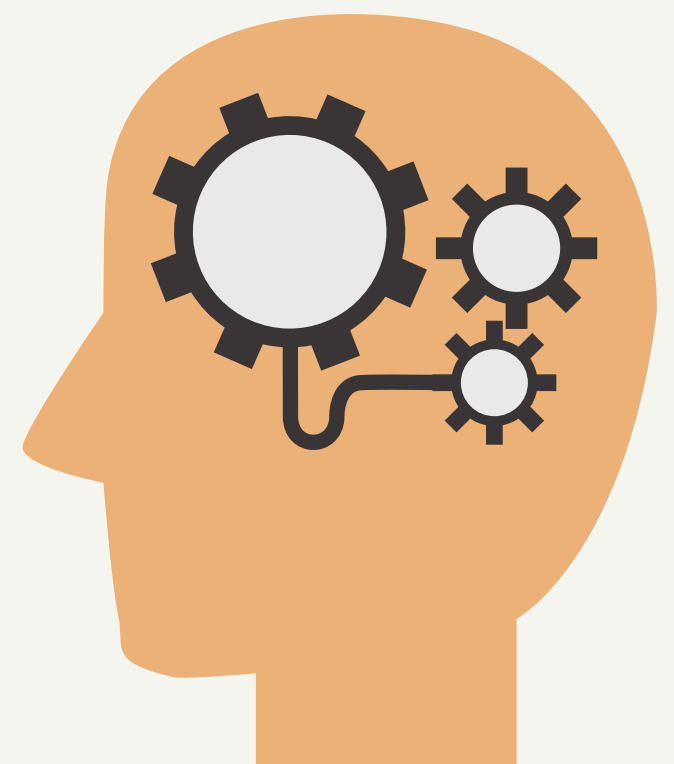




# SMARTER THAN THE REST?

# Brain Doping

Humans have always desired to improve their physical and cognitive abilities (such as attention, attentiveness, and memory). The use of legal or nonprescription psychoactive chemicals by healthy persons with the goal of cognitive enhancement is referred to as pharmacological neuroenhancement. **Caffeine**, for example, is used as a natural stimulant all over the world.



However, brain doping refers to the use of illegal substances or prescription medications that have not been approved for the aim of cognitive improvement. Only amphetamines, methylphenidate, and modafinil have substantial impacts on attentiveness, concentration, and alertness, but anti-dementia medicines and anti-depressants failed to show cognitive enhancement in healthy volunteers.

According to numerous research conducted on the American continent, the prevalence rate of **NMUPS** in university students ranges from **8.1 %** (Midwestern University in the United States) to **27.6 %** (Midwestern University in the United States) (Puerto Rico).

In surveys of young adult and adolescent populations in North America, the prevalence of NMUPS (Methylphenidate and Amphetamines) ranged from **5% to 35%**, with **25.6 %** and **8.3 %** in college students in a university in the Pacific Northwest and a university in the Midwest, respectively. Similar findings were found in other studies conducted across the United States. NMUPS is found in **0.78 %** of German university students and **6.2 %** of European university students (in Switzerland).





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## Methylphenidate and amphetamines

Methylphenidate (MPH), a substance from the group of phenylethylamines, is approved as a component of a multimodal treatment concept for **ADHD**. Doses of the same order of magnitude are used for brain doping as for the treatment of ADHD. The substance was synthesized in 1944; the (trade) name Ritalin derives from the name of the developer's wife, who was amazed at the increase in performance in tennis after taking MPH. The substance has a stimulating and exciting effect (psychoanaleptic), suppresses tiredness and inhibitions and increases physical performance in the short term.

The central mechanism of action is an increase in catecholamine release, v. a. of dopamine, by inhibiting reuptake from the synaptic cleft. Recent work also describes a modulation of attention-relevant neural networks. In healthy people, there is an increase in vigilance and attention as well as a decrease in reaction time, especially when tired. Mood, memory and subjective self-assessment are not clearly affected in the approved dosage, but higher doses have a euphoric effect.

The spectrum of side effects is wide and includes **loss of appetite, sleep disturbances, restlessness, headache, rash, dizziness, nausea, hypertension, tachycardia, abdominal pain, weight loss, tics and dyskinesia**. Difficulty concentrating, somnolence and dysphoria can also occur; there is also a risk of triggering psychoses.

