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Pharmacological cognitive enhancement: a promising or an inevitable future?

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Abstract

Human cognitive functions are often targets of curiosity, study and reflections, since they are essential for human beings. Understanding our cognitive boundaries, the processes that originate them, and how to overcome them means comprehending the human condition and the consequences of manipulating cognition. In recent years, growing interest has been observed in cognitive enhancement with the help of drugs, resulting in several important ethical, medical, and legal dilemmas. This article analyzed the ethical issues involved in this process and concluded that pharmacological cognitive enhancement needs further studies at the pharmacodynamic level, so that its application – regulated and in specific contexts – can benefit individuals and society, without undermining the authenticity of the human condition.

Keywords: Biomedical enhancement. Ethics, medical. Nootropic agents.

Resumo

Melhoramento cognitivo farmacológico: futuro promissor? Ou futuro inevitável?

Funções cognitivas são alvo frequente de curiosidade, estudo e reflexão, pois são estruturantes para o ser o humano tal como o conhecemos. Compreender os limites cognitivos, os processos que os originam e a forma de os ultrapassar é, por isso, forma de entender a condição humana e de perceber as consequências da potencial manipulação da cognição. Nos últimos anos tem havido interesse crescente no melhoramento cognitivo mediante o uso de fármacos, e com ele têm surgido diversos e importantes dilemas éticos, médicos e legais. O objetivo deste ensaio é refletir sobre os problemas éticos levantados. Pode-se concluir que o melhoramento cognitivo farmacológico tem de ser mais bem estudado no nível farmacodinâmico para que sua aplicação – regulada e em contextos específicos – possa beneficiar indivíduos e sociedade, não pondo em causa a autenticidade da condição humana.

Palavras-chave: Melhoramento biomédico. Ética médica. Nootrópicos.

Resumen

Mejoramiento cognitivo farmacológico: ¿Un futuro prometedor? ¿O un futuro inevitable?

Las funciones cognitivas humanas son objeto frecuente de curiosidad, estudio y reflexión, ya que estructuran el ser humano tal como lo conocemos. Comprender los límites cognitivos, los procesos que los originan y la forma de superarlos es, por lo tanto, una forma de entender la condición humana y percibir las consecuencias de la potencial manipulación de la cognición. En los últimos años ha habido un interés creciente en el mejoramiento cognitivo a través del uso de productos farmacéuticos, y con ello han surgido una serie de importantes dilemas éticos, médicos y legales. El propósito de este ensayo es reflexionar sobre los problemas éticos planteados. Se puede concluir que el mejoramiento cognitivo farmacológico debe estudiarse mejor en el ámbito farmacodinámico, de modo que su aplicación, regulada y en contextos específicos, pueda beneficiar a individuos y a la sociedad sin comprometer la autenticidad de la condición humana.

Palabras clave: Refuerzo biomédico. Ética médica. Nootrópicos.

Research

The authors declare no conflict of interest.

Pharmacological cognitive enhancement (PCE) is the use by healthy individuals of prescription drugs for cognition enhancement. PCE, with all its advantages and problems, has spread as a practice and as a topic of neuroethical debate. The number of scientific articles available on the subject increased from 1,300 between 1980 and 2000 to around 17,000 between 2000 and 2017 [1], and the media have also reported this practice more frequently. This article aims to discuss the various ethical and neuroethical dilemmas resulting from PCE, as well as the advantages and limitations of this procedure for patients and the social contexts where they are inserted.

Method

This study did a bibliographic search in the PubMed database, with the keywords "cognitive enhancement," "ethics," and "pharmacological cognitive enhancement". It included articles in English and Portuguese published in the last eight years and whose full text was available free of charge. After a manual search, some scientific papers considered relevant that were listed in the references of the selected articles were also included. We excluded articles whose abstract or text, after analysis, significantly diverged from the topic.

