Overview

Neuroethical issues in pharmacological cognitive enhancement

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Neuroethics is an emerging field that in general deals with the ethics of neuroscience and the neuroscience of ethics. In particular, it is concerned with the ethical issues in the translation of neuroscience to clinical practice and in the public domain. Numerous ethical issues arise when healthy individuals use pharmacological substances known as pharmacological cognitive enhancers (PCEs) for non-medical purposes in order to boost higher-order cognitive processes such as memory, attention, and executive functions. However, information regarding their actual use, benefits, and harms to healthy individuals is currently lacking. Neuroethical issues that arise from their use include the unknown side effects that are associated with these drugs, concerns about the modification of authenticity and personhood, and as a result of inequality of access to these drugs, the lack of distributive justice and competitive fairness that they may cause in society. Healthy individuals might be coerced by social institutions that force them to take these drugs to function better. These drugs might enable or hinder healthy individuals to gain better moral and self-understanding and autonomy. However, how these drugs might achieve this still remains speculative and unknown. Hence, before concrete policy decisions are made, the cognitive effects of these drugs should be determined. The initiation of accurate surveys to determine the actual usage of these drugs by healthy individuals from different sections of the society is proposed. In addition, robust empirical research need to be conducted to delineate not only whether or not these drugs modify complex higher-order cognitive processes but also how they might alter important human virtues such as empathy, moral reasoning, creativity, and motivation in healthy individuals.

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THE USE OF PCEs BY HEALTHY INDIVIDUALS

As society becomes more dependent on technology and the boundaries between humanity and artificial intelligence become blurred, heavy demands are increasingly placed on the individuals' cognitive and physical functions. Thus among healthy individuals the pursuit to enhance cognition might become commonplace. To simply keep up with these ever increasing demands to overproduce, healthy individuals are resorting to ever more creative ways of boosting their cognition, using any means of improving their attention.[1] Recent scientific and philosophical debates about human enhancement indicate a growing interest in PCEs,[2] where healthy non-sleep deprived individuals are using medications that are licensed for patients with clinical disorders to enhance their cognitive functions.[1]

Overview of this Paper

The aim of this paper is to give an overview of the neuroethical issues in pharmacological cognitive enhancement. The first section of this paper will give an overview of the reported use of PCEs. It will attempt to define the term cognitive enhancement and will describe how these drugs might alter higher-order cognitive processes. It then highlights the current reported trends in the use of these drugs by healthy individuals. The second section of the paper focuses on the neuroethical issues in pharmacological cognitive enhancement. These include the culture wars in the cognitive enhancement debate, the advantages and disadvantages of using these drugs non-medically, and the bioethical issues that might arise from their use such as coercion, the lack of distributive justice and informed consent, and the importance of implementing the principles of benevolence and non-malfeasance. The overview concludes on recommendations on how a balanced neuroethical analysis could benefit society, particularly the healthy individual.

WHAT IS COGNITIVE ENHANCEMENT?

There is currently no agreed definition of the term cognitive enhancement and it is unclear whether a principled enhancement and/or treatment distinction can be offered. However, the distinction between enhancement and treatment may relate to the former being concerned with healthy individuals attempting to improve their cognition through neuroscientific technologies such as the use of these drugs for non-medical purposes while the latter is concerned with treating patients with recognizable clinical disorders.[1] This distinction is very blurred and needs further in-depth discussion, which is not addressed here. However, three useful definitions of cognitive enhancement have been proposed.

Definitions

An information-processing definition of enhancement argues that cognitive enhancement is the amplification or extension of core capacities of the mind through improvement or augmentation of internal and external information processing systems.[3] A welfarist definition of enhancement argues that enhancement is any change in the biology or psychology of a person which increases the chances of leading a good life in the relevant set of circumstances.[4] However, bioethicists do not agree with above definitions. They argue that enhancement is an intervention which is beyond what is necessary to sustain good health.[5,6] Because healthy individuals are using these drugs non-medically to amplify their cognition and are in essence going beyond what is necessary to sustain their good health,[2] PCEs can be seen as one form of cognitive enhancement.[7] Other forms of enhancement techniques include exercise and coffee but they are not considered here.

Pharmacological Cognitive Enhancers (PCEs)

Current Interests

The argument that these drugs improve cognitive performance in healthy individuals has been widely reported in the media[8] and in research.[1] This has generated an increased interest among the general public, particularly among healthy individuals who might want to use these drugs non-medically, especially for boosting higher-order cognitive processes.[2]

HIGHER ORDER COGNITIVE PROCESSES

Executive Functions

Higher-order cognitive processes include executive functions, which are a set of cognitive processes that enable humans to plan ahead, solve complex problems, shift between mental mind-sets, inhibit unhelpful responses, and update relevant information.[9]

Working Memory

Working memory is the ability to hold temporarily relevant information active over a short interval and to manipulate this information online.[10]

