



Key messages

- ▶ OTC products such as energy drinks or dextrose are the preparations most commonly used with the aim of boosting mental performance.
- ▶ About 1.8% of women and 1.3% of men take medicines or illegal substances that can be used to enhance mental performance.
- ▶ These agents are used mainly by 18- to 44-year-old women and men.
- ▶ A long working week increases people's risk of using medicines or illegal substances to enhance their mental performance.

Pharmacological Neuroenhancement

The consumption of substances that affect a person's waking state and mental performance is not a new social phenomenon. Since time immemorial, people have tried to improve not only their physical performance but also their mental capacity by using drugs, substances or preparations. The consumption of coffee and alcohol, to name just two examples, has always been widespread and largely accepted by society. However, the development of psychostimulants – such as amphetamines in the 1930s, antidepressants in the 1950s, or modafinil and anti-dementia agents in the 1990s (Franke, Lieb 2010) – opened up new ways of influencing mental performance.

Substances that can be used to boost mental performance are known as neuroenhancers. When healthy people use neuroenhancers, they usually have one of two aims in view: either to boost such intellectual skills as learning, memory, mental attentiveness and vigilance (alertness), or to improve functional social skills by improving their mood, avoiding stress and nervousness, and reducing social anxiety (Norman et al. 2010).

However, most drugs that can be used for neuroenhancement only have a limited benefit. Some agents only make people more alert and improve their concentration and attentiveness for a short time – if at all – and do not seem to directly improve a person's memory. In particular, anti-depressants and anti-dementia agents do not have any verifiable effect on healthy people. Apart from which, there is a risk of undesirable side effects, for example mental disorders and addictions (Franke, Lieb 2010). Apart from the possible side effects, the abuse of prescription drugs also raises legal issues.

Since the results of a study commissioned by the science magazine *Nature* were published in 2008, the use of neuroenhancers has been the subject of much discussion in the international scientific community and especially in the media. In this study, 1,400 readers were interviewed on the subject of brain doping (see box). About 20% of the respondents from 60 countries stated that they had taken drugs to enhance their concentration and memory without medical reasons; 62% had taken methylphenidate, 44% modafinil and 15% beta blockers (Maher 2008).

In Germany, the 2009 Health Report of the Deutsche Angestellten Krankenkasse (DAK, a health insurance fund) took up the theme of »doping at the workplace« and conducted both a survey of experts and an online survey of 3,000 people insured by the DAK. The experts suspected »that drug use seems to be a socially accepted form of behaviour in everyday life and at work for coping with pain, discomfort, work pressure, stress, etc.« (DAK 2009, page 84). The evaluation of the online survey, however, showed that about 5% of people in regular employment between the ages of 20 and 50 took brain-doping agents without medical necessity.

Definition pharmacological neuroenhancement

The use of psychoactive substances of all kinds to boost mental or cognitive performance is subsumed under the term pharmacological neuroenhancement.

The term brain doping is also frequently used in this context. According to a definition given by Franke and Lieb (2010), this term relates to doping in sport and refers exclusively to the improper use of psychoactive substances and preparations that are either subject to prescription or illegal. They include psycho- and neurotropic drugs that have been approved for treating dementia, attention-deficit or sleep disorders and depression, as well as beta blockers and synthetic chemical stimulants such as amphetamine (Franke, Lieb 2010).

The DAK study focused exclusively on prescription psychostimulants (methylphenidate, modafinil), agents against dementia (e.g. donepezil) and depression (e.g. fluoxetine), and beta blockers. Other studies, by contrast, do not restrict themselves to the use of prescription neuroenhancement drugs, but also include over-the-counter (OTC) substances, such as ginkgo biloba, and illegal psychostimulants such as amphetamines, cocaine and ecstasy (Teter et al. 2006. Maher 2008; Franke et al. 2009).