Cognitive and pharmacological enhancement

Cognitive enhancement (CE) is a recent topic in the field of neuroethics, which studies the ethics of neuroscience and the neuroscience of ethics [2]. The definition of CE is not absolutely consolidated, and it is unclear whether "enhancement" and "treatment" can be distinguished [3]. However, the following definitions are the most common. First definition: CE is the extension or amplification of core cognitive abilities by improving information processing systems by mechanism internal or external to the individual [3,4]. Second definition: CE is any change in an individual's biology or psychology that increases their likelihood of a better quality of life in the circumstances in which they live [5].

Several experts in bioethics suggest a third definition: CE is any intervention in cognitive capacities that goes beyond what is strictly necessary for an individual's health [6,7]. Another more general definition was proposed by Franke, Lieb and Hildt [8], and supported by other authors: CE is the use by healthy individuals of drugs, appropriate biotechnology, or other means to enhance cognitive functions such as memory, concentration, or alertness without medical need [9,10].

Besides these seemingly divergent concepts, the threshold of "enhancement" also differs: it can be considered as any increase of a certain cognitive ability relative to an individual's baseline level that may increase their probabilities of having a better quality of life [11]. In this definition, "enhancement" occurs regardless of the baseline level of a given capacity [5]. Alternatively, we have more restrictive definitions, which assume that a cognitive ability is improved if it is enhanced beyond a limit considered normal, or beyond the lower threshold for the correction of pathologies [11].

Despite all differences, common aspects can be found in these definitions. For the purposes of this study, CE will refer to any improvement in a given cognitive capacity of a healthy individual that is likely to improve quality of life. Individuals' cognitive capacities can be improved in several ways, including PCE and non-pharmacological cognitive enhancement (NPCE).

The latter is associated with the idea that cognitive capacities can be maintained or even improved with adequate nutrition, regular physical activity, proper sleep hygiene and rest, and various forms of meditation and yoga or by using mnemonics and other memorization systems [12,13]. This concept is also associated with other non-invasive methods, such as computerized training (specific games) [13]. We also have other methods, such as electrical stimulation of the brain using transcranial direct current stimulation, transcranial magnetic stimulation, direct vagus nerve stimulation or deep brain stimulation, the latter considered the most invasive technique [13].

PCE is currently one of the most frequently discussed forms in the scientific community [14] and the media [15], and its impact and neuroethical issues are more evident than non-drug associated

cognitive enhancement. Given those definitions, PCE can be considered the use of drugs by healthy individuals aiming to increase certain cognitive abilities without medical need.

Main drugs used in pharmacological cognitive enhancement

Drugs commonly associated with PCE are methylphenidate (Ritalin), amphetamine-dextroamphetamine compounds/multiple amphetamines salts (Adderall) and modafinil (Provigil) [3,16]. Methylphenidate is a dopamine and noradrenaline synaptic reuptake inhibitor used to treat attention deficit hyperactivity disorder (ADHD). Also used in ADHD, amphetamine-dextroamphetamine increases dopamine release. Modafinil is a drug with multiple mechanisms of action, used to treat narcolepsy and sleep disorders [3].

Other substances, such as donepezil, galantamine, and rivastigmine (among other dopamine agonists), are also used, but their effect on PCE is less noticeable and less studied [11]. Some research admits a null or even harmful effect of these substances on PCE [11,17-19]. But most available studies, including those addressing the main nootropics (cognitive enhancers), show disparate results, from negligible increases in the cognitive functions studied to negative effects on these or other functions [3,14].

Other drugs used for performance enhancement, but in a different scope, are beta blockers, which are taken by performing artists to reduce tremors or anxiety [3]. All these drugs, due to their use as potential cognition enhancers in healthy individuals, can also be considered nootropics.

Social context of pharmacological cognitive enhancement

The use of nootropics by the general public reflects the individuals' desire (or the pressure put on them) to improve their cognitive functions, even if they are healthy [19], being encouraged by different reasons, such as stress associated with work or competitiveness in academic and scientific environments [19,20]. Despite that, several studies indicate that PCE is not the norm among university students [10,21-25]. Moreover, students may be children and adolescents, who may be subject to various pressures to start PCE programs [19].

