

Opinion Paper

The Medical Ethics of Cognitive Neuroenhancement

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Abstract: Prescription stimulant medications have been sought for cognitive “neuroenhancement”, the practice of enhancing ostensibly normal cognitive function such as attention span, focus, and memory. This trend, particularly studied in college students, has driven a debate about many ethical aspects related to cognitive enhancement; however, the central role of physicians and the medical ethics of this practice have been minimally investigated. In this paper, a clinical case serves as the focal point to review the current state of prescription stimulant use for enhancement, beginning with the medical and legal problems related to the surreptitious, yet common, behaviors of diversion and malingering. In contrast, there may be a growing trend for individuals to seek prescription stimulants “openly” (without malingering or diversion) as a direct request from their physician, which leads to complex ethical questions. A model of clinical-ethical decision making (the “four-box model” from Jonsen et al.) is applied to analyze the factors that a physician must consider when deciding whether to engage in the open prescribing of a stimulant neuroenhancer to otherwise healthy, autonomous adults. Four domains are explored in depth: medical indications, quality of life / beneficence, patient preferences, and contextual factors. Relevant experiences from the medical disciplines involved in athletic enhancement and cosmetic enhancement are discussed. Although an overall ethical framework for neuroenhancement continues to evolve, from a perspective of medical ethics there are presently significant reasons to be wary of cognitive neuroenhancement with stimulant medications.

Keywords: Neuroenhancement; cognitive enhancement; stimulant enhancement; neuroethics; medical ethics; cosmetic enhancement; athletic enhancement

1. Introduction: clinical case

Martin is a 26 year-old self-employed man who recently relocated to a new city and has scheduled to see a new psychiatrist. He reports being diagnosed with attention-deficit hyperactivity disorder (ADHD) 4 years ago, when he started business school, and has been prescribed several types of stimulant medications. Martin describes the challenges of his work, which requires him to spend as many as 12 hours per day manipulating large databases of information. He feels increasingly distracted and bored after 2 to 3 hours of consecutive work in front of the computer screen, and has trouble sustaining his attention and motivation.

As the psychiatrist gathers a detailed history, he is increasingly doubtful about a diagnosis of ADHD. At the end of his assessment, he confronts Martin with the lack of evidence to validate the diagnosis. Martin uncomfortably confesses that he doesn't think that he has ADHD either, and that he was diagnosed previously by a psychiatrist who was, "let's just say, very willing to prescribe medications." Martin then genuinely offers several ways stimulants do help him, including boosting his concentration and motivation, helping him get a "competitive edge," and providing an overall "better feeling" about his performance.

Neuroenhancement can be broadly defined as any attempt to augment or enhance ostensibly normal aspects of brain functioning, including, but not limited to cognition, mood, appetite, or sexual functioning. Over the past decade, the neuroenhancement of cognition, in particular, has drawn significant attention from the public and the scientific community, in large part due to the apparent rates at which prescription medications have been sought for this purpose. While there are many ways to potentially enhance cognitive function (see Table 1), the "classic" ADHD stimulants (methylphenidate and amphetamine products) have been specifically obtained and used for the purpose of cognitive enhancement by otherwise healthy, autonomous adults, and are therefore the focus of this paper's medical-ethics analysis [1–6].

Several initial questions are raised by Martin's clinical case: Does Martin have an illness? Did he misrepresent his symptoms in order to falsely obtain a psychiatric diagnosis and treatment? Was Martin's prior psychiatrist "duped", or did he assign a diagnosis to justify the use of a stimulant? What are the laws pertaining to the acquisition and use of prescription stimulants as enhancers? This article begins with a review of the current state of surreptitious stimulant use as cognitive enhancing agents, then examines the complex ethical dilemmas physicians face in deciding whether to prescribe stimulant enhancement to healthy adults "openly", that is, in full acknowledgement of the absence of any diagnosed illness.

2. The current state of cognitive enhancement: illicit prescription stimulant use

It is estimated that 8.5% of all Americans have used prescription stimulants illicitly at some point in their lifetime, and 12% of people between ages 21 and 25 reported lifetime use [7]. The preponderance of epidemiologic research on cognitive enhancement with stimulants has been conducted in college populations, where students are two to three times more likely to use "non-medical" or illicit prescription stimulants than non-students of the same age [9]. Past-year prevalence rates among college students may be as high as 25–35% depending on the geographic location of the school, with half using at least monthly, if not more often [9,10].

