Enhancing the mind: A neuroethical perspective on diverse brain enhancement techniques

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Abstract. Advances in medical science have expanded our ability to manipulate health, extending beyond treating diseases to enhancing cognitive and emotional functions. This practice, known as cosmetic neurology, involves using neurologic interventions and psychotropic drugs to improve brain performance, resilience to stress, and overall mental well-being, even in healthy individuals. While these interventions raise critical ethical concerns—such as issues of authenticity, beneficence, non-maleficence, and justice—emerging evidence suggests promising alternatives. Non-invasive brain enhancement techniques and experimental biohacking practices, including lifestyle adjustments and technological interventions, offer innovative pathways for cognitive enhancement. However, ethical investigations into these alternatives remain limited. This paper provides a comprehensive neuroethical analysis of invasive and non-invasive enhancement methods, emphasizing the relative advantages of non-drug-based approaches. It argues that non-invasive techniques present a less ethically fraught and more sustainable alternative to psychotropic drugs, positioning them as viable solutions for advancing the field of brain enhancement.

Key words: brain enhancement, cosmetic neurology, neuroethics, psychotropic drugs, non-invasive techniques, cognitive enhancement, neurohacking, justice in healthcare, mental performance optimization, neurologic interventions

Introduction

From the moment we became increasingly aware of our capability to treat diseases and lessen their symptoms, we found ourselves able to manipulate health. The term cosmetic neurology refers to the use of neurologic interventions and psychotropic drugs to enhance our brain's performance, resilience to stress and trauma and simply to become better, even if we are healthy individuals (1). The investigation of these practices and their implications is utterly important, especially if we take into account various perspectives such as cognition, mood, and feelings, but also considering the ethical issues of Authenticity, beneficence and Non-maleficence, and Justice. However, there is significant evidence guiding us towards the idea that, even though cosmetic neurology can be considered problematic, there can be, sooner than later, a concrete and plausible alternative to it (2), represented by non-invasive and not related to drugs brain enhancement techniques. Unfortunately, little research has been carried out concerning the ethical investigation of these techniques. Another alternative that is worth looking at is surely Neurohacking, which is a broad and experimental practice involving the application of DIY (do-it-yourself) biology techniques, including diet and lifestyle changes, and technological interventions to optimize physical and mental performance (3). This paper aims to ethically analyze both invasive and non-invasive cosmetic neurology techniques including Neurohacking, claiming that the latter group is far less problematic when compared with the use of psychotropic drugs. Therefore, the ethical use of non-invasive brain enhancement techniques would provide a better alternative and an important solution to drug use in cosmetic neurology.

Types of enhancement

At this moment there are three known kinds of enhancement: pharmacological enhancement, external brain stimulation, and biohacking. In this section, we will define these concepts to clarify their meanings. Pharmacological approaches to cognitive enhancement involve the use of various compounds, commonly referred to as nootropics or smart drugs, to augment cognitive function (4). These compounds act on neurotransmitter systems, neuronal metabolism, or neurovascular mechanisms to enhance attention, memory, creativity, and other cognitive domains. Examples of commonly used nootropics include modafinil, methylphenidate, and racetams. Modafinil is a wakefulness-promoting agent, and it is believed to enhance cognitive function and mitigate fatigue without the addictive properties or adverse effects associated with traditional stimulants. Similarly, methylphenidate, a psychostimulant primarily prescribed for attention deficit hyperactivity disorder (ADHD), has been repurposed off-label for cognitive enhancement due to its ability to increase dopamine and norepinephrine levels in the brain. Racetams are a class of compounds including piracetam and aniracetam, that are believed to modulate glutamate receptors and cholinergic systems, therefore they should improve memory, learning, and cognitive flexibility. External stimulation techniques for cognitive enhancement involve the application of non-invasive methods to modulate brain activity and enhance cognitive function. Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are among the most researched modalities in this domain (5). Biohacking, on the other hand, is intended as the use of natural foods and activities in order to improve cognitive ability (6). This practice has gained substantial interest today as individuals seek to optimize their physical and mental performance through accessible and natural means. This approach is based also on the use of caffeine, which is widely recognized for its cognitive-enhancing properties, improving alertness and concentration (7). Natural supplements, such as omega-3 fatty acids and curcumin, have been used to benefit brain health and stimulate inflammation reduction(8), (9). Additionally, practices like yoga and mindfulness are integral to biohacking, offering profound benefits for stress reduction, emotional regulation, and overall well-being. Yoga, through its combination of physical postures and breath control, has been shown to enhance flexibility, strength, and most importantly mental clarity (10). Finally, mindfulness practices, including meditation, can significantly lower stress levels and improve cognitive function by fostering a state of focused attention and awareness (11). These natural interventions provide a synergistic effect, promoting a balanced and enhanced lifestyle without the need for synthetic compounds or medical procedures (12). In conclusion, pharmacological interventions, external stimulation techniques, and biohacking techniques offer some interesting options for cognitive enhancement. However, especially in the first two options, further research is needed to elucidate their mechanisms of action, optimize protocols for effectiveness and safety, and address ethical considerations surrounding their use in healthy individuals, since they could raise some neuroethical concerns that we aim to address in the present work.