Neuropsychiatric Disorders

There are primary deficits in executive functions and working memory in a number of neuropsychiatric disorders.[11] These cognitive deficits are sometimes a result of a traumatic brain injury or from clinical neuropsychiatric disorders such as schizophrenia, attention deficit hyperactivity disorder (ADHD), Parkinson's, or Alzheimer's disease (AD). When these disorders occur, the affected patients are impaired in the capacity to plan, maintain goals, shift between different goals, update goals in the light of new information, and filter out irrelevant information.[9] Consequently, these patients suffer from impaired day-to-day cognitive functioning. In these patients, drugs that pharmacologically alter neurotransmitter modulation of cognition lead to improvements in attention, acquisition of new information, better executive functioning, and working memory.[1] However, these drugs are reported to be increasingly used non-medically by healthy individuals for enhancing their cognition.[2]

Current PCEs

Among healthy individuals, most popular PCEs include methylphenidate (®Ritalin), a dopamine (DA) and noradrenaline (NA) reuptake inhibitor; dextroamphetamine (®Adderall), a mixed amphetamine salt that increases DA, and is licensed for the treatment of ADHD; and modafinil (®Provigil), a wake-promoting drug with multiple mechanisms of action that is licensed for narcolepsy. Other drugs that improve cognition include atomoxetine (®Strattera), a selective NA reuptake inhibitor (SNRI); and guanfacine (®Tanex), a α^2 adrenergic agonist. Furthermore, ampakine has excitatory effects on glutamate receptors, and induces long-term potentiating processes to improve learning and memory[12] in AD patients[13] and in some healthy volunteers.[14,15] Cholinesterase inhibitors boost acetylcholine in the brain,[13] and are moderately effective in regulating attention and memory in AD.[16] In contrast, β-blockers, that are prescribed to reduce anxiety in clinical patients, have been used by musicians to dampen physiological tremors in order to improve their performances on stage.[17]

CURRENT TRENDS IN THE USE OF PCEs

Data from US Surveys

In the past few years, it has been reported that there has been an unprecedented rise in the use of PCEs among healthy university students[18] and academics[1] who are aiming to improve their cognitive functions. More specifically, it has been reported that students are specifically taking PCEs to improve academic performance,[19] and are framing their actions as both physically harmless and morally acceptable.[18] For example, in the United States, 16% of college students[20] and 8% of undergraduates reported having illicitly obtained and used prescription psychostimulants.[21] Furthermore, a 2005 survey by the US National Institute on Drug Abuse (NIDA)[22] found that 2.5% of 13- to 14-year-olds, 3.4% of 15- to 16-year-olds, and 5.1% of 17- to 18-year-olds abused methylphenidate. In 2009, the figures for these groups were 1.8, 3.6, and 2.1%, respectively.[23] The 2012 report by NIDA showed that non-medical use of prescription and over-the-counter medicines still remain a significant part of the teen drug problem.[24] According to the Monitoring The Future Study, which is a long-term epidemiological study that surveys trends in legal and illicit drug use among American adolescents and adults,[25] 14.8% of high-school seniors used a prescription drug non-medically in the past year. Data for specific drugs show that the most commonly abused prescription drugs by teens are the psychostimulant Adderall and the pain reliever Vicodin.[24]

Underachievers Using PCEs

The most recent figures show a rise in the illicit use of PCEs among male, academically underachieving students[26] and the most up-to-date evidence suggests that young healthy individuals are obtaining psychostimulant drugs from illicit sources (e.g., from others who have prescriptions to these drugs as medications or they are purchasing them via the internet or street dealers).[27]

Problems with Epidemiological Studies

Nevertheless, these epidemiological prevalence studies are based on survey data from college and university students in the United States,[28] and there is a lack of evidence in the prevalence of the use of these drugs in Europe, and more specifically in the UK. Furthermore, these surveys do not enquire about the motivations behind the use of these drugs. In the bioethics debate, analysis of the current available literature suggests that most of these drugs are being used for recreational purposes.[29] However, in the UK, a newspaper survey of 1000 students from Cambridge University showed that 1 in 10 were illicitly taking prescription drugs for cognitive enhancement.[30] In England, prescription rates of psychostimulants have been rising steadily from 220,000 in 1998 to 418,300 in 2004.[31] The reasons for this steep rise have not been explained,

but instead it has been implicitly assumed that these increases in prescription rates are related to emerging PCE use for cognitive enhancement.[1]

Survey Responses from Academics

In 2008, the scientific journal *Nature* conducted a poll about the use of PCEs by healthy academics, to which 1400 scientists from 60 different countries responded.[32] One in five respondents used drugs for cognitive enhancement purposes, with 52% of them obtaining the drug by prescription, 34% obtaining the drug via the internet, and 14% through their pharmacy. The most popular drug was methylphenidate, with 62% of users; 44% reported taking modafinil mainly to improve concentration, and 15% reported taking β-blockers for anxiety. Although this data from these academics might be biased and unrepresentative of the general population, the figures nonetheless suggest the increased use of PCEs among healthy academics and students.[28]

Currently, the global market share of modafinil is more than US$700 million per year.[33] It is now estimated that around 90% of modafinil is predominantly used off-label by healthy, non-sleep deprived individuals who are not aiming to get 'high' but are aiming to increase attention and wakefulness.[34,35] Consistent with this, Greely[36] previously claimed that healthy physicians on call, students, and academics are increasingly using PCEs to enhance cognitive abilities. This is further supported by recent evidence showing increased use of illicit and prescription drugs for cognitive or mood enhancement among students and surgeons.[26,37]

Fierce Academic Competition Could Lead to Drug Use

The reported widespread use of these drugs is unsurprising given that the Academy of Medical Sciences[38] argued that small percentage of increments in performance may lead to significant improvements in functional outcome. Indeed, they argue that a 10% improvement in memory score could lead to an improvement from an A grade to an A+ A-level grade (or from a 2.1 (69%) to first class (70%) degree in the UK). Presumably, healthy individuals are taking PCEs to improve their academic performance.

