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Ethical Considerations and Implications of Smart Drugs

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ABSTRACT
The current generation marks a milestone in the development and use of methods to extend and improve our cognitive abilities, from the external repository of the internet to the increasing focus on cognitive enhancers. One of these methods is through drugs. Drugs exist in many classes from stimulants and painkillers to hypnotics, which cut across lines of legality, and are used across cultures for different uses such as mental disorder treatment, improved performance in military personnel, and educational purposes. Drugs play a role in many facets of our lives, often in a way that enhances our work ethic and the way we feel. While naturally occurring cognitive enhancers (CEs) such as coffee and other caffeinated drinks have been around for thousands of years, a new class of human-made drugs known as nootropics is defining a multi-billion dollar market: drugs specifically developed to increase cognitive abilities and enhance learning and memory in healthy people. Questions have importantly arisen about whether drug-based cognitive enhancers that improve our ability to process information may just be an extension of technological inventions like the internet. From an ethical perspective, it can be argued that these drugs provide us with a new, unparalleled, opportunity to improve the human mind. Unlike the large majority of psychopharmaceutical substances, these supplements are marketed to the healthy, general public as lifestyle brands and these so-called 'smart drugs' lack clarity in their potential long-term negative consequences. Smart drugs are designed to enhance cognition in healthy people, and may do so via alterations in perception, mood, or consciousness. As the use and development of smart drugs increases, we must seriously consider the ethical issues associated with such use, including (but certainly not limited to) their perceived societal value, their safety and distribution, and whether fair access to such drugs is necessary. While I will being using front-line comments to further illustrate some of these ideas, they are not radical opinions in that they are supportive of the main underlying research and claims.

KEYWORDS
Smart Drugs, Cognitive Enhancers, Neuroethics, Nootropics, Learning Acquisition, Psychostimulants, Medical Ethics, The Role of Medicine, Psychological Treatments, Competitive Fairness

SMART DRUGS ENHANCE COGNITION AND THEY ARE DECADES OLD

Contrary to popular belief, the concept of 'smart drugs' emerged decades ago. Romanian psychologist and chemist, Corneliu E. Giurgea, coined the term nootropics in 1972 to describe a class of psychotropic drugs that "characteristically interfere with the higher telencephalic integrative activity by a direct and selective attention" (Giurgea and Salama 1997, 235). Since then, different classes of drugs have emerged under smart drugs. For example, drugs such as Adderall have become popular treatments for attention deficit hyperactivity disorder (ADHD) as they increase alertness, reduce impulsivity, and improve concentration in these patients (Sahakian and LaBuzetta 2015, 67). More recent smart drugs such as modafinil have been developed and used to treat drowsiness and daytime fatigue. We will see that the clinical evidence for these drugs achieving these effects is clear, but healthy individuals report feeling more attentive and energetic when using them, too. Psychologist and professor of clinical neuropsychology Barbara Sahakian writes that these chemicals affect the catecholamine system, which produces increased executive functioning, "improving their abilities to focus their attention, manipulate information in working memory and flexibly control their responses" (Sahakian et al. 2008, 702). One study from which Sahakian draws this conclusion looks at Adderall's effect on selective enhancement of memory consolidation in healthy volunteers (Linssen et al. 2011, 614-615). Depending on the smart drug type, they work in different ways and by different mechanisms, but all have the same general intended effects to increase focus and learning acquisition. While the smart drug's ability to expand psychological capability in healthy humans should be embraced, it should also be evaluated on a number of ethical questions.

CONCEPTUAL CHALLENGES TO SOCIETAL ACCEPTANCE: NATURAL VS. UNNATURAL CE

One ethical issue associated with cognitive enhancing drug use outside a clinical purpose is whether the intervention is natural or artificial. As Sahakian states, "Drugs may seem distinctive among enhancements in that they bring about their effects by altering brain function, but in reality so does any intervention that enhances cognition" (Sahakian et al. 2008, 703). Despite this analysis, people have a tendency to make negative moral judgements such as the belief that artificial is worse than natural or that taking a drug is bad. For instance, one study found

