

Responding to requests from adult patients for neuroenhancements

Guidance of the Ethics, Law and Humanities Committee



Dan Larriviere, MD, JD
Michael A. Williams,
MD, FAAN
Matt Rizzo, MD, FAAN
Richard J. Bonnie, LLB
On behalf of the AAN
Ethics, Law and
Humanities
Committee*

Address correspondence and
reprint requests to Dr. Dan
Larriviere, Department of
Neurology, Box 800394,
University of Virginia,
Charlottesville, VA 22908
dgl6t@virginia.edu

ABSTRACT

In the last decade, persons who have no diagnosed medical or mental health condition are increasingly seeking and utilizing, for the ostensible purpose of enhancing their memory or cognitive skills, prescription drugs that were originally developed to improve executive function or memory in persons diagnosed with disorders such as attention deficit hyperactivity disorder or Alzheimer disease. Evidence suggests that this practice, now known as neuroenhancement, is gathering momentum. As a result, neurologists may be encountering patients without a diagnosed illness asking for medications with the goal of improving their memory, cognitive focus, or attention span. Strong arguments have been made for and against this practice, often reflecting strongly held convictions concerning the appropriate practice of medicine. The purpose of this report is to provide neurologists with an overview of the ethical, legal, and social issues surrounding the use of pharmaceuticals prescribed to enhance or augment normal cognitive or affective functioning, as well as practical guidance for responding to an adult patient's request for neuroenhancement.

Neurology® 2009;73:1406-1412

GLOSSARY

ELHC = Ethics, Law and Humanities Committee; **FDA** = Food and Drug Administration.

In the last decade, persons with no diagnosed medical or mental health condition have been increasingly seeking and utilizing, for the purpose of enhancing their memory or cognitive skills, prescription drugs originally developed to improve executive function or memory in persons with disorders such as attention deficit hyperactivity disorder or Alzheimer disease.¹⁻³ This practice, now known as neuroenhancement, is gathering momentum.^{4,5} As a result, neurologists may be encountering patients without illness who request medications with the goal of improving their memory, cognitive focus, or attention span. Arguments have been made for and against this practice, often reflecting strongly held convictions concerning the appropriate practice of medicine.^{6,7}

Although much has been written about prescribing drugs for the purpose of neuroenhancement, the current literature consists mainly of ethically informed opinion that provides little or no practical

clinical guidance for neurologists who may face these questions.^{5,8} Also, no professional or societal consensus exists regarding how clinicians should approach the issue. The purpose of this report is to provide neurologists with 1) an overview of the ethical, legal, and social issues surrounding the use of pharmaceuticals prescribed to enhance normal cognitive or affective functioning; and 2) practical guidance for responding to an adult patient's request for neuroenhancement. This report and guidance should not be construed either to promote or discourage the prescription of neuroenhancements.

Notwithstanding debate regarding the definition of normal or abnormal, "normal patients" in the present context may be defined as patients who do not have sufficient signs, symptoms, or abnormalities of test results to satisfy criteria for a medical or mental health condition (referred to in this article as "normal" or "well"). Admittedly, the boundary be-

Supplemental data at
www.neurology.org

e-Pub ahead of print on September 23, 2009, at www.neurology.org.

*Members and staff of the AAN Ethics, Law and Humanities Committee who participated in development of this report and guidance are listed in the appendix.

From the Department of Neurology and School of Law (D.L.) and Schools of Medicine and Law (R.J.B.), University of Virginia, Charlottesville; Sandra and Malcolm Berman Brain & Spine Institute (M.A.W.), Department of Neurology, Sinai Hospital of Baltimore, MD; and Department of Neurology (M.R.), Roy J. and Lucille A. Carver College of Medicine, Iowa City, IA.

Approved by Ethics, Law and Humanities Committee on April 28, 2009; approved by the AAN Board of Directors on September 3, 2009.

Disclosure: Author disclosures are provided at the end of the article.

tween disease and nondisease states is sometimes unclear, even to medical experts. However, this report assumes that the neurologist has correctly characterized the patient's clinical condition (e.g., disease state or normal state).

