsewhere for pharmacological approaches to memory enhancement in normal individuals. Recent advances in the molecular biology of memory have presented drug designers with many entry points through which to influence the specific processes of memory formation, potentially redressing the changes that underlie both normal and pathological declines in memory. Most of the candidate drugs fall into one of two categories: those that target the initial induction of long-term potentiation and those that target the later stages of memory consolidation. In the first category are drugs that modulate AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) receptors to facilitate depolarization, including Cortex Pharmaceuticals' Ampakines[12]. In the second category are drugs that increase CREB (the cAMP response element-binding protein), a molecule that in turn activates genes to produce proteins that strengthen the synapse. One such drug is the molecule MEM1414, which is being tested by Memory Pharmaceuticals[7] (a company co-founded by one of the authors (E.K)).

The pursuit of mastery over our own memories includes erasing undesirable memories as well as retaining desirable ones. Traumatic events can cause lifelong suffering by the intrusive memories of post-traumatic stress disorder (PTSD), and methods are being sought to prevent the consolidation of such memories by pharmacological intervention immediately after the trauma[15]. Drugs whose primary purpose is to block memories are also being developed by the pharmaceutical industry[7]. Extending these methods beyond the victims of trauma, to anyone who wishes to avoid remembering an unpleasant event, is another way in which the neural bases of memory could be altered to enhance normal function.

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Enhancement of executive function. Executive function refers to abilities that enable flexible, task-appropriate responses in the face of irrelevant competing inputs or more habitual but inappropriate response patterns. These include the overlapping constructs of attention, working memory and inhibitory control. Drugs that target the dopamine and noradrenaline neurotransmitter systems are effective at improving deficient executive function, for example in ADHD, and have recently been shown to improve normal executive function as well[16,17].

For example, one of the authors (B.J.S.) found that healthy young volunteers performed the Tower of London problem-solving task more accurately after being given methylphenidate than after being given a placebo when the task was novel[16]. Methylphenidate also increased accuracy in a complex spatial working memory task, and this was accompanied by a reduction in the activation of areas of the brain that are related to working memory, as shown by positron emission tomography (PET)[17]. For the latter task, the amount of benefit was inversely proportional to the volunteers' working memory capacity as assessed by a different working memory task, digit span, with little or no benefit to those with the highest digit span performances. This is of interest in discussions of enhancement, because it indicates that, for this medication and this cognitive ability at least, those with lower levels of performance are more likely to benefit from enhancement than those with higher levels. Indeed, it is possible that some drugs would compress the normal range of performance in both directions. One of the authors (M.J.F.) found that the dopamine agonist bromocriptine improved performance on various executive function tasks for individuals with lower-than-average working memory capacity, but lowered the performance of those with the highest working memory capacities[18]. Whether enhancement can boost the performance of already high-performing individuals must be determined empirically for each drug and for each type of cognitive ability.

Newer drugs might improve executive function in different ways, influencing different underlying processes and interacting in different ways with individual differences (for example, in working memory capacity) and states (such as restedness). The newest potential neurocognitive enhancer is the drug modafinil, which is approved for the treatment of narcolepsy and is increasingly prescribed off-label for other purposes[19]. One of the authors (B.J.S.) found that it increases performance among healthy young adults on a set of executive function tasks that differs partly from those that are influenced by methylphenidate, with its effects resulting at least in part from an improved ability to inhibit impulsive responses[20].

What should we do?

Ethical problems and policy solutions. Neurocognitive enhancement raises ethical issues for many different constituencies. These include academic and industry scientists who are developing enhancers, and physicians who will be the gatekeepers to them, at least initially. Also included are individuals who must choose to use or not to use neurocognitive enhancers themselves, and parents who must choose to give them or not to give them to their children. With the advent of widespread neurocognitive enhancement, employers and educators will also face new challenges in the management and evaluation of people who might be unenhanced or enhanced (for example, decisions to recommend enhancement, to prefer natural over enhanced performance or vice versa, and to request disclosure of enhancement). Regulatory agencies might find their responsibilities expanding into considerations of 'lifestyle' benefits and the definition of acceptable risk in exchange for such benefits. Finally, legislators and the public will need to decide whether current regulatory frameworks are adequate for the regulation of neurocognitive enhancement, or whether new laws must be written and new agencies commissioned.