Lack of Reliable Data and the Need for Informative Data

However, an accurate estimation of PCE use, as well as accurate responses of when and why healthy individuals use these drugs (e.g., to increase motivation or attention), is currently lacking. Besides, these surveys are based on academics and students' views who are knowledgeable about the cognitive enhancement debate. Therefore, there is a need to conduct large surveys on large diverse populations to establish who takes PCEs as well as when and why they are taken. There is also a need for empirical data on how these drugs alter cognition and behavior in healthy individuals who are using them non-medically.

Experimental Studies

In experimental settings, it is important to emphasize that improvement from these drugs in healthy individuals is very modest. For instance, data from experimental laboratory studies with healthy individuals show that PCEs improve performance on neuropsychological tasks in an inverted U-shaped fashion, where optimal enhancement is dependent on both dose and baseline of cognitive function.[39] Small doses work best and help individuals low in working memory.[40] However, how these experimental findings map on to the proposed definitions of cognitive enhancement is unclear. The effect sizes, which calculate the size of improvements associated with these drugs, are rather small.[41] Furthermore, these drugs increase levels of numerous neurotransmitters that are already at a steady level in healthy individuals, and taking them might lead to over-focusing and impairments in cognitive flexibility.[42] Relevant to the neuroethical debate, in some cases healthy individuals even become impaired in cognition when they take these drugs.[42–48] Hence, the use of PCEs by the healthy individuals raises numerous ethical issues, which are discussed below.

NEUROETHICAL ISSUES

As the initial goal for prescribing these drugs was not to improve cognitive functions in healthy individuals with no psychiatric disorders but to treat cognitive dysfunction in clinical patients, the non-medical use of drugs by healthy individuals for enhancement purposes have raised numerous ethical issues in the emerging field of neuroethics.[49] This has prompted significant interests in academia,[1] the media, and in the public.[8]

What Is Neuroethics?

Neuroethics is a broad emerging field that deals with the ethics of neuroscience and the neuroscience of ethics.[50] In particular, neuroethics is concerned with the ethical issues in the translation of neuroscience

to clinical practice and in the public domain.[51] One important ethical issue that neuroethics deals with is pharmacological cognitive enhancement practices.[49] This is the use of drugs, which are licensed to treat cognitive disabilities in patients with neuropsychiatric disorders, for improvements in cognitive function in healthy individuals.[1] As there is an absence of a clinical disorder to ameliorate, some bioethicists argue that the use of these drugs for enhancement purposes is beyond what is necessary to sustain good health.[5]

Culture Wars in Cognitive Enhancement

Neuroethics scholars have been divided between those who promote the use of pharmacological drugs for cognitive enhancement[7] and those who are against this type of use.[52] This divide has been termed as the culture wars in cognitive enhancement.[49] The former scholars argue that the pursuit of cognitive enhancement through drugs is permissible as long as they meet moral acceptability criteria.[49] According to Racine,[49] this requires that enhancement technologies fulfill scientific (e.g., risk assessment), ethical (e.g., informed consent), social (e.g., health coverage), and regulatory criteria (e.g., approval mechanisms). The latter group of scholars argues that society should not engage in pharmacological enhancement practices because pursuing enhancements through pharmacological means lacks moral praiseworthiness.[49]

Multifaceted Nature of Brains and People

However, as cognition is multifaceted, and healthy individuals fall into a wide spectrum of normality, altering the healthy brain with pharmacological agents has both advantages and disadvantages for the individual and for society. For instance, for the healthy individual, using these drugs for enhancement purposes run greater risks of unanticipated health problems,[53] while for society, if PCEs increase cognitive function without any significant side-effects in healthy individuals, the benefits from enhanced cognition are substantial.[54] As there are several important considerations in the use of PCEs by healthy individuals, the following section discusses the general ethical issues that have been raised in the neuroenhancement debate. Particular attention is paid to the advantages and disadvantages of using PCE non-medically by the healthy.

ADVANTAGES OF USING PCEs

The advantages of using PCEs relate to the demonstrated improvements that they have on those with low cognitive performance.[55] These advantages meet both prudential and moral goals for the individual and for society. For the individual, the advantages include improved cognitive function and greater productivity, while the advantages to society include a more focused, more productive society, which might mitigate societal problems, such as financial troubles and poverty.

However, it is unclear how taking pharmacological drugs non-medically could bring about such lofty goals. Furthermore, given that high IQ does not increase health and wealth outcomes later in life,[56] using PCEs to increase cognitive function will not necessarily lead to a higher well-being and life satisfaction. Nonetheless, these drugs boost cognition and normalize function in patients with debilitating neuropsychiatric disorders[1] and even in healthy individuals, there is some empirical evidence showing that those with lower baseline of working memory performance are moderately improved by drugs like modafinil and Ritalin.[40,55] Hence, using PCEs might be beneficial for some sectors of the population.

