Pharmacological Enhancement

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The Facts and Myths About Brain Doping

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SUMMARY

PHARMACOLOGICAL ENHANCEMENT
THE FACTS AND MYTHS ABOUT BRAIN DOPING

Since the turn of the millennium, the possibility of using pharmacological methods to improve people's performance has been the subject of intense discussion. Experts from science and ethics usually use the term 'neuroenhancement' or 'brain doping' in this context. It has also been regularly reported in the media that using pharmacological methods to enhance academic performance is already commonplace among 25% of students.

Stephan Schleim has researched this topic intensively at the University of Groningen (The Netherlands) and as part of the 'History of Neuroethics' research project funded by the Dutch Research Council (NWO). This report summarizes results from 60 years of research and disentangles numerous facts and myths about brain doping. Below is a summary of the key findings.

1. NEUROENHANCEMENT/BRAIN DOPING IS NOT A WIDESPREAD PHENOMENON

There is no conclusive scientific evidence to support the notion of brain doping as a widespread phenomenon, which has been propagated by both experts and the media. The fact is that stimulant and sedative psychotropic drugs were already commonly used during certain periods of the twentieth century. For example, amphetamine (street name: 'Speed') and tranquillizers such as Librium and Valium were frequently used until the 1960s. *Instrumental* use, in other words the use of substances to achieve specific purposes other than medical treatment, has also been documented.

The more recent studies on prevalence present a very mixed picture: there is no consensus among experts on the definition of the phenomenon. Most research groups investigate the 'non-medical use' of such substances, and the more significant surveys actually reported numbers of consumers in the single-digit percentage range (i.e., less than 10%). However, this usually concerns *infrequent* or *occasional* use; according to the studies, more frequent use is even rarer. Furthermore, other reasons for substance use – such as to have more fun while partying or to lose weight – are sometimes mentioned more frequently than to enhance mental performance.

Conversely, the marked increase in use of certain psychotropic drugs for *medical* purposes since the 1990s is well documented. This coincides with the much more frequent diagnosis of mental disorders, for example, attention or anxiety disorders, and depression. Whether doctors are diagnosing these disorders too often, and prescribing certain drugs too frequently, is a discussion in itself.

2. WHICH SUBSTANCES ARE WE ACTUALLY TALKING ABOUT?

Although current and prospective drugs for the treatment of age-related dementia and technical methods for brain stimulation are occasionally mentioned in the debate, in practice the focus tends to be on the psychostimulants amphetamine, methylphenidate (the active ingredient in Ritalin), and modafinil (the active ingredient in Vigil). These drugs are often prescribed for the treatment of attention and sleep disorders. More recently, the debate has also turned to psychedelic substances (such as ayahuasca, LSD, and psilocybin). It is claimed that the consumption of very small amounts of these substances, known as 'microdosing', improves creativity and mental performance.

However, there is as yet no conclusive scientific evidence to support the idea that psychostimulants or psychedelics significantly improve the performance of *healthy* people. In fact, various studies suggest that the effects are primarily *subjective*: test subjects feel better and are more motivated or more interested after consuming the substance. On top of that, the majority of these studies involve abstract laboratory-based tasks that are difficult to transfer to everyday life.

A rare exception to this is the study involving chess players, which is discussed in more detail in the report. But even here, the results were rather modest when compared with, for example, the effect that can be achieved using caffeine that is freely available. Nevertheless, it is worth noting that even very minor differences in performance can be crucial in highly competitive situations.

