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The Ethical Implications of Cognitive Enhancers

Sydney Shearouse[a], Shanaz Tejani-Butt[b*]

[a,b]*Department of Neuroscience and*

[b]*Department of Pharmaceutical Sciences, University of the Sciences in Philadelphia, PA USA*

[b]*Email: S.Tejani@Usciences.Edu*

Abstract

This review will explore the ethical use of cognitive enhancers which alter and improve cognitive function and performance. Cognitive enhancers are not only used in the treatment of certain cognitive disorders, such as schizophrenia and attention deficit hyperactivity disorder (ADHD), but also by individuals to change or enhance certain cognitive abilities. The review will explore and understand the possible ethical implications of the availability of these enhancers to the general population.

Keywords: cognitive enhancers; pharmacological; non-pharmacological; ethics.

1. Introduction

Cognitive enhancement is often defined as the amplification of core capacities of the mind by improving information processing systems [1]. Cognition is the process of higher-level thinking in the brain which encompasses a large variety of processes [2]. A popular method to enhance cognitive functions, such as attention, learning, memory, and planning is the usage of drugs or supplements known as pharmacological cognitive enhancers (PCE) [3,4]. These supplements are commonly used to treat patients suffering from cognitive dysfunctions due to neuropsychiatric disorders or traumatic brain injuries (TBI). While the usage of PCEs in the treatment of disease is rarely disputed, it has raised neuroethical concerns particularly when compared with their non-pharmacological counterparts.

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* Corresponding author.

1.1 Pharmacological Cognitive Enhancers

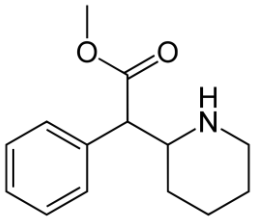
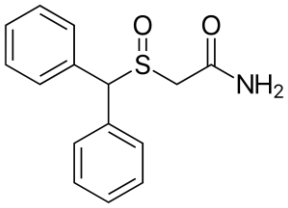
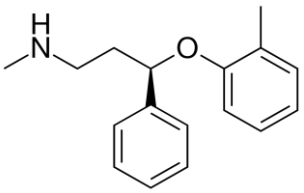
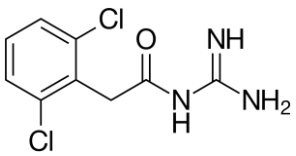
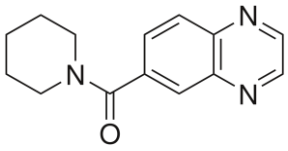
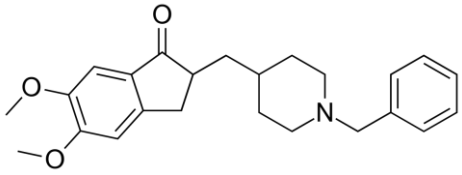
Impairment of cognition as the core of many neuropsychiatric diseases, has been well-researched and reported [5]. Specifically, PCEs have been shown to improve cognitive deficits in depression [6], addiction [7], multiple sclerosis [8,9], Parkinson's disease (PD) [10], Alzheimer's disease (AD), schizophrenia, and ADHD by altering neurotransmitter modulation in the brain. The previous studies listed above all focus on how PCEs improve such conditions and what positive functions these medications may serve within the medical field. By contrast, non-pharmacological cognitive enhancers focus on methods of improving cognitive function that are more natural. Some examples include nutrition, physical exercise, meditation, brain stimulation, computer training, mnemonic devices, and sleep [11]. Non-pharmacological cognitive enhancement methods are also commonly used in the treatment plan for neuropsychiatric diseases. However, outside of the realm of medicine, both non-pharmacological cognitive enhancers and PCEs are commonly utilized by individuals to improve their own cognitive functioning to compete in an academic or workplace environment. The usage of these substances for personal gain calls into question many different ethical perspectives regarding implications of class and how using these may create division in academic and work-place environments.