Pharmacological enhancement

The ability to manipulate one's own cognitive ability is something very appealing to many of us, especially to people working in academia or having highly stressful jobs (13). The very possibility of being less tired, more mindful, and controlling our mental health has been traditionally linked to the practice of pharmacological enhancement in healthy individuals. This practice has usually been referred to as cosmetic neurology or neuroenhancement. It comprehends the use of psychotropic drugs to enhance our brain's performance, our resilience to stress and trauma, and the possibility of improving on a cognitive level, that is to become better, even if we are healthy individuals (14). Of course, in this case, the drugs we are mentioning are always taken off-label, and we have very little evidence that they help enhance our cognition, also inter-individual variety in the brain seems to be decisive when it comes to the actual effects of drug-related cosmetic neurology. The other side of this story is linked to the possible side effects of the drugs taken, which are already worrying in case of illnesses, and even more worrying in the case of a healthy individual taking off-label drugs for enhancement purposes. However, even if research, especially neuroethics, has always been concerned with psychotropic drugs prescribed off-label when it comes to neuroenhancement, there is some scientific evidence telling us that in the foreseeable future, enhancement could also be done with a drug-free, noninvasive clinical procedure that consists in brain stimulation of some specific areas and networks (15). Unfortunately, there is a scarcity of clinical trials and research in this direction, however, from what we know, such enhancement techniques seem to be extremely promising and a very good alternative to cosmetic neurology with psychotropic drugs. It has been largely established that a higher IQ has higher perks during the lifespan of individuals (16). This has also been shown by research and tests on brain resilience to trauma. For instance, in a 2015 study (17) it has been shown that human intelligence seems to be intertwined with several brain properties that are both structural and functional. In this study, simulated injuries were modeled on different individuals with different IQs, the outcome was a higher resilience to trauma and robustness showed by those who had a higher IQ. What was important in this study was the idea of a strict link between brain robustness and “Full Scale, Verbal and Performance IQ scores” (17). The robustness parameter is indeed a very vague neuroscientific term to explain several cognitive and brain functions. However, it has been defined as a ubiquitously observed property of complex, evolvable systems (18). So, to be more resilient to stress, one should be more intelligent, i.e. one should have a higher IQ and higher cognitive functions, more generally. More and more people try to do so by using psychotropic drugs, and from both a pharmacological and neuroethical point of view, this is extremely problematic. First, we should notice that a great part of cognitive enhancers work by targeting neuromodulatory systems such as: cholinergic, dopaminergic, noradrenergic, and serotonergic (13), these systems are ascendant, i.e., they ascend from the brainstem’s nuclei and innervate the cortical system as well as the subcortical one. Such drugs, even though their enhancement power is somewhat modest (13) have been the object of interest by many people looking for a way to be more efficient. The most used compounds for such a goal are: methylphenidate and modafinil, they are usually called neuromodulators (13), but do they work? First of all, it is important to notice that there cannot be a one-to-one mapping of a specific neurotransmitter and a specific cognitive function. In the case of dopamine, for example, we can see that it has some strong effects on working memory and attention, but this description is only on a general level: because of inter-individual brain variety, there is no way to tell what other effects neurotransmitters can have on an individual’s brain, and especially on its cognitive functions that are all different in power and expression. Also, it is important to notice that neurotransmitters such as dopamine work thanks to a cluster of various receptor systems that can give very different outcomes. For example, in the case of serotonin, we know that it acts via seventeen receptors, therefore it can have extremely different effects, depending on the receptor it acts upon. Finally, we can say that the question about what is enhanced, in the case of a beneficial cognitive effect, remains open. It is unknown whether psychotropic drugs used as enhancers have effects on several cognitive processes or just one, single mechanism; this uncertainty is because the studies we have only refer to clinical populations, and the parameters of those studies are very different from what we should look for in the case of a healthy brain. For instance, in Alzheimer’s disease’s pharmacological trials, the level of cognitive enhancement is evaluated and measured. However, these evaluations (CIBIC-Plus) are incredibly subjective and extremely clinical-driven what is measured are both general cognitive and behavioral functions but also daily activities. In addition to that, there are some trials (NPI) that include delusions, dysphoria, hallucinations, agitation, anxiety, aggression, euphoria, disinhibition, apathy, and also nighttime behavior disturbances as parameters to evaluate. As you can see, the clinical evaluation of these studies is already too individual-driven and too pathology-driven to be able to create some collateral data on healthy brain enhancement, and the scoring systems used have also the same issues.

Side effects

The drugs used for cognitive enhancement have, like all drugs, several side effects. The aforementioned side effects can have their outcomes not only in the brain but also in the entire body. Some common side effects of these kinds of drugs are gastrointestinal issues, nausea, verbal impairment (in the case of rivastigmine), and reversal learning (in the case of serotonin in young people) (19), while compulsive shopping, gambling, and hypersexuality are common side effects of dopamine agonists (20, 21). This collection of side effects is quite extensive, and not complete at all. When considering drug assumption, one should always consider also subjective side effects and singular differences in people. This has raised several concerns from a neuroethical perspective that will be further investigated in the course of the present analysis. There have been a couple of systematic reviews that investigated the issue in a more in-depth way (22, 23) but what can be said is that overall, the amount of side effects, both known and expected and unknown ones is extremely concerning and raises important questions about the actual admissibility of drug-related neuroenhancement. In the end, neuroethics is mainly concerned with the translation of neuroscience from a merely clinical practice to a more public discussion. Therefore, in this context, the issues caused by the off-label use of pharmacological cognitive enhancers by healthy individuals are especially concerning.