Self-Medication Hypothesis

It has been argued that some 'healthy' individuals have undiagnosed attentional problems, and are actually self-medicating with drugs such as Ritalin.[57,58] Although these individuals are self-medicating, rather than enhancing their cognition per se, if PCEs boost cognition in those with lower cognitive ability, there is a good reason for their use as they have the potential benefits of removing disparities in society and in mitigating undiagnosed neurocognitive disorders.

Social Benefits

Savulescu[59] argues that human enhancement might lead to dramatic social benefits by reducing natural inequality and promoting social justice, because increasing cognitive ability on an individual level could have dramatic and positive effects on society and the economy as a whole.[60] Sandberg and Savulescu[54] used data simulations, and evaluated the social and economic impact of cognitive enhancement to society. Their analyses reveal that even small enhancements to the individual and to society would have profound positive effects. They argue that relatively small upward shift of the distribution of cognitive abilities would substantially reduce the incidence of learning problems that prevent many from flourishing, and would help large average groups to perform better.[54] To illustrate this, it has been estimated that a 3% population wide increase in IQ would reduce poverty rates by 25%,[61] and would lead to an annual economic

gain of US $165–195 billion and up to 1.5% GDP growth.[62]

Will PCEs Actually Improve Well-Being?

Nevertheless, it is important to note that this data is based on simulations rather than actual evidence, and it is not exactly clear what positive effects and what performing better mean for healthy individuals who are already functioning normally. The simulated data does not show whether using PCEs will directly or indirectly improve well-being in healthy individuals. Again, greater economic benefits do not equal greater well-being or happiness for society.

PCEs Are Used during Stressful Situations

Nonetheless, even healthy individuals who normally function well, are not always performing normally due to sleep deprivation, jet lag, or other stressors, and some might need cognitive enhancers to perform at their best possible level on some occasions.[1] For instance, psychostimulants have been employed to boost cognition in military,[63] soldiers in combat,[64] shift workers,[65] pilots,[63] surgeons,[66] and school pupils diagnosed with ADHD that are performing below average.[67] The US military has been using a cognition intervention program, which includes medications, to enhance soldiers' memory and cognition through technology when soldiers are under conditions of interrupted sleep and stress.[68] This suggests that different sections of the population are interested in improving their wakefulness and that using PCEs during stressful situations might be advantageous for highly domain specific cognitive processes. Hence, if proven to be safe, PCEs may be utilized for improving attention during periods of challenged sleep and stress.

Nevertheless, if one is suffering from jet lag or insomnia, it is still unclear whether improving wakefulness with PCEs will count as an enhancement. It might be that these drugs are working to normalize cognitive functions where they raise attention and wakefulness to one's normal baseline level of performance. This in itself might be an advantage if one needs to boost wakefulness at a specific or crucially important situation. However, there are also disadvantages to using psychoactive medications non-medically.

DISADVANTAGES OF USING PCEs

Unknown Risks

The disadvantages of using PCEs include the lack of safety and possible harms that they might cause to healthy individuals. For instance, the disadvantages include greater unknown risks and long-term harms to children and adolescents, where the brain is still in development.[7] Lewens[69] succinctly addresses the substantial risks associated with pharmacological cognitive enhancement practices and, using a bioethical precautionary principle[6] evaluates their benefits and risks. Based on such analysis, Lewens[69] objects to the uses of these drugs on the basis that their benefits to healthy individuals are small and they carry the substantial risks of causing harm to healthy individuals.

Coercion in Children

Singh et al.[70] discuss specific ethical issues that arise from neuroenhancement in young children. These include lack of capacity to consent, and coercion from teachers and parents. However, even in healthy adults who can consent, the same safety concerns still arise, as these drugs carry risks and side-effects that might outweigh the beneficial effects of their use.[1] Exposing psychoactive agents to the healthy brain runs the risk of damaging receptors that allow smooth communications between neurons in the brain.[13] Using a pharmacological agent could also lead to a neurotransmitter imbalance in specific parts of the healthy brain, which can lead to long-term detrimental effects.[71]

Neurotransmitter Imbalance in ADHD

A good example in this neurotransmitter imbalance is the case of ADHD disorder, which has been implicated in structural abnormalities in the fronto-striato-circuitry[72] and dysfunctions in catecholamine neurotransmission, specifically in the NA and DA pathways in the prefrontal cortex.[73] This dysfunction leads to inefficient information processing and hypo-activation in the frontal lobes.[13] As a result, patients diagnosed with ADHD have significant impairments in executive functions and working memory performances.[74]

Safety Concerns for Healthy Individuals

However, it is currently unclear whether exposing the healthy brain to pharmacological agents for neuroenhancement purposes could result in this very dysfunction in catecholamine neurotransmission that is reported in the ADHD disorder. These safety concerns are amplified in the absence of informative data from healthy individuals. Accordingly, Lewens[69] predicts that the use of these drugs for enhancement purposes carry substantial risks to health. However, it is important to note that Lewens'[69] arguments are based on potential substantial risks to the health of the healthy individuals which currently there is no data. It would

be ideal to specify the probability of these risks occurring in healthy individuals.

