Smart drugs for cognitive enhancement: ethical and pragmatic considerations in the era of cosmetic neurology

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ABSTRACT

Reports in the popular press suggest that smart drugs or "nootropics" such as methylphenidate, modafinil and piracetam are increasingly being used by the healthy to augment cognitive ability. Although current nootropics offer only modest improvements in cognitive performance, it appears likely that more effective compounds will be developed in the future and that their off-label use will increase. One sphere in which the use of these drugs may be commonplace is by healthy students within academia. This article reviews the ethical and pragmatic implications of nootropic use in academia by drawing parallels with issues relevant to the drugs in sport debate. It is often argued that performance-enhancing drugs should be prohibited because they create an uneven playing field. However, this appears dubious given that "unfair" advantages are already ubiquitous and generally tolerated by society. There are concerns that widespread use will indirectly coerce non-users also to employ nootropics in order to remain competitive. However, to restrict the autonomy of all people for fear that it may influence the actions of some is untenable. The use of potentially harmful drugs for the purposes of enhancement rather than treatment is often seen as unjustified, and libertarian approaches generally champion the rights of the individual in deciding if these risks are acceptable. Finally, whether the prohibition of nootropics can be effectively enforced is doubtful. As nootropics use becomes widespread among students in the future, discussion of this issue will become more pressing in the years to come.

In ancient Greece, it is said that students would entwine rosemary sprigs into their hair in the belief that it would improve their memory.[1] Although the desire to enhance one's cognitive abilities has not abated since then, modern advances in psychopharmacology now offer the possibility of one day realising this ancient dream. Cognitive enhancing drugs, smart drugs or "nootropics" (from the Greek roots noo-, mind and -tropo, turn, change), not only represent important pharmacotherapies for neurocognitive disorders such as dementia, attention deficit disorder and schizophrenia, but might also augment the minds of the healthy.[2] The possibility of purchasing "smartness in a bottle" is likely to have broad appeal to students with normal or above average cognitive functioning to begin with.

Need to finish that 5000-word paper on contemporary Russian literature by the morning? Then pop the psychostimulants modafinil (Provigil) or methylphenidate (Ritalin). Or, for the old fashioned, there is still always caffeine or amphetamine (Dexedrine). Need to memorise all of the steps in the Krebs cycle? Fear not, for the likes of brahmi, piracetam (Nootropil), donepezil (Aricept) and galantamine (Reminyl) are your trusty companions! Overcome by a lack of motivation? Perhaps selegiline (Deprenyl) is for you.

As the latest incarnation of "cosmetic neurology"—the off-label and non-prescription use of drugs in the healthy for the purposes of enhancement rather than treatment[3]—nootropics have captured the imagination of popular media as a sign of the brave new world in which we now live.[4–8] A world where we must be bigger, better and faster, where to err is all too human, and to realise one's highest potential demands that one be unfettered by their own biological limitations.

As the post-war baby boomer generation ages, there will be an increase in demand for and development of drugs that treat neurocognitive disturbances such as Alzheimer's disease, and it is likely that nootropics for the purposes of cosmetic neurology will be derived from this therapeutic market.[9] Although they currently offer modest improvements in cognitive performance at best, it is thought that future nootropics will encompass a wide array of drugs that enhance memory, attention, alertness, motivation, executive function, creativity or the need for sleep. Refer to Lanni *et al*[10] and de Jongh *et al*[11] for a review of current nootropics and future drug targets.

As evidenced by the literature,[3 12–14] the increasing use of nootropics and other forms of cosmetic neurology have been presaged for some time. However, although several authors[15–18] have considered the issue of "academic doping", none have examined the main ethical issues to any large extent. This is despite the widespread non-medical use of psychostimulants such as methylphenidate across universities for the purposes of enhancing concentration.[19] It seems apparent that cognitive enhancing drugs would be highly attractive to high school and university students, and the largest non-therapeutic market for future nootropics could very well be this demographic. As a corollary, the ethical and pragmatic issues that will emerge from the use of nootropics by students warrants earnest consideration.

In the absence of any existing ethical framework with which to view this issue, it may be relevant to examine the one paradigmatic human endeavour that has already wrested with the problem of performance-enhancing drugs for several decades: competitive sport.[14 20] This article will briefly

consider four critical themes regarding the use of drugs in sport as they apply to nootropics in academia: (1) the argument that they are a form of cheating because they offer an unfair advantage; (2) the problem of indirect coercion; (3) the argument that they are dangerous; and that (4) regardless of the ethical implications of their use, prohibition is likely to fail. Although this is by no means an exhaustive treatise on the matter, it is hoped that this article will provoke greater discussion of the issue than is presently the case.