Table 1. A spectrum of cognitive neuroenhancement

Type of cognitive neuroenhancement	Description and examples
Non-prescription	Behaviors and technology Some ethicists describe advances in “human ingenuity” as a means of cognitive enhancement, citing for example: written language, printing, and the Internet. Other examples of behaviors and technology that may enhance performance include: education, good health habits (exercise, sleep, healthy diet), information technology, cognitive enhancing courses (such as Luminosity or “brain boot camps”) and test preparatory courses (such as Kaplan, Princeton Review, etc.).
	Foods, dietary supplements, nutraceuticals, and other non-prescription substances Certain foods, substances, and dietary supplements or nutraceuticals have varying degrees of evidence for cognitive enhancing potential, such as: caffeine (or l-theanine), nicotine, piracetam, gingko biloba, vitamin E, fish oil, sadenosylmethionine (SAM-E), acetyl-L-carnitine, among many other supplements.
Prescription	ADHD stimulants Amphetamine and methylphenidate products, the “classic” ADHD stimulants, are the most commonly sought (and studied) prescription cognitive neuroenhancers at this time. These medications are predominantly obtained through illicit means (diversion or malingering). They may be increasingly obtained by a direct or “open” request to a physician. Amphetamine and dextro-amphetamine products include: Adderall, Dexedrine, Desoxyn, and Vyvanse. Methylphenidate products include: Ritalin, Concerta, Daytrana, Metadate, Methylin, Focalin.
	Other stimulants Modafinil and armodafinil (Provigil and Nuvigil) are FDA approved for narcolepsy, obstructive sleep apnea, or shift-work disorder, and appear to be gaining popularity as cognitive enhancing agents.
	Dementia drugs Medications that are commonly used in the treatment of dementia and cognitive impairment are of interest for cognitive neuroenhancement, specifically the augmentation of memory. It is unclear how frequently these medications are being used for enhancement at this time. The primary example is donepezil (Aricept), though there are several experimental drug classes being investigated (such as ampakines).

The use of stimulant medications for the purpose of cognitive enhancement has many terms in the literature, including: “non-medical”, “non-prescription”, and “illicit prescription” stimulant use. Of these, *illicit prescription stimulant use for cognitive enhancement* is likely the most accurate term given that the medications are invariably obtained through diversion or malingering, both of which are federal crimes (charged as a misdemeanor or felony based on state laws and/or the discretion of the prosecutor). Diversion describes when individuals who are being treated for ADHD share, trade, or sell their prescribed stimulants with others, and the research suggests that the overwhelming majority of stimulant enhancers are obtained in this manner [10,11]. It is estimated that as much as 30%

of the stimulants intended for people with ADHD are diverted to other users [12]. More than half (54%) of prescribed college students reported being approached to divert their medications [5,13,14].

Returning to the clinical case, Martin did not obtain his stimulants through diversion; rather, he was coached by a friend to recite the symptoms of ADHD in order to obtain a prescription from a doctor. The deliberate misrepresentation or manufacturing of symptoms for secondary gain is clinically termed “malingering”. The rates of malingering ADHD for stimulants are not well known, though one study reported that 20% of past-year illicit users obtained their stimulants in this manner [8]. While diversion and malingering are today’s prevailing methods to obtain prescription drugs for neuroenhancement, these practices are neither legal nor consistent with safe medical care or societal ethics.

3. An uncertain future for cognitive enhancement: open prescribing of stimulant medications

Although Martin does not have ADHD, does that mean a physician should not prescribe him a stimulant? Several authors have anticipated an increasing likelihood that patients will directly and openly request cognitive enhancers from their physicians. Some have called for active development of such an open pathway to enhancement, favoring it as “innovative”, and arguing that with “appropriate research and evolved regulation” it would be possible to maximize the benefits and minimize harms for society [2].

In 2009, the American Academy of Neurology published a practical guideline for how physicians might respond to open requests for neuroenhancement from adult patients, where the authors stated that the practice is legal and ethically permissible, but not obligatory [15]. According to this perspective, a psychiatrist evaluating a patient like Martin could transition from a *treatment* to an *enhancement* practice with the following steps: 1) remove the diagnosis of ADHD 2) change the financial structure of the visit to a fee-for-service (enhancement is not covered by third party insurers) 3) screen for contraindications, obtain the patient’s “informed consent”, and respect his autonomy to do what he wants with his body, and 4) establish future appointments for monitoring and prescribing of stimulants.

Recommendations paving a path for open cognitive enhancement have by no means been universally accepted. In fact, while there has been vigorous ethical debate about neuroenhancement, the central role of the physician and the relevant ethics in this scheme have been minimally addressed [2,16–18]. A small but growing body of literature on physicians’ attitudes demonstrates little enthusiasm and significant reservations for the opportunity to enhance patients’ normal cognition [18–20].