External brain stimulation: TBS and TDcs

As we have seen in the Introduction section, an alternative to pharmacological enhancement exists and has been copiously studied (24), and its results are very promising. External brain stimulation techniques, such as Theta Burst Stimulation (TBS) and Transcranial Direct Current Stimulation (tDCS), have emerged as promising non-invasive methods for modulating neural activity and enhancing cognitive functions. Both techniques offer distinct mechanisms and applications, contributing to their growing use in both research and clinical settings.

Theta Burst Stimulation (TBS)

TBS is a form of repetitive transcranial magnetic stimulation (rTMS) characterized by delivering short bursts of high-frequency stimuli. These bursts are typically delivered at theta frequency (5 Hz), which has been shown to induce long-lasting changes in cortical excitability. There are two main types of TBS: intermittent (iTBS) and continuous (cTBS). iTBS tends to enhance cortical excitability, whereas cTBS generally reduces it (25). Some studies have demonstrated the efficacy of TBS in treating various neuropsychiatric conditions, including depression and anxiety (26). For instance, Blumberger (27) conducted a randomized sham-controlled trial which provided evidence that iTBS can be a viable alternative to traditional rTMS for treatment-resistant depression. Additionally, TBS has been explored for its potential for cognitive enhancement, such as improving memory and executive function in healthy individuals (28). Chung and colleagues (29) highlighted the potential of TBS to modulate cortical networks associated with cognitive processes, suggesting that this technique could be used to enhance cognitive performance in both clinical and non-clinical populations. Furthermore, TBS has shown promise in neurorehabilitation, with studies indicating its potential to aid recovery in stroke patients by enhancing motor function and plasticity (30, 31).

Transcranial Direct Current Stimulation (tDCS)

tDCS involves the application of a low, constant electrical current through electrodes placed on the scalp. This method modulates neuronal activity by altering the membrane potential, making neurons more or less likely to fire. Anodal stimulation typically increases cortical excitability, while cathodal stimulation decreases it (32). tDCS has gained attention for its potential in cognitive enhancement, motor rehabilitation, and the treatment of mood disorders (33, 34). For example, Dedoncker and colleagues (35) found that tDCS can improve working memory and attention in both clinical populations and healthy subjects. Their meta-analysis provided a comprehensive overview of the effects of tDCS, supporting its use as a cognitive enhancement tool. Moreover, tDCS has been investigated for its therapeutic potential in various neurological and psychiatric disorders. Studies have shown that tDCS can alleviate symptoms of major depressive disorder, enhance motor recovery post-stroke, and improve cognitive function in patients with Alzheimer's disease (36, 37). The non-invasive nature and ease of application of tDCS make it an attractive option for both clinical and at-home use. However, the variability in individual responses to tDCS necessitates further research to optimize stimulation parameters and identify predictors of efficacy (38).

Working processes

The mechanisms underlying TBS and tDCS are still being elucidated, but both techniques are thought to modulate synaptic plasticity. TBS likely induces long-term potentiation (LTP) or long-term depression (LTD)-like effects depending on the stimulation pattern, thus altering synaptic strength and network connectivity (39). Conversely, tDCS is believed to influence neuronal excitability by modulating the resting membrane potential and affecting synaptic efficacy (40). These modulations can lead to changes in neurotransmitter levels, receptor activity, and intracellular signaling pathways, ultimately impacting cognitive and motor functions. While both TBS and tDCS show promise, their comparative efficacy and optimal protocols remain areas of active investigation. Studies suggest that TBS may offer more robust and immediate effects due to its higher-intensity stimulation pattern, whereas tDCS provides more subtle, yet sustained changes in cortical excitability (41). Comparative studies are crucial to understand the differential impacts of these techniques and to develop tailored interventions based on individual needs and conditions. Future research should focus on elucidating the underlying mechanisms, optimizing stimulation parameters, and exploring the long-term effects and safety of these techniques. Personalized approaches, considering individual variability in response to stimulation, also hold the potential for enhancing the efficacy of these interventions, efficacy seems, linked to frequency of treatment (42). Additionally, the integration of neuroimaging and electrophysiological methods can provide deeper insights into the neural correlates of TBS and tDCS effects, facilitating the development of more effective and targeted brain stimulation protocols (43).

External stimulative enhancement on healthy individuals

In this section, we present a study made by Santarnecchi et al. (17) testing TDcs on healthy individuals. Cognitive enhancement could be interpreted as something strictly linked to our biological neural networks and, therefore has the aim to stimulate the prefrontal cortex via transcranial oscillatory potentials. The individuals' IQ was tested both before and after the stimulation via the administration of Raven's Matrixes tests. The type of stimulation was an imperceptible frequency stimulating the gamma band located specifically over the left middle gyrus via an application of electrodes over the scalp. It is utterly important to notice that this kind of enhancement is rather similar to what happens when we train ourselves to meditate and make it a daily practice (44). This study on brain stimulation showed that when stimulation of the kind described is administered to a healthy individual, then the time taken to complete a certain task is shortened, giving a different IQ score, demonstrating that there is an actual alternative to psychotropic drugs for brain enhancement. In addition, this alternative can actually and selectively avoid any harm or risk: here, we just stimulate what is already there: neural networks. Of course, this study also has a strong potential in the case of cognitive impairments and cognitive rehabilitation, since it can improve the cognitive ability of patients who are already using many drugs for their condition, hence reducing the number of drugs used in therapy but also enhancing the effects of cognitive therapies. Reiterating and testing multiple times what was done here, would be essential to create an actual clinical protocol and then an actualization of these practices as therapies.