For this report, neuroenhancement is defined as prescribing medications to normal adults for the purpose of augmenting their normal cognitive or affective function. Examples include the use of stimulants (e.g., methylphenidate) to improve performance on academic tests or to learn new skills, and the use of cholinesterase inhibitors (e.g., donepezil) to treat normal age-related memory changes. Evidence suggests that these medications can improve memory and executive function in normal individuals.⁹⁻¹¹ However, other evidence suggests that these effects are complex, may not be uniformly positive across all dose levels or age groups, and do not enhance all aspects of executive function or memory.^{12,13}

While medications currently prescribed for neuroenhancement were developed to treat patients with disease, it is conceivable that medications will be developed and approved explicitly for improving cognition and memory in normal persons.^{14,15} Because such drugs do not yet exist, this report and guidance will address the use of Food and Drug Administration (FDA)-approved medications for the off-label purpose of neuroenhancement.

METHODS We conducted a literature search in PubMed, PsycInfo, Web of Science, LexisNexis Academic, EBSCO host, and Google Scholar, using the terms listed in table 1. We then developed an annotated bibliography, summary, and preliminary recommendations, which the Ethics, Law and Humanities Committee (ELHC) examined to identify the key issues to be addressed.

The authors generated a series of drafts that were reviewed by the ELHC at each of 5 meetings between the fall of 2007 and spring of 2009. A draft was then distributed to the AAN Board of Directors and Committee Chairs for review, consistent with AAN procedures for development of position statements. The guidance statements (table 2). were presented to the AAN membership for public commentary at the Ethics Colloquium on April 27, 2009, during the annual meeting in Seattle. As a result, the ELHC further modified the report and the guidance at its meeting on April 28, 2009. The final report and guidance statements were submitted for publication on May 28, 2009, and after peer review, revision, and acceptance for publication were approved by the AAN Board of Directors on September 3, 2009.

NEUROENHANCEMENT AND THE GOALS OF MEDICINE Neuroenhancement in the context of the physician-patient relationship. It might be argued that normal persons who request neuroenhancement are not patients because they do not require treatment for symptoms, disease, injury, or disorder. However, the existence of a physician-patient relationship is not dependent on the patient's state of

Table 1	Search terms
	Neuroethics
	Intelligence enhancement
	Neural prosthetics (prostheses)
	Neuroprosthetics
	Neural augmentation
	Neuroaugmentation
	Brain boosting
	Neural enhancement
	Neuroenhancement
	Cognitive enhancement
	Mood enhancement
	Neural implants
	Memory enhancement
	Biotechnology and neurology
	Nanotechnology and neurology
	Brain-machine interface
	Neuroengineering
	Cognition/drug effects
	Cognitive science/trends
	Intelligence/drug effects
	Biomedical enhancement/ethics

health; it is only dependent on the mutual decision of the patient and physician to enter into the relationship (except in emergency circumstances). Thus, a person who requests neuroenhancement at the first encounter with a neurologist becomes a patient when the neurologist agrees either to evaluate the person or to prescribe a medication for neuroenhancement. If a patient with normal cognitive or affective function is in an existing patient-physician relationship with a neurologist, a request for neuroenhancement neither negates that relationship nor alters the neurologist's ethical and professional responsibilities to the patient. In either circumstance, the prescription of a medication for neuroenhancement occurs in the context of the physician-patient relationship, and the neurologist's ethical and professional responsibilities to the patient continue until the relationship is ended in accordance with professional standards for doing so.¹⁶

The goals of medicine. The traditional goals of medicine include physicians' obligations to 1) prevent and diagnose disease or injury; 2) cure or treat the disease/injury; 3) reduce suffering or, if that is not possible, help patients to cope with a disease or injury; 4) educate patients about disease/injury and prognosis; 5) help patients to die in peace and with dignity; 6) reassure the "worried well" who do not have a disease/injury.¹⁷ The traditional goals reflect the values and practices of the medical profession, provide a

Table 2 Guidance for responding to requests from adult patients for neuroenhancement medications*