Accordingly, a physician could also refuse to prescribe stimulant enhancement for Martin. But on what grounds would a physician base either decision? Currently, there is no framework that specifically addresses the ethics related to clinical decision making in cases of enhancement. Therefore, an ethical analysis of openly prescribing cognitive enhancement to Martin is undertaken by applying an existing framework from Jonsen et al.’s *Clinical Ethics* [21], and incorporating perspectives on enhancement from the fields of sports medicine and aesthetic/cosmetic surgery. The four primary domains to be addressed are: medical indications, quality of life / beneficence, patient preferences, and contextual features.

3.1. Medical indications and the ethical rationale for cognitive enhancement

What is the medical indication for Martin’s treatment? What are the diagnosis, prognosis, and treatment options? This usual starting place in medical decision making is an obvious stumbling block in cases of enhancement, where there is no “medical illness” diagnosed as the goal of treatment.

To medically and ethically justify cognitive enhancement, a physician must first and foremost believe that he or she is not limited to practicing within the “traditional” goals of medicine, which include: 1) promotion of health and prevention of disease 2) relief of symptoms, pain and suffering 3) cure of disease 4) prevention of untimely death 5) improvement of compromised status 6) education and counseling of patients, and 7) avoidance of harm to the patient [15,21]. Proponents argue that practicing outside of these time-honored goals might be considered “fringe,” but nevertheless ethically permissible so long as the practices are “socially useful” and acceptable to the profession and society [2,15]. Arguments against fringe practices include the need to uphold “virtue-based” ethics in medicine (considered by some to be the highest ethical standard in medicine), where there is specific emphasis on avoiding practices that lie at the margin of moral responsibility [22].

Careful patient selection and stratification of risks are common procedures in medical treatment, where the ethical duty of non-maleficence, or “do no harm”, is the core ethical principle. A physician must consider what level of risk to the patient is ethically acceptable when prescribing for the sole purpose of enhancement. The psychopharmacology of stimulants, which has been well described, provides a neurobiological background for understanding the potential benefits and risks (see Table 2). The side effects of stimulants are predictable based on the sympathomimetic pharmacology, and the risk of addiction is strongly correlated to the pro-dopamine effects in the brain’s “reward pathways” (see Table 3).

Table 2. Summary of stimulant psychopharmacology

- Methylphenidate appears to inhibit the re-uptake of dopamine (DA), and to a lesser degree norepinephrine (NE), and thereby increases extracellular levels of these neurotransmitters. Amphetamines act similarly, but, in addition, they likely increase the rate of release of DA and NE [71,72].
- The benefits of increased attention, and decreased impulsivity and hyperactivity, appear related to modulation of adrenergic neurotransmission in the meso-limbic and meso-cortical pathways of the brain, and relevant cortical and sub-cortical projections to the pre-frontal cortex [71,73].
- The high potential for addiction to stimulants is related to activation of the brain’s “reward pathways” (increased DA levels in the nucleus accumbens, medial prefrontal cortex, amygdala, and thalamus [74], whereby behaviors are maintained that lead to repeat administration [75].

Studies of college-users provide a reasonable foundation for stratifying the risks associated with use of stimulants as cognitive enhancers. Interestingly, although stimulant enhancement users in college perceive the overall medical risks as “low” [4,23], they paradoxically report experiencing a higher than expected rate of side effects such as anorexia (63%), insomnia (60%), irritability (50%), headaches (18%), stomachaches (18%), dizziness or lightheadedness (18%), and sadness (16%) [24].

From a medical perspective, the incidence of these side effects is alone a cause for concern. Further caution should be raised about the potential for a “slippery slope” of prescribing, whereby side-effects like insomnia and irritability might be managed with *additional* drugs such as benzodiazepines or sedative-hypnotic sleep aids.

Stimulants also have a significant risk of serious or life-threatening adverse effects (see Table 3). The U.S. Food and Drug Administration issued two “black box warnings” (the agency’s highest level of warning) for the risks of cardiovascular events and death, and the high potential for abuse and dependence. More recently, the Canadian government issued a warning for increased risk of suicidal thoughts and behaviors [25]. Studies of college stimulant enhancement users have consistently identified an overrepresentation of drug and alcohol use, binge alcohol use, and a greater odds of meeting diagnostic criteria for substance use disorders compared to non-users [26,27]. Multiple surveys have verified that the primary motivations for stimulant use are to improve concentration, increase alertness, and to aid in study and test performance [13,23,24]. However, one study found that only 26% of students used prescription stimulants *solely* for academic enhancement, while the remainder (74%) used for academic *and* recreational purposes (54%), or recreation only (20%) [28]. Other studies have reported similar rates of use for the explicit purpose of “getting high” (31–43%) [9,24].