Neurohacking

Neurohacking involves practices such as diet manipulation, fasting, meditation, exercise, and the use of cognitive-enhancing supplements or devices. Neurohacking with natural foods and activities has gained substantial interest as individuals seek to optimize their physical and mental performance through accessible and holistic means. Key components of this approach include the use of caffeine, which is widely recognized for its cognitive-enhancing properties, improving alertness and concentration (45). Natural supplements, such as omega-3 fatty acids and turmeric, have been linked to benefits in brain health and inflammation reduction, respectively (46, 47). Additionally, practices like yoga and mindfulness are integral to biohacking, offering profound benefits for stress reduction, emotional regulation, and overall well-being. Yoga, through its combination of physical postures and breath control, has been shown to enhance flexibility, strength, and mental clarity (48). Mindfulness practices, including meditation, can significantly lower stress levels and improve cognitive function by fostering a state of focused attention and awareness (49). These natural interventions provide a synergistic effect, promoting a balanced and enhanced lifestyle without the need for synthetic compounds or invasive procedures (50).

Nutrition-related aspects of neurohacking

When it comes to nutritional Neurohacking it must be said that caffeine is one of the most used natural substances for enhancement, it acts as an adenosine receptor antagonist, enhancing noradrenaline turnover in the brain and reducing neural inhibition, which leads to increased alertness, elevated mood, and better-sustained attention (51-53). It improves motor-skill performance (54) and speeds up response to new stimuli (55, 56). However, a general consensus on caffeine's effects on complex cognitive tasks and memory is far from achieved and the opinions one could find in the literature are mixed, with some studies showing improved performance (57) and others finding no significant effects (58, 59). However, caffeine tolerance (60) and withdrawal symptoms such as headaches and fatigue have been (61-63). Also, psychological factors play a role in withdrawal effects and perceived caffeine effects (64-66). Another common natural substance that could generate some sort of enhancement is glucose. Glucose is the primary fuel for cells and is regulated by insulin and glucagon. Low glucose levels can impair cognitive functioning and reaction times. Glucose administration has been shown to improve attention, response speed, and working memory (67-70). It particularly enhances declarative memory, with significant effects on demanding tasks and more pronounced benefits in the elderly (71-75). The hippocampus is a key region mediating these memory effects, involving mechanisms related to insulin, acetylcholine, and glucose availability. Overall, caffeine and glucose enhance mood, energy, vigilance, attention, and memory, potentially in a synergistic manner (76), but in the end, individual differences such as glucose tolerance and caffeine consumption habits affect these outcomes.

Non-nutritional aspects of neurohacking

Physical Exercise, a correct sleep schedule, and meditation are factors that can effectively improve people's lives, but these elements can also generate some form of brain enhancement in the terms we are going to discuss in this section of the present work. For instance, regular physical activity is widely recognized for its benefits in preventing cardiovascular diseases and promoting overall health. Early research showed that athletes outperformed inactive individuals in cognitive functions, and contemporary studies confirm that aerobic exercise benefits brain function and cognition (77). Studies often focus on children and elderly adults. In children, physical exercise enhances academic achievement and cognitive skills (78). In older adults, exercise programs improve various cognitive functions (79, 80). A meta-analysis revealed that aerobic exercise improves attention, processing speed, executive function, and memory, though effects on working memory are less consistent (81). Research on younger and middle-aged adults is limited, with most data coming from studies on older adults where they serve as control groups. However, studies on the acute effects of exercise in young adults show improvements in long-term memory and learning speed (82, 83). A meta-analysis indicates that mental speed and memory processes are enhanced after acute exercise, with small to medium effect sizes (84). Motivational factors and increased arousal levels are potential mechanisms (85). Exercise improves resting functional efficiency in cognitive networks, including the frontal, posterior, and temporal cortices (86). Greater activity in fronto-parietal networks is linked to cardiovascular fitness and cognitive benefits (87). Exercise also increases hippocampal blood flow and connectivity (88)and is associated with preserved gray matter in some areas typically declining with age (89). Aerobic exercise increases brain volume in gray and white matter regions and enhances spatial memory through increased hippocampal size and BDNF levels (46, 90-92). In general, we could say that cerebral blood volume measurements correlate with neurogenesis and cognitive function (93). Humans spend about one-third of their lives sleeping, which offers significant cognitive benefits, particularly for memory and creativity (6, 94). Numerous studies have confirmed sleep's positive effects on memory consolidation (94) even in non-sleep-deprived conditions (95, 96). Daytime naps can also benefit memory, with even short naps promoting memory performance (97, 98). Sleep effects vary by memory system, with declarative memory showing medium effect sizes and procedural or perceptual learning showing larger effects (99). Also, sleep not only stabilizes but also enhances certain memories (96). The neural mechanisms of sleep's effects on memory are not fully understood but it has been postulated that it may involve passive homeostatic processes or active consolidation (100). Animal studies show neuronal replay during sleep (101), and human studies suggest a causal role for sleep in memory consolidation (102). Instead of global sleep stages, physiological microprocesses like hippocampal ripples, thalamocortical spindles, and slow cortical oscillations are crucial for memory consolidation (103). Sleep also enhances creativity. Studies show that this daily necessity also promotes creative problem-solving (104) and REM sleep, associated with dreaming, enhances associative networks for problem-solving (105), and selective REM sleep deprivation impairs creativity (106). Sleep facilitates creative ideas by fostering defocused attention and hyper-associativity, processes typical of dreaming (107, 108). Therefore, sleep provides optimal conditions for creative insights. The last element that has come to our attention when considering the discourse on biohacking is certainly meditation. This practice, while traditionally associated with mental well-being, also benefits cognitive functions. It involves various practices like focused attention and open monitoring meditation, which enhance emotional and attentional regulation (109, 110). Studies show that meditation improves attention, cognitive flexibility, and other cognitive capacities (111, 112). Even brief meditation training enhances visuospatial processing, working memory, and executive functioning (49). A systematic review found that early mindfulness meditation training improves selective and executive attention, while later training improves sustained attention (113). A meta-analysis reported medium to large effects on emotionality and attention, with smaller effects on memory(114, 115). Neurophysiological studies show that meditation increases alpha and theta brain activity (116, 117) and activates brain areas such as the prefrontal cortex and anterior cingulate cortex (118) . Long-term meditation enhances brain activation in specific areas and promotes attention sustainability (119). Meditation modulates plasticity in attention-related neural circuits (120), and reduces neural responses in conceptual processing regions, indicating enhanced neural efficiency (121, 122). PET studies show increased dopamine release in the ventral striatum during meditation, suggesting regulation of conscious states (123). Structural brain changes associated with meditation include larger volumes of the right hippocampus and orbitofrontal cortex in long-term meditators (124), and greater cortical thickness in attention-related regions (125). Longitudinal studies show gray matter increases in the hippocampus and other regions after meditation training (126).