1.2 Pharmacological Cognitive Enhancers (PCEs) & Ethical Implications

There are many different PCEs available to the general public and many more that require a doctor's prescription to access. These drugs generally target specific areas of the brain. Primarily, they target neuro modulatory systems such as the cholinergic, dopaminergic, noradrenergic, and serotonergic systems, ascending from brainstem nuclei and innervating both subcortical and cortical systems. These drugs work primarily on the prefrontal cortex (PFC), but also have action in the mesolimbic pathway, the hippocampus, and the amygdala [12]. PCEs that are most used by individuals for cognitive enhancement are also used to treat ADHD such as methylphenidate (Ritalin) and modafinil [13]. These drugs generally function to increase dopamine (DA) and norepinephrine (NE) levels in the PFC which helps to increase attention and other 'executive functions' in the brain [14]. Methylphenidate is a DA and NE reuptake inhibitor, while modafinil is a DA reuptake inhibitor. Many national epidemiological studies have found that non-medical use of these prescription stimulants has become a growing problem among young adults, in particular college students, in the United States [15,16]. For example, one study found that 5.7% of college students reported higher rates of non-medical usage of methylphenidate (Ritalin) than their same-age peers not attending college (2.5%) in the past year [16]. Continually, studies have found that non-medical users of prescription stimulants were usually from families of a higher socioeconomic class [17]. This indicates one major moral implication regarding the use of PCEs, in that when used to enhance performance in realms such as school it will provide an inequitable advantage to individuals of a higher socioeconomic status. Other drugs that are considered to be PCEs but are often less commonly abused are: atomoxetine (Strattera), guanfacine (Tanex), ampakine, and cholinesterase inhibitors. Atomoxetine is a selective NE reuptake inhibitor (SNRI) which is also commonly used in the treatment of ADHD. Guanfacine functions as an a-2 adrenergic agonist which treats both ADHD and high blood pressure in many individuals. Ampakines are a class of drugs with excitatory effects of glutamate receptors. They are used to treat Parkinson's, Alzheimer's, schizophrenia, treatment-resistant depression, and ADHD. Furthermore, ampakines are thought to improve learning and memory by inducing the process of long-term potentiation in the

brain. Another common type of PCE are the cholinesterase inhibitors (ChEI), such as donepezil, which inhibit acetylcholinesterase and help to boost acetylcholine in the brain [18]. As they are thought to have effects on learning and memory, ChEIs are commonly used in the treatment of Alzheimer's disease [19].

Table 1: Chemical Structures of Common Cognitive Enhancers

Compound Name	Structure
Methylphenidate	
Modafinil	
Atomoxetine	
Guanfacine	
Ampakine	
ChEI (example: donepezil)	

1.3 Adverse Effects of PCEs

Methylphenidate is reported to cause adverse effects such as increased heart rate, increased blood pressure, headache, anxiety, nervousness, dizziness, drowsiness, and insomnia [20]. Modafinil results in adverse reactions such as headache, dizziness, gastrointestinal complaint, increased diuresis, palpitations, nervousness, restlessness, sleep disturbances and insomnia [20]. Atomoxetine has been shown to cause increased blood pressure, seizures, aggression and hostility, gastrointestinal problems, suicidal ideation, and possible liver damage [21]. Side effects of guanfacine include drowsiness, dizziness, dry mouth, constipation, tiredness, nausea, headache, and stomach pain. While several of the same side effects are reported with use of ampakine, they are less severe when compared to other PCEs. ChEIs also have many reported side effects (insomnia, nausea and vomiting, accidental injury, headache, dizziness, bradycardia, hypotension, ecchymosis, and sleep disturbance). This, the use of PCEs without prescription is associated with various potential health issues as listed above [22].