Table 3. Common side effects and warnings of stimulant medications

Side effects*	Percent reporting side effects	Warnings
Hypertension	7–35%	• U.S. Black box warning*: high potential for abuse and dependence
Insomnia	12–27%	• U.S. Black box warning*: misuse may cause sudden death, stroke or heart attack
Headaches	26%	• Canadian prescribing warning**: stimulants may increase suicidal thoughts and behaviors.
Anorexia	22–36%	
Dry mouth	2–35%	
Abdominal pain	11–14%	
Increased heart rate	6%	
Irritability or emotional problems	2–9%	
Anxiety	8%	
Agitation	8%	
Dizziness	2–7%	

References: *[33,34]; **[25]

These characteristics of college-users underscore an essential need for physicians to carefully monitor patients’ usage and potential for misuse, but also trigger immediate concerns about the difficulty in accomplishing that task. As one indicator of the problem, the number of emergency department visits related to stimulant medications tripled between 2005 and 2010 [29]. Of those visits, approximately a third involved illicit prescription stimulants and nearly half involved co-ingestion of other drugs or alcohol.

A cautionary tale is provided by the field of sports medicine, and the challenges experienced in monitoring patients’ usage of prescribed enhancers [30]. In the 1980’s, Dr. Robert Kerr, an outspoken physician and author of the book “The Practical Use of Anabolic Steroids with Athletes,” was notorious for prescribing steroids for athletes, bodybuilders, and policemen [31]. He argued that with safe controls and medical monitoring, the risks of steroids could be minimized and the benefits

maximized. Dr. Kerr eventually stopped this practice when he realized that athletes could not be trusted to limit their consumption in accordance with his instructions [30,32].

Additional details of the clinical case are revealed as the psychiatrist explores the benefits, side effects, and risks of abuse with the patient: *Martin reports that the benefits include improvements in his attention, motivation, and a subtle boost in his mood. However, he also reports mild anxiety, jitteriness, suppressed appetite, and the next day he feels exhausted and more irritable than usual. Martin prefers the instant release Adderall over the extended release because it is less expensive and he can “feel it working”, even though it wears off more quickly and he wonders if taking more would help. Martin used to binge drink in college, but states that he only drinks socially and moderately now.*

3.2. Quality of life and beneficence

Improving an individual's subjective well-being and quality of life (the primary goal in the principle of beneficence) are cited as major reasons why physician-administered enhancements, such as cosmetic surgery and enhancements, are ethically accepted by society, consumers, and the medical establishment [35,36]. Consumers of cosmetic surgery seek to fulfill a personal wish by correcting a self-perceived deficit in their appearance that causes emotional dissatisfaction or discomfort, or in some cases social handicap [37,38].

By extension, cognitive enhancement may be similarly sought to address self-perceived deficits or psychosocial factors that include a level of dissatisfaction, anxiety, fear, behavioral problems, or external pressures, though the rationale is often framed in innocuous phrases such as “people just want to do their best and be productive” or “perform at one's highest ability” [2,39,40]. The driving forces for cognitive enhancement also resonate with the competitive motivations of athletes who seek sports enhancement, which include pressures to perform and win, economic motives, and dissatisfaction with one's innate performance limitations [41]. The motivations for cosmetic, athletic, and cognitive enhancement may overlap considerably, with potentially common core psychological or social issues or needs (see Table 4).

Students who use stimulant enhancers are motivated by hopes of achieving better concentration, attention, memory, and tangible benefits in academic performance, especially before tests or during finals week [13]. Yet, the evidence that stimulant use among healthy adults produces objective improvements in measures of cognition is inconclusive. It appears that there may be modest benefits in consolidating long-term declarative memory, though these effects are highly variable based on the type of experimental task given and the individual's baseline cognitive ability level and personality [12,13,42]. In contrast, stimulant enhancement does not currently appear to provide meaningful improvements in cognitive control, working memory, or executive functioning [13]. There is a lack of evidence from healthy subjects to demonstrate that enhancement translates into any real-world, objectively measurable benefits such as an improvement in test scores, grade point average, or level of academic or occupational functioning.