Bioethical analysis

As we have seen during the course of the present work, advancements in neuroscientific research have opened up new possibilities for enhancing brain function. As shown in Table 1, these enhancements can be achieved through pharmacological means, TBS or TDCs, or via neurohacking.

However, especially when it comes to the use of pharmacological enhancement these practices are very problematic because they could raise ethical concerns surrounding a classical bioethical discourse. These

Table 1. Comparison of different methods for brain enhancement

	Pharmacological enhancement	**TMS & External stimulation**	**Neurohacking**
Side effects	Major	Mild	Mild to non-existent (depending on the combination of employed techniques)
Availability	Moderately available	Scarcely available	Widely available
Measuring parameters, i.e. what is enhanced	Unclear	Prefrontal cortex and its neural pathways	Many processes at work, depending on the enhancers' combination
Target Population	Healthy, non-pathological individuals	Healthy, non-pathological individuals	Healthy, non-pathological individuals

practices raise bioethical concerns related to safety, informed consent, equity of access, and the potential for unintended consequences along with ethical concerns about authenticity and fairness due to their widespread illicit use for cognitive enhancement purposes and their potential to create an uneven playing field in academic and professional settings. These bioethical issues need to be carefully considered and addressed to ensure responsible and ethical practices in the field of brain enhancement. A recent article about closed-loop neuromodulation of the prefrontal cortex (127) provides insights into the challenges of closed-loop approaches in brain stimulation and highlights the need for objective characterization of mental states and effective strategies for neurostimulation interventions. Also, the ethical dimension of biohacking must be confronted with some reflection on neuromarketing and brain hype (128) and how commercialized products are advertised to the public (129). In this section, we are going to explore and address such issues considering the singular kinds of enhancement and giving a final analysis as to which one or which ones are more bioethically acceptable than others starting from both scientific and bioethical evidence. The first issue concerning drug-related cognitive enhancement is certainly due to the unknown risks of this practice, the aforementioned risks concern the lack of safety and possible harm that it can cause to healthy people, especially when it comes to long-term consequences in adolescents and children: during this period the brain is still in development (130), in these cases, the use of pharmacological cognitive enhancers is even riskier. Other safety concerns are about possible abuse of cognitive enhancers and, as is the case with every drug assumption, contraindications in the case of pre-existing conditions such as heart or hepatic impairments, and this could be utterly dangerous if such conditions are still unknown by the person using enhancers (131, 132). Authenticity (133) is another ethical issue that is worth taking into account in our case: it concerns the individual's identity first, i.e. the way a person is, the way they interact with the external world, their decision-making processes, and their morality and values.

Consequently, the issue of authenticity concerns also the behavioral outcomes of such an individual, i.e. the way a result of a university exam is achieved, the moral judgments this person expresses, and the whole set of actions whose outcomes have a certain impact on the community in which the individual lives their daily life (13). Of course, the other side of this issue also concerns the work of others: e.g., can we consider exactly equal two papers written by an individual A and an individual B, whereas individual A has used cognitive enhancers? This represents an authenticity concern.