Given the side effects on the cardiovascular system, reports of an association between stimulant use and an increased risk of sudden cardiac death are not surprising, although this risk has not been unanimously confirmed. Basically, it should be noted that stimulants have a potential for dependency. A significantly increased coincidence of ADHD and addictions could be shown. Amphetamines are not approved as medicinal products in German-speaking countries; consumption is therefore always illegal.





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## Modafinil



Modafinil is approved for the treatment of narcolepsy associated with excessive daytime sleepiness with and without cataplexy. A direct inhibition of central dopamine and noradrenaline uptake transporters is assumed to be the mechanism of action, resulting in an increase in catecholamine levels. Secondly, there is also an increase in the levels of serotonin, histamine, glutamate and orexin, while the levels of  $\gamma$ -aminobutyric acid (GABA) are reduced. Modafinil is subjectively mostly well tolerated and can reduce fatigue; cognitive performance and mood are raised. An increase in vigilance, a decrease in reaction time and an improvement in attention and executive functions are to be objectified.

The effects are more pronounced when you are tired. Undesirable effects include **nervousness, headache, palpitations, tremor, restlessness, dizziness, trouble sleeping, lightheadedness and dry mouth**. Nausea, vomiting and diarrhea have also been reported. Rarely, severe skin reactions and neuropsychiatric disorders such as suicidal ideation and mania occur.



Comparative neuropsychological studies with modafinil, dextroamphetamine and caffeine in healthy young adults suggest that there are no significant differences in the effects on attention and vigilance between the substances.

# SMARTER THAN THE REST?

# Brain Doping

## Anti-dementia and nootropics

It seems obvious to use 2nd generation cholinesterase inhibitors (ChEH) (donepezil, galantamine, rivastigmine), which are approved symptomatically for mild and moderate Alzheimer's dementia, also to increase cerebral performance in healthy individuals. The basis for this approach is an acetylcholine deficiency that has been demonstrated in Alzheimer's disease, particularly in the basal forebrain. Clinically, there is an improvement in attention and memory. Studies on healthy people are available for donepezil, galantamine and rivastigmine. The results are disappointing as no effect could be observed; in some older subjects, there was even a deterioration in memory function. This is consistent with study results showing that in mild cognitive impairment (MCI), ChEH have no impact on cognitive performance and progression. Only one study was able to show an immediate improvement in cognitive functions after taking donepezil, with a connection to peak plasma levels being noticeable. Side effects described include nausea, diarrhea, loss of appetite, hallucinations, agitation, tremor and urinary incontinence.

Under the designation nootropics, numerous preparations are used to maintain or increase brain performance, which in current terminology can be subsumed under the term "neuroenhancement". Various biological mechanisms of action have been described. The target parameter is usually the improvement of blood circulation. An increase in oxygen and glucose utilization is also cited, as is the influence on various neurotransmitters. Many of these substances are still approved today for the indication "improvement of cerebral performance", although there is a lack of robust data on clinical efficacy.

Pleiotropic effects have also been demonstrated in animal models for the neuropeptide cerebrolysin, which has been approved for various diseases (stroke, craniocerebral trauma, dementia) for many years: This preparation has an antioxidant, anti-inflammatory effect, reduces the activation of microglia and their deposition of  $\beta$ -amyloid as well as the rate of apoptosis; in addition, a positive influence on synaptophysin and an increase in neuroplasticity have been demonstrated. While studies have shown beneficial effects on the course of cognitive disorders and in neurorehabilitation, no data are available for healthy people.



### Sources:

Franke AG, Lieb K. Pharmakologisches Neuroenhancement und "Hirndoping" : Chancen und Risiken [Pharmacological neuroenhancement and brain doping : Chances and risks]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2010 Aug;53(8):853-9. German. doi: 10.1007/s00103-010-1105-0. PMID: 20700786.  
Iglseder B. Doping für das Gehirn [Doping for the brain]. Z Gerontol Geriatr. 2018 Feb;51(2):143-148. German. doi: 10.1007/s00391-017-1351-y. Epub 2017 Dec 5. PMID: 29209802.  
Majori S, Gazzani D, Pilati S, et al. Brain doping: stimulants use and misuse among a sample of Italian college students. J Prev Med Hyg. 2017;58(2):E130-E140.