PCE may have benefits for individuals whose professions involve high levels of pressure or risk or require a higher adaptation and learning capacity [19]. Today, in different professional environments, workers are expected to be more efficient for longer periods. Besides being required more flexibility, motivation and productivity, the competitive environment and the desire for success are constant [19,26]. Using nootropics is thus more frequent in demanding professions [19,26]. Even the performance of workers with sleep deficit can be improved with PCE, increasing their efficiency, performance, and safety at work [19,26].

The desire for cognitive and performance enhancement is not, however, limited to students and professionals. The so-called "psychonauts" use drugs with cognitive enhancing properties and regulate the use of various drugs, recording their experiences [19]. Moreover, the practice of microdosing psychedelic drugs, such as lysergic acid diethylamide (LSD), psilocybin (mushrooms), and mescaline, has become increasingly common [19] to improve cognitive functions such as creativity or perception, for professional or recreational purposes.

But one of the limitations of understanding and using PCE (and nootropics) is the lack of studies assessing each drug and the lack of information about their side and long-term effects [11,19]. This raises several questions regarding PCE safety and relevance, which will be briefly explained in the next section, along with other important neuroethical issues related to the use of nootropics in the contexts here addressed.

Essential neuroethical issues of pharmacological cognitive enhancement

With the dissemination of PCE and growing interest in the topic, controversial neuroethical issues

related to PCE have emerged [3,10,12]. These issues, along with PCE advantages and disadvantages, are discussed in the following subsections.

Lack of information about long-term efficacy and effects

One of the main limitations of PCE is the lack of information about its effects on the brain (and the remaining physiology) associated with the consumption of nootropics [12,19]. Some studies report cognitive enhancements in healthy individuals, but only as unexpected side effects [27], as these studies had other objectives. It is unknown whether cognitive enhancers will be effective for PCE, and especially their safety profile and side effects in healthy individuals [11,12], since they are studied in disease or deficit contexts as a method of prevention, diagnosis or treatment [12].

Continued consumption of nootropics (or psychotropic drugs) may lead to changes in neuronal circuits or synapses, with unknown effects that may be harmful in the long term [3,12]. Negative effects of methylphenidate have been reported in healthy students concerning sleep quality and increased depressive symptoms in these individuals [3]. All this is particularly important in the case of its use by parental or teacher pressure [12,19,28] in children and adolescents, whose brains are still developing.

Lack of information regarding the effects and risks of nootropics may justify limiting their use to short periods or specific circumstances, and only for valid reasons [12,29]. The basic principles of non-maleficence and beneficence apply here.

Possible changes in personality, individuality, and authenticity

The consumption of nootropics has caused growing ethical concern due to possible changes caused by these substances in the individual's personality [3], as they may alter characteristics considered essential for human beings [3,30]. Questions include, for example, whether PCE will change the natural trends and convince us that emotions should also be altered or modulated by PCE [3,16]; and whether the continued consumption of these drugs will lead individuals to perceive themselves as something different from human beings and to undervalue some characteristics of the human condition itself [3,31].

As for children and adolescents, important biological and psychological issues must be considered. The biological impact of PCE on developing brains is even more alarming than on adults, as alterations may be more serious, leading to changes in the individuality, personality, and authenticity (and feelings of authenticity) [3]. Psychologically, children and younger individuals partially attribute their behavior (especially bad behaviors) to peaks of abstinence from these drugs, which raises immediate (and long-term) questions regarding the perception of morality and ethics by these individuals [3,28,32,33]. This highlights the issues about individuality and authenticity discussed above.

Unequal and unfair access to nootropics

Access to these drugs may increase social disparities [34-36]. But if such access does not depend on individuals' financial capacity or is planned to favor the needy, the effect can be diametrically opposed, reducing disparities [34,35,37]. Prioritizing and supporting the use of PCE in disadvantaged individuals, limiting access as social benefits increase, may help improve social status [3]. Small cognitive gains can significantly improve academic results, for example [38], and it is known that greater access to undergraduate and graduate education by students from more privileged families is already a problem.