Table 4. Motivations to seek enhancement and potential core psychosocial issues

Motivations to seek cognitive enhancement	Examples	Potential core psychosocial issues	Potential ways to address core issues
To compensate for self-perceived deficits, or to feel better about oneself. To meet excessive, self-imposed demands or expectations.	A college student worries excessively before each exam, striving to achieve an “A”, has difficulty accepting variations in performance. Feels that she is not “doing enough” or is not “smart enough” to get into grad school.	Dissatisfaction with one’s authentic “best effort” or anything “less than perfect”. High self-criticism, low self-worth, or unstable self-confidence.	Address perfectionism and develop healthier personal value systems. Address self-criticism and low-self esteem. Address rigid thinking, and cognitive distortions such as all-or-nothing thinking, discounting the positive, and catastrophization.
To meet excessive demands or expectations imposed by others such as parents, peers, employers, or society. To be recognized or praised by others.	Pressure from employer to increase productivity. Pressure by parents to get into “the top college”. Societal or pop culture messages that convey “winning is everything”.	Fear of failure, inadequacy, or shame. Fear of loss or rejection. Belief that self esteem must be earned.	Improve assertiveness to decide what expectations are reasonable. Improve self-confidence, develop the ability to “think one’s own thoughts”. Address low self-esteem and need for external validation, develop self-acceptance.
To increase motivation, “sustain” attention, or to make work or tasks seem more interesting.	Lack of interest in subject matter of school or work. Trying to remain focused for extended, un-interrupted periods of time.	Mismatch in goals and desires. Intolerance of boredom, challenging material, or less stimulating activities. Unrealistic expectations for the capacity of human attention span.	Improve tolerance and management of boredom. Evaluate personal goals and desires. Reset or “ground” expectations for what is humanly capable.
To compensate for “real deficits”, or objective problems in functioning or performance (i.e. self-treatment).	An “A” college student is now a “C” student, leading parents to wonder if he has ADHD or some other problem.	Possible psychosocial stressors impacting functioning. Possible underlying psychiatric illness.	Evaluation for psycho-social stressors, mal-adjustment, anxiety, depression, substance abuse, ADHD, or other potential medical or mental health etiologies.
To get a competitive advantage, or to “maximize” or “boost” performance. To achieve “success” or financial or material gain. To do as much as possible with the least amount of effort, or in the least amount of time.	Student seek an “edge” during finals or high-stakes entrance exams. Aim to be more “competitive” in workplace, seeking financial rewards. A person is over-subscribed and feels fatigued in trying to keep up with competing social, academic, familial, and occupational commitments.	Fear of loss of opportunity or rewards, fear of failure. Dissatisfaction with not being “at the top”, or being “just average”.	Address “hypercompetitive” mentality that may cause undue anxiety or worries. Address and modify detrimental consequentialist mentality (“the ends justify the means”). Assess and re-calibrate school-life or work-life balance. Develop acceptance of natural limits of time, and human limits of energy and attention. Work on prioritizing goals.

To keep up with others who are using stimulant enhancers.	A person knows that his peer or co-worker is using stimulant medications to enhance occupational performance.	Fear that one cannot compete. Concerns about fairness that lead to a modified prisoner's dilemma ("everyone else is using, therefore I must use").	Address anxiety and preoccupation about competition. Re-focus on the deontological value that "the process of an endeavor, is as important as the result."
To compensate for detrimental behaviors.	Poor time management or planning, irresponsibility, excessive alcohol or drug use, or excessive socialization (i.e. staying out late) that may interfere with performance.	Conflict in priorities, unwillingness to accept or acknowledge trade-offs or consequences of one's own choices.	Modify detrimental behaviors, develop better "limit setting" or self-discipline, develop healthier personal value systems, address any problematic substance use.

3.3. Patient preference and informed consent

Martin and his psychiatrist engage in further detailed discussion. Martin feels pressured for time, especially since he works from home and his 2-year old child is competing for his attention. His goals are to enhance his job performance, avoid mistakes, make better "investments", and maximize his financial profit. Martin admits that despite using stimulants it has been hard to increase his revenue. Nonetheless, he says he is a "risk taker" by nature, and firmly believes that his subjective benefits are enough to outweigh any of the risks or side effects.

In order to ethically prescribe stimulant enhancement, does the physician need to agree with Martin's calculation of the benefits versus risks, or is it sufficient to simply accept that it is Martin's prerogative to make this decision? Personal autonomy is often a dominating factor in justifying enhancement, an argument that generally takes the form: "a person should be free to do what he wants with his own body" [40]. The moral and philosophical values of personal autonomy and freedom imply that a person is free to take risk, small or large, so long as it does not harm others. The medical ethics principle of "patient autonomy" is similar, though applies specifically to the patient-doctor relationship and states that a competent patient has the right to accept or refuse care when provided with informed consent. The physician inherently bears some degree of risk by participating in this shared decision making.