PERFORMANCE-ENHANCING DRUGS CREATE AN UNEVEN PLAYING FIELD

One of the most frequently invoked arguments against the use of performance-enhancing drugs in sport is that they confer an unfair advantage to those who use them.[21–23] If the difference between winning and losing were determined not on the running track but in the chemical laboratory, it would result in an "uneven playing field" because athletes would not be competing on equal grounds. It is often concluded, therefore, that doping in sports is a form of cheating, because it provides doping athletes an unfair advantage over their clean competitors.[22 23]

The contention that a student's use of nootropics would produce an uneven playing field is a peculiar one. One implicit assumption of this argument appears to be the belief that without the use of nootropics, an even playing field either exists or is entirely possible. However noble an aspiration this may seem, it assumes the validity of the level playing field concept without reconciling itself with the reality of widespread biological and environmental inequalities that already exist.[12 24]

Unsurprisingly, cognitive ability is a significant predictor of academic performance[25] and twin studies indicate that IQ has a heritability of approximately 50%.[26] That is, a sizeable proportion of one's academic successes are due to the genes with which one has been naturally endowed. Moreover, resources that influence academic performance are also unevenly distributed across social classes. Home computer access,[27] private tuition[28] and even better childhood nutrition[29] are all examples of environmental factors that contribute to improved academic performance, factors that are less readily available to individuals from lower socioeconomic backgrounds.

It is clear, then, that some students have a distinct genetic or environmental advantage over others from the offset. Academic performance is not merely the product of hard work, discipline and other laudable personal attributes, but, it would seem, is a competition partly won by the genes and socioeconomic background of one's parents. It follows, therefore, that prohibiting nootropics would not even the playing field, because there never was an even playing field to begin with.

To be sure, nootropics would probably make an already uneven playing field more unfair, and one that is likely only to favour the wealthy who can afford to purchase them.[2 17] Not only do the rich get richer, but in the future it seems that they might also get smarter. However, using unequal distribution to justify the prohibition of nootropics is akin to prohibiting private tuition, which also increases academic performance while exacerbating educational inequalities between social classes. If socioeconomic inequalities in education are readily tolerated by society, then it would be hypocritical to apply this criterion selectively to nootropics and not to other performance-enhancing strategies.[3 12]

It is interesting to consider under what conditions society might have an obligation to ensure universal access to nootropics should highly effective compounds emerge.[14 18] If nootropics represented the most cost-effective means of enhancing academic performance, social programmes might seek to make them accessible to the underprivileged. Moreover, it is entirely possible that some nootropics would primarily benefit those in whom cognitive deficits are present, with little, no, or perhaps even deleterious effects upon the healthy.[11 12] This appears to be the case with modafinil, in which the greatest improvements in cognitive performance are seen in those with lower IQs.[30] Nootropics might therefore free underperforming students from their "neurological handicaps"—rather than creating an uneven playing field, nootropics could help to level it, increasing standards in academic performance in the process.

EVERYBODY ELSE IS TAKING THEM

Some athletes are motivated to use performance-enhancing drugs because they believe their competitors are doing so.[20 22 31] Although it is difficult to determine the prevalence of drug use in sports, anecdotal reports suggest up to 95% of elite athletes have taken them[31] and the general opinion of athletes is that few successful Olympians do not dope.[32] Therefore, in order to compensate for what might be considered an unfair advantage against them, an athlete who would otherwise not be compelled to dope may decide that this is the only avenue through which they can remain competitive against those who do.[20 31]

One concern surrounding the widespread use of nootropics is that it may indirectly coerce other students into taking them in order to keep up with their peers.[2 12 33] For example, if the majority of students were to use modafinil and their doing so vastly improved their academic performance, then the remaining non-users would feel a certain amount of pressure to follow suit in order to remain competitive. The Red Queen Principle applies here, in which an individual must continue developing in order to maintain their fitness relative to others with whom they are competing.[3] Ergo, a student must make use of every possible advantage afforded to them, eg, nootropics, as failing to do so might result in a relative loss of academic performance.

It would appear that for a student to be indirectly coerced into using nootropics, several criteria must be fulfilled. First, nootropics would need to confer substantial improvements in performance such that not taking them would place one at a distinct academic disadvantage against those who do. In addition, a sufficiently high proportion of the student's peers must use nootropics in order to edify the perception that "everybody else is taking them". Moreover, it is likely that the most successful students would need to use nootropics, so as to perpetuate the presumption that it is either impossible or prohibitively difficult for a drug-free student to attain high grades.