Consequently, we can also consider the issue of Justice (134, 135), both in an academic environment and, more generally, society-wise. Considering our last example, we can see how an issue of justice also arises, and it would be even larger in the case of a university exam. We could say that the use of enhancers is morally unjustifiable because it could cause an individual to the violation of the Standard of Excellence that a workplace or an academic setting should have (136) Starting from this idea we could extend the issue to other endeavors such as the military, but also corporate jobs and medical jobs. Enhancing the brain relates also to the risks and harm to others that can result from the use of enhancers by healthy individuals. Since we have a severe lack of knowledge in this sense, we could say that we do not know the consequences of drug assumption to society and, more specifically, to other people. We know that these drugs can cause some very serious behavioral side effects and that we cannot control those side effects, therefore it is still unclear whether a healthy individual could harm other people because they are under the effect of an enhancer, i.e. harm to other people remains in this context a possible outcome of cognitive enhancers assumption, therefore the respect of the principle of non-maleficence cannot be guaranteed (137). When it comes to external stimulation the situation shifts. This kind of non-invasive enhancement has some ethical advantages that are of interest to us. First, the health concerns about any possible side effects and harm can be addressed and solved with this kind of practice: it seems that there are no unknown risks in stimulating one's own brain and neural pathways. Also, an issue of justice is still present, and, in this case, it would be related to the effective availability of this kind of therapy and the related possible cost of it. If this kind of enhancement is considered not essential, especially for healthy individuals, it is plausible that a procedure of this kind would be extremely expensive and therefore not accessible to everyone. While these technologies promise substantial cognitive benefits, including improved memory, attention, and mental health outcomes, they are also extremely costly. For this very reason, their accessibility remains a contentious issue, raising important ethical concerns about equity and justice. One of the primary barriers to accessing high-cost brain enhancement techniques is their significant financial burden. For instance, transcranial magnetic stimulation (TMS) can cost between $300 to $500 per session, with a full course of treatment often requiring multiple sessions, thus accumulating substantial costs (138) This price range makes it unaffordable for many individuals, particularly those from lower socioeconomic backgrounds. In contrast, individuals with higher income levels or comprehensive health insurance plans are more likely to afford such treatments, thereby exacerbating existing health disparities (139). Health insurance could be a way to solve this problem, at least in the middle class when it comes to European countries however, the bureaucratic hurdles involved in obtaining insurance approval for these treatments can be prohibitive, further limiting access for those in (140) Of course, global disparities also play a crucial role in the accessibility of brain enhancement technologies. When it comes to low- and middle-income countries, the availability of advanced medical technologies, including high-cost brain enhancement methods, is often limited or non-existent (141) This lack of availability is compounded by inadequate healthcare infrastructure and insufficient funding, leaving a significant portion of the global population without access to these potentially life-changing treatments. Naturally, the inaccessibility of high-cost brain enhancement techniques raises significant ethical concerns. The principle of justice in healthcare ethics demands fair distribution of resources and equal access to medical treatments (134) In our case, only a privileged part of the global population can adequately access such cognitive enhancement methods, this creates a troubling issue in equal opportunity and its validity. Such reasonings can be applied to the whole global healthcare system, but this inequity is particularly important in the context of cognitive enhancement because access to these technologies could confer enormous advantages in many areas of life: from basic to higher education, to employment, affecting the overall quality of life. The accessibility of high-cost brain enhancement techniques is a complex issue that intersects with socioeconomic status, health insurance coverage, and global disparities. Addressing these barriers is essential to ensure equitable access to cognitive enhancement technologies, thereby promoting a fairer and more just society. Ethical considerations must guide policy decisions to bridge the gap in accessibility and ensure that the benefits of these advanced treatments are available to all, regardless of their financial or geographic circumstances (142) When it comes to authenticity the problem is extremely complicated and it has been discussed in the case of another similar practice that involves a surgical procedure of deep brain stimulation, however, we think this reasoning can also be extended to non-invasive stimulative methods such as our subject matter (143). Accordingly, we should say that the authenticity issue, in this case, would arise only if we think that an individual stays authentic to their personhood (144) only if they stay just the way they are born both physically and mentally: therefore, in this case also cosmetic surgery would be an issue (145). Contrarily, if we consider the beneficence and non-maleficence principles, we could safely say that since there is no harm to external individuals and since no possible behavioral change has been detected in external stimulation practices, then this enhancement option would be ethically justifiable. In the context of natural biohacking, the principle of autonomy is paramount. Techniques such as mindfulness and dietary choices empower individuals to take control of their mental health and cognitive function. However, the principle of autonomy can be only compromised if individuals lack access to accurate information or if societal pressures unduly influence their choices. For example, the commercialization of certain neurohacking practices may lead to exaggerated claims and misinformation, undermining true informed consent (146). When it comes to the principle of non-maleficence, we could say that biohacking practices generally pose low physical risks to the individual and none to society, therefore we believe such a principle is respected. Since the principle of beneficence involves promoting the well-being of individuals and society (134), we could say that natural neurohacking has the potential to offer significant benefits, including improved mental health, enhanced cognitive function, and greater overall well-being. As we have seen mindfulness meditation, has been shown to reduce stress and improve emotional regulation (147) However, ensuring beneficence requires that these practices are based on solid scientific evidence and that the benefits are communicated. Overstating the benefits or ignoring the potential downsides can lead to mistrust and harm, counteracting the intended positive outcomes. Furthermore, psychological techniques such as intensive meditation may induce distress or exacerbate underlying mental health issues in some individuals (147, 148). Natural neurohacking practices often require resources such as time, money, and access to information, which can create disparities. For instance, individuals from lower socioeconomic backgrounds may find it more challenging to engage in certain neurohacking practices due to cost or lack of availability. This inequity raises concerns about fairness and the right of all individuals to benefit from health-enhancing practices (149-151). Therefore, we could say that the issue of justice, though mitigated concerning our previous examples, is not completely respected also in the case of biohacking. In the end, the accessibility of high-cost brain enhancement techniques is a complex issue that intersects with the socioeconomic status of individuals, the possible presence of health insurance and its coverage, and, most importantly, global disparities. Addressing these issues is essential to ensure equitable access to cognitive enhancement via external stimulation and promoting a fairer and more just society. While both drug-related enhancement and external stimulation methods present bioethical issues, we believe that external stimulation poses significantly fewer problems. However, issues of justice and authenticity remain pressing concerns. These challenges can only be resolved through comprehensive policies and regulations that strictly monitor the application and progress of TMS and tDCS (152) Ultimately, the only bioethically acceptable method for enhancement remains neurohacking due to its lower risk profile and its guarantee of personal autonomy (153). Nevertheless, as a society, we should strive to make external stimulation techniques safe and widely available. This would provide an alternative for individuals who either do not wish to pursue neurohacking techniques or cannot modify their lifestyle for various reasons (154). Through such efforts, we can ensure that the benefits of cognitive enhancement are accessible to all, regardless of their financial or personal circumstances (141).