Arguments that favor cognitive enhancement based on the primacy of patient autonomy have the potential to minimize or obscure the ethical obligations of physicians who are the "gatekeepers" for prescription medication. At a minimum, a physician who enhances a healthy patient must verify the patient's capacity to make the decision, assess for contraindications, monitor and manage unforeseen negative effects (and/or manage those that were predictable), before administering the enhancement. Some say that a physician's role in practicing enhancement approximates one of a "technician" or "service vendor" [22,43], with little ethical control over the indications for enhancement other than the physician's own character traits and moral conscience [22,36].

Informed consent, the process by which an autonomous patient engages with the physician in shared decision-making about the risks, benefits, treatment alternatives, and option of no-treatment, is an ethical obligation in prescribing medical treatments. Arguably, a high level of informed consent

is even more important in enhancement, where one thing is certain: the risks of no-treatment are, by definition, *none* [35,37]. Yet, informed consent for cognitive enhancement is significantly hampered by a lack of studies and evidence on these aforementioned basic required elements. One major reason is that research funding has been historically aimed at understanding and treating illnesses, not enhancement [13].

In turning to the field of cosmetic enhancement for “lessons learned”, there is little published work on the ethics of informed consent, despite the fact that such enhancement procedures have been practiced in their modern form for over 100 years [36]. In fact, it has been identified as a problem by authors within the field of cosmetic enhancement that there are few quality studies that characterize clear selection and exclusionary criteria for enhancement, outcomes (especially long-term), and alternative treatments or no-treatment comparisons [38,44–46].

Beyond risks and benefits, to explore *alternatives* to stimulant enhancement it is necessary to consider whether the patient’s motivations are indicators of psychosocial issues that would be appropriate targets for interventions such as psychotherapy or behavioral modification (see Table 4). Cognitive behavior therapy might be useful to address underlying feelings of inadequacy, self-criticism, or negative attitudes that are rooted in cognitive distortions. Addiction treatment or behavioral modification would be appropriate where substance use/abuse or balancing of social, academic, and occupational priorities are problematic. Supportive or psycho-dynamic psychotherapy might address cases where unrealistic or harmful pressures have been exerted by family, friends, or society, or where a patient struggles with an overly rigid or punitive expectation of oneself. Children and adolescents may be particularly vulnerable to such pressures. Finally, if cognitive enhancement is withheld, does this mean that a patient must “struggle” with being “normal”, “average”, or feelings of being somehow disadvantaged?

3.4. Contextual factors: enhancement and society

Some experts believe that society stands to gain broadly from the general public use of cognitive enhancement as it “favors innovation” [2]. Pharmaceutical enhancements are viewed on the spectrum of innovative cognitive aids like writing, computers, caffeine, and test preparatory courses (see Table 1). The “innovation” of physician-administered enhancements (especially prescriptions drugs and minimally- or non-invasive procedures) includes the relative simplicity, the rapid effects and reward, and the low requirement of personal effort. To address fairness, it is argued that enhancements should *ideally* be available to all.

In consideration of this view, cosmetic enhancement is a service that is theoretically available to all, but in reality it is limited to those with financial means and access. Cosmetic enhancement has historically been practiced with little ethical attention to distributive justice or fairness [47,48]. These traditional concerns may have been side-stepped by the medical profession and society, however new ethical issues have emerged as the demand for cosmetic enhancement has increased enormously in the past decade. In 2014, more than 11 million cosmetic surgical and nonsurgical procedures were performed in the United States, totaling more than 12 billion dollars in revenue [49], of which Botulinum toxin (“Botox”) procedures alone comprises a dominant share. There is little doubt that enhancement practices are financially lucrative for physicians [37,50]. This potential reward raises several ethical concerns about financial conflicts of interest, “practice drift”, physician workforce shortages, and the unscrupulous advertising of services (see Table 5). The degradation of patient care

is potentially at the center of these issues [37,51].

Conflicts of interest relate to a physician's fiduciary duty to act solely in the patient's best interest, and not in self-interest or financial reward. The psychiatrist working with Martin is confronted with the conflicts that 1) Martin desires a stimulant, though it's not clear there are objective benefits 2) Martin is a normal, healthy patient, therefore relatively "easy" to manage compared to patients with severe mental illness, and 3) Martin would pay out-of-pocket, thus eliminating commonly bemoaned "hassle" and "paperwork" that is endemic with third-party payers.