To focus our discussion, we will dispense with some ethical issues that are important but not specific to neurocognitive enhancement. The first such issue is research ethics.

Research on neurocognitive enhancement, as opposed to therapy, raises special considerations mainly insofar as the potential benefits can be viewed as smaller, and acceptable levels of risk to research subjects would be accordingly lower. This consideration is largely academic for those neurocognitive enhancers that come to market first as therapies for recognized medical conditions, which includes all of the substances that are now available for enhancement, although this might not be true in the future. Another important ethical issue concerns the use of neurocognitive enhancement in the criminal justice system, in which a large proportion of offenders fall in the lower range of cognitive ability in general[21] and executive inhibitory control in particular[22]. Although neurocognitive enhancement brings with it the potential for subtle coercion in the office or classroom, 'neurocorrection' is more explicitly coercive and raises special issues of privacy and liberty that will not be discussed here. Finally, the ethical problems that are involved in parental decision-making on behalf of minor children are complex and enter into the ethics of neurocognitive enhancement in school children, but will not be discussed here.

The remaining issues can be classified and enumerated in various ways. Four general categories will be used here to organize our discussion of the ethical challenges of neurocognitive enhancement and possible societal responses.

Safety. The idea of neurocognitive enhancement evokes unease in many people, and one source of the unease is concern about safety. Safety is a concern with all medications and procedures, but our tolerance for risk is smallest when the treatment is purely elective. Furthermore, in comparison to other comparably elective treatments such as cosmetic surgery, neurocognitive enhancement involves intervening in a far more complex system, and we are therefore at greater risk of unanticipated problems. Would endowing learners with super-memory interfere with their ability to understand what they have learned and relate it to other knowledge? Might today's Ritalin users face an old age of premature cognitive decline? The possibility of hidden costs of neurocognitive enhancement might be especially salient because of our mistrust of unearned rewards, and the sense that such opportunities can have Faustian results.

With any drug, whether for therapy or enhancement, we can never be absolutely certain about the potential for subtle, rare or long-term side effects. Instead, our regulatory agencies determine what constitutes a sufficiently careful search for side effects and what side effects are acceptable in view of a drug's benefits. Although consensus will have to be developed on these issues in connection with neurocognitive enhancement, we see no reason that the same approach cannot be applied here.

Coercion. If neurocognitive enhancement becomes widespread, there will inevitably be situations in which people are pressured to enhance their cognitive abilities. Employers will recognize the benefits of a more attentive and less forgetful workforce; teachers will find enhanced pupils more receptive to learning. What if keeping one's job or remaining in one's school depends on practicing neurocognitive enhancement? Such dilemmas are difficult but are not without useful legal precedent. Many of the relevant issues have been addressed in legislation such as Connecticut's Statute "Policies regarding the recommendation of psychotropic drugs by school personnel"[23] and case law such as Valerie versus Derry Cooperative School District[24].

"What if keeping one's job or remaining in one's school depends on practicing neurocognitive enhancement?"

Of course, coercion need not be explicit. Merely competing against enhanced co-workers or students exerts an incentive to use neurocognitive enhancement, and it is harder to identify any existing legal framework for protecting people against such incentives to compete. But would we even want to? The straightforward legislative approach of outlawing or restricting the use of neurocognitive enhancement in the workplace or in school is itself also coercive. It denies people the freedom to practice a safe means of self-improvement, just to eliminate any negative consequences of the (freely taken) choice not to enhance.