1. Neuroenhancement is defined as prescribing medications to normal adult patients for the purpose of augmenting their normal cognitive or affective function.
2. "Normal adult patients" in the context of neuroenhancement may be defined as patients who, after appropriate evaluation, neither 1) satisfy accepted criteria for medical or mental health disease, disorder, or injury (collectively described as medical or mental health condition), nor 2) satisfy accepted criteria to be considered at risk for a medical or mental health condition that can be prevented with appropriate measures.
3. The prescription of medications for neuroenhancement occurs within the context of the physician-patient relationship.
4. Neurologists who provide neuroenhancement have ethical and legal responsibilities to patients.
5. Neurologists should respond to a request for neuroenhancement as they would respond to a chief complaint.
6. The prescription of medications for neuroenhancement is 1) not legally obligatory, 2) not legally prohibited, and therefore, 3) is legally permissible in the United States.
7. The prescription of medications for neuroenhancement is 1) not ethically obligatory, 2) not ethically prohibited, and therefore, 3) is ethically permissible.
8. Limited evidence exists regarding the efficacy and safety of medications prescribed to normal adults for neuroenhancement.
9. The liability risks associated with prescribing medications for neuroenhancement are uncertain.
10. A refusal to prescribe medications for neuroenhancement is ethically and legally permissible.
11. The medical principles for prescribing medications for neuroenhancement are identical to those for prescribing medications to treat medical conditions.
12. The principles of informed consent apply to the use of medications for neuroenhancement.
13. The potential influence of neuroenhancement medications on the patient's decision-making capacity should be considered.
14. Ending the prescription of a neuroenhancement medication after it has been initiated is ethically and legally permissible.

*The full annotated guidance is available as appendix e-1 on the *Neurology*® Web site at www.neurology.org.

basis for medical education, establish boundaries for the content and evaluation of medical practice, and provide a reference for patients' expectations of their physicians.

Practices consistent with the traditional goals of medicine compose a core of legitimate medical practices. However, some physicians have also embraced practices that are outside the traditional goals of the profession, such as expert witness testimony. Moreover, some areas of clinical practice, such as aesthetic forms of cosmetic surgery, represent uses of medical knowledge and skill to enhance the well-being of normal persons. These practices have generally been regarded as acceptable because they serve useful social purposes without compromising the profession's ca-

capacity to fulfill its traditional goals. However, some roles, such as participating in executions or other forms of punishment^{18,19} or participating in interrogations of detained persons,²⁰ are regarded as unacceptable because they undermine the profession's core values. Thus, the practice of medicine consists of a core domain of practices that serve the traditional goals of medicine, surrounded by a domain of other socially useful practices that are acceptable to the profession and society, surrounded by a group of practices that are considered illegitimate and should be prohibited.²¹

Practices in the core domain are often considered to be ethically obligatory (provided that the physician has the competence and the resources to provide them), while practices in the secondary domain are considered ethically permissible (whether they are encouraged or not), and those in the outer domain are considered ethically impermissible. From this perspective, prescribing neuroenhancement therapies lies outside the core domain of traditional medical practice and is not ethically obligatory. The key question is whether prescribing medications for neuroenhancement should be considered illegitimate and ethically impermissible, or whether it may be regarded as an acceptable practice—and therefore ethically permissible.

Prescribing neuroenhancement therapies is likely to be considered ethically permissible by society and by the profession for several reasons. First, like cosmetic surgeons, neurologists who provide neuroenhancement therapies will presumably do so for the purpose of improving the well-being of their patients.

Second, it is possible that as evidence accumulates about the trade-offs involved with prescribing medications to improve executive function or memory, many physicians will conclude that the benefits sufficiently outweigh the risks of harm. The FDA drug approval process would serve to keep the risk-benefit ratio within an acceptable range. Discussions with officials at the FDA indicate that any claims by pharmaceutical or device manufacturer that a product enhances the cognitive function of normal persons would be considered health claims that are subject to FDA regulation because neuroenhancement would "affect the structure or any function of the body of man."²²

Finally, pharmaceutical companies have financial incentives to develop medications that are effective and safe with an acceptable risk-benefit ratio. Medications that are found to be harmful by postmarketing surveillance (e.g., Vioxx) can be costly to pharmaceutical companies because of protracted litigation, large settlements or jury verdicts, and market devaluation of the company's shares.²³

REGULATORY, ETHICAL, AND LEGAL ISSUES TO CONSIDER BEFORE PRESCRIBING NEUROENHANCEMENT Authority for off-label prescribing. Until medications designed specifically for neuroenhancement in a normal population are developed, neuroenhancement will consist of “off-label” use of medications that were developed and clinically studied in cohorts of patients with a defined disease state.²⁴