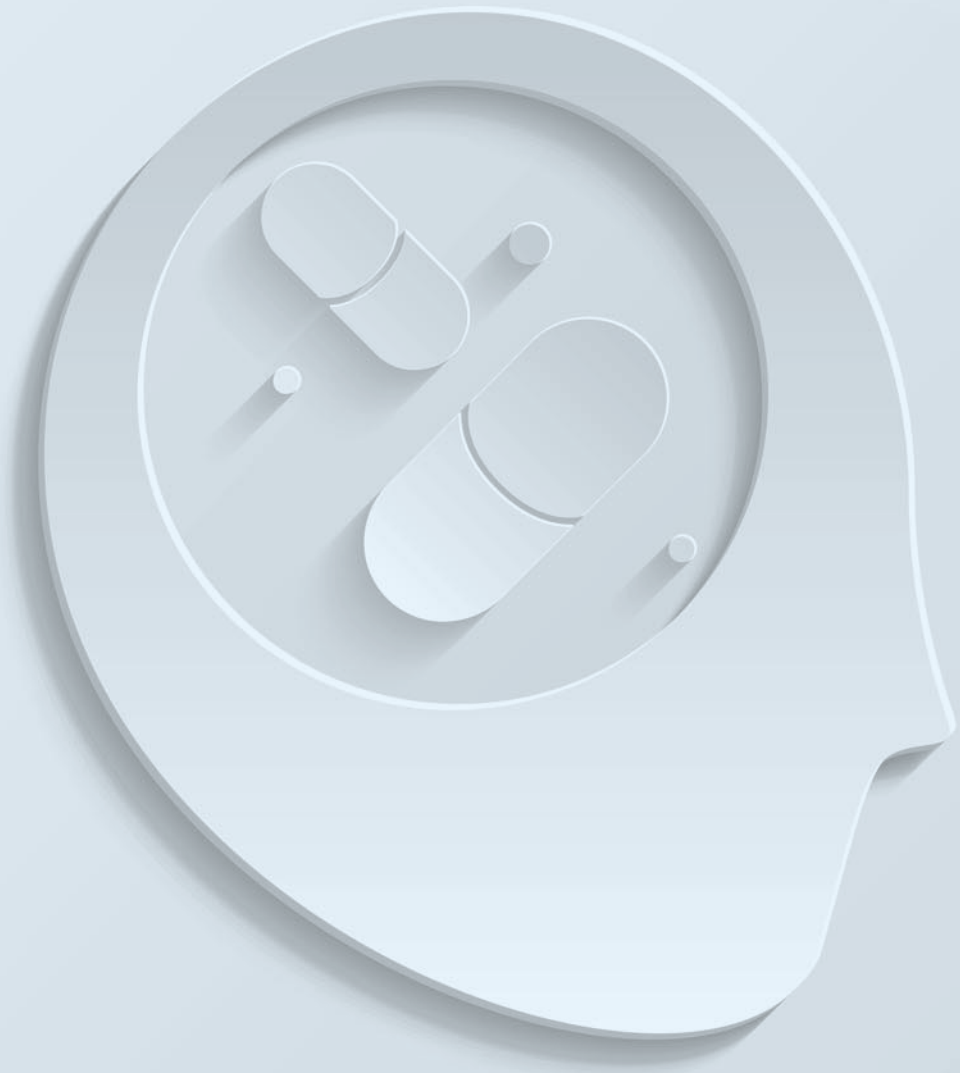
3. INSTRUMENTAL SUBSTANCE USE

The previous conclusion raises the question as to whether a specific discussion of neuroenhancement or brain doping is at all useful. The use of substances that affect the psyche to achieve certain goals has been documented for centuries and has probably always been part of our culture. In other words, substances can be used as *instruments*. This shifts the focus to our moral values and drug policy. In doing so, we must remember that the boundary between permitted stimulants and food supplements, regulated medicines, and prohibited drugs is flexible and changes over time.

4. SUBSTANCES AND VALUES

This, too, was the subject of an informative debate as early as the 1970s. The firmest opposition to instrumental substance use invokes the 'wisdom of nature' and rejects artificial intervention from outside; this position, however, neglects the fact that some of the substances mentioned are of natural origin and there is a long record of their instrumental use in cultural history. Another stance emphasizes the adaptability and versatility of human beings and welcomes the availability of new methods; however, this position often overlooks that the demands on people's performance are shaped by society.

A democratic middle ground is therefore geared towards correctly informing citizens about the prevalence and benefits of substance use as well as changing societal demands. This approach emphasizes the *autonomy* of people, which includes the shaping of their social framework. This report aims to make a useful contribution to this.



WHAT IS BRAIN DOPING/ NEUROENHANCEMENT?

The concepts generally refer to the enhancement of mental performance through direct intervention in the brains of healthy people, for example using pharmacological substances (e.g. drugs and medicines) or electrical stimulation. The term 'brain doping' invokes a comparison with institutionalized sport, where certain performance-enhancing substances are banned. The term 'neuroenhancement' (or 'cognitive enhancement') is more commonly used in scientific discussions. Further on it will be argued that 'instrumental substance use' is actually the most appropriate term.

In scientific discussions and in debates in the media, the impression has often been given that this is a new and growing trend. But in fact, research findings on prevalence have often been misrepresented or one-sided, and results from the 1960s to 1980s have even been ignored altogether (see below). Already in 2007, a review of the pharmacological studies with healthy subjects suggested that the public might be promised too much (Schleim & Walter, 2007).

This report thus starts out with a discussion of the prevalence of this phenomenon in society – now as well as in the past. The most commonly used substances will be presented subsequently, including information about their effects and side effects. After this, the alternative framework of instrumental substance use is introduced and relevant ethical values associated with it are presented. At the end of this report answers to frequently asked questions can be found.

HOW WIDESPREAD IS BRAIN DOPING/NEUROENHANCEMENT?

This question was the subject of a comprehensive review of 28 individual studies as early as 2011 (Smith & Farah, 2011). However, the results ranged between 1.7% and 55% – a clear indication of inconsistent approaches among researchers. For example, how do you define the phenomenon, and how do you subsequently measure it in practice? Each research group seems to have different answers to these questions.

More recently, a new paper was published that comprises 111 studies (Faraone et al., 2020). Their results vary even more, between 2.1% and 58.7%. The authors also regret that, due to the significant differences between the individual studies, they were unable to conduct a formal meta-analysis that would allow them to summarize the scientific results in a standardized manner. So, the evidence base in 2020 has hardly improved since 2011.

The honest answer to this question is, therefore, that we cannot really say *with any certainty*. We can, however, reflect on what is *plausible*.

KEY INDICATORS OF PREVALENCE

For example, the results of studies that are more methodologically sound, in which significantly more people (N > 10,000) were surveyed – ideally using a representative method and conducted at different locations – are usually in the single-digit percentage range. By contrast, the extreme value of 55% originated from a non-representative survey of a few (N = 307) male members of fraternities at only one North American university (DeSantis, Noar & Webb, 2009). Nowadays, young men and members of such fraternities are known for their excessive substance use.

On the other hand, the nationally representative (N = 102,000) *US National Survey on Drug Use and Health 2015-2016,* found that only 2.1% of respondents had used prescription stimulants such as amphetamine (street name: 'speed') or methylphenidate (known from the drug Ritalin) without a prescription (Compton et al., 2018). A large-scale, international comparative study also found that substance use is higher in English-speaking countries (e.g. Canada, USA, United Kingdom) than in German-speaking countries (Germany, Austria, Switzerland; Maier et al., 2018).

Many of these studies do not specifically focus on brain doping/neuroenhancement, but on 'non-medical use' of stimulants and other substances. This encompasses motivations such as wanting to party longer, wanting to overcome social anxiety or shyness, wanting to lose weight (some drugs

suppress hunger), or simply wanting to experience a 'high'. However, these crucial differences are often overlooked in many reports, both in scientific and general media.

Improved concentration while studying or staying awake longer to study were also frequently mentioned as reasons for substance use, which is consistent with the concept of brain doping/neuroenhancement. However, this could simply reflect the fact that most of the surveys were conducted among students. In their stage of life and situation, these are, after all, essential activities. Incidentally, those studies that focus exclusively on enhancing mental performance, rather than asking about 'non-medical use' in general, report considerably lower frequency of use.

The clearest indication that there has been any increase at all was provided by researchers at the University of Michigan (McCabe et al., 2014). Between 2003 and 2013, they repeated a non-representative survey at the same university on six occasions. For the period in question, this revealed an increase in non-medical use of prescription stimulants from 5.4% to 9.3%. It should be noted here that survey participants were asked whether they had consumed stimulants *at least once in the last year*.