Distributive justice. It is likely that neurocognitive enhancement, like most other things, will not be fairly distributed. Ritalin use by normal healthy people is highest among college students, an overwhelmingly middle-class and privileged segment of the population. There will undoubtedly be cost barriers to legal neurocognitive enhancement and possibly social barriers as well for certain groups. Such barriers could compound the disadvantages that are already faced by people of low socioeconomic status in education and employment. Of course, our society is already full of such inequities, and few would restrict advances in health or quality of life because of the potential for inequitable distribution. Unequal access is generally not grounds for prohibiting neurocognitive enhancement, any more than it is grounds for prohibiting other types of enhancement, such as private tutoring or cosmetic surgery, that are enjoyed mainly by the wealthy. Indeed, in principle there is no reason that neurocognitive enhancement could not help to equalize opportunity in our society. In comparison with other forms of enhancement that contribute to gaps in socioeconomic achievement, from good nutrition to high-quality schools, neurocognitive enhancement could prove easier to distribute equitably.

Personhood and intangible values. Enhancing psychological function by brain intervention is in some ways like improving a car's performance by making adjustments to the engine. In both cases the goal is to improve function, and to the extent that we succeed without compromising safety, freedom of choice or fairness we can view the result as good. But in other ways the two are very different, because modifying brains, unlike engines, affects persons. The fourth category of ethical issue encompasses the many ways in which neurocognitive enhancement intersects with our understanding of what it means to be a person, to be healthy and whole, to do meaningful work, and to value human life in all its imperfection. The recent report of the President's Council on Bioethics[25] emphasizes these issues in its discussion of enhancement.

Attempts to derive policies from these considerations must contend with the contradictory ways in which different values are both challenged and affirmed by neurocognitive enhancement. For example, we generally view self-improvement as a laudable goal. At the same time, improving our natural endowments for traits such as attention span runs the risk of commodifying them. We generally encourage innovations that save time and effort, because they enable us to be more productive and to direct our efforts towards potentially more worthy goals. However, when we improve our productivity by taking a pill, we might also be undermining the value and dignity of hard work,

medicalizing human effort and pathologizing a normal attention span. The self-transformation that we effect by neurocognitive intervention can be seen as self-actualizing, or as eroding our personal identity. Neither the benefits nor the dangers of neurocognitive enhancement are trivial.

In weighing the dangers of neurocognitive enhancement against its benefits, it is important to note the many ways in which similar tradeoffs are already present in our society. For example, the commodification of human talent is not unique to Ritalin-enhanced executive ability. It is probably more baldly on display in books and classes that are designed to prepare preschoolers for precocious reading, music or foreign language skills, but many loving parents seek out such enrichment for their children. Americans admire the effort that was expended in Abraham Lincoln's legendary four-mile walk to school every day, but no-one would do that (or want their child to do that) if a bus ride were available. Medicalization has accompanied many improvements in human life, including improved nutrition and family planning. And if we are not the same person on Ritalin as off, neither are we the same person after a glass of wine as before, or on vacation as before an exam. As these examples show, many of our 'lifestyle' decisions end up on the right side of one value and the wrong side of another, but this does not necessarily mean that these decisions are wrong.

Disentangling moral principle and empirical fact. Since pre-Socratic times, philosophers have sought ways of systematizing our ethical intuitions, to identify a set of guiding principles that could be applied in any situation to dictate the right course of action. All of us have ethical intuitions about most situations; one goal of ethics is to replace case-by-case intuitions with principled decisions. A practical social advantage of ethical principles is that they can provide guidance when intuitions are unclear or inconsistent from person to person. The success of an ethical discussion depends on the discussants' ability to articulate the relevant principles as well as the relevant facts about a situation to which the principles apply.

In the ethics of neurocognitive enhancement we are still feeling our way towards the relevant principles and we still have much to learn about the relevant facts. Is it a matter of principle that 'medicalization' is bad, or that hard work confers 'dignity'? Or are these moral heuristics, rules of thumb that might be contradicted in some cases? And is it a matter of fact that Ritalin reduces our opportunities to learn self-discipline, or could it in fact have no effect or even help us in some way? Until we have disentangled the *a priori* from the empirical claims, and evaluated the empirical claims more thoroughly, we are at risk of making wrong choices.