1.4 Ethical Implications of Elective PCE Usage

In order to understand the major ethical debates regarding the use of PCEs, one must first understand the concept of neuroethics. Neuroethics is a growing field surrounding the ethics of neuroscience as well as the neuroscience of ethics [23]. This field most specifically focuses on the translation of neuroscience research from experimental studies to medical practices and public usage [24]. One of the major emphases of researchers in this field is to evaluate the practice of PCEs as well as the elective usage of PCEs [25]. Before the ethical concerns regarding the usage of PCEs are analyzed, some of the advantages of these should be discussed. For one, many have argued that it can be used as self-medication for individuals with undiagnosed attentional or cognitive problems [26]. This can be seen as a major advantage as it allows individuals who would otherwise be suffering from lower cognitive abilities to gain equal footing in society. Another advantage of PCEs are the possible social benefits. It has been argued by different researchers that cognitive enhancement could provide a route for reducing natural inequality and promoting social justice [27]. A simulation study indicated that a 3% population wide increase in IQ would reduce poverty rates by 25%; therefore, these social benefits also expand to possibly reinforcing the economy and allowing larger groups of people to live comfortably [28]. Another major benefit of PCEs is their usage to alleviate stress in highly stressful situations. This allows individuals suffering from sleep deprivation, jet lag, or a wide variety of other stressors to perform as they would normally under ideal conditions. These advantages of using PCEs are not commonly talked about but do paint a picture of why the individual may decide to utilize elective enhancement. There are a wide range of ethical concerns regarding the use of PCEs for elective reasons. For one, there is a concern regarding the medical safety of taking these enhancers. While several short-term studies have been performed, few studies have examined the long-term effectiveness or possible side effects regarding the usage of PCEs. Another major ethical concern is related to the authenticity of using such enhancement methods. Does the use of these substances change a person's central being and cause them to become an entirely different person [29]? The idea behind moral problems related to authenticity are based on the idea that a human is most themselves in a natural and unaltered state. Therefore, by consuming unnatural substances in pursuit of altered cognitive activity, is thought to undermine that person as their 'true self' [30]. However, as a significant number of people are using enhancers to improve

their cognition and achieve goals, one can argue in favor of their usage and not as undermining their authenticity. The authenticity debate also argues about naturalism or the 'pharmacologization of life' [31]. The idea being that using unnatural products to boost human cognition draws individuals out of their natural state of being and poses the risk of an overcompensation of technology for human failings. One of the biggest concerns regarding the elective use of PCEs is the socio-economic divide and how these products may allow the rich more advantage over those in less ideal economic conditions. There is great potential for PCEs to further the divide between socio-economic classes, especially if they are unevenly distributed across society to those who can afford to pay for them [32]. Usage of PCEs can potentially create a divide in competitive fairness and also facilitate cheating in academic and workplace settings. For example, college students have a strong history of abusing methylphenidate and modafinil in order to get ahead in school and perform better on exams and assignments. This is considered to be a major form of academic dishonesty at most Universities and can once again create a division between those who can afford to take these PCEs recreationally and those who cannot. Another area of concern is the usage of such drugs in sports which undermines the fairness of these activities. One PCE commonly abused by athletes is modafinil in order to maintain focus in times of stress [33]. Overall, there are a lot of ethical concerns surrounding the elective usage of PCEs, just as there would be with the abuse of any drug outside of medical recommendation. Much more research is required to understand whether the benefits of these drugs actually outweigh the potential downfalls. However, even if it is found that the side effects are mild compared to the cognitive improvements, the division in society and the problem of pharmacologizing human life remains.

1.5 Non-pharmacological Cognitive Enhancers

Non-pharmacological cognitive enhancers come in various shapes and forms. Different foods and drinks claim to increase energy or enhance memory. Caffeine, an adenosine receptor antagonist increases turnover of biogenic amines in the brain to cause a stimulating effect shortly after consumption [34]. Some of the behavioral effects which are commonly associated with caffeine are elevated mood, increased alertness, and better sustained attention; however, effects on memory and learning are often disputed [35]. Caffeine is also thought to improve motor-skill performance on tasks that are impaired with low arousal and increases the speed of encoding and response to new stimuli [36]. However, caffeine usage is associated with the development of tolerance and withdrawal, which can lead to headaches, increased perception of stress and reduced alertness [37]. Overall, caffeine has been shown to serve as a major non-pharmacological cognitive enhancer. Glucose provides the primary energy for our cells and comes from the breakdown of carbohydrates. There have been many subjective reports of individuals experiencing increased mental energy due to higher glucose metabolism in the brain [38]. Glucose has been reported to increase attention, response speed, and working memory [39,40,41]. However, these effects have been found to be most significant for declarative memory [42], and related to remodeling in the hippocampus due to glucose [43]. Some other common non-pharmacological cognitive enhancers are physical exercise and sleep which appear to be associated with hippocampal activity [44]. Inactive individuals have been shown to perform much worse on cognitive tasks compared to athletes [45]. While literature suggests that sleep enhances memory, creativity and has a positive effect on memory consolidation [46], the relationship between sleep and memory is also impacted by differing personal factors. Meditation is a frequently used non-pharmacological cognitive enhancer that is reported to promote all aspects