In the absence of empirical data, one can only speculate if any of these factors presently hold true in academia. For example, caffeine is a widely used nootropic that can reduce fatigue and promote alertness and vigilance,[34] but it is unlikely that its use is necessary for academic success and that many feel coerced into consuming it. However, some speculate that indirect coercion may already be felt by students who attend schools with high rates of methylphenidate use.[12 35]

McCabe *et al*[19] report that in the USA the non-medical use of methylphenidate and amphetamine in the previous year is as high as 25% in some college campuses. The most commonly cited reason for using these stimulants is to enhance concentration (58%) and increase alertness (43%), indicating that they are being used for their performance-enhancing properties.[11] Others have reported similar findings.[36 37] Interestingly, that the

prevalence of methylphenidate is over two times greater at colleges with more competitive admission criteria[19] hints at indirect coercion, but this remains to be evaluated explicitly.

Although indirect coercion would imaginably be an unpleasant experience in those who feel it, the expectation that one restrain their actions for fear that it may evoke feelings of coercion in others is not a particularly cogent reason for prohibiting these actions. Students who are not employed are more likely to perform better academically than those who are.[38] As a consequence, nootropics would be no more coercive than the pressure that one should not work to support oneself financially in order to remain academically competitive. Placing constraints on people's actions so as to protect others from feelings of coercion is arguably no less an attack on personal freedom.

However, difficulties in this reasoning arise when considering indirect coercion with respect to dangerous or toxic nootropics. Should individuals be protected from the pressure of taking potentially dangerous drugs such as methylphenidate in order to succeed academically? What if the nootropic were innocuous? Would this relegate indirect coercion to a moot point? It seems reasonable to argue that few would raise the same level of concern about indirect coercion regarding caffeine use as they would towards methylphenidate. It is apparent then, that the issue of indirect coercion to use performance enhancers hinges upon the safety profile of the drug in question and that this may be a major determinant of future policy towards nootropics use.

PERFORMANCE-ENHANCING DRUGS ARE DANGEROUS

According to the World Anti-Doping Agency (WADA) one criterion for prohibiting a drug in sport is whether or not it poses an actual or potential risk to an athlete's health.[39] Chronic use of anabolic steroids, for instance, may produce hepatic disease and cardiovascular complications resulting in death.[40] Although the dangers of drugs are often overstated, these dangers seemingly justify their prohibition because legalisation may be perceived as tacit endorsement of their use. Indeed, the safety profile of a performance-enhancing drug appears to be a large determinant of whether or not it is prohibited. Caffeine, for example, reliably increases performance in a range of sports including swimming, cycling and running at doses allowed by WADA.[41] Yet despite being a form of ''cheating'' in the same vein as anabolic steroids, caffeine's use in sport is permitted because it is relatively harmless.[22]

Similar considerations can been made with regard to nootropics.[2] For nootropic psychostimulants such as methylphenidate, the dangers are real and relatively well known. Aside from its abuse potential, methylphenidate may aggravate mental illness, produce sleep disturbances and is associated with cerebrovascular complications.[42] Therefore, inadequacies of prohibition notwithstanding, restricting methylphenidate's use would be justified in the eyes of many.

In contrast, common nootropics such as caffeine and brahmi have an extensive history of use and are generally well tolerated.[41 43] For the majority of nootropics, however, there are few data on the effects of long-term use of these drugs on humans. Although many display minimal adverse effects and in some cases appear to be neuroprotective, eg, modafinil,[44] it remains to be seen whether nootropics represent a pharmacological ''free lunch'' or if the enhancement of some cognitive functions can only be realised at the expense of others.[10 12] For example, transgenic mice with increased expression of the NR2B protein subunit of the *N*-methyl-D-aspartate receptor display improved learning and memory functioning.[45] However, they also possess a greater ability to recall aversive events;[46] enhancing memory might not only increase the ability to recall exam material, but also negative and traumatic experiences that might otherwise be forgotten. Happiness, as they say in the classics, is good health and a bad memory, and augmenting the latter may have untoward effects upon general mental well-being.