FDA review and approval of a new drug application is limited to the uses for which the manufacturer has conducted safety and efficacy studies.^{25,26} To avoid constraining physicians’ ability to treat patients, the FDA’s position is that lack of approval of a drug or device for a particular use (e.g., neuroenhancement) does not imply that such off-label use is either disapproved or improper.²⁷ Thus, neurologists, in their professional judgment, and based on an individualized assessment of patients, may prescribe FDA-approved drugs or devices for any clinical indication or purpose that they believe will benefit their patients.²⁸ This prerogative includes 1) prescribing drugs for conditions other than those for which they were approved; 2) prescribing drugs for patient groups other than those for which they were originally approved; and 3) varying from the approved dosage or method of administering drugs.²⁸

Clinicians should have a medical basis or plausible rationale when prescribing medications for off-label use, which should be based on relevant medical principles and available evidence, including the pathophysiology of the disease, pharmacologic properties of the medication, studies or case reports in the professional literature, or professional experience. Neurologists must also consider whether doing so would be consistent with the practice of other neurologists in similar circumstances (i.e., standard of care). Physicians who consider prescribing medication for neuroenhancement are disadvantaged by the dearth of valid clinical studies concerning the effects and safety of these drugs on normal persons.⁹⁻¹³ Whether the effects shown in these studies can be extrapolated to the general population is unknown.

Before prescribing medications for off-label use of enhancement, neurologists should 1) inform patients that the medication has not been approved by the FDA for such use; 2) explain possible side effects, including potential risks to cognitive function; 3) discuss potential short-term and long-term risks of the medication; and 4) explain the alternatives to the medication (including not taking it).

AN ETHICAL FRAMEWORK FOR RESPONDING TO REQUESTS FOR ENHANCEMENT THERAPIES Neurologists should consider well-known medical and ethical principles when responding to requests for neuroenhancement by their patients.

Thorough assessment of the patient. A patient’s request for enhancement does not obviate a neurologist’s clinical responsibilities or ethical duties to the patient and should not automatically lead a physician to assume that the patient is well. A request for an enhancement may reflect a symptom the patient cannot articulate or may be the result of the patient’s interpretation of his or her own symptoms. The patient’s request for neuroenhancement should first be interpreted as a chief complaint that deserves further investigation. Neurologists must consider the possibility that patients who request neuroenhancement may have an underlying medical or mental health condition, including psychiatric disease, and undertake appropriate evaluations and referrals prior to initiating therapy.

Beneficence and nonmaleficence. As in any physician–patient relationship, physicians who contemplate prescribing neuroenhancement should maximize benefits and minimize harms.²⁹ In traditional medical practice, this involves weighing harms due to illness or injury against the risks and probable benefits of the proposed therapy. With neuroenhancement, however, the risks must be weighed against the putative benefit a patient hopes to gain by the intervention, such as becoming more competitive at work or school. However, putative benefits are difficult to quantify in risk–benefit analysis. Therefore, the better a patient and physician can articulate the specific goal of an enhancement therapy, the better they will be able to analyze the risks and benefits.

Clearly articulating the goals and hoped-for outcomes will allow the neurologist to identify and respond to unrealistic expectations at the outset and to reconsider whether to proceed with neuroenhancement if it appears that the patient’s expectations cannot be met. The physician and patient may also be able to find ways to achieve their goals that do not involve the use of pharmaceuticals; for example, referring the patient to a therapist for cognitive-oriented psychotherapy if affective issues are impeding the patient’s performance.

As is done when prescribing medications for disease, neurologists who write a prescription for neuroenhancement should work with the patient to identify when and why medication adjustment or cessation will be considered. For example, the patient can be referred for neuropsychologic evaluation to establish a baseline for future comparison. Alternatively, the neurologist and patient may agree to rely on reports from the patient’s family members to judge effectiveness of the intervention. While neurologists may rely on patient self-reports about the success or failure of the enhancement, they should be aware of the likelihood of a placebo response—both

when initiating and when discontinuing a medication. Clearly specified goals, along with agreed-upon measures of success or failure, are particularly important when the long-term risks of neuroenhancement medications in normal patients are unknown. In general, the medication should be stopped whenever the goals have been met or when they cannot be attained. When the goals depend on continuation of the medication (e.g., a patient who requests stimulant medication to use at work in order to be more productive), the patient and neurologist should agree ahead of time about the appropriate reasons to stop taking the medication.