The same research group examined the frequency of this behaviour in more detail in a separate investigation (Teter et al., 2010). According to this study, 82.1% of the users had taken stimulants *less than ten times* in total. So, even though more students had tried the substances, around four out of five stopped taking them after a few times.

CONCLUSION ON PREVALENCE

These and many other findings strongly suggest that brain doping/neuroenhancement has never been a mass phenomenon and by no means can we say with any certainty that it has increased in the last 20 years. Contemporary figures may even be lower than those of surveys from the 1960s to the 1980s, which are summarized in other publications (Schleim, 2020a; Schleim & Quednow, 2017; 2018).

To give an example, one review paper covered 21 individual studies from 1966 to 1980 (McAuliffe et al., 1984). Here, between 11% and 54% of the participants stated that they had previously taken amphetamines, mainly for the purpose of staying awake longer or to perform better on a test or in sports. (Methylphenidate/Ritalin was not well known at the time.)

Not long after, the same research group published a detailed but non-representative survey of health science professionals and students (N = 1308; McAuliffe et al., 1986). Some 16% of the doctors and 17% of the medical students surveyed reported that they had taken drugs or medication to stay awake longer, to work more effectively, or to be better at sports. The professionals estimated that they had done so roughly 44 times on average; for the students, that figure was 66 times.

This is significantly higher than the figures presented by American researchers in 2010 (Teter et al., 2010). It is therefore entirely conceivable that brain doping/neuroenhancement was even more widespread in the past than it is today, even if people did not call it that yet.

GRAPHS: PREVALENCE NOW AND IN THE PAST

Figure 1

Stimulants (amphetamines in particular) were popular from the 1930s to the early 1970s. Here, we can see the results of surveys conducted at secondary schools in San Mateo County, California. As many as a quarter of the pupils in the 10th (red) and 12th grade (blue; dotted lines) had previously used stimulants. About 5% said that they used them every week (solid lines). Source: Ferrence & Whitehead, 1980

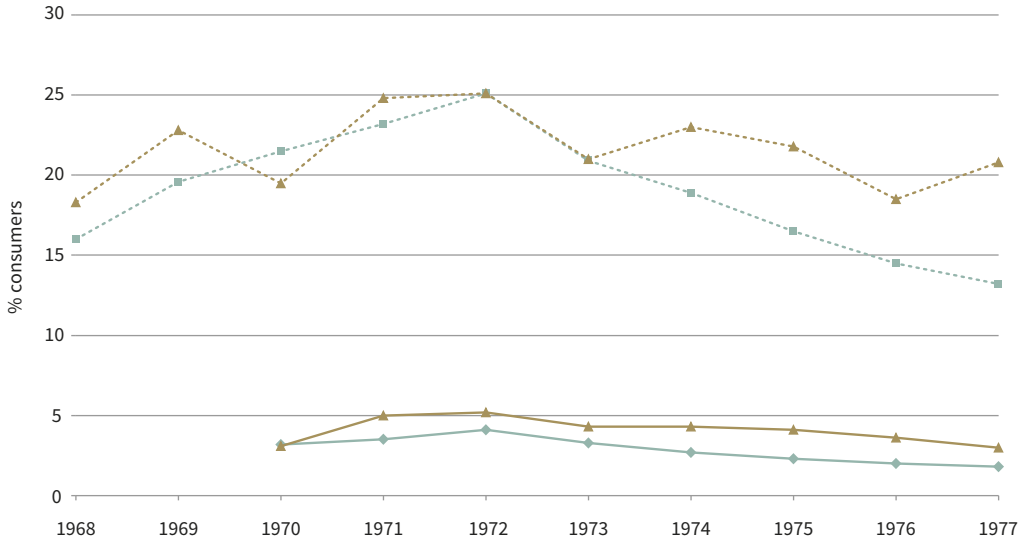


Figure 2

Tranquillizers (especially Librium and Valium) became very popular at the end of the 1950s. Around 1960, almost 500,000 kg of these drugs were produced annually in the USA. The number of adults who had taken such a drug at least once rose from 7% in 1957 to 27% in 1967. Source: Parry, 1968; these are average values for 1957-59, 1960-62, and 1963-65; intermediate values have been added.

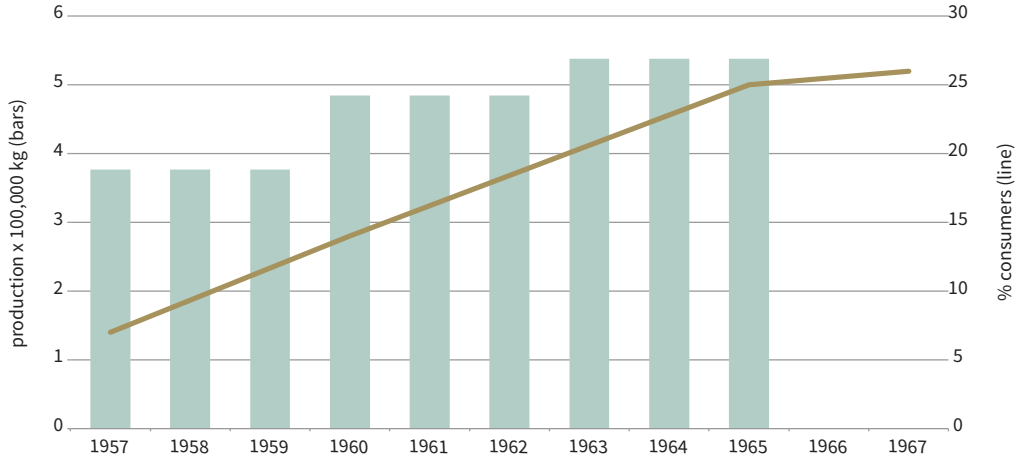
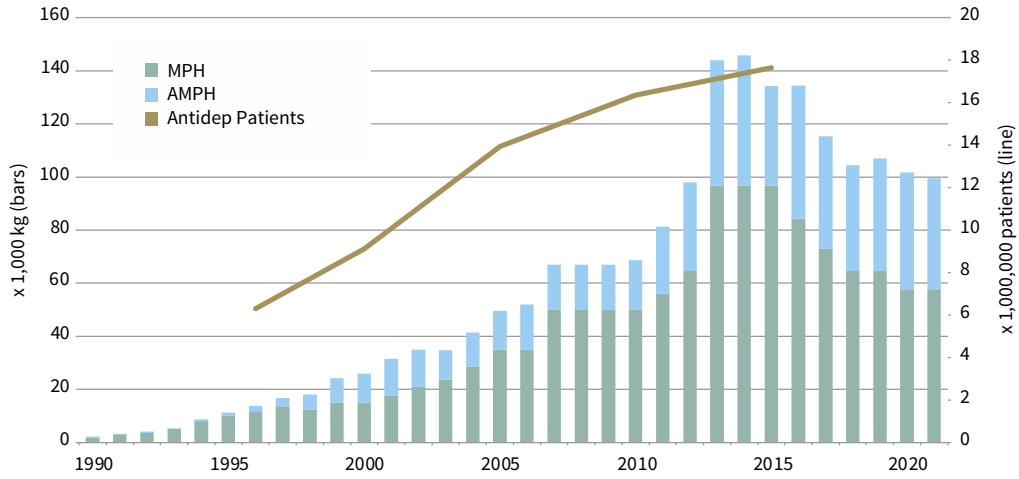