of mental well-being [47]. A study comparing individuals who meditated regularly versus those who did not, showed an increase in attentional performance and cognitive flexibility [48,49]. This is thought to be closely tied to neuroimaging studies which have indicated that meditation activates the PFC and anterior cingulate cortex [50]. Mnemonics are another common method of non-pharmacological cognitive enhancement. Mnemonics are simply internal cognitive methods which allow people to enhance their memory abilities. Many individuals have been categorized as "super" memorizers and these individuals have developed this skill through training with mnemonics [51]. Music is another method for enhancing cognition. Music therapy consists of two major types: receptive and active [52]. For example, piano lessons have led to increased performance on working memory, perceptual speed, and motor skills in the elderly [53]. Music therapy also functions to improve an individual's psychological and physiological well-being, social cohesiveness, and ability to express emotions [54]. Music has been reported to have many positive effects on behavioral aggression problems in adolescents [54] as well as relief of negative and cognitive symptoms for individuals suffering from schizophrenia [54]. One of the more contested methods used for non-pharmacological enhancement is brain stimulation. These techniques involve stimulating certain regions of the brain and can be either invasive (Deep Brain Stimulation (DBS) and direct vagus nerve stimulation (dVNS)) or non-invasive (Transcranial Direct Current Stimulation and Transcranial Magnetic Stimulation). The method for non-invasive brain stimulation involves the placement of two electrodes on the scalp and using an electrical current to change the likelihood of neuron firing in parts of the cortex [55]. The vast majority of brain stimulation methods help with encoding and learning, while certain methods such as DBS can directly impact and modulate memory systems [56]. Some studies have documented the effectiveness of brain stimulation on improving learning ability [56,57,58]. Brain stimulation techniques also enhance cognitive abilities by improving verbal fluency [59], picture word verification [60], and picture naming [61]. Thus, brain stimulation can be considered as an effective non-pharmacological cognitive enhancer which impacts a wide variety of cognitive domains.

1.6 Ethical Implications of Non-pharmacological Enhancer Usage

Although there are far fewer ethical issues with non-pharmacological cognitive enhancers compared to PCEs, some common issues still arise regarding their usage. One major ethical concern is the ideas of doctors 'playing Gods' by trying to enhance humans beyond what they naturally inherited. The issue of a wealth gap in some methods of non-pharmacological enhancement continues to be an issue, especially when looking at methods like brain stimulation. However, when compared to PCEs, most methods of non-pharmacological enhancement are viewed in a more positive light since they are more natural and do not represent short-cuts for achieving goals. However, the non-pharmacological enhancement techniques are viewed to be less effective and not worth the amount of time and effort that has to be invested in order to achieve results similar to those found with PCEs.

2. Discussion

The ethical implications and downfalls of using the PCEs versus the non-pharmacological enhancers indicates that in general, there are more ethical implications to be found within the realm of PCE usage. However, a downfall of this assumption and a constraint of this review may be related to the amount of literature existing on both topics. While there is a wide breadth and amount of published research regarding the ethics of PCE usage,

literature regarding non-pharmacological enhancement usage is much more limited.

3. Recommendations

There is a lot of potential for future research directions in this area, as there is much that is not yet understood. Further investigations into PCEs and the possible long-term effect of consuming these medications is essential. Such research will allow the scientific community to better understand the issues associated with healthy individuals abusing these medications and will lead to educated and mechanistic decisions regarding the consumption of these drugs. Another area with potential for future research would be to specifically compare the effects of PCEs vs non-pharmacological methods in the brain. This will provide researchers with the ability to perform a clear cost-benefit analysis for the different methods to determine which method of enhancement is best suited for a particular goal. Expanding research in this area will improve our understanding of the safety of these methods for use on an individual level.

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