Study on the consumption of performance-enhancing substances (KOLIBRI)

A Germany-wide survey of 6,142 people was conducted in 2010 on the consumption of performance-enhancing substances in everyday life and leisure time as part of the Robert Koch Institute's KOLIBRI study. It covered the use of prescription and illegal substances (e.g. amphetamines), as well as OTC products, by the general population over 18 years. These data enable representative conclusions to be drawn on the use of substances for pharmacological neuroenhancement by the adult population in Germany. The analysis is based on the use of such agents – not to treat an illness – at least once during the last twelve months. The choice of neuroenhancement agents is modelled on those chosen in the DAK study and include prescription psychostimulants (methylphenidate, modafinil), anti-dementia and anti-depression agents, and beta blockers. Both fluoxetine and St. John's wort were listed as examples in the same response category in the group of antidepressants. Fluoxetine, and some preparations containing St. John's wort used to treat mild or moderate depression, require a prescription; however, most St. John's wort products are available without a prescription. Illegal substances, such as amphetamines, were also taken into account.

The above set of preparations is referred to in the following as »medicines or illegal substances for neuroenhancement«.

Use is not widespread

In the KOLIBRI study a total of 74 respondents said they had used medicines or illegal substances for neuroenhancement at least once during the last twelve months. This corresponded to a 12-month prevalence among adults in Germany of 1.5 %. The prevalence rates for men and women were approximately at the same level (Table 1).

The use of antidepressants without medical necessity was reported most often by both women and men. The second most frequently consumed substances were synthetic chemical stimulants such as amphetamines. Beta blockers were used by only 0.1 % (n=6) without medical necessity. Antidepressants were more likely to be used by women. The use of methylphenidate or anti-dementia agents was measured in tenths of a percent among women. Only one respondent reported using each type. Modafinil was not used by any participant without medical necessity.

Preparations are used mainly by younger people

The percentage of women and men who use medicines or illegal substances for neuroenhancement tends to fall as they grow older (Figure 1). Just under 3 % of women and men between the ages of 18 and 44 used such substances without medical necessity, compared to only 0.7 % of women and men over 45. Women between the ages of 30 and 44 used medicines or illegal substances for neuroenhancement most frequently: 3.7 %. Among men, the use of these products was most widespread in the 18-to-29 age group; the figure here was 3.3 %.

Odds ratios (OR) with corresponding 95 % confidence intervals (CI) were calculated as a measure of the correlation between people's age and their use of medicines or illegal substances for neuroenhancement. According to this measure, the risk of younger adults (aged 18 to 44) using these agents without medical necessity was more

Study on the consumption of performance-enhancing substances in everyday life and leisure time (KOLIBRI)

<i>Data holder:</i>	Robert Koch Institute
<i>Objectives:</i>	To provide data on the prevalence of the use of performance-enhancing substances in the general population
<i>Survey method:</i>	Population-based, written, postal survey
<i>Population:</i>	Residential population of Germany aged 18 and over
<i>Sample:</i>	6,142 women and men who agreed in the GEDA 2009 and 2010 surveys to take part in a further survey
<i>Response rate:</i>	62.2 %
<i>Survey period:</i>	March to July 2010

Table 1
Use of medicines without medical necessity and illegal substances for neuroenhancement during the last 12 months
 Data basis: KOLIBRI 2010

	Women		Men		Total	
	%	(95% CI)	%	(95% CI)	%	(95% CI)
Beta blockers	0.1	(0.0–0.2)	0.0	(0.0–0.1)	0.1	(0.0–0.1)
Synthetic chemical stimulants	0.5	(0.2–1.3)	0.5	(0.2–1.1)	0.5	(0.3–1.0)
Methylphenidate	0.0	(0.0–0.2)	n. a.	n. a.	0.0	(0.0–0.1)
Anti-dementia agents	0.0	(0.0–0.1)	n. a.	n. a.	0.0	(0.0–0.1)
Antidepressants	1.2	(0.7–2.0)	0.7	(0.4–1.3)	1.0	(0.7–1.4)
Modafinil	n. a.	n. a.	n. a.	n. a.	n. a.	n. a.
Total	1.8	(1.2–2.8)	1.3	(0.8–2.0)	1.5	(1.1–2.1)