"The question is therefore not whether we need policies to govern neurocognitive enhancement, but rather what kind of policies we need."

When not to decide is to decide. Neurocognitive enhancement is already a fact of life for many people. Market demand, as measured by sales of nutritional supplements that promise cognitive enhancement, and ongoing progress in psychopharmacology portend a growing number of people practicing neurocognitive enhancement in the coming years. In terms of policy, we will soon reach the point where not to decide is to decide. Continuing our current *laissez-faire* approach, with individuals relying on their physicians or illegal suppliers for neurocognitive enhancement, risks running afoul of public opinion, drug laws and physicians' codes of ethics. The question is therefore not whether we need policies to govern neurocognitive enhancement, but rather what kind of policies we need. The choices range from minimal measures, such as raising public awareness of the potential practical and moral difficulties of neurocognitive enhancement, to the wholesale enacting of new laws and the creation of new regulatory agencies. In between these extremes lie a host of other options, for example the inclusion of neurocognitive enhancement policies in codes of ethics of the professional organizations of physicians, scientists, human resource managers and educators, and short-term moratoria on neurocognitive enhancement.

Francis Fukuyama[26] has argued for new legislation to control the use of neurocognitive enhancement, among other biotechnologies. He characterizes the work of groups such as the President's Council on Bioethics in the USA and the European Group on Ethics in Science and New Technology as the "intellectual spade work of thinking through the moral and social implications of biomedical research", and suggests that "it is time to move from thinking to acting, from recommending to legislating. We need institutions with real enforcement powers."

We admit to being less certain about the right course of action. With respect to the first three categories of issue, concerning safety, freedom and fairness, current laws and customs already go a long way towards protecting society. With respect to the fourth category of issue, we believe that there is much more 'spade work' (in Fukuyama's words) to be done in sorting out the moral and social implications of neurocognitive enhancement before we move from recommendations to legislation. We should draw an object lesson from the history of federal stem cell legislation in the USA, which was enacted hastily in the wake of reported attempts at human reproductive cloning with limited public understanding of the issues. That legislation is now viewed by many as a setback for responsible biomedical research, and two states have now enacted their own laws to permit a wider range of research activity.

The need for more discussion of the issues is a predictable conclusion for an article like this one, but nevertheless a valid one. One urgent topic for discussion is the role of physicians in neurocognitive enhancement[27]. Although western medicine has traditionally focused on therapy rather than enhancement, exceptions are well established. Cosmetic surgery is the most obvious example, but dermatology, sports medicine and fertility treatments also include enhancement among their goals. Enabling a young woman to bank her eggs to allow later childbearing, for example, is not therapeutic but enhancing. Will neurocognitive enhancement join these practices? If so, will it be provided by specialists or family practitioners? What responsibility will physicians take for the social and psychological impact of the enhancements they prescribe, and by what means (for example, informal or formal psychological screening as used by cosmetic surgeons or fertility specialists)?

Beyond these immediate practical issues, we must clarify the intangible ethical issues that apply to neurocognitive enhancement. This requires interdisciplinary discussion, with neuroscientists available to identify the factual assumptions that are implicit in the arguments for and against different positions, and ethicists available to articulate the fundamental moral principles that apply. As a society we are far from understanding the facts and identifying the relevant principles. With many of our college students already using stimulants to enhance executive function and the pharmaceutical industry soon to be offering an array of new memory-enhancing drugs, the time to begin this discussion is now.

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doi: 10.1038/nrn1390

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Acknowledgements

This paper is based, in part, on a meeting held at the New York Academy of Sciences in June 2003, supported by a grant to J.I. from the National Science Foundation with co-sponsorship of a Mushett Family Foundation grant to the Academy. The writing of this paper was supported by NSF and NIH grants to M.J.F. and an NIH grant and a Greenwald Foundation grant to J.I.

Competing interests statement

The authors declare competing financial interests: see Web version for details.

Online links

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