One medical ethicist warned that when the temptation of self-interest is elevated, "we are all too good at rationalizing what we want to do so that personal gain can be converted from vice to virtue" [22]. While it may remain unknown if physicians are truly adding enhancement procedures to their offerings out of self-interest, the public perception of such financial conflicts of interest has the potential to negatively impact the integrity of medicine as a whole [51,52]. Martin described his prior physician as "more than willing to prescribe", and the portrayal of some doctors as "pill pushers" could conceivably be worsened by practices of cognitive neuroenhancement. Preoccupation about revenue, whether real or perceived, justifiable or self-interested, is fundamentally lamented in medicine and contradicts most basic codes of medical ethics [53,54].

In contrast to cosmetic enhancement, the issue of fairness was central in the case against athletic enhancement [30,55–57]. Individuals like Martin often advocate for stimulant enhancement from the perspective that college academics and the global economic marketplace are "competitive fields" where gaining even a slight edge might translate into substantial payoffs, such as the difference in a promotion, a college admission, or major financial consequences [2,13,40,58]. These "small but significant" differences in competitive outcomes are the athletic equivalents of playing on the varsity or junior varsity high school team, the "big leagues" or the minors, and a first or second place finish. In fact, these effects on "fairness" (exemplified by the use of steroids, amphetamines, tranquilizers, and erythropoietin) constituted one of the very fundamental reasons society has opposed athletic enhancement and the governing bodies of sport have instituted bans and regulations (see Table 5) [57,59].

The arguments voiced today for cognitive enhancement resemble those that have been historically made in favor of athletic enhancement by a significant minority of sports physicians and a faction of public opinion. In both cases the enhancement is viewed as 1) innovative 2) in favor of personal autonomy and freedom 3) ethically indistinguishable from other performance enhancing techniques or equipment 4) necessary to compete effectively, and 5) safe when administered under a physician's supervision as opposed to self-medicated [43]. While the medical community has largely renounced their role in athletic enhancement, it remains to be seen what stance will be taken on cognitive enhancement.

4. Conclusion

Significant and concerning rates of illicit prescription stimulant use, especially among college students and young adults, have driven the debate about cognitive neuroenhancement. The current methods by which most individuals obtain stimulants for cognitive enhancement are through diversion or malingering, both of which are illicit and should be firmly rejected by physicians, institutions and organizations, policymakers, and society.

Table 5. Contextual factors in cognitive enhancement

Contextual factors	Description and examples	Potential implications and questions for cognitive enhancement
Financial conflict of interest	A conflict of interest lies in the physician's fiduciary duty to act solely in the patient's best interest, and not in self-interest or financial reward. Enhancement practices are potentially more gratifying and "easier" compared to traditional medical practices (financially, administratively, and clinically) [60].	How does a physician evaluate "the patient's best interest" when there is no medical indication, and a patient's best interest amounts to his/her subjective desire and self-perceived benefits? Conflicts of interest are potentially damaging to the integrity of medicine.
Practice drift	Practice drift describes when a physician practices outside of one's training or specialization. A variety of physicians now offer cosmetic enhancements, sometimes in "medi-spa" facilities [51,60–63]. Concerns have been raised about the potential degradation in the quality of care being provided, or outright concerns about safety [37,51,64].	Which types of physicians are "qualified" to prescribe and manage cognitive enhancement? Does society and/or the medical establishment have reservations about family doctors (as one example) potentially offering their patients stimulant medications alongside Botox injections?
Physician workforce shortage	It is predicted that the U.S. will face a shortage of 46,000–90,000 physicians by 2025 [65]. Concierge medical practices are increasing, and aim to provide "enhanced services and amenities", while lowering practice volumes as much as 10-fold [66].	The lure of practicing cognitive enhancement is a potential slippery slope away from the treatment of mental and physical illnesses, possibly worsening access to care.
Advertising practices and commercialization of medicine	Increased competition among cosmetic enhancement providers has led to questionable advertising practices (such as offering medical care in beauty salons, spas and health clubs), blurring the distinction between medical practice and cosmetology or beauty industry services [36,67–70].	Is it possible that future advertisements for cognitive enhancement will target college campuses, business parks, and appear in airlines' in-flight magazines? The commercialization of medical services bears consequences on the public's perception of medicine as a whole.
Fairness, distributive justice, and competition	Enhancement is available to those with the financial means or access. Specific enhancements are banned in competitive athletics if they 1) may enhance performance 2) possess actual or potential risks or 3) violate the spirit of sport (i.e. equal opportunity, role modeling for youth and public, "cheating" other competitors or oneself of the "process" of discipline and natural self-improvement [57].	Academia and the global economic marketplace are described as competitive fields. Does it violate a "spirit of academia" if a stimulant aids one person's entry into graduate school, over another candidate who did not enhance? If an older-age worker wishes to enhance to compete with a younger worker, what is more "fair": enhancing the older worker only, or enhancing both individuals?
Bias and value judgments	It is unclear whether a physician's own value or moral judgments (or even the value judgments of society) about a patient's "need" or "appropriateness" are proper grounds to restrict enhancement to certain persons, purposes, or professions.	Is it ethical to enhance college students, nurses, and aid-workers, but not professional gamblers or night-club entertainers?