Figure 3

In the 1990s, stimulants – primarily methylphenidate (Ritalin, blue bars) – were once again produced in greater quantities in the USA. Amphetamine ('Speed', red) also experienced a comeback. In 2014, the previous record was surpassed; the production level rose to 140,000 kg. In the same period, more and more antidepressants were prescribed. The yellow line shows the number of patients in the USA in millions who were prescribed such drugs annually. In 2015, this figure was almost 18 million. Source: Schleim & Quednow, 2018; Luo et al., 2020



EXAGGERATIONS IN MEDIA AND SCIENCE

One thing that can be said with certainty, however, is that the figures on prevalence have been regularly exaggerated both in the media and in relevant scientific publications (Partridge et al., 2011; Quednow, 2010a; Schleim, 2010).

For example, right at the beginning of the discourse, a study was repeatedly cited, according to which 16% of students engaged in brain doping/neuroenhancement (Babcock & Byrne, 2000). Besides the poor quality of the non-representative survey, it explicitly did *not* ask about mental performance enhancement, but about the use of various drugs/medications 'for fun'.

Another way was to refer to what was in itself a sound nationwide study conducted at various colleges in the USA with a large number of participants (N = 10,904; McCabe et al., 2005). Among the 119 educational institutions at which students were surveyed, there *was only one* where 25% of respondents had answered 'yes' to the question of whether they had used non-medical prescription stimulants at least once in the past year. By comparison, this figure was 0% at 21 colleges. The average for all respondents was 4.1% (incidentally, for use in the past month, this figure was only 2.1%).

Despite this, leading media outlets and even leading research figures repeatedly reported the 25% as if this applied to all (American) students. This is a gross distortion of the scientific evidence. And this does not even take into account the fact that this study did not explicitly examine brain doping/neuroenhancement, but rather the broader concept of 'non-medical use'. These are just two striking examples of how the phenomenon has been and is still being turned into an urgent problem.

There is no doubt that the media have a vested interest in generating a lot of attention. But researchers are also in competition with each other for research funding; those who can convince their intended audience that they are tackling an urgent and societally relevant problem have an advantage over the competition. However, adopting such a strategic approach could lead to a situation where the public no longer believes science when it comes to really important issues (for example, climate change or infectious diseases).

SO, WHICH SUBSTANCES ARE WE ACTUALLY TALKING ABOUT?

When it comes to substances or drugs that *could* improve mental performance, the possibilities are virtually endless. Besides preliminary experiments with electrical or magnetic brain stimulation methods, such as transcranial direct current stimulation (TDCS) or transcranial magnetic stimulation (TMS), and potential anti-dementia drugs, research has largely focused on the psychostimulants amphetamine (street name: 'Speed'), methylphenidate (used in the drug Ritalin, among others), and modafinil (in the drug Provigil), which is prescribed for the treatment of certain sleep disorders.

These drugs affect the availability of neurotransmitters such as dopamine and noradrenaline in the brain, although the mechanisms of action – especially of modafinil – are not yet fully understood. It is worth noting that research into amphetamine has been going on for over 100 years, methylphenidate since the 1940s, and modafinil since the 1970s. All three substances are suspected of having a potential for addiction and abuse and are therefore subject to specific regulation, although modafinil is regulated to a lesser extent than the other two.

As for scientific studies *with healthy test subjects*, the group size is often very small and the test exercises are usually rather abstract, which reduces the significance of the results. In addition, the effects are very much dependent on the respective dosage and on individual health factors.

PLAYING CHESS IN THE NAME OF SCIENCE

One in this respect extraordinary investigation examined 39 healthy male chess players with an average age of 37.3 years (Franke et al., 2017). They were asked to play several games on different days against a chess computer that was adapted to the level of the respective player after the administration of methylphenidate (Ritalin), modafinil (Provigil), caffeine, or a placebo. The playing time was limited to 15 minutes per game.

On average, the chess players who had used stimulants scored 6.3% (methylphenidate) to 8.2% (modafinil) more points per game compared to those who had taken the placebo. However, these differences did not reach the statistical significance threshold. There was almost no difference between the results achieved under the influence of caffeine and methylphenidate (Ritalin). Compared to caffeine, the chess players scored an average of 1.7% more points under the influence of modafinil (Provigil). This difference was also not statistically significant.

Interestingly, chess players under the influence of the substances took *more* time per game. They therefore lost more often because they had reached the time limit. They also completed 2.1% (modafinil) to 2.8% (methylphenidate) fewer games compared to the placebo. The researchers speculated that the test subjects would have performed better under the influence of the active substances without a time limit. This once again emphasizes the importance of concrete parameters for such experiments.