The social impact of cognitive enhancement in several individuals could be significant, reducing learning difficulties and the incidence of intellectual disability. This improvement could also have major effects on the economy, technology and culture, given the increase in the intelligence quotient (IQ) of the general population [27]. Some argue that an increase of just 3% in the global average IQ could reduce the poverty rate by 25% [3,39], produce economic gains of 165 to 195 billion dollars and a 1.5% growth in the GDP [7].

Coercion and soft peer pressure

Although university students may not be so concerned with the legal restrictions to use these substances [3,21,40,41], the same may not be true for

other groups. The most paradigmatic case is PCE in children and adolescents due to parental or teacher pressure [3], a situation in which potentially harmful effects of PCE may be more pronounced, as already described. This is not an atypical situation, as highlighted in a survey conducted by *Nature*, in which 33% of respondents admitted feeling pressured to give nootropics to their children if other students were using them [42].

Indirect social peer pressure, or soft peer pressure, seems to concern students more than coercion [3,21]. This pressure consists of the student's perception that a group where he is inserted is consuming nootropics for PCE purposes, and not him. This consumption is commonly associated with North American fraternities and sororities [10] and common friends exactly for this reason [10]. But this soft peer pressure may lead to an opposite behavior in societies or groups that culturally see PCE as something to be avoided [21], often using the argument that these drugs are illegal for non-therapeutic purposes [43].

Coercion and soft peer pressure are also seen in the workplace (especially in the most demanding environments), where workers are expected to be increasingly more effective and productive. Reducing failures related to human factors is a possible advantage of PCE [26], but it can quickly become a requirement from employers or the State [26,31]. The scientific community itself is not immune: according to Mohamed [3], in 2008 a survey conducted by *Nature* reported that, among 1,400 healthy members of the scientific community in 60 countries, one in five respondents used nootropics for PCE – methylphenidate and modafinil being the most popular substances (62% and 44%, respectively). Some authors, however, consider it risky to accept PCE as a normal practice in institutions and society [21].

Cognitive trade-off

The enhancing effect of various drugs taken for PCE seems to depend on the basal level of cognition and capacity of each individual [3], but some studies show that enhancement in this case is only a trade-off phenomenon, where a certain cognitive capacity is improved but, in exchange, another capacity would be reduced [3,11]. A recent study with children diagnosed with ADHD showed that methylphenidate consumption increased the number of errors in the Wisconsin Card Sorting Test, which requires cognitive flexibility and capacity for adaptation [44].

Thus, this topic needs more in-depth studies to see if such drug-induced cognitive enhancement is only achieved by reducing another cognitive aspect. Some studies suggest this cognitive trade-off between, for example, long-term memory stability and flexibility, short-term working memory stability and flexibility, long-term memory itself and working memory, or between cognition and emotion and mood [11]. Trade-off may cause problems in people's cognitive liberty [13,26], which in various circumstances may be subjected to PCE coercion, as already discussed. Currently, cognitive liberty is not legally protected [26].

Academic use, competitive fairness, and valorization of results

PCE is largely associated with the academic community, especially in the United States, where the use of non-prescription drugs for PCE can range from 5% to 35% [10,45], depending on the university, and is particularly high in fraternities and sororities [10]. Studies show that the use of PCE can reach 55% in some fraternities [21]. In the European Union, it is estimated that PCE is adopted by 0.8% to 16% of university students, depending on the country, the university and the drug [10,43,46]. It is difficult, however, to determine the use in European universities, since the samples, methods, and study designs are quite different [10,21].

University students point to the competitive and stressful environment and the feeling of concentration and alertness offered by nootropics as the main reasons for using these substances [19]. Despite this, a clear distinction can be observed – especially in the European context [10,46] – between easy access drugs (such as coffee, caffeine pills, and energy drinks) and prescription cognitive enhancers [21]. The first are commonly found and more prevalent, consumed daily by most students [21], without social stigma [21,31], while prescription nootropics have a bad reputation and are sometimes discriminated, as they are seen

as an unwanted phenomenon, typical of North American universities [10,21].