Conclusions

In conclusion, there is significant evidence guiding us toward the idea that, even though cosmetic neurology can be considered problematic, there can be methods that are safe and bioethically acceptable, or at least improvable. As we have seen, such methods, even though not completely free from bioethical consequences and risks can be deemed acceptable if carried out responsibly and backed up by policies and regulations, preferably on a global level. Finally, it is rather clear that since the need for enhancement is a real and concrete necessity of today's society, enhancement systems are to be considered as a way to improve ourselves and our cognitive abilities. The scope of a bioethical analysis in this context is moving forward to guarantee their safety and availability while addressing major ethical issues.

References

1. Steinbock B. The Oxford handbook of bioethics. New York: Oxford University Press; 2007.
2. Rossi S, Santarnecchi E, Feurra M. Noninvasive brain stimulation and brain oscillations. Handb Clin Neurol 2022; 184:239–47.
3. Santos D. Conceptualizing the democratization of innovation through transitions theory: A case study of biohacking in community science labs. Environ Innov Soc Transit 2023; 49:100783.
4. Mohamed AD. Neuroethical issues in pharmacological cognitive enhancement. Wiley Interdiscip Rev Cogn Sci 2014; 5(5):533–49.
5. Salvador R, Biagi MC, Puonti O, et al. Personalization of Multi-electrode Setups in tCS/tES: Methods and Advantages. In: Makarov SN, Noetscher GM, Nummenmaa A, editors. Brain and Human Body Modeling 2020. Berlin: Springer; 2021. p. 119–135.
6. Dresler M, Sandberg A, Bublitz C, et al. Hacking the Brain: Dimensions of Cognitive Enhancement. ACS Chem Neurosci 2018; 10(3):1137.
7. Einöther SJL, Giesbrecht T. Caffeine as an attention enhancer: reviewing existing assumptions. Psychopharmacology (Berl) 2013; 225(2):251–74.
8. Bozzatello P, Brignolo E, De Grandi E, BellinoS. Supplementation with Omega-3 Fatty Acids in Psychiatric Disorders: A Review of Literature Data. J Clin Med 2016; 5(8):67.
9. Lopresti AL, Smith SJ, Pouchieu C, et al. Effects of a polyphenol-rich grape and blueberry extract (Memophenol™) on cognitive function in older adults with mild cognitive impairment: A randomized, double-blind, placebo-controlled study. Front Psychol 2023; 14:1144231.
10. Cramer H, Lauche R, Anheyer D, et al. Yoga for anxiety: A systematic review and meta-analysis of randomized controlled trials. Depress Anxiety 2018; 35(9):830–43
11. Schumer MC, Lindsay EK, David CreswellJ. Brief mindfulness training for negative affectivity: A systematic review and meta-analysis. J Consult Clin Psychol 2018; 86(7):569–83.
12. Bruce SE, Werner KB, Preston BF, Baker LM. Improvements in concentration, working memory and sustained attention following consumption of a natural citicoline-caffeine beverage. Int J Food Sci Nutr 2014; 65(8): 1003–7.
13. Husain M, Mehta MA. Cognitive enhancement by drugs in health and disease. Trends Cogn Sci 2011; 15(1):28–36.
14. Sahakian BJ, Bruhl AB, Cook J, et al. The impact of neuroscience on society: cognitive enhancement in neuropsychiatric disorders and in healthy people. Philos Trans R Soc Lond B Biol Sci 2015; 370(1677):20140214.
15. Santarnecchi E, Polizzotto NR, Godone M, et al. Frequency-Dependent Enhancement of Fluid Intelligence Induced by Transcranial Oscillatory Potentials. Current Biology 2013; 23(15):1449-53.
16. Batty GD, Shipley MJ, Gale CR, Mortensen LH, Deary, IJ. Does IQ predict total and cardiovascular disease mortality as strongly as other risk factors? Comparison of effect estimates using the Vietnam Experience Study. Heart 2008; 94(12):1541–4.
17. Santarnecchi E, Muller T, Rossi S, et al. Individual differences and specificity of prefrontal gamma frequency-tACS on fluid intelligence capabilities. Cortex 2016; 75: 33–43.
18. Kitano H. Biological robustness. Nat Rev Genet 2004; 5(11):826–37.
19. Cools R, Roberts AC, Robbins TW. Serotoninergic regulation of emotional and behavioural control processes. Trends Cogn Sci 2008; 12(1):31–40.
20. Weintraub D, Koester J, Potenza MN, et al. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. Arch Neurol 2010; 67(5):589–95.
21. Weintraub D, Siderowf AD, Potenza MN, et al. Association of dopamine agonist use with impulse control disorders in Parkinson disease. Arch Neurol 2006; 63(7):969–73.
22. Sahakian BJ, Morein-Zamir S. Neuroethical issues in cognitive enhancement. J Psychopharmacol 2011; 25(2):197–204.
23. Mohamed AD. Neuroethical issues in pharmacological cognitive enhancement. Wiley Interdiscip Rev Cogn Sci 2014; 5(5):533–49.
24. Erker TD, Arif Y, John JA, et al. Neuromodulatory effects of parietal high-definition transcranial direct-current stimulation on network-level activity serving fluid intelligence. J Physiol 2024; 602(12):2917–30.
25. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron 2005; 4(2):201–6.
26. Blumberger DM, Vila-Rodriguez F, Thorpe KE, et al. Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial. Lancet 2018; 391(10131):1683–92.
27. Blumberger DM, Mulsant BH, Daskalakis ZJ. What is the role of brain stimulation therapies in the treatment of depression?. Curr Psychiatry Rep 2013; 15(7):368.
28. Katagiri N, Yoshida S, Koseki T, et al. Interindividual Variability of Lower-Limb Motor Cortical Plasticity Induced by Theta Burst Stimulation. Front Neurosci 2020; 14:563293.
29. Chung SW, Sullivan CM, Rogasch NC, Hoy KE, Bailey NW, Cash RFH, Fitzgerald PB. The effects of individualised intermittent theta burst stimulation in the prefrontal cortex: A TMS-EEG study. Hum Brain Mapp 2019; 40(2):608–27.