Experts assume that psychostimulants primarily increase the alertness, excitation, and motivation of users and not their intelligence or creativity (Quednow, 2010b; Vrecko, 2013). In other words, when under the influence of these substances, people may simply feel more motivated or more 'on the ball' to accomplish specific – often rather monotonous – tasks.

The study with the chess players was mentioned here because it investigated a comparatively realistic scenario. Such experiments typically use neuropsychological tests. These were often developed to examine cognitive deficits of psychological and psychiatric patients. Translating such test results into the everyday environment of healthy people therefore runs the risk of a 'clinical fallacy' (Schleim, 2014); just because you score a few extra points on a test like this on the computer does not automatically make you smarter or any more efficient at work or in your studies.

Nevertheless, the benefits of these substances should not be completely dismissed. In highly competitive situations, even minor differences that do not reach the significance threshold in such studies can be decisive. Take a chess tournament, for example, where players of virtually the same ability play against each other. In this case, a 1.7% increase in performance (in the case of modafinil compared to caffeine) could be the difference between winning and losing. However, in unfavourable conditions, such as the above-mentioned time limit, an active substance could actually be disadvantageous.

Therefore, for the vast majority of people, the only marginal and potential added value is unlikely to outweigh the risk of side effects – which can be quite severe in individual cases, especially when combined with other medical problems (such as cardiovascular disease). Anyone considering using such substances should seek medical advice first. However, the most common side effects – nervousness, sweating, headaches, palpitations, and sleep problems – are also rather mild.

PSYCHEDELICS

Recently, psychedelics are getting more attention with respect to our topic. The most relevant substances are psilocybin which is contained in particular mushrooms, ayahuasca which is used for religious ceremonies in South America – with the active ingredient *N,N*-Dimethyltryptamine (DMT) – as well as LSD which is well known from the time of the hippies.

After a long period characterized by prohibition, scientists now again investigate these substances as potential treatments for psychiatric disorders (Vollenweider & Preller, 2020). There are promising

findings that, in combination with psychotherapeutic counseling, these substances can help terminal patients to reduce their fear of dying or people with depression or other mood disorders (Sarris et al., 2022).

The experience of illusory states with severely altered perception does not sound like the ideal precondition to better solve cognitive tasks. That is why some consumers are experimenting with 'microdosing'. This means to take in very little amounts which do not cause illusions or other psychedelic experiences, but may perhaps improve emotional well-being or cognitive performance (Liokaftos, 2021).

Several new studies suggest, though, that the effects of this kind of consumption are rather subjective without demonstrably increasing performance (de Wit et al., 2022; Marschall et al., 2022; Petranker, Kim & Anderson, 2022; Polito & Stevenson, 2019). It thus seems that the reported benefits are rather placebo effects. But it should be noted that the samples studied so far are very small and the results thus have to be considered as preliminary.

CONCLUSION ON THE EFFECTS

The substances that have been the subject of research into brain doping/neuroenhancement to date are by no means miracle drugs. In many situations, it is likely that a similar effect can even be achieved using freely available caffeine. As part of a new meta-analysis, researchers evaluated 47 individual studies on the effects of amphetamine ('Speed'), methylphenidate (Ritalin), and modafinil (Provigil) on healthy people (Roberts et al., 2020). They concluded the following:

> 'Methylphenidate has the strongest effects on cognition of the three stimulants observed. However, the positive effects are small to moderate, and limited to recall, inhibitory control and sustained attention. […] D-amphetamine produces no improvements in cognition, and so can probably be ruled out of future investigation for safe, effective cognitive enhancement. The data with these stimulants is far from positive if we consider that effects are small and likely transient, in experiments that do not accurately reflect their actual use in the wider population.' (Roberts et al., 2020, p. 20-21)

The researchers also drew attention to the risk of side effects, especially in the case of an overdose. This can lead to agitation, headaches, sleep problems, tremors, hallucinations, paranoia, seizures, or cardiovascular problems.

Finally, a study that compared pharmacological with non-pharmacological techniques for enhancing mental performance shall be mentioned (Caviola & Faber, 2015), the latter being computer-assisted learning, sleep, and exercise. The conclusion reads:

‘We find that all of the techniques described can produce significant beneficial effects on cognitive performance. However, effect sizes are moderate, and consistently dependent on individual and situational factors as well as the cognitive domain in question. […] [W]e can conclude that pharmacological cognitive enhancement is not more effective than non-pharmacological cognitive enhancement.’ (Caviola & Faber, 2015, p. 1)

In other words, the rather modest effects that might be achieved with substances could probably also be achieved with non-pharmacological methods.

INSTRUMENTAL SUBSTANCE USE

In light of these facts, we have to ask ourselves whether talking about brain doping/neuro-enhancement is useful: it was and is not a widespread phenomenon, it is unlikely to have increased significantly in the twenty-first century, and the effectiveness of substances for mental performance enhancement is questionable (Schleim, 2020a). Misrepresentation or biases in relevant specialist publications and in the media, as well as the failure to take into account older findings from the 1960s to 1980s, also call into question the integrity of the entire debate. Which leaves us with the question: is it just a 'hype' after all?

Admittedly, for decades there has been and still is a dramatic increase in the use of psychostimulants such as amphetamine ('Speed') and methylphenidate (Ritalin). This, however, is for *medical* use, which is excluded from both the definition of brain doping/neuroenhancement and from the aforementioned studies on prevalence. Whether new disorders such as ADHD (Attention Deficit/Hyperactivity Disorder), which hardly anyone knew about a few decades ago, justify the widespread prescription of such substances is a discussion in itself (Beeker et al., 2021; Davis, 2020; Rose, 2018; Schleim 2018a, 2020b).

However, we are left with the phenomenon that humans (and arguably even some animal species) use substances to achieve certain goals. Christian Müller, Professor of Addiction Medicine at the University Hospital in Erlangen, therefore refers to 'instrumental drug use' and has identified nine purposes (Müller, 2020; Müller & Schumann, 2011), namely: (1) improving social interactions; (2) facilitating sexual behaviour; (3) improving cognitive performance or reducing fatigue; (4) improving recovery or coping with stress; (5) self-medicating mental disorders; (6) expanding consciousness; (7) experiencing a high or euphoria; (8) improving physical attractiveness; and finally (9) improving spiritual or religious experiences.