cognitive enhancement drug use to be considered more wrong and threatening if drugs were artificial rather than herbal regarding drinks and injections. Specifically, on a moral judgment scale ranging from scores 0 (perfectly okay) to 5 (extremely wrong), 44 undergraduates responded with an average of 3.5 for an artificial drink compared to a 2 for an herbal drink and a 4 for an artificial injection compared to a 3 for an herbal injection (Scheske, Christel, and Schnall 2012, 512). In general, it is a fallacy to think that naturally occurring or human-made drugs are more likely to alter brain function and structure and there is ample evidence for natural interventions altering brain function in the same way as cognitive enhancing drugs. Such a moral intuition is difficult to justify when considering the role of cognitive enhancers in society. Social psychologist Jonathan Haidt coined the concept 'moral dumbfounding', which occurs when people declare a behavior wrong in the absence of supporting evidence (Hindriks 2015, 237). This seems to be an applicable case as people still remain unaware that many of the activities in which they engage affect brain function. Yet, natural interventions indisputably act on the brain to produce cognitive enhancing effects like smart drugs do.

One example of a non-drug cognitive enhancer is meditation. For example, Yoga Nidra (a relaxed meditative technique that promotes the dissociation and loss of conscious control of one's actions (Kjaer et al. 2002, 255)), was tested in one study looking at eight healthy male meditation teachers aged 31–50 with 7-26 years of daily practice. Using a C-raclopride tracer (a selective antagonist on D2 dopamine receptors) in a combined positron emission tomography (PET) and magnetic resonance imaging (MRI) study, five brain regions of interest which were previously related to cognitive enhancement were scanned: the right caudate, left caudate, right putamen, left putamen, and ventral striatum (Kjaer et al. 2002, 257). Findings revealed increased dopamine release in the ventral striatum during relaxation meditation, providing evidence for the meditators' ability to regulate conscious states at a synaptic level and influence patterns of brain activation and deactivation. Since dopamine is a neurotransmitter tied to reward-motivated behavior, these findings suggest that natural meditative practices can activate the medial forebrain reward-related circuit just like that of typical pharmacological drugs of abuse. Yet, this does not mean both alter the same behaviors, release dopamine in the same way, or imply they have the same long-term term effects. While smart drugs are human-made and meditation is natural, both natural and

unnatural cognitive enhancers may act on similar brain circuits, and so all drugs should not be considered unique in their ability to alter brain function or structure.

Again, putting aside our unbiased reasoning, we can appreciate the effects of exercise, another non-drug cognitive enhancer that acts similarly to pharmaceutical drugs. In one animal study, scientists found that running causes neurochemical adaptations in brain reward pathways in the same way as addictive drugs (Brené et al. 2007, 5). For example, opioids activate dopamine cells of the ventral tegmental area (VTA), a region implicated in the drug and natural reward circuit, which in turn stimulates the medial forebrain reward-related circuit. We know that running activates this same region and can consequently also be addictive. Voluntary exercise can have an antidepressant effect - through mechanisms that likely overlap with the aforementioned opioids - blunting physical and emotional strength, and promoting neurogenesis and other biological changes (Linden 2012, 150). In terms of cognitive enhancement, exercise "is the single best thing one can do to slow down the cognitive decline that accompanies normal aging" and it is associated with long-term improvement in mental functioning (Linden 2012, 150). Accompanying your morning cup of coffee with a drug may become just as thoughtless as running on a treadmill for thirty minutes. Ample research shows beneficial neural changes in the intervention of exercising, so why would we not accept new innovative methods that improve brain function?

CONCEPTUAL CHALLENGES TO SOCIETAL ACCEPTANCE: DRUG VS. NON-DRUG CE

It seems people are concerned about non-drug versus drug, yet for centuries, we have been using both methods with negligence. The fact that caffeine is a drug does not stop people from continuing to line up for their Starbuck's lattes and coffees each morning. Research has shown that caffeine increases alertness, mood, and motor and cognitive performance. For instance, one study investigated the cognitive and subjective effects of caffeine in combination with L-theanine, another naturally occurring ingredient in tea, and tested for improvements in attention. Forty-four participants, twenty-eight of which were female, aged between 18-34 years, were randomly assigned to a placebo or experimental group and then asked to perform various cognitive tasks. The experimental group consumed a combination of 97 mg of L-theanine and 40 mg of caffeine (Giesbrecht et al. 2010, 284). One example of a cognitive test was the two-choice reaction time

task where three symbols appear on a computer screen for 500 ms and then are replaced by a target letter (A or B) alone or with various accompanying distractor stimuli. By way of a key press, participants indicated whether the target was A or B as quickly and accurately as possible (Giesbrecht et al. 2010, 285). In the drug condition, findings showed an improvement in task switching accuracy as well as other attentional benefits. Caffeine's ability to improve the capacity of one's overall psychological functioning helps us realize the societal value of a very common artificial drug.