The reported increase in the use of these substances in the academic community [3] has highlighted the issues of competitive fairness among students and the value of the results they obtain after using PCE. In an increasingly competitive university environment, some experts compare PCE to drugs consumed by high-level athletes to increase performance [10,40]. Others claim the achievements under PCE influence may be less valued, both socially and individually, as they were obtained with the support of substances [11]. Among students, the issue of unfairness seems to be relevant [31], since the results obtained by individuals with the help of PCE can be superior when compared to peers only due to these drugs [3]. Despite this fact, the legal and medical implications of nootropics are becoming more important, particularly supporting non-use of PCE [10].

Increasing consumption and dependence

Despite the media exaggerating PCE levels and describing unprecedented increases, especially in the academic community [10,21,41], the truth is that some studies have reported an effective growth of PCE in both academic and scientific communities [3]. In the United Kingdom, the number of prescriptions for these drugs has increased steadily and inexplicably from 220,000 in 1998 to 418,300 in 2004 [3]. Moreover, about 90% of modafinil are used by healthy individuals (without sleep disorders) to increase alertness and attention [3], so it is clear that the consumption of nootropics has spread over the past few years, highlighting the issue of dependence on these products.

Studies have shown blockade of dopamine transporter by modafinil and the consequent increase of this neurotransmitter in areas of the brain typically associated with substance dependence and addiction [3,47]. Others report that one in 20 users of cognitive enhancers fulfill the criteria for dependence or abuse [11]. Addiction can also be associated with the fact that individuals feel less prepared when they do not use these drugs, resulting in pressure to use them.

Discussion: a promising or an inevitable future?

Growing consumption and discussions about CE in general, and PCE in particular, are pertinent factors in this reflection, as it seems to be still in its early stages and will become more relevant in the future. It is important to discuss this practice based on current ideas and guidelines due to the variety of issues related to this topic and the lack of definition on what regulations should be adopted for PCE.

Will it be legally banned in certain contexts? Will it be ethically acceptable or mandatory in others? To what extent will this practice require regulations? How can we draw a line between treating a healthy individual and improving someone's cognitive impairment? Providing immediate or simple answers to these questions means doubting the relevance of the discussion.

First, PCE must always be contextualized at the social and individual level, because that context – whether an individual desire for improvement or a social desire for better individuals in our society – is the fundamental incentive for this practice. PCE can become an important tool to help individuals in difficult social circumstances, or it can aggravate social disparities if it is available only to upper classes. Less favored social situations are often caused and perpetuated by cognitive problems and difficulties in these circumstances. Due to their intellectual limitations, they are also called low-achievers or underachievers [1,3,12,28].

Several studies report a standard dose-response relationship for PCE drugs [11], often described as an inverted U-shaped curve that relates dopamine levels to cognitive capacities. That is, individuals with very low or very high levels of dopamine will have worse cognitive capacities when compared to individuals with ideal levels of this neurotransmitter [11]. Thus, individuals in the ascending part of the curve tend to have much better results with PCE than those in the middle or at the bottom of the curve. For example, individuals with lower baseline working memory capacity tend to obtain better results than subjects with very good working memory, who may not be affected or even be harmed by PCE.

All these reflections lead to a question: is it fair to assume PCE as an important and necessary reality for these low-achievers? Once again, it reflects the impact individuals have on the society they help create – a society that often affected individuals by not ensuring them (or their ancestors) the conditions to have a life better than the one they have now [34].

When assuming the existence of a minimum IQ that provides someone with the ability to live a better life, the importance of PCE for these low-achievers is almost self-explanatory, and the possibility of a "promising" future for these subjects can have major social impacts. Would it be fair, then, in a technologically advanced society, where IQ is essential to complete a certain level of education, to condemn an individual to have quality education only rarely and, with that, the possibility of a better life? Is there a real difference between improving this individual and treating someone with cognitive impairment when that situation refers to a level established by society? And will it become inevitable in the future? The difference between the so-called "normal individuals" and low-achievers is just a line drawn by us. If this difference is always exacerbated thanks to PCE, it will inevitably become almost mandatory using current or future drugs.