The Abuse Liability of PCEs

Notwithstanding these points, all drugs have side effects. Yet, while in patients the benefits of using cognitive boosting drugs often outweigh the side-effects,[75] in healthy individuals, the risks include possible unknown, long-term negative consequences, including personality change and addiction.[52] The abuse liability of some of the PCEs such as methylphenidate and modafinil is also increasing, which is becoming a concern. For example, a recent study showed that modafinil blocked DA transporters and increased DA in the caudate, putamen, and nucleus accumbens in healthy human brains.[76] These are well-known areas in a network known to be involved in drug-seeking behavior and addiction.[48] This indicates the need for awareness about the risks involved in PCE use among healthy individuals, and shows that a full ethical consideration of their use is required.

Lack of Longitudinal Data on the Abuse Potential of PCEs

To date, there have not been systematic randomized psychopharmacological trials investigating the short- and long-term use, as well as the positive and negative effects of PCE drugs on healthy individuals.[1] Thus, without any concrete evidence on their cognitive enhancing effects and safety profile, using the precautionary principle is prudentially useful.[6] For instance, it could be argued that their use can be objected to on the basis that they might cause risks and harms to healthy individuals. Furthermore, if doctors prescribe these drugs for enhancement purposes, healthy individuals might find it difficult to make informed and autonomous decisions on whether the risks involved in neuroenhancement outweigh the purported benefits. There are still further safety concerns about the risks of ingesting toxic or impure substances that are advertised as PCEs and are purchased over the internet.

UNINTENDED CONSEQUENCES

The disadvantages associated with the use of PCEs also include unintended consequences that may result from their use. Adderall has been shown to impair creativity performance in healthy individuals high in creativity.[77] Furthermore, DA agonist, bromocriptine, improved the performance of executive function tasks in individuals with lower than average working memory capacity, but impaired performance of those with high working memory capacity.[78] Recent evidence suggests that in non-ADHD adults PCEs may actually impair performance of tasks that require adaptation, flexibility, and planning.[42]

Cognitive Trade-Offs

A recent double blind placebo-controlled study with children diagnosed with ADHD disorder showed that methylphenidate increased perseverative errors in the Wisconsin Card Sorting Test,[79] a task of cognitive flexibility and set shifting. One might argue that cognitive flexibility is an important cognitive process and constricting it with psychoactive drugs in healthy individuals and in patients diagnosed with ADHD could be problematic both for individuals and for society.[80] As mentioned above, research indicates that off-label psychostimulant use, including methylphenidate, is highest in US college students,[81] but this off-label use has been reported to negatively affect subjective sleep quality[82] and to increase depressive mood in this particular cohort.[21] This is an example of PCEs having unintended consequences in healthy individuals. As these drugs are not licensed for enhancement use and are not prescribed by a qualified doctor they might not be suitable for healthy individuals.

Contraindications

For instance, contraindications of atomoxetine and modafinil include heart problems and hepatic impairments.[83] Additionally, if one is taking other medications there might be drug–drug interactions, which could be dangerous in some cases. On the other hand, if these children find it difficult to focus, the drug might help them concentrate better and might enable them to achieve important life goals such as obtaining a college or a university degree. In any case, given that the way these drugs change cognitive processes are currently not well delineated, their effects on cognition and behavior could lead to both good and bad unintended and unanticipated consequences.

COERCION

Healthy individuals might be coerced to use PCEs. Coercion typically carries the important implications of diminishing the targeted agent's freedom and responsibility, and that it is pro tanto wrong because it violates personal autonomy.[84] There are ethical concerns about healthy individuals being coerced into using PCEs to enhance their abilities. Society might

force healthy individuals to take psychoactive agents in order to perform better, or to be in a particular mental state. For example, authorities in the United States ordered a mentally ill inmate, in criminal proceedings, to take psychotropic medications to improve his competence to stand trial and be executed.[85,86] This illustrates an example in which PCEs can be used coercively and can raise considerable ethical and moral problems for society.

Social Coercion

There is also considerable potential for indirect coercion resulting from a highly demanding '24/7 society' where healthy individuals feel compelled to take PCEs in order to meet social or workplace demands. Healthy individuals may resort to self-medication for inadequate sleep or overexertion at work. For example, 33% of respondents of the poll by *Nature* indicated that they would feel pressure to give PCE drugs to their children if other children at school were taking them.[32] There might still be social pressures to use PCEs, particularly in young people. Riis et al.'s[87] survey revealed that US college students are more likely to take PCE drugs if such drugs were effective, and were framed as non-threatening to their individuality. Therefore, this raises the ethical issue that arises from the use of PCEs because of social pressure, nudging, or indirect suggestions to try to achieve non-forced compliance and clever marketing of drugs for non-medical use.