30. Chen L, Chung SW, Hoy KE, Fitzgerald PB. Is theta burst stimulation ready as a clinical treatment for depression?. Expert Rev Neurother 2019; 19(11):1089–102.
31. Sharbafshaaer M, Cirillo G, Esposito F, Tedeschi G, Trojsi F. Harnessing Brain Plasticity: The Therapeutic Power of Repetitive Transcranial Magnetic Stimulation (rTMS) and Theta Burst Stimulation (TBS) in Neurotransmitter Modulation, Receptor Dynamics, and Neuroimaging for Neurological Innovations. Biomedicines 2024; 12(11):2506.
32. Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol 2000; 527(3):633–9.
33. Vitor-Costa M, Okuno NM, Bortolotti H, et al. Improving Cycling Performance: Transcranial Direct Current Stimulation Increases Time to Exhaustion in Cycling. PLoS One 2015; 10(12):e0144916.
34. Douglas KM, Peckham A, Porter R, Hammar A. Cognitive enhancement therapy for mood disorders: A new paradigm?. Aust N Z J Psychiatry 2019; 53(12):1148–50.
35. Dedoncker J, Brunoni AR, Baeken C, Vanderhasselt MA. A Systematic Review and Meta-Analysis of the Effects of Transcranial Direct Current Stimulation (tDCS) Over the Dorsolateral Prefrontal Cortex in Healthy and Neuropsychiatric Samples: Influence of Stimulation Parameters. Brain Stimul 2016; 9(4):501–17.
36. Flöel A. tDCS-enhanced motor and cognitive function in neurological diseases. Neuroimage 2014; 85(3):934–47.
37. Kuo HI, Paulus W, Batsikadze G, Jamil A, Kuo MF, Nitsche MA. Chronic Enhancement of Serotonin Facilitates Excitatory Transcranial Direct Current Stimulation-Induced Neuroplasticity. Neuropsychopharmacology 2016; 41(5): 1223–30.
38. Lefaucheur JP, Antal A, Ayache SS, et al. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Clin Neurophysiol 2017; 128(1): 56–92.
39. Ridding MC, Ziemann U. Determinants of the induction of cortical plasticity by non-invasive brain stimulation in healthy subjects. J Physiol 2010; 588(13);2291–304.
40. Stagg CJ, Nitsche MA. Physiological basis of transcranial direct current stimulation. Neuroscientist 2011; 17(1): 37–53.
41. Wischnewski M, Schutter DJLG. Efficacy and Time Course of Theta Burst Stimulation in Healthy Humans. Brain Stimul 2015; 8(4):685–92.
42. Horvath JC, Forte JD, Carter O. Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS). Brain Stimul 2015; 8(3):535–50.
43. Bergmann TO, Karabanov A, Hartwigsen G, Thielscher A, Siebner HR. Combining non-invasive transcranial brain stimulation with neuroimaging and electrophysiology: Current approaches and future perspectives. Neuroimage 2016; 140:4–19.
44. Lutz A, Greischar LL, Rawlings NB, Ricard M, Davidson RJ. Long-term meditators self-induce high-amplitude gamma synchrony during mental practice. Proc Natl Acad Sci USA 2004; 101(46):16369–73.
45. Camfield DA, Stough C, Farrimond J, Scholey AB. Acute effects of tea constituents L-theanine, caffeine, and epigallocatechin gallate on cognitive function and mood: a systematic review and meta-analysis. Nutr Rev 2014; 72(8): 507–22.
46. Gómez-Pinilla F. Brain foods: the effects of nutrients on brain function. Nat Rev Neurosci 2008; 9(7):568–78.
47. Gupta VK, Scheunemann L, Eisenberg T, et al. Restoring polyamines protects from age-induced memory impairment in an autophagy-dependent manner. Nat Neurosci 2013; 16(10):1453–60.
48. Ross A, Thomas S. The health benefits of yoga and exercise: a review of comparison studies. J Altern Complement Med 2010; 16(1):3–12.
49. Zeidan F, Johnson SK, Diamond BJ, David Z, Goolkasian P. Mindfulness meditation improves cognition: evidence of brief mental training. Conscious Cogn 2010; 19(2):597–605.
50. Pascoe MC, Bauer IE. A systematic review of randomised control trials on the effects of yoga on stress measures and mood. J Psychiatr Res 2015; 68:270–82.
51. Smith A, Brice C, Nash J, Rich N, Nutt DJ. Caffeine and central noradrenaline: effects on mood, cognitive performance, eye