These could be narrowed down to four basic needs, namely: (1) psychological activation/enhancement; (2) psychological dampening/relaxation; (3) new experiences; and (4) body shaping. To satisfy these needs, people resort to very different methods – and some to substances such as drugs or medication.

SUBSTANCES AND VALUES

American psychiatrist Gerald Klerman (1928-1992), who was a professor at Harvard University and later director of a prominent drug prevention programme under President Jimmy Carter, suggested several useful terms for this: 'psychotropic hedonism' versus 'pharmacological Calvinism' (Klerman,

1970, 1972). The latter reflects the Protestant work ethic, which can be summarized as 'No pain, no gain'. Psychotropic hedonism, on the other hand, focuses on the now: 'Why wait when I can fulfil my needs and achieve my goals now, if necessary, by pharmacological methods?'

At the time, however, the renowned American medical ethicist Robert Veatch, now professor emeritus at Georgetown University in Washington D.C. and researcher at the Kennedy Institute of Ethics, criticized Klerman's explanation for being too simplistic (Veatch, 1977). Drawing on Max Weber's analysis of the Protestant work ethic (Weber, 1905), he concludes that substance use to increase efficiency would be permissible from a Protestant perspective. However, advocates of an ethic that is based on the 'wisdom of nature' and is critical of artificial interventions in the body would be particularly opposed to this.

Klerman's psychotropic hedonism most closely corresponds to Veatch's so-called 'Protean ethic', which is named after Proteus, the Greek god of rivers and oceanic bodies of waters, who was able to change his form. Substances are therefore used to perpetually change and to adapt to external demands. Proponents of this ethic contest the existence of a permanent essence of human beings. Today, these ideas from the 1970s resemble precursors of globalization, competitive pressure, and lifelong learning.

Klerman and Veatch did agree on one thing, however: that *social values* are articulated in the way people treat substances; values that, according to Klerman, create divisions between different social groups – the old and the young, the better and the less educated, the poor and the rich, groups with different religious or cultural backgrounds (Klerman, 1970). Here, the psychiatrist lamented that we lack a suitable word for non-medical substance use:

'In our society there is no suitable label for the use of drugs to enhance pleasure or performance. It is sometimes called social drug use, but this term is not part of our scientific lexicon. […] The fact that we don't have an established nomenclature for nontherapeutic drug use is in itself an indication of society's conflict.' (Klerman, 1970, p. 316)

DRUGS AND MEDICATION

'Instrumental substance use' could potentially fill this gap. We should remember here that the distinction between drugs and medications is based on conventions and that it changes over time (Schleim, 2018b). For example, when coca leaves were first brought to Europe in the second half of the nineteenth century, many doctors were interested in the parts of the plant that were used to make cocaine. In 1883, for example, the pharmacologist and military doctor Theodor Aschenbrandt gave soldiers 'cocaine wine' during a military manoeuvre – without their knowledge, one might add – and subsequently noticed their increased ability to cope with hunger, physical stress, and fatigue (Holmstedt & Fredga, 1981).

This inspired the young Sigmund Freud (1856-1939), who was still working as a doctor in Vienna at the time, to conduct his own cocaine experiments (Freud, 1884). However, his attempt to treat opium addiction with the new drug turned into a public disaster for him: some patients then became addicted to opium *and* cocaine, and his reputation was severely damaged. But Freud's colleague, ophthalmologist Carl Koller (1857-1944), made medical history thanks to the substance; he observed its anaesthetic effect (Bernfeld, 1953). He discovered the first local anaesthetic, which meant that once-dreaded eye operations could be performed more comfortably for patients – thanks to cocaine.

Nowadays, there are much better anaesthetics available. Throughout the course of the twentieth century, cocaine – like many other substances – was demonized and banned under a number of international treaties. This development was spearheaded by the USA with its puritanical morals and, from the 1970s onwards under the conservative president Richard Nixon, the 'war on drugs'.

Today, drug cartels earn billions from the substance, while indigenous groups in South America continue to use coca leaves in their daily lives; you might even say *instrumentally*. As Müller and other researchers note, however, only a minority of users actually become addicted (Müller, 2020; Müller & Schumann, 2011).

A SOCIAL PERSPECTIVE

Individuals who make a rigid distinction between drugs and medicines probably do so because of a value system: substance use is bad unless it alleviates a medical condition. However, this distinction exposes a double standard in our society.

On the one hand, alcohol and tobacco are used liberally and, due to the increasing diagnoses of vaguely defined mental disorders – leading epidemiologists now consider almost half of our society to be 'mentally disturbed' (Wittchen et al., 2011) – psychopharmacological drug prescriptions are becoming increasingly normal. For example, children and adolescents are prescribed amphetamine ('Speed') or methylphenidate (Ritalin) to help them perform better at school or in their studies. On the other hand, if people obtain the same drugs on their own volition, for the same reasons or to have more fun when partying, they are committing a criminal offence (Schleim, 2018b).

We should remember that contemporary 'common diseases' such as ADHD, depression, and social anxiety disorder were very rarely diagnosed just a few decades ago: depression was little known before it was redefined in the 1960s and 1970s; hardly anyone knew about social anxiety disorder before the end of the 1990s (Davis, 2020; Horwitz & Wakefield, 2007). The term 'ADHD' was first formalized in 1987, and the disorder has only been increasingly diagnosed since the 1990s (Schleim, 2018a). These days, it has become increasingly common to interpret deviations from the social norm and hardships as a biochemical problem in the brain (Beeker et al., 2021; Davis, 2020; Rose, 2018), so treating them more and more with substances is the obvious response.

The use of antidepressants and stimulants, tranquillizers, sleeping pills, and painkillers has penetrated almost all areas of society. Even people who are prescribed these drugs can become dependent on them and may have to deal with withdrawal symptoms later on (Fava et al., 2015). Combined with what we still refer to today as 'substance abuse' or simply alcohol consumption and smoking, many people rely on substances to cope with their daily lives and to achieve their goals. 'Instrumental substance use' fits the bill as an overarching term for this. It would also accommodate scientific initiatives that advocate for more common-sense and, above all, more consistent drug policies (e.g. Nutt et al. 2010; van Amsterdam et al., 2010; 2021).