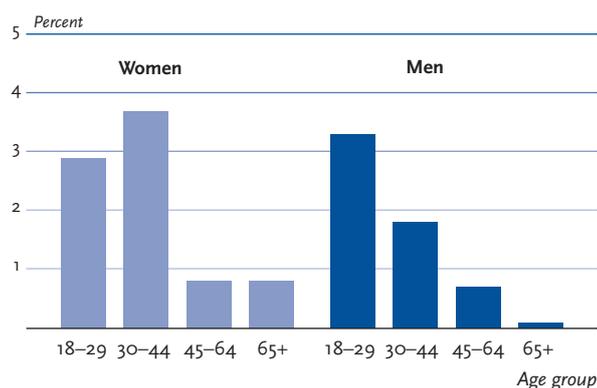
n. a. = no answer

than four times higher than those aged 45 and over (OR 4.3; 95% CI 2.2 to 9.1). This was observed in both women (OR 4.2; 95% CI 1.6 to 11.3) and men (OR 5.1; 95% CI 2.0 to 12.9). Statistical control of the influence of age did not reveal any significant influence of educational attainment on the use of medicines or illegal substances for neuroenhancement either in women or in men.

A long working week increases the risk of using neuroenhancement

The data of the KOLIBRI study show that the use of medicines or illegal substances that can be used to improve cognitive or social skills is related to employment (Figure 2). About 2.6% of men who worked more than 40 hours a week used medicines or illegal substances for neuroenhancement without medical necessity. By contrast, the figure was 0.7% among men who were not employed or worked less than 40 hours.

Figure 1
Use of medicines or illegal substances for neuroenhancement in the last 12 months, by age and gender
 Data basis: KOLIBRI 2010



In women, the difference between the employment groups regarding the use of medicines or illegal substances for neuroenhancement was lower overall. Approximately 3.1% of women with a working week of more than 40 hours used medicines or illegal neuroenhancers. The figure was 1.7% among women who were not employed or worked less than 20 hours.

Statistical confirmation of the results using logistic regression analyses shows, when controlling for the influence of age, that the differences according to weekly employment are only statistically significant among men. According to this, the risk of men with a working week of more than 40 hours using preparations to enhance their mental and social skills (OR 3.0; 95% CI 1.2 to 7.7) is three times that of men of the same age who are not employed or work less than 40 hours.

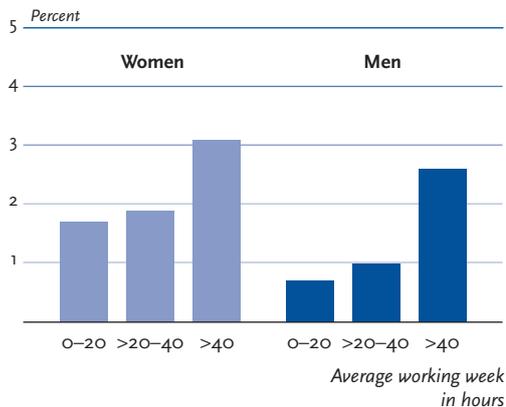
OTC products are most commonly used

In addition to medicines and illegal substances, KOLIBRI also covered OTC (over-the-counter) products that can be used for neuroenhancement (e.g. energy drinks). Respondents were summarily asked about possible motivations for using all of these substances if they reported using at least one of them without medical necessity. In addition to physically oriented motives, one option was »to improve or enhance mental performance (e.g. concentration)«.

Overall, 16.9% of the men and 12.8% of the women used substances with the aim of enhancing their mental performance. This meant that men used such substances significantly more frequently than women with this aim in view.

However, the majority of people who gave this motive were using OTC products like dextrose, energy drinks or isotonic drinks. Medicines such as antidepressants, anti-dementia agents, modafinil, methylphenidate and beta blockers, or illegal substances such as synthetic chemical

Figure 2
Use of medicines or illegal substances for neuroenhancement, by length of working week and by gender
 Data basis: KOLIBRI 2010



stimulants, were only used by a very small number of women and men with this motivation (Figure 3). Antidepressants accounted for the largest share here.