SOME SMART DRUGS CAN BE HIGH-RISK

One of the more significant concerns of smart drug use among healthy people is safety. Whether it is a natural intervention like meditation and exercise or a drug such as caffeine, these methods are not highly debated forms of cognitive enhancement. However, they may produce negative consequences in high doses or frequency. By virtue of these powerful negative effects, concerns regarding smart drugs' overall impact on health are certainly legitimate; accordingly, this is what we would expect every time a new medication is introduced to the market. Currently, drugs are regulated by the Center for Drug Evaluation and Research (CDER), which operates under the Food and Drug Administration (FDA). Note that while the FDA does conduct limited research, it is the responsibility of the company seeking to market a drug (the sponsor) to test it and submit evidence to the FDA that it is safe and effective. In order to gain FDA approval, the sponsor must submit evidence as part of an application and the FDA CDER claims to have very high standards for this research and evidence. Such a claim is well-founded considering the complexity of this process from testing the drug compound on animals to submitting an intricate Investigational New Drug application to the FDA. It comes to no surprise that almost all smart drug developers even bother to seek FDA approval for their products.

However, smart drugs specifically intended for a clinical purpose demonstrate research about their risks. Particularly, one of the more questionable smart drugs is methylphenidate (trade name is Adderall), which is a popular treatment for patients with attention-deficit hyperactivity disorder. Its cognitive enhancing effects are supported by discoveries in a study conducted by Elliott et al., who tested the effect of methylphenidate on the spatial working memory and planning of twenty-eight healthy males. Half of them received methylphenidate and the

other half a placebo; half of the experimental group ingested 20 mg and the other 40 mg. All participants performed tests in the same order, beginning with a verbal fluency test, a spatial span task, and spatial working memory test. Additionally, they performed The Tower of London task, an attentional shifting task, a sequence generation test, and the Rapid Visual Information Processing test (Elliott et al. 1997, 197-198). These tests focused on testing various cognitive aspects including sustained attention and explicit planning. Results showed that methylphenidate produced corresponding improvements in accuracy of performance on all spatial and planning tasks with no effect for the Rapid Visual Information Processing test. These results show that methylphenidate not only facilitated cognitive performance in relatively unfamiliar situations, but also increased the amount of response output and speed of performance by participants (Elliott et al. 1997, 202-203).

While methylphenidate increased cognitive performance, research shows that it potentially produces adverse side effects too. Alexander J. Covey, M.D., asserts, whether clinically prescribed or not, "The side effects (both short and long term) vary according to the specific nootropic drug, but using Adderall as an example, one might experience appetite suppression and unhealthy weight loss, insomnia and, more dangerously, cardiac issues including not only hypertension but arrhythmias and even sudden death" (Personal Interview 2017). Other reported minor side effects include dry mouth, repetitive movements (tics), and mild forms of depression as well as more major cases of psychosis, seizures, and previously mentioned cardiovascular events such as hypertension and tachycardia (Lakhan, Shaheen, and Kirchgessner 2012, 661). The Drug Enforcement Administration (DEA) declares methylphenidate and stimulants similar in profile as schedule two drugs, characterized by a high potential for abuse and severe psychological dependence. Despite widespread use of methylphenidate in ADHD patients since the 1950's, research about its long-term effects is not well grounded and is lacking. Nevertheless, not all smart drugs yield inherent danger with their use.

Accessibility is another issue associated with safety. Since a drug like Adderall (methylphenidate) is available only through prescription, people may try to get it illegally, even over the internet and from other countries. Dr. Covey asserts, "There are no guarantees that these drugs are real, not contaminated with other more dangerous substances, and therefore even fatal" (Personal Interview 2017). Healthy college students without ADHD diagnoses are typically aware of the cognitive

enhancing effects of smart drugs and their wide abuse across college campuses shows students have little concern for safety as discussed below. Specifically, they abuse these drugs to gain a competitive advantage in their school work. Clinical psychologist, Marcus Hotaling, PhD, says, "I had a student tell me the other week, after not doing well on a paper, that she was frustrated by her peers that had an ADD/ADHD diagnosis and can get ... help from ... medication … she knew she would be able to just pop a pill and do better herself if she wanted to" (Personal Interview 2017). This student is likely to find the desired smart drug via her college campus black market or on the web. While we must take into account that this is anecdotal evidence, in principle, students who meet the criteria set for specific diagnoses should be administered a prescription for smart drugs.