Any talk of 'brain doping' or 'neuroenhancement' then does not seem to have added value. Neither did the phenomenon emerge in the early 2000s, as proponents of 'neuroethics' often claim, and nor are the drugs 'intelligence pills' or 'smart drugs'. Consistent with research findings on people's reasons for using these substances, they instead seem to serve as pills for motivation and perseverance (Faraone et al., 2020; Quednow, 2010b; Vrecko, 2013). If we want to explore the social causes underlying these trends, we need to focus more on the success, performance, and optimization mindset of our time.

FREQUENTLY ASKED QUESTIONS

At what point does neuroenhancement actually begin? Isn't eating chocolate or drinking coffee then also classed as enhancement?

Why does it matter? First of all, I would argue that it is more appropriate to use the term 'instrumental substance use' rather than 'brain doping' or 'neuroenhancement'. If we use Professor Müller's nine categories, or even the four needs I have identified, a lot actually falls under instrumental consumption.

But I see this as an advantage: the distinction is then no longer one of principle, but one of fluidity. Since many people (and probably even some animals) use substances instrumentally, we avoid stigmatizing or even criminalizing ordinary behaviour.

If you are nevertheless concerned that you may be engaging in brain doping/neuroenhancement or instrumental consumption yourself, then you can perhaps ask yourself which of your values are responsible for this. For example, how do you feel about the values described by professors Klerman or Veatch? What are your convictions based on?

So, instrumental substance use isn't an ethical problem at all?

In liberal democracies, we have agreed (among other things) on two fundamental points: Firstly, anything that is not explicitly forbidden is permitted, and secondly, one's own freedom ends where the freedom of others begins.

At the same time, however, there is an obvious risk of peer pressure and social conformity: if, for example, so many of your competitors in your field use stimulants such as amphetamines ('Speed') that you are also required to do so yourself, this presents a problem. Not only do you run the risk of experiencing side effects and becoming addicted, but you are also breaking the law (unless you can find a doctor who will prescribe this or similar drugs). Some people (myself included) might also experience this as an invasion of their personal integrity.

I believe that it is primarily the responsibility of political parties, trade unions, and occupational medicine and social medicine to ensure healthy learning and working conditions that help to limit the pressure to perform. During a previous amphetamine epidemic in the USA, long-distance hauliers, for example, were under a lot of pressure to drive longer and longer distances every day

and to suppress fatigue with stimulants (Rasmussen, 2008). In the long run, that was probably detrimental to both the long-distance hauliers and to road safety.

There are many reasons as to why burn-out is such a hot topic today and why more and more people are taking early retirement due to psychological problems. Psychological and sociological studies play a key role here (e.g. Neckel & Wagner, 2013) as they provide a basis for maintaining or, where necessary, re-establishing a healthy working and living environment. No one should be forced or even compelled to use substances instrumentally in order to live their life.

What are the implications of your views on drug policy? Do you think all drugs should be legalized?

I was and still am rather reluctant to use substances myself: I see them – including medication – as a last resort when nothing else helps. I have also witnessed among my circle of friends and acquaintances that certain substances (especially alcohol and tobacco) can be harmful to people. Scientists have been calling for a more rational and consistent drug policy for many years (e.g. Nutt et al. 2010; van Amsterdam et al., 2010; 2021).

Drug policy is deeply rooted in traditions and prejudices. The conservative movement has also often used a ban on substances to oppress marginalized groups: in the past, people didn't want Afro-Americans, hippies, or labour migrants from China and South America ('Hispanics') in their country, or more specifically, they rejected their value systems. So, substances that were popular with these groups (such as hashish, opium, and LSD) were criminalized. With the USA at the helm, many countries adopted a policy of prohibition in the twentieth century.

This approach becomes particularly perfidious when it comes to the oppression of the poor: they may turn to prohibited substances so that they can better cope with the experience of social exclusion. If they are subsequently caught by the police, they are threatened with harsh punishments that plunge them even deeper into hardship. This turns in to a vicious cycle. Mainstream society quickly labels them as 'antisocial', 'junkies', etc., and further marginalizes them, even though they are often not responsible for their disadvantaged starting position.

As recently as the nineteenth century, nation states were the biggest 'drug dealers' around – just think, for example, of the opium wars waged by the colonial powers Britain and France against China. Contemporary drug policies are full of contradictions. I don't think radical legalization would solve all the problems, but a more liberal approach would probably alleviate a lot of unnecessary suffering and help to cut down on crime.

Let's not forget that bans and punishments are the sharpest sword of the rule of law. But the constitutional principle of proportionality dictates that the least severe effective means be chosen.

What advice would you give to anyone interested in brain doping/neuroenhancement?

I hope that my analysis has made it clear that you should not expect miracles from these substances. In my opinion, one key criterion is whether instrumental substance use is a way of overcoming a brief period of stress or a lack of motivation or desire, or whether the use is permanent.

In the latter case, I would consider whether your current situation is right for you: is your degree or job really right for you if you are only able to endure it using substances? If it is more about getting by in your day-to-day life more generally, you should consider seeing a coach, psychotherapist, or psychiatrist.

Some people (myself included) think that you have to solve everything on your own. This can, of course, point to a high degree of self-reliance, but if you are trying to solve a current problem, you should also look for other effective methods. And in the process, other people – even your friends or family – may point you towards alternatives that you would not discover as quickly or consider as readily on your own.

Would your opinion change if more effective drugs were available?

People use substances to achieve certain goals. The ethics of the 'wisdom of nature' that I mentioned above initially seems to reject unnatural interventions. But what is 'natural' these days? And what about naturally occurring substances? Or therapeutic interventions to treat a disease?

I think it is difficult to develop a principled counter-argument that applies to everyone (while I might pour myself a glass of wine to help me relax). For me, the important thing is *who* defines the goals. We live in a meritocracy, a competitive society. Many, many people feel under pressure to constantly improve. Some perhaps internalize this pressure so much that they no longer realize that it is being imposed on them by society.