Medications currently used for neuroenhancement do not appear to act uniformly to improve executive function or memory across age groups (e.g., elderly/young), populations (high/low IQ), or tasks (novel/repetitive), and in some cases may make cognitive function worse.¹⁵ Thus, the idea of simply “making people smarter” by prescribing these medications ignores the complex nature of cognitive function. In addition, the risks of the long-term use of off-label medications for neuroenhancement in normal patients without a medical or mental health condition are not known and may not be known for many years. The complex effects that the medications may exert, combined with a lack of information on long-term effects, may dissuade many physicians from offering enhancement medications except in the form of a clinical trial.³⁰

Respect for autonomy. Respect for autonomy does not always supersede other ethical principles, and at times neurologists may (and probably should) decline to honor the request for neuroenhancement based on their clinical judgment and their obligation to protect the patient’s welfare. As with any drug, the safety of neuroenhancement medications is a concern. The neurologist’s perception of the risk of harm may be very different from the patient’s perception of risk. The patient may view the risk as minimal, while the neurologist may view it as significant. Thus, neurologists who have reason to believe that neuroenhancement will result in more harm than benefit to a patient may ethically refuse to provide it on the basis of nonmaleficence. While such refusal may appear paternalistic, physicians have no ethical obligation to provide patients with treatments or medications simply because they want them. However, physicians are obligated to explain their refusal in terms that are understandable to patients without being demeaning or disrespectful. Furthermore, physicians may wish to continue their relationship with a patient aside from the use of neuroenhancement and should express this desire as a way of fostering the

relationship and avoiding the appearance of abandonment or disrespect.

Neuroenhancement drugs may alter cognition, emotion, and personality, and could potentially alter the decision-making capacity of autonomous individuals who must decide whether the benefits outweigh the risks of continuing to take the drug, especially those drugs that have potential for addiction or that stimulate the same neural pathways associated with addictive behaviors.³¹ Neurologists should consider this possibility and make appropriate plans with the patient. For example, they could agree that the patient’s spouse or other family member will have decision-making power about the cessation or continuation of the enhancement medication in the event the patient is unable to make these decisions.

Distributive justice. Neuroenhancement therapies are likely to be seen as “lifestyle” drugs and therefore are unlikely to be covered by third-party payers. Their use might thus be limited to a relatively small segment of the population who can afford them. Whether such an inequality of distribution will provide a sufficient basis to prohibit the use of neuroenhancement at all is an issue that will have to be addressed by the medical profession and society. For the time being, neurologists may wish to consider the effects such limited access may have on society when deciding whether to provide enhancements to patients who request them. The fact that our society tolerates inequality of distribution by virtue of ability to pay (e.g., cosmetic surgery, concierge medical practices) does not imply that neurologists are under an obligation to tolerate or promote inequality of distribution of neuroenhancements.

Conflicts of interest. In general, neurologists should avoid financial arrangements that could influence patient care decisions.³² Neurologists who would potentially benefit by prescribing neuroenhancement to their patients (e.g., by owning a significant amount of stock in the company that manufactures the medication) have an ethical obligation to so inform their patients.³² Neurologists may dispense medications for neuroenhancement from their offices if and only if the practice provides a convenience or accommodation to their patients without taking financial advantage of them. Patients should be given a choice to purchase the medication from the neurologist or to have the prescription filled elsewhere.³³

LIABILITY ISSUES The primary legal concern for neurologists is not whether the off-label prescription of neuroenhancement is legal—it is—but rather whether the practice may expose them to liability for malpractice. There is good reason to believe that in-

jury claims arising from prescription of medications for neuroenhancement will be analyzed by courts along traditional medical negligence lines, which is how the courts have generally analyzed injuries associated with elective cosmetic surgery.³⁴ However, it is possible that judicial application of the legal doctrines could tilt in a more aggressive direction (in order to shift more risk to the physician and thereby discourage such treatments) or in a less aggressive direction (to shift the risk of injury to the patient).

The following case illustrates how a court might shift the liability “set point” to favor a patient who is seeking to recover damages for harms caused by an elective cosmetic procedure. *Zalazar v Vercimack*³⁵ stands for the proposition that expert witness testimony is not necessary to prove causation in an informed consent case when the underlying medical procedure is elective because there is no medical issue that requires explanation for the jury. This means, in effect, that the jury is permitted to take the plaintiff’s word at face value when he or she says he or she would not have agreed to the procedure if he or she had known about a risk that was not disclosed. Other courts might use the same rationale in enhancement cases in which informed consent is at issue. In so doing, the end result may be to increase the risk of liability for physicians who prescribe neuroenhancement and thereby push risk-averse physicians away from this type of practice.