Ethical Blind Spots in Mislabeling Medication Drugs

Forlini and Racine[88] argue that the medical community and the media have already contributed to the misconception of terming prescription drugs as 'miracle drugs' and this has misled lay people into thinking that these drugs are 'smart drugs', enhancing everybody without side effects. According to them, this creates an ethical blind spot that masks the importance of investigating the long-term harm and side effects of PCEs in healthy individuals. They argue that describing the phenomenon as 'enhancement' does not do justice to the unknown risks of long-term non-medical use of prescription drugs as this has generated many polarized debates, framed in terms of 'to enhance or not to enhance', while paying less attention to the conditions under which enhancement of function could become ethically acceptable. They further argue that framing the use of PCEs by healthy individuals as 'lifestyle' contributes to the ethical blind spots that indirectly coerce people to take PCEs. Other prominent bioethicists share this view, and argue that calling these drugs cognitive enhancers will inevitably lead to overuse, abuse, and addiction in healthy individuals.[52]

Cognitive Liberty

In contrast, other ethicists argue for the existence of strong negative right to cognitive enhancement, where individuals exercise cognitive liberty, privacy interest, and interest of persons in protecting and developing their own minds and capacity for autonomy.[85] In practical ethics, one would argue that healthy individuals are free to take or not to take PCEs because they are autonomous. However, Merkel et al.[89] argued that refusing to be part of a (*pharmacologically*) enhanced society, and thus staying 'natural', would mean intentionally choosing to live one's life at a lower baseline of functioning than the average person. However, some individuals choose not to take PCEs and yet can still function well, so the argument that everyone will be enhanced if they took PCEs is not tenable simply because these drugs do not have the same effect on cognition in all individuals. Some individuals will benefit from a drug and others will not, and some might even become impaired in cognitive function. As discussed earlier, experimental studies on psychostimulants support the view of baseline dependency for cognitive improvement.

Low Cognitive Function and PCEs

Research is corroborating the evidence that individuals with low working memory capacity may benefit from PCEs while high working memory capacity individuals are over stimulated and, in some cases, show deterioration in cognitive performance.[39,55] Furthermore, many null and negative results are not reported in the literature, which suggests that the cognitive enhancing effects of PCEs are even smaller than the positive results that have been consistently reported.

AUTHENTICITY

Authenticity is a complex concept that is multidimensional but it essentially means that the individual experiences their true, natural self without feeling alienated and psychologically, socially, spiritually, or existentially coerced.[90]

Ethicists argue that memory modification through PCE use poses a threat to authenticity[91,92] in that modifying our inherent self, character, and

individuality poses the threat of what it means to be a human being.[53] It is important to distinguish between two concerns of authenticity. One concern relates to being authentic to one's true individual self,[93] while another relates to staying human, or retaining what is valuable in our humanity. For some bioethicist, there is the worry that using PCEs will change our natural tendencies that might lead us, in the outset, to believe that our emotions need altering with PCEs (e.g., using β-blockers to dampen physiological tremors in order to improve performances on stage). For example, when we feel sorrow, or emotions that serve important functions, such as feeling empathy toward others, it is by no means clear that we would be better off without such emotions. Kass[6] argues that: 'the lack of "authenticity" sometimes complained of in these discussions is not so much a matter of "playing false" or of not expressing one's "true self," as it is a departure from "genuine," unmediated, and (in principle) self-transparent human activity'. Thus, there is a concern that PCEs will threaten our notion of personhood and will dampen essential characteristics of what it means to be human.[53] In this context, the notion of personhood is related to what makes us who we are as humans, as opposed to the subsets of characteristics related to our rational capacities that can be argued to be related to our developed brains.

Altering Self-Identity Versus Cognitive Performance

Consistent with this view, the study by Riis et al.,[87] which investigated the preferences for psychological enhancements by young Americans, found that young healthy individuals are not interested in enhancing or altering traits that are fundamental to self-identity, including motivation and social skills, as opposed to mental faculties like memory, ability, and concentration. Hence, healthy individuals might object to using PCEs if they impair important human characteristics such as authenticity, creativity, and other traits related to self-identity.[80]

Technology and Authenticity

Other philosophers argue that new technologies, such as PCEs, which alter the self, need not be threatening to the authentic self, but rather might bring the actual self in line with the ideal self. For this reason, Levy[94] argues that enhancement technologies can be seen as enhancing our authenticity. If PCEs are safe and effective, we might not object to utilizing them as a form of cognitive enhancement, and as Levy[94] argues, using PCEs might be a way of developing our authentic self and might aid both our self-discovery and self-creation. Indeed, some patients diagnosed with ADHD feel as though their true self emerges only while on medication, while others feel a loss of self while on medication.[95]

Undervaluing Work and Personal Achievement

However, although philosophers might argue that using drugs for enhancement can aid authenticity, public health researchers do not agree with this account and might object to their use.[52] If healthy individuals take drugs that focus their attention and memory, could their perception of themselves change from being human to being mechanistic beings with a modicum of emotions? Farah et al.[53] also argue that using neuroenhancers could undervalue hard work and achievement. Similarly, children diagnosed with ADHD have been shown to give excuses for, and attribute bad behavior to forgetting to take psychostimulants, rather than to their own behavior.[70,96] In contrast, parents have been shown to attribute positive behaviors to psychostimulant use.[97,98] Therefore, it is arguable that, because children are attributing their bad behavior due to not taking psychostimulants, using psychostimulants pose threats to self-identity and the understanding of moral agency. However, Singh et al.[70] argue the opposite and show that the use of psychostimulants in children can positively contribute to their moral self-understanding and self-identity. Singh[99] recently used an empirical approach to evaluate the claim whether psychostimulant drugs pose threats to authenticity and to children's capacity for moral agency. Drawing on empirical data from studies involving families in the United States and UK, Singh[99] shows that, although children are able to report threats to authenticity related to psychostimulant drug treatments, the majority of children are not concerned with such threats. On balance, Singh[99] argues that children report that psychostimulant drugs improve their capacity for moral agency, and they associate this capacity with an ability to meet normative expectations. Singh[99] further argues that this association raises an important question about whether the use of psychostimulant drugs in children in fact threaten the capacity to protest bad conditions and, as a consequence, allows bad conditions to prevail. Singh[99] suggest that medical professionals should play a role in ensuring that the risks of psychostimulant drug treatment are minimized, and the benefits are maximized. A further issue is how insightful children are in attributing their good behavior to taking psychostimulants, given that their responses