Better mental performance is a motive, especially among younger people

The motivation for using substances to improve or enhance their mental performance was markedly more pronounced in young adults between 18 and 29 than in the older age groups. Approximately 42.8 % of consuming men and 37.4 % of the women between 18 and 29 stated this motivation, compared to less than 10 % in the 45-to-64 age group and less than 5 % among the over-65s (Figure 4).

Discussion

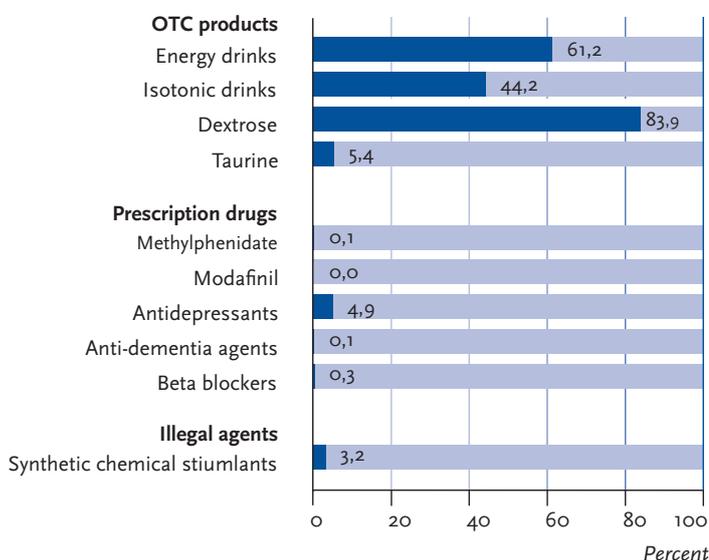
No population-level data on pharmacological neuroenhancement have been available up to now, but these have now been presented with the KOLIBRI study (please go to: www.rki.de for a report [in German]). The results of the KOLIBRI study show that pharmacological neuroenhancement with medicines or illegal substances is not widespread in Germany's adult general population. About 1.8 % of women and 1.3 % of men used drugs without medical necessity or illegal substances for neuroenhancement. There was nevertheless a willingness among young adults to increase their mental performance by consuming substances. However, it was primarily OTC products that were used to enhance mental performance.

To date, information on the use of prescription or illegal psychostimulants – such as methylphenidate, amphetamines, cocaine or ecstasy – for neuroenhancement in Germany is only available relating to students of senior secondary schools and vocational schools in small towns and large cities, as well as for university students of medicine, pharmacy and economics (Franke et al. 2009; Middendorf et al. 2012).

The study's findings on school and university students on the use of prescription and illegal psychostimulants show that 1.5 % of school students and 0.8 % of university students have ever used prescription psychostimulants (methylphenidate) (Franke et al. 2009). The lifetime prevalences of illegal neuroenhancers (amphetamines, cocaine, ecstasy) – 2.4 % for school students and 2.9 % for university students – are higher than those for the use of prescription neuroenhancers.

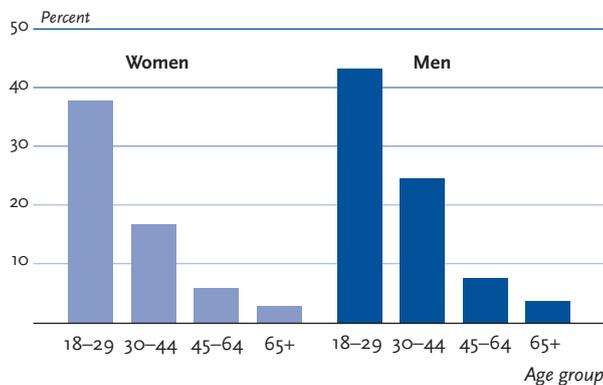
In addition, an online survey on »academic brain doping« conducted among 8,000 students by the HIS-

Figure 3
Use of performance-enhancing substances by people who said their motivation was »to improve or enhance mental performance«, by product group
 Databasis: KOLIBRI 2010



Institute for Research on Higher Education in December 2010 showed that 5 % of the respondents resorted to prescription drugs or illegal substances to enable them to cope with their studies better. 18 % of these took methylphenidate, 12 % beta blockers, 9 % amphetamines and 4 % modafinil. In addition to the psycho- and neuropharmaceuticals included in KOLIBRI, the HIS study also included the consumption of painkillers, barbiturates and sedatives, as well as cannabis, cocaine and MDMA (ecstasy's active ingredient) in the analysis. While just under half used such agents »very rarely«, 17 % did so »frequently« and a further 36 % »now and then« (Middendorf et al. 2012).