Another aspect reveals an important problem related to the cost of PCE, which foresees that regulated or non-regulated cognitive enhancement would be reserved for higher social classes. In other words, less favored individuals would be subjected to a plutocracy where only the richest can afford PCE, which would contribute to maintain or increase social inequalities. Or they would be subjected to a plutocracy where richer social classes would have no interest in ensuring PCE access to less favored classes, as they would not see personal advantage in it (although they may recognize the social benefits of a potential increase in the population IQ) [48].

Non-regulation or illegalization of PCE will probably lead to this second scenario, associated with a clandestine market for purchasing and selling these products and the lack of medical supervision of users. These three aspects are clearly harmful to PCE use at the social level. If they are not promising factors, are they truly inevitable?

The individual/society duality is evident in several other issues involved in PCE. The academic environment is undoubtedly the most frequently discussed in the literature and media regarding this topic, especially in the United States. When linking this argument with the aforementioned aspects, we should emphasize that the North American academic environment is known to have individuals from higher social classes, and the greatest adherence to PCE is mainly reported in the most competitive universities [21].

More important than knowing the rates of PCE use, however, is to understand that most students do not consider PCE inherently bad. They mostly question the degree of fairness of results obtained with PCE, and this depends on whether they are students who adhere to this practice or not. Fundamentally, this seems to be the only ethical issue of relevance for this population, highlighted when compared to major problems of cognitive enhancers for these individuals: its legality and the lack of information about its secondary and long-term effects [10]. It is important to stress that students value more the free choice about PCE use than the fairness of the results obtained.

Increasing competition in universities and the pressure to produce results are undeniable factors. Using enhancers seems to be more related to pressure and stress than to actual results. Improvements seem scarce, and PCE seems to be used more to tolerate stress and make tedious tasks more interesting. Those who advocate its use admit that it is useless if it is not accompanied by proper studies, considering that, in an academic context and with the available nootropics, the effects appear to be very small. Perceived enhancements may be superior to actual improvement [49], and this placebo effect is also relevant.

Also, the most frequently used drugs today are intended to increase the capacity for attention and alertness, and, in some cases, memory. Using different substances to improve other cognitive abilities may, in certain contexts, be considered absolutely inadequate, for example, adhering to a PCE plan that deliberately increases creativity in

an exam that involves developing a work. A parallel question would be: outside the context of the exam, is it relevant to develop such work using PCE? Is the use of other psychotropic substances, such as stimulants, not commonly associated with art itself? It is difficult to have a final judgment because countless contexts would have to be considered.

On the other hand, PCE is often compared to the illegal use of substances to improve the performance of high-level athletes. Students do not seem to consider this comparison as a relevant factor [10], mainly because the purpose of a competition is precisely to achieve a ranking at that moment, while, in the academic context, the result of an exam or a number of exams ranks the individual only, although always compared to their peers, and does not constitute the end of a process.

This is much more evident in the professional context. For instance, in a surgery outcome, it will be irrelevant whether the surgeon has used PCE, because the purpose of the process is not a competition or to compare the surgeon to other surgeons, but the success of the surgery and the patient's well-being.

In the professional context, we still have other problems, mainly in occupations of high risk and responsibility or which involve high pressure. The examples of PCE associated with surgeons (among other medical specialties), airline pilots and air traffic controllers, military personnel and intervention forces are paradigmatic. These professionals are often in risky situations, with human lives at stake. Thus, the issue of "new obligations" has been discussed for this type of professional [26]. Is it not to be expected that the state of art will request these professionals to use PCE?

This question is posed because these "new obligations" are just similar rules to those imposed in the past to obtain better results or make procedures safer. Sterilization of surgical materials or hand washing between surgeries (and between consultations) was not imposed until they were recognized as essential measures. Is PCE an indispensable (and therefore inevitable) measure in certain professions?

Once again, the individual/society duality is evident. Society often requires that some individuals abdicate something for the benefit of all. Military personnel abdicate their safety and well-being to defend their country, airline pilots have more troubled family lives due to constant flights, physicians abdicate family time and assume continued training in their short free time. It all implies an exchange between the individual and society, often to the greater benefit of society.