However, I see two fundamental objections to using substances as a way of improving performance, even if they do not have any side effects (which is a very unrealistic assumption). I have written about this before (Schleim, 2011). Firstly, if we hone in on the level of performance, we are faced with the question: if we are unhappy with a 100% performance level, why should we suddenly be satisfied with a 110% performance level? Will we then not want to increase that by another 10%?

Secondly, we do not make this decision in isolation, but in competition with others. Following the principle of continuous improvement, these people would naturally also use substances to achieve their goals. In this case, either many people use the drugs and thereby lose their individual advantage – or other people are prevented from doing so, for example through high prices, thereby reducing equal opportunities.

The first idea demonstrates that brain doping/neuroenhancement is unlikely to make you happier. This, incidentally, is also a hallmark of the Protestant work ethic and capitalism; that the level

reached is never enough (Weber, 1905). The second idea suggests that it either amounts to a zero-sum game or even results in a more unjust world.

The point sometimes raised to counter the zero-sum-game argument is that while this would apply on an individual level relative to others, humanity as a whole would attain a higher level. This is a very idealistic argument and overlooks the fact that we are becoming smarter and more efficient even without substances – and yet (or precisely because of this), we are consuming more and more resources and increasingly doing more damage to the environment.

Many problems are human-made and their underlying causes could just as easily be eliminated by humans. It is completely implausible to think that new pills or brain stimulation would suddenly change this, given the technological developments of the last few centuries. In my opinion, self-reflection, ethical conduct, and ethical institutions are the only way out of the dilemma.

But you cannot force people to do this. Instead, I try to convince them with arguments. These are my tools as a philosopher and scientist.

Who actually practises neuroenhancement/brain doping?

As I explained above, the studies on prevalence interpret the phenomenon under investigation very differently. However, as far as non-medical stimulant use is concerned, most individuals are male, aged between 18 and 25 years old, and are more likely to have poor grades and to have had traumatic childhood experiences and also to consume alcohol and other drugs (Faraone et al., 2020).

What do you think would be the worst-case scenario regarding neuroenhancement/brain doping?

Suppose the trend were to become widespread: more and more people would consume more and more substances to increase their mental performance. This would put increased pressure on other people to do the same. Following a brief period in which the forerunners of brain doping would have a head start, everyone's performance would probably level off again. So, essentially, you would end up with more or less the same situation, except that a huge number of people would now spend time and money on brain doping and accept the health risks that go along with it.

The forerunners would then probably turn to newer, less tested, and riskier substances; after all, they wanted to pull away from the others. And the game would start all over again. It would end up being a kind of 'arms race'. Let's not forget that this has already happened in the world of sport – and people have even died as a result of doping because they took even greater risks to win. So, in the end, neuroenhancement/brain doping would actually leave humanity in a worse state than if it had not happened at all.

Neuroenhancement is not explicitly prohibited. Why should it then be regarded as cheating or doping?

This is actually the argument put forward by several leading researchers in the field of 'neuroethics' (e.g. Greely et al., 2008; Schermer, 2008). But, as I see it, they are overlooking the fact that most of the substances discussed here are already banned – in other words, there are already legal regulations in place regarding the purchase of many stimulants and other drugs. For example, you can only buy amphetamine or methylphenidate if you have a doctor's prescription.

No one would ever think that you can murder your fellow students at university simply because it is not *expressly* prohibited there. You do not need to prohibit murders at universities, because prohibition under criminal law already applies to society as a whole. A key trait of criminal law is its universal binding nature; unlike house rules, it does not just apply when you enter a particular establishment.

Of course, this does not prevent an ethical discussion of prohibition and its consequences. But then we are entering the realm of drug policy, and in my opinion, many neuroethicists have so far overlooked this.

That being said, universities and other schools and colleges are free to set their own house rules. In fact, Duke University in Durham, North Carolina, USA, has incorporated a regulation to this effect into its catalogue for academic misconduct: the unauthorized use of prescription drugs to enhance academic performance is explicitly regarded as cheating.

However, we should also broach the conflicting situation that educational institutions find themselves in here: on the one hand, educational institutions are supposed to make people more educated and more intelligent, and even to improve their intellectual performance. On top of that, students are under pressure to compete through selection procedures and in terms of grades. On the other hand, however, not all methods of achieving these goals or dealing with pressure should be legitimized. These distinctions must be soundly justified in a liberal country.

Under what circumstances would you resort to neuroenhancement/brain doping?

From what we know today, I cannot imagine any circumstances under which I would do it. As I see it, our society (and the nature that is suffering under it) does not need increasingly higher levels of performance, but more contemplation and relaxation. That's actually the main reason why I became a yoga teacher.

Speaking of nature... The debates tend to revolve around us humans, but the mass consumption of stimulants and other substances also affects the environment. Not only do the substances have to be produced, but they also eventually end up in the environment after passing through our bodies.

Chemists at Poznan University of Technology in Poland have already documented how methylphenidate, modafinil, and other substances can end up in sewage and harm animals and plants (Wilms et al., 2019). Our sewage treatment plants are said to be ill-equipped to handle this kind of purification.

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PHARMACOLOGICAL ENHANCEMENT

THE FACTS AND MYTHS ABOUT BRAIN DOPING

These days, everyone is talking about brain doping, or neuroenhancement. But is there really widespread consumption among professionals and students of substances that allegedly improve mental performance? This report presents a summary of the fundamental findings from sixty years of research. It provides scientifically substantiated answers to key questions such as: How widespread is the phenomenon? Is it a new trend or has it always existed? What are the substances in question and how do they work? What are the salient ethical questions and which values underpin them?

Dr Stephan Schleim is an Associate Professor of Theoretical Psychology at the University of Groningen in the Netherlands. He has been researching the topic since 2005 and has published many articles on it. He has also been interviewed on the subject many times in the media. At the end of this report, Schleim answers the main questions that people from various disciplines have asked him about brain doping and neuroenhancement over the last 15 years.