Figure 4
Percentage of people who consumed in the last 12 months and said their motivation was »to improve or enhance mental performance (e.g. concentration)«, by age and gender
 Data basis: KOLIBRI 2010



In the online survey conducted as part of the DAK's 2009 Health Report (DAK 2009), in which about 3,000 people in regular employment aged between 20 and 50 were interviewed, 17 % of the respondents reported that they had taken medicines to improve their mental performance or psychological well-being; 5 % of the respondents used these drugs without medical necessity. 2 % used neuro- or psychotropic drugs frequently and/or regularly without a doctor's prescription.

Although a certain amount of information on the use of medicines or illegal drugs for pharmacological neuroenhancement can be obtained by from secondary analyses of data from the 2009 Drug Report of the GEK (Gmündener Ersatzkasse, a health insurance fund) (Glaeske, Schick-tanz 2010), the 2009 Epidemiological Survey on Addiction (Kraus et al. 2010a) and the 1998 Federal Health Survey on drug use (RKI 2003), this information sheds little light on the distribution of a set of agents for neuroenhancement that contain both components. Moreover, the reported prevalences were based on different periods. A comparison of the 12-month prevalences for the use of amphetamines or antidepressants in the KOLIBRI study with the results of the 2009 Epidemiological Survey on

Addiction shows a high degree of correlation. The latter reported a prevalence of 0.8 % for the use of amphetamines in the last twelve months among 18- to 59-year-olds and of 4.5 % for antidepressants in the 18-to-64 age group (Kraus et al. 2010a; 2010b). The directly comparable prevalences for amphetamines in KOLIBRI – i. e. irrespective of whether they were used to treat one or more diseases – are 0.9 % for 18- to 59-year-olds and 3 % for antidepressants among 18- to 64-year-olds. Differences between women and men as regards frequency of use are similar for all compared substances. It should be noted that the level of frequencies determined essentially depends on the composition of the set of agents for neuroenhancement or the population group studied.

Nevertheless, the above-mentioned studies show similar prevalences of neuroenhancement or brain doping in the populations examined. However, there is a suspicion that, in the case of survey studies on the use of illegal substances or prescription drugs without medical necessity, social desirability plays a major role and influences the answers to the questions. As a result, it can be assumed that the reported prevalences underestimate the true extent of the use of brain-doping substances.

In the light of the study data described here, there is currently no scientific evidence to suggest that a large number of people in Germany practise brain doping. Summing up, the authors of the 2009 DAK Health Report say that, taken as a whole, the survey results do not support »the assumption that doping at the workplace or enhancement by active employees is (already) a widespread phenomenon. Rather, there is a growing impression that a distorted picture is being presented to the public« (DAK 2009, p.60).

The conclusion that the use of prescription psycho- and neuropharmaceuticals without medical necessity is not widespread in the population is corroborated by the results of the KOLIBRI study, although the latter indicate that, despite the low prevalences for the use of brain-doping agents, there is definitely a willingness among parts of the adult population to resort to performance-enhancing substances to improve mental performance.

In general, however, prescription or illegal substances are not used, but primarily OTC and therefore easily accessible products. However, the risks associated with the frequent use of these agents have hardly been studied up to now. In light of the findings presented, it seems advisable to address the indiscriminate use of pharmacological neuroenhancers, to educate people about the consequences of using these substances, and to encourage health-related behaviour that enables people to live without consuming such agents.

Furthermore, the results of the KOLIBRI study and other studies refer to the connection between neuroenhancement and (psychosocial) workloads. However, the data provide no information on whether such substances really are used to compensate for such stress, or, if so,

which occupations are affected. Further research is therefore needed before any reliable conclusions can be drawn on the connection between pharmacological neuroenhancement and workloads.

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