It is clear that there are risks inherent in the use of any drug, and given that the use of nootropics by the healthy would be for the purposes of enhancement rather than treatment, some clinicians would deem any risk unacceptable.[2 3] On the other hand, the general libertarian perspective argues that provided that the individual is cognisant of the potential side effects, they are free to make their own decision to take nootropics.[3] If we take this perspective to its logical and extreme conclusion, however, is this no different to allowing the use of any nootropic, no matter how dangerous, eg, methamphetamine, provided that individuals are aware of the dangers in doing so? It would appear that both extremes are untenable—on one hand people should have a right to decide whether or not the risks of nootropics are acceptable, but civil liberties must also be balanced by the need to safeguard the public good.[47]

DRUG USE WOULD BE IMPOSSIBLE TO CONTROL

The widespread access to and use of performance-enhancing drugs in sport despite their prohibition suggests that current anti-doping measures are inadequate.[22] The competitive advantages derived from their use, the low likelihood of drug testing and the relatively minor punishment for getting caught make them attractive to many athletes.[48] As a consequence, Foddy and Savulescu[22] contend that any attempt to prohibit performance-enhancing drugs is condemned to failure. This is not influenced by ethical considerations concerning such use, but rather the belief that any attempt at prohibition is not pragmatic and possibly more harmful than regulation.[21 22 24 49] Let us consider a future scenario in which highly effective nootropics are developed: would the prohibition of these drugs for academic gain even be possible?

As in the case of controlled substances such as methylphenidate and amphetamine, the high rates of non-medical use and the ease with which they can still be obtained[36] demonstrate the inability of prohibition to control their illicit supply effectively. As nootropics would probably have legitimate therapeutic applications in the treatment of neurocognitive disorders such as dementia,[50] diversion from legitimate sources—as is the case with the aforementioned—would be highly likely.

Considerations of supply notwithstanding, just how the prohibition of nootropics in academic contexts could be enforced remains unclear. One conjures to mind the scenario of students taken to one side, cup in hand, and asked to provide a urine sample to test officials.[15] Scandal would erupt and rumours abound when the magna cum laude is stripped of his title for testing positive for modafinil—a drug that gave him near-superhuman levels of mental endurance. As laughable as it may seem, it is possible that scenarios such as this could very well come to fruition in the future. However, given that the benefits of nootropics can also be derived from periods of study at any time leading up to examinations, this would also require drug testing during non-exam periods.[14] If the current situation in competitive sport is anything to go by, any attempt to prohibit the use of nootropics will probably be difficult or inordinately expensive to police effectively.

CONCLUSIONS

In any highly competitive environment it is inevitable that people will seek to gain advantages over their competitors. This is no more apparent than in competitive sport, in which pharmacologically based performance enhancers are prohibited yet widely used. Therefore, with the development of highly effective nootropics in the future, it is likely that their use by healthy students will become more widespread. With this come a number of ethical dilemmas that warrant deeper consideration. Is there something intrinsically wrong about enhancing our minds pharmacologically? What is it about swallowing a pill to improve our cognitive abilities that offends our sensibilities, when we will happily drink a cup of coffee to increase our alertness? Should the use of nootropics by students be prohibited, and if so, on what grounds? Finally, would it even be possible to enforce the prohibition of drugs in academia?

In this article I have briefly touched upon these issues by examining some themes that have arisen from the drugs in sport debate. Ostensibly, academia is not as competitive as sport, in which the mantra ''nobody remembers second place'' governs the latter. However, high school and university are the primary competitive spheres of many people's lives, and ones that have significant bearing upon their lives in terms of both career opportunities and future earning capacity. The pressure to succeed academically is very real and in a climate in which high-stakes public examinations have increased demand for private tuition,[51] it is likely that all avenues for performance enhancement will be exhausted. Whether this culminates in the widespread use of performance-enhancing drugs to the level seen in sports remains unclear, and will probably be influenced by the competitiveness of the scholastic setting, eg, university or school entrance exams versus end of semester final exams.

By examining the main considerations from the drugs in sport debate, we may draw from almost 50 years of discussion regarding the use of performance-enhancing drugs. Those who forget history are doomed to repeat it, and it is apparent that the failures and inconsistencies inherent in anti-doping policy in sport will be mirrored in academia unless a reasonable and realistic approach to the issue of nootropics is adopted. Taking caffeine as an exemplar nootropic whose use is both safe and culturally endorsed, it is likely that drug safety will be an important factor in determining the acceptability of nootropics use within academia. If this is to be the case, then there is a greater need to examine the safety and efficacy of putative nootropics in the healthy rather than only in clinical populations. However, the widespread non-medical use of methylphenidate[36] suggests that students will use nootropics regardless of their safety or legality. Perhaps the most that can be hoped for is to have a better understanding of the dangers of nootropics so that students will take this into consideration when deciding whether or not to use them.

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