might be based on conforming to and feeling good about fitting within social norms and expectations. It also raises questions regarding as to what extent doctors might become complicit in giving children medications to behave better and, as a consequence, might further perpetuate unhealthy norms in society. Hence, from this analysis, the use of PCEs in young healthy individuals has implications for authenticity, individuality, and personal identity. Using PCEs will have an impact on how we relate to them, how they think of their behavior and, more importantly, their individuality and moral understanding.

DISTRIBUTIVE JUSTICE AND COMPETITIVE FAIRNESS

Disparities in Society

Another argument against the use of PCEs is that, if only the wealthy can access them, they might further exacerbate the ever-growing inequality in society.[100] This raises questions about distributive justice, where the uses of enhancement technologies in general, and PCEs in particular, might divide those who have access from those who have not. The disparities in access to a potentially cognitive boosting drug might increase injustice.[91] This is particularly relevant, given the argument that small cognitive improvements can lead to significant academic gain.[38] If this is the case, using PCEs to improve academic performance could lead to even more disparities in academic attainment. A recent survey of University of Cambridge students indicated that students are opposed to using PCEs because of the potential risks that they might cause to healthy individuals and the inequality of access which might lead to disparity in academic performance.[101] These views were similar to Australian students who expressed strong objections to the uses of these drugs in academic contexts.[102]

CHEATING

As discussed above, whether the use of PCEs constitutes cheating becomes relevant. For instance, is it morally justified to use PCEs during exams, and does it give the user an unfair advantage over those who are equally capable but are not using PCEs? This is particularly important since young healthy individuals in the United States are more willing to use PCEs to enhance their cognition, especially if PCEs allow them to gain an unfair advantage over others.[87] The issue of cheating has been frequently debated in the cognitive enhancement literature. By definition, cheating constitutes violating the rule that these drugs should be gained through prescription by only for those with clinical and neuropsychiatric disorders. One way that cheating has been argued to be unethical is that cheaters break rules in order to gain an unfair advantage over others.[103] For this reason, it has been argued that using drugs for enhancement purposes during academic examinations is a form of cheating.[103]

Lack of Clear Academic Policy

However, many universities have no formal policy about the off-label uses of PCEs during exams.[1] Nevertheless, if PCEs enable individuals to compete better than those who do not have them, it can be argued that PCE users are gaining positional goods because they have the competitive advantage that depend on others not having access to PCEs[104] and, therefore, their use constitutes to cheating.[103] If this is the case, then the problem of cheating can be remedied by either changing the rules, or by instituting controls and sanctions against the use of PCEs.[103]

Violating Internal Goods and Standards of Excellence

However, even if this does not lead to banning PCEs, another objection to using PCEs, at least in academic contexts, is that it violates 'practices' with their own internal goods and standards of excellence. For instance, it might violate the practice of honestly striving to study for exams and working hard. Nevertheless, although healthy individuals are currently not breaking explicit rules, as there is currently no policy against the use of PCEs for academic purposes, by taking PCEs to perform better in exams, they are breaking the implicit rule of the practice of fair competition, hard and honest work. As a result, they might be gaining a competitive advantage over others who are not taking them.

INFORMED CONSENT

If the full mechanisms of these drugs are not well known can healthy individuals be consenting to the use of these drugs when doctors prescribe them for enhancement purposes? Children under 16 years of age cannot consent to the use of PCEs, while adolescents might not have the full capacity to make an informed decision about the consequences of using psychoactive drugs for cognitive enhancement. Informed consent is likely to raise different ethical issues in the enhancement field as opposed to the treatment field. The ethical issues about consenting to taking drugs for medications are far more developed

than in cases where young children are illicitly taking medications for enhancement. Hence, another ethical issue that is relevant to taking PCEs for enhancement purposes relates to whether healthy individuals, especially when they are young, are exercising their full informed consent when doctors prescribe these drugs for enhancement purposes.

Autonomy

Bioethicists argue that healthy individuals are responsible for their actions, and therefore we ought to expect that they know the consequences of using PCEs. Glannon[5] argues that, as autonomous individuals, healthy individuals have the right to use PCEs, as long as they do not harm others, and they access these drugs on their own (without being coerced). Glannon[5] also argues that if these drugs cause harm to healthy individuals, they can be banned on public health (paternalistic) grounds. However, for healthy individuals to exercise their informed consent, it might be necessary to provide full information about how these drugs work on their body and brains.