Neurologists who decide to provide neuroenhancement should refrain from guaranteeing a specific outcome and will need to become familiar with the laws in the states in which they practice in order to better understand the legal risks associated with this practice.

SUMMARY Although society may embrace the idea of physicians prescribing medications for neuroenhancement, physicians have no obligation to do so and may ethically refuse to do so. Neurologists must exercise their clinical and ethical judgment to decide whether to prescribe medications for neuroenhancement. It is ethically permissible for neurologists to prescribe such therapies, provided that they adhere to well-known bioethical principles of respect for autonomy, beneficence, and nonmaleficence. Because the prescription of medications for neuroenhancement occurs within the context of a physician–patient relationship, neurologists have ethical and legal obligations to their patients, even if neuroenhancement is the sole or primary aim of the treatment plan. Neurologists who prescribe medications for the off-label use of neuroenhancement are acting lawfully. Courts will likely analyze allegations of negligence in this context, using traditional malpractice

theory, but the possibility exists that legal rules might be altered to make it easier for a plaintiff to prove negligence.

ISSUES FOR FUTURE CONSIDERATION This report and guidance do not address neuroenhancement for normal children, a subject that may engender even more controversy than it does for adults.^{36,37} Issues that warrant attention include the long-term effect of medications on the developing brain; the distinction between normal and disordered cognitive and affective development; and the determination of decision-making capacity for children, adolescents, and teens whose wishes regarding neuroenhancement medications may differ from those of their parents. A comprehensive review and set of recommendations would require further effort by the American Academy of Neurology and related specialty societies.

ACKNOWLEDGMENT

The authors thank Drs. Jim Childress and Carol Manning for their critiques of earlier versions of this report. The authors also thank Tzipora Sofare, MA, Medical Editor, Sandra and Malcolm Berman Brain & Spine Institute, for her assistance in editing the manuscript.

DISCLOSURE

Dr. Larriviere has received honoraria for serving on the American Association for the Advancement of Science Faculty and has received an unrestricted educational grant from Allergan, Inc. Dr. Williams’ life partner holds stock in Medtronic, Inc. Dr. Rizzo reports no disclosures. Prof. Bonnie serves as a paid consultant to the Ethics, Law and Humanities Committee.

APPENDIX

**Members and staff of the AAN Ethics, Law and Humanities Committee who participated in development of this report and guidance: Michael A. Williams, MD, FAAN (Chair 2003–2009); Dan Larriviere, MD, JD (Chair 2009–); James Gordon, MD, FRCP, FAAN (Vice-Chair 2003–2009); James L. Bernat, MD, FAAN; Patricia Evans, MD, FAAN, FAAP; Elizabeth Habersfeld, MD; Peter L. Jacobson, MD, FAAN; Don W. King, MD, JD, FAAN; Dawn McGuire, MD; Tyler Reimschisel, MD; Matt Rizzo, MD, FAAN; Russell D. Snyder, MD, FAAN; Murray G. Sagsveen, JD, CAE (AAN General Counsel); John C. Hutchins, JD (AAN Staff Liaison); Karen M. Kasirski (Assistant).*

Received May 28, 2009. Accepted in final form August 10, 2009.

REFERENCES

1. Farah MJ. Neuroethics: the practical and the philosophical. *Trends Cogn Sci* 2005;9:34–40.
2. McCabe SE, Teter CJ, Boyd CJ, Knight JR, Wechsler H. Nonmedical use of prescription opioids among U.S. college students: prevalence and correlates from a national survey. *Addict Behav* 2005;30:789–805.
3. McCabe SE, Teter CJ, Boyd CJ, Guthrie SK. Prevalence and correlates of illicit methylphenidate use among 8th, 10th, and 12th grade students in the United States, 2001. *J Adolesc Health* 2004;35:501–504.
4. Maher B. Poll results: look who’s doping. *Nature* 2008; 452:674–675.
5. Farah MJ, Illes J, Cook-Deegan R, et al. Neurocognitive enhancement: what can we do and what should we do? *Nat Rev Neurosci* 2004;5:421–425.