This phenomenon of abuse is reflected in a national survey from 2005, conducted by Sean Esteban McCabe that aimed to calculate the prevalence of nonmedical use of prescription stimulants among United States college students. A representative sample of about 11,000 students across 119 four year undergraduate institutions revealed that seven percent of students used psychostimulant chemicals to increase their work production, and on some campuses, up to twenty-five percent used within the past year (McCabe et al. 2005, 96). While psychostimulant use is primarily used for people diagnosed with attention deficit disorder and ADHD, their wide abuse on college campuses reflects a non-medical desire. As new drugs that aim to enhance cognitive functions such as attention and memory, primarily for healthy individuals, grow into a multibillion dollar market, an obvious concern is one of safety considering they are widely abused outside of their medicinal purposes.

Similar in profile to traditional stimulants, modafinil (with one common trade name being Provigil) is a more recent, popular, and safer smart drug option for healthy populations. Modafinil is used to treat disorders such as narcolepsy, shift work sleep disorder, and excessive daytime sleepiness and it has been shown to treat other conditions (without FDA approval) such as ADHD, Schizophrenia, cocaine addiction, and multiple sclerosis. Similar to other psychostimulants such as methylphenidate, modafinil's clinical case is promising for helping patients with mental disorders and neurological conditions. Moreover, it promotes improved memory and accuracy of decision making and responses for healthy individuals, too. In a study by Turner et al., sixty healthy young adult male volunteers received either a single oral dose of 100 mg or 200 mg of modafinil, or a placebo before

performing a variety of tasks designed to test attention and memory. Results revealed a specific pattern of cognitive enhancement, improving performance on tests of visual and spatial planning and slowing response times on gambling tasks (Turner et al. 2003, 266). Modafinil's effect of increased response inhibition is partly why it is an effective treatment for the impulsive symptoms associated with ADHD. Nonetheless, the essence of this study aimed to test its effects for healthy individuals and results demonstrated that it improves their performance on neuropsychological-related tasks. While altering brain functioning, modafinil has not been shown to produce the same side effects and addictive behaviors like methylphenidate and other psychostimulants. Dr. Hotaling asserts, "I have personally worked with too many students who have had issues with Adderall and similar stimulant based medications. Even with a prescription, sometimes the medication is abused/used incorrectly which can lead to a drug induced psychosis. So, modafinil is certainly, at this point a better alternative than Adderall" (Personal Interview 2017).

SAFE SMART DRUG USE SERVES CERTAIN CONTEXTS

Once we understand the risk of bodily harm and unintended side effects posed by smart drugs, we can discuss the ethics of their application. Modafinil's wakefulness promoting properties have led to its approval in jobs that routinely challenge one's bodily rhythms associated with arousal and timing. One instance is in the military such as Air Force personnel who are required to have top cognitive function and vigilance while fatigued. In the medical world, some experts say any form of stimulant use by physicians delivering patient care is unethical. However, studies show that "physicians engaged in patient care during episodes of sleep deprivation tend to make more errors and perform procedures more slowly" and that "patient care may be compromised" (Westcott 2005, 333). Specifically, one study analyzed the effects of sleep loss and fatigue on residents' performance on cognitive and neuropsychological tests and patient tasks. The results showed two concerning trends: 1. Tasks that dependent on high levels of vigilance and sustained attention were more vulnerable to the effects of short-term sleep loss and 2. Efficiency of task performance was often sacrificed in favor of preserving accuracy (Owens 2001, 414). In the best interest of the patient, it seems modafinil use by doctors performing long surgeries may prove to be an effective alternative to caffeine, which can cause anxiety and affect the psychomotor system. When

we are talking about smart drug use by people who need to stay hyperfocused - military, potentially physicians in surgery, there is an ethical argument to prescribe and take the medication during these time-limited periods.