BENEFICENCE AND NON-MALFEASANCE

Enhancing the brain, with its higher cognitive processes, demands strong ethical and practical policy considerations. An important ethical issue that can arise from neuroenhancement relates to the risks and harm that can result from their use by healthy individuals. Hence, a clear consideration of the benefits and harms of the use of these drugs in healthy individuals is required. Although neither the British Psychological Society[105] nor the American Psychological Association[106] have specific ethical guidelines for the use of PCE drugs, both bodies have put forward the principle of placing greater responsibility to limit detrimental effects to animals and human volunteers. These guidelines can be extended to limit the possible risks associated with the use of drugs for cognitive enhancement purposes. Thus, the principles of beneficence and non-malfeasance can preserve autonomy on moral and prudential grounds. This means that society can implement policies that safeguard individuals while individuals resist social coercion and exercise responsibility to oneself and obligations to society.[107]

Enhancement Policy Criterion

Bostrom and Roche[108] argued for the need to establish a baseline for acceptable risks involved in cognitive enhancement. Glannon[5] asserts that, with PCEs, such acceptable risks should include a benefit ratio for healthy individuals; if using PCEs pose risks of adverse effects in the central nervous system and the benefits are modest, there is no justification for doctors prescribing them to healthy individuals.[5] Thus, for further decision making, an enhancement policy criterion could be that before PCE drugs are prescribed off-label to healthy individuals, their cognitive enhancing effects and their effectiveness must be fully tested to provide important facts about their benefits.[1] To provide this, scientific studies need to be carefully conducted with each putative cognitive enhancer and the empirical results should be reported. Moreover, empirical studies that focus on understanding one specific PCE which alongside analyse the ethical issues that might arise from such PCE use need to be conducted. Such comprehensive understanding of a particular PCE would inform both the neuroscience and neuroethics of cognitive enhancement. This approach would enable researchers, clinicians, parents, teachers, policy makers, and regulatory bodies to evaluate whether each PCE has beneficial or detrimental effects on diverse cognitive functions that might have positive or negative implications for optimal well-being and functioning. This will contribute toward the reduction of harm and in the promotion of the well-being of healthy individuals who want to use these drugs for cognitive enhancement.

GENERAL CONCLUSIONS

This article gave an overview of the current neuroethical issues that arise when healthy individuals use pharmacological substances as a way of enhancing cognitive processes. It is clear that there are several gray areas in the neuroethical issues that arise from the use of drugs for cognitive enhancement purposes. Most pressing neuroethical issues include the lack of accurate information regarding their actual use, their benefits and harms to healthy individuals, including young children; it is clear that the use of drugs for enhancement purposes carry substantial unknown risks to the healthy individual, such as the negative side effects that they might have on the healthy brain. There are also concerns that they might alter authenticity and personhood in the healthy individual. Hence, these drugs might enable or hinder children and healthy adults to gain better moral and self-understanding and autonomy. Although current evidence suggests that these drugs have small effects on cognition in healthy individuals, if in the future they actually improve cognition they might have implications on distributive justice and competitive fairness, in that they might exasperate the inequality of access that can arise from

enhanced cognition and well-being in those who have access to these drugs. Other neuroethical issues that arise in neuroenhancement relate to healthy individuals being coerced by social institutions that force them to take cognitive enhancing drugs to function better. However, before concrete ethical claims and practical policies can be made, the cognitive enhancing effects of these drugs should be determined. It is of paramount importance that accurate surveys are conducted to better determine actual usages of these drugs by healthy individuals from different sections of society. In addition, robust empirical research needs to be conducted to delineate not only how these drugs modify memory, attention, and executive functions but also how they alter important human virtues such as empathy, moral reasoning, creativity, and motivation in healthy individuals. Finally, this overview did not address the underlying motivations of different stakeholders who are either promoting or opposing the use of drugs for neuroenhancement purposes. It could be argued that if these motives are not based on the principles of beneficence and non-malfeasance they may themselves raise ethical issues that merit thorough neuroethical analysis and discussion.

CONCLUSIONS

The use of pharmacological agents for cognitive enhancement purposes has been one of the most frequently talked about issue in the cognitive neurosciences, philosophy, and in the media. There are polar views on whether or not healthy individuals should use these drugs for cognitive enhancement purposes. Some scholars are currently staunch advocates of pharmacological cognitive enhancement while others are completely opposed to it. This has created what is known as the culture wars in cognitive enhancement. What is clear from this overview is that the empirical evidence to support the cognitive enhancing effects of pharmacological agents in otherwise healthy individuals is inconclusive. The neuroethical issues that arise from their use are also numerous and are tinged with clashes in opinion and the advocacy of specific points of views. The culture wars in cognitive enhancement may itself pose an ethical issue as it hinders proper and honest dialog in the field. Therefore, it might be useful that researchers, clinicians, parents, teachers, policy makers, and regulatory bodies initiate more balanced and unbiased dialogs that aim to evaluate whether or not PCEs have beneficial or detrimental effects on diverse cognitive functions and well-being in healthy individuals. This will contribute toward the reduction of harms and in the promotion of well-being of healthy individuals who are interested in using these drugs for cognitive enhancement. This article has contributed to this dialog by giving an overview of the diverse neuroethical issues in the use of pharmacological drugs for cognitive enhancement by healthy individuals. In conclusion, it is important to evaluate each specific putative PCE, both empirically and ethically, before rejecting it or advocating for its use for enhancement purposes. Such evaluation is a worthy pursuit that offers an alternative option to the culture wars in cognitive enhancement. Finally, attempting this interdisciplinary endeavor would indeed advance both the emerging field of neuroethics and the more advanced field of cognitive neuroscience.

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