6. Chatterjee A. Cosmetic neurology: the controversy over enhancing movement, mentation, and mood. *Neurology* 2004;63:968–974.
7. Kass L. The President's Council on Bioethics. *Beyond Therapy: Biotechnology and the Pursuit of Happiness*. Washington, DC: The President's Council on Bioethics; 2003.
8. Greely H, Sahakian B, Harris J, et al. Towards responsible use of cognitive-enhancing drugs by the healthy. *Nature* 2008;456:702–705.
9. Yesavage JA, Mumenthaler MS, Taylor JL, et al. Donepezil and flight simulator performance: effects on retention of complex skills. *Neurology* 2002;59:123–125.
10. Gron G, Kirstein M, Thielscher A, Riepe MW, Spitzer M. Cholinergic enhancement of episodic memory in healthy young adults. *Psychopharmacology* 2005;182:170–179.
11. Mehta MA, Owen AM, Sahakian BJ, Mavaddat N, Pickard JD, Robbins TW. Methylphenidate enhances working memory by modulating discrete frontal and parietal lobe regions in the human brain. *J Neurosci* 2000;20:RC65.
12. Elliott R, Sahakian BJ, Matthews K, Bannerjee A, Rimmer J, Robbins TW. Effects of methylphenidate on spatial working memory and planning in healthy young adults. *Psychopharmacology* 1997;131:196–206.
13. Turner DC, Robbins TW, Clark L, Aron AR, Dowson J, Sahakian BJ. Relative lack of cognitive effects of methylphenidate in elderly male volunteers. *Psychopharmacology* 2003;168:455–464.
14. Lynch G. Memory enhancement: the search for mechanism-based drugs. *Nat Neurosci* 2002;5 suppl:1035–1038.
15. de Jongh R, Bolt I, Schermer M, Olivier B. Botox for the brain: enhancement of cognition, mood and pro-social behavior and blunting of unwanted memories. *Neurosci Biobehav Rev* 2008;32:760–776.
16. American Academy of Neurology. Code of Professional Conduct, Sect 1.3. St. Paul: American Academy of Neurology; 2008.
17. Brody H, Miller FG. The internal morality of medicine: explication and application to managed care. *J Med Philos* 1998;23:384–410.
18. Gawande A. When law and ethics collide: why physicians participate in executions. *N Engl J Med* 2006;354:1221–1229.
19. American Academy of Neurology. Code of Professional Conduct, Sect 7.4. St. Paul: American Academy of Neurology; 2008.
20. Bloche MG, Marks JH. Doctors and interrogators at Guantanamo Bay. *N Engl J Med* 2005;353:6–8.
21. Miller FG, Brody H, Chung KC. Cosmetic surgery and the internal morality of medicine. *Camb Q Healthc Ethics* 2000;9:353–364.
22. Food Drug and Cosmetic Act, Section 201 (g)(1)(C).
23. Merck settles Vioxx litigation. *Nat Rev Drug Discovery* 2007;6:946–947.
24. Farah MJ. Emerging ethical issues in neuroscience. *Nat Neurosci* 2002;5:1123–1129.
25. 21 USCA sec 360e(d) (1)(A).
26. 21 CFR sec 314.50–54, 807.92(a)(5), 807.100(b)(1)(1999).
27. *Richardson v Miller*, 44 S.W. 3d 1 (Tenn. Ct. App. 2000).
28. *Richardson v Miller*, 44 S.W. 3d 1 (Tenn. Ct. App. 2000), p. 13.
29. Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*, 6th ed. Oxford: Oxford University Press; 2009.
30. McNutt RA. Shared medical decision making: problems, process, progress. *JAMA* 2004;292:2516–2518.
31. Volkow ND, Fowler JS, Logan J, et al. Effects of modafinil on dopamine and dopamine transporters in the male human brain: clinical implications. *JAMA* 2009;301:1148–1154.
32. American Academy of Neurology. Code of Professional Conduct, Sect 5.2. St. Paul: American Academy of Neurology; 2008.
33. American Academy of Neurology. Code of Professional Conduct, Sect 5.3. St. Paul: American Academy of Neurology; 2008.
34. Carmichael ML. Liability of physicians or hospital in performing cosmetic surgery upon the face. *A.L.R.* (3d) 54; 1255 Sec 2[a](1973);54.
35. *Zalazar v Vercimack*, 633 N.E. 2d 1223 (Ill. App. 3rd Dist. 1993).
36. Gill DG. “Anything you can do, I can do bigger?” The ethics and equity of growth hormone for small normal children. *Arch Dis Child* 2006;91:270–272.
37. Mayes R, Bagwell C, Erkulwater J. ADHD and the rise in stimulant use among children. *Harv Rev Psychiatry* 2008; 16:151–166.