In certain situations and under certain circumstances, professionals may be expected to adopt PCE. It may be expected that a surgeon, after long hours in the operating room, will be ethically or legally required to take modafinil, for example, for safety reasons. Some studies suggest that this situation does not happen only because caffeine is frequently used, for being easily available [26].

A neuroethical dilemma emerges then, which refers to making the consumption of a potentially cognition-enhancing drug mandatory due to an individual's profession. But assuming that a particular professional has worked for long hours and that his cognitive abilities are reduced, could this professional be compared to a low-achiever? If that individual is now on the ascending section of the inverted U-shaped curve that shows the relationship between dopamine levels and cognitive ability, PCE drugs will only restore the normal levels of this individual. This is similar to the case of professionals who operate heavy machinery and who suffer from epilepsy or diabetes and must take a certain drug, that potentially alters some brain functions, to prevent adverse effects on other individuals. In a high-risk profession, won't an exhausted professional be in almost the same situation?

However, at the professional and academic level, the demand may increase beyond control, and not for a good social reason. In some cases, PCE will be required from employees of a given company just to increase profit, and not for technical or safety reasons. These cases are more dangerous because this so-called "cognitive liberty" (or cognitive integrity) is not legally protected like physical integrity [26]. Several bioethics experts argue that enhancers may involve problems regarding the individuals' authenticity and personality and may even threaten what is to be human [3]. This is particularly worrying if PCE is a deregulated

professional imposition to benefit only a certain company, not society.

Everything explained here depends critically on the study of PCE action: what effects do cognitive enhancers have on the brain and other physiological conditions of healthy individuals? The lack of prospective studies (or other types of study) with significant samples of users taking different nootropics and from different contexts represent an obstacle to discuss this topic. In the case of risky professions, PCE with studied effects would be more easily recommended (or mandatory) circumstantially, if secondary or long-term effects were not problematic.

Today, studies show good tolerance to nootropics, but some cases have reported increased heart rate, blood pressure, headache, anxiety, dizziness, nausea and insomnia with methylphenidate, as well as gastrointestinal problems, polyuria, palpitation, sleep problems, depression, psychosis and cardiovascular effects with modafinil [11]. Caffeine has been, for this reason and because it is a known xenobiotic, more widely consumed as a central nervous system stimulant [11] and cognitive enhancer. Its brain effects have been studied in detail and, apparently, they seem to be less comprehensive than prescription nootropics [8].

Finally, PCE in children and adolescents must be mentioned. The lack of information about the effects of these drugs makes its application in children extremely questionable. Since consent cannot be presumed, this may be an illegitimate interference in the future exercise of that young individual's autonomy.

The fact that their brains are in development must be considered for cognition itself, but not only. Cognition does not exist without morality or emotion [48,50], so for individuals who are still developing facets of personality and learning what is to be human, affecting this balance with the use of drugs will question their future. Interfering in this stage of development calls into question the basis of human condition, as the child ends up lacking full opportunity to develop and understand it. One example is that children with ADHD attribute much of their bad behavior to situations when they are not medicated.

What can be expected if more children are medicated without a reason? Dependence on these drugs – although not only in this case and not necessarily physiological – must be avoided since several individuals may consider themselves capable of certain tasks only under the influence of drugs. An even worse situation will emerge if these individuals doubt their humanity when not under the influence of nootropics.

Final considerations

The various neuroethical, medical and legal issues that PCE involves make this topic a challenge and a concern. One should always consider the beneficence and non-maleficence of the whole process for individuals, assessing their autonomy and condition. In children, precautions must be reinforced, as it may not only limit personal autonomy in the future (right to an open future), but also condition the personal identity.

For all these reasons, to further study the pharmacodynamics of each nootropic is crucial, and the regulation of these products should not be ignored either by the medical professions or society. Cognitive enhancement has always been pursued by this or other methods. The most important thing is to understand how far each enhancement, no matter how promising it may be, takes us away from or brings us closer to our notion of humanity.

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