A discussion about modafinil's approval in the military and potential benefit among health care providers raises the possibility of use by other healthy populations who may benefit from its cognitive enhancing effects, such as in the everyday workplace. Twenty-four year old healthy male and entrepreneur Jesse Grushack takes 200 mg of modafinil orally once a day in the morning. Compared to Adderall, which often disrupted his sleep cycles, appetite, and left him moody, modafinil achieved the same effect for him without the harsh side effects. He asserted, "Jet lag is a non issue and working 80 hours a week has become pretty standard and not unmanageable" (Personal Interview 2017). Finding himself under constant pressure to deliver at a new job, Grushack attributes much of his success to modafinil, which improves his wakefulness. The experience of Jesse Grushack is not a comment about the 'goodness' or badness' of using modafinil, but rather, it points to the appeal of cognitive enhancement in a modern workplace that demands long hours, an intense work ethic, creativity, and travel. These exhausting conditions fuel what thought leaders call 'the power through culture', marked by increased productivity in less time. An article in TechCrunch labeled modafinil as the Silicon Valley entrepreneur's drug of choice (Cederström 2017). A demand for cognitive enhancement exists in the workplace, especially among those who are trying to build companies.

CHALLENGES TO DISTRIBUTION: CE TECHNOLOGIES ARE NOT FAIRLY ACCESSIBLE EARLY ON

An interrelated issue of smart drug implementation is their availability to people of different socioeconomic classes; however, such an attitude limits human ingenuity. Yes, not everyone will be able to improve their functioning with smart drugs, but not everyone can afford a Dunkin Donuts coffee, pay to have their children tutored after school, or hire acclaimed athletic trainers either. In fact, distribution will likely be unfair based on current evidence that shows college students, a privileged middle class segment of the population, tend to be the largest abusers of cognitive enhancers. Low socioeconomic status among other social barriers already exist in many facets of our lives. When humans develop advanced technologies, exposure is limited to those who can afford them first

before they later become widely available for the masses. For instance, the first computer built in 1946 cost about $500,000, the equivalent of six million dollars today, weighing over twenty-five tons and taking up the space of a sizable room. Today, one out of every three people in the world owns a smartphone - and it fits in their pocket. The argument for distributive fairness does not ground obstructing the progress of smart drug development.

FURTHER ASSESSMENTS OF SMART DRUG USE CASES

Another layer in addressing the ethics of smart drugs is their competitive fairness, which will depend on the context. The wide use of smart drugs will require institutions and organizations to review their values and determine smart drug permissibility. For example, in the modern workplace, several ethical challenges surface: 1. Does employee smart drug use provide an unfair advantage over his colleagues? 2. Will employers encourage use among employees and favor job candidates who use? 3. Should we be concerned that smart drug use may further fuel today's rigorous work routine? Such questions are important to consider, but once again, do not pose enough of a threat for banning smart drug use in the workplace when we appreciate the reward of their cognitive enhancement.

Whether in the space of sports or education, different concerns arise depending on the context of the smart drug implementation. For example, athleticism involves an admiration of the natural human body. In professional sports, cognitive enhancers may be deemed the equivalent of a machine powered throwing machine. With this claim, we would expect smart drugs to be prohibited because they are seen as diminishing an athlete's accomplishment or self-worth. This same logic explains why anabolic steroids are prohibited. Conversely, cognitive enhancers might be accepted in schools because they facilitate human learning and improvement through their increased learning acquisition abilities. Then again, Dr. Alexander Covey poses the question, "Is it fair for students of similar aptitude to compete on an exam if one student has access to a drug which could potentially enhance his performance?" (Personal Interview 2017). His judgment is that the playing field is no longer equal. In any case, a reasonable implication of increased smart drug use is their legitimacy and permissibility by different establishments.

CONCLUSIONS

We are prepared right now to define appropriate use of cognitive enhancers for fully developed adults. We know research undoubtedly supports that smart drugs enhance a human's psychological capabilities and that some seem to have a safer profile than others. The most critical issue in discussing the ethics of smart drug use is one of safety. As the public consumes new smart drug supplements, we must closely monitor possible side effects and conduct comprehensive research so we can make informed decisions about their regulation and dosages. Subsequently, we may address different contexts in which smart drugs should be implemented; we anticipate an immense effect on family life and all layers of society. Both military and healthcare related applications make strong cases for smart drug use. They help us realize the value of smart drugs in other contexts such as in the workplace and in education, but this does not come without reservations about fairness among other implications.

The use of smart drugs becoming part of mainstream pharmacology requires as shift in western medicine from focusing on drug implementation after disease onset and neglecting advances for healthy people to solutions that prevent and improve the human species. Rather than allow these ethical concerns to impede progress, we must evaluate how smart drug use manifests itself in different facets of life and society and adapt in time. This requires accepting the inherent risk that comes with all novel practices. With increased use of cognitive enhancement among healthy populations, this is the approach we must have in addressing the smart drug revolution and movement.

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