Factions of society and academia are curious, if not in some cases optimistic, about a medical practice of cognitive enhancement where patients may openly request and receive stimulants and other “brain boosters” from their physicians. Physicians and their professional organizations are rightfully called upon to engage in the debate, particularly in the interests of patient safety, the ethics of medical practice, and the integrity of the medical profession. The analysis of ethics in medical decision-making is a common standard of practice in the “traditional” care of patients with illness, disease, or suffering [21]. Given the absence of any framework specifically tailored for analyzing the ethics of medical enhancement, it is even more incumbent upon individual practitioners and their professional societies to carefully consider the ethics of practices where there is no medical indication and decision-making weighs disproportionately on patient preferences, autonomy, and self-stated quality of life.

The experiences of the medical profession with athletic enhancement are informative to the degree that cognitive enhancement appears to be driven by the same human proclivity to be competitive or to have difficulty accepting one’s innate physical or mental limitations. Enhancement for athletics was broadly rebuffed, restricted, and regulated by the governing bodies of sport and medical establishment as unfair, potentially dangerous, and a negative portrayal for the public and youth. Alternately, where cognitive enhancement has the potential to become a minimally-regulated and lucrative medical practice that honors patients’ autonomy to address self-perceived deficiencies and desires, the experiences from the rapidly expanding field of cosmetic enhancement are especially relevant. Society and medicine can be forewarned about the potential to encounter problems with ethical conflicts of interest in the practice of cognitive enhancement, with the added uncharted concerns about (further) flooding the market with medications that have a high potential for addiction and diversion.

The psychiatrist evaluating Martin chooses not to engage in cognitive neuroenhancement, based on the following clinical-ethical analysis aligned to Jonsen’s four boxes:

1. Medical indications: Enhancement has no medical indication. Although cognitive neuroenhancement may be considered ethically permissible to some physicians, it is largely inconsistent with the traditional core purpose and mission of medicine. The objective benefits of stimulant enhancement may be limited to modest, individually variable, and task-limited improvements in memory or concentration. There is no current evidence that stimulant enhancers produce measurable “real-life” benefits for most normal healthy people. The ability for a physician to monitor “responsible use” of stimulant enhancements is problematic, especially in light of known side effects and warnings about abuse.
2. Quality of life and beneficence: Though patients may subjectively believe they benefit from cognitive enhancement, there is concern about the motivations to “need” or “want” enhancement that may be rooted in psychosocial issues including dissatisfaction, anxieties, fears, problematic self-perceptions or expectations, and external pressures (see Table 4). The prescription of a stimulant medication in these circumstances is not clearly in the patient’s best interest.
3. Patient preferences: Respect for autonomy and the fulfillment of a patient’s preference seem medically insufficient to justify exposing a patient to commonly encountered

side-effects and the risk for severe adverse reactions. Informed consent is significantly hampered by a lack of data on outcomes related to enhancement, alternatives to cognitive enhancement, and consequences of no-enhancement. An exploration of alternatives could conceivably begin with interventions to address any identifiable underlying psychosocial issues.

4. Contextual Features: Cognitive enhancement of healthy people would be a potentially lucrative and “easy” practice for physicians, directly raising concerns about conflicts of interest. Real *or* perceived conflicts of interest have the potential to damage the integrity of medicine. The practice of cognitive enhancement would likely lead to the further commercialization of medicine. Physicians who enhance would need to resolve ethical problems with fairness and value judgments in determining which patients to enhance, and for what purposes and professions.

The medical-ethical dilemmas of cognitive enhancement range from a complex, non-traditional benefit-risk analysis on an individual case basis, to a consideration of the “benefits to society” *versus* the “integrity of medicine”, institutions of higher learning, and workplace ethics. There are currently few compelling reasons for physicians to engage in the practice of stimulant cognitive enhancement of normal healthy individuals, and there are many reasons from a perspective of medical ethics to discourage this practice.

Conflicts of interest

All authors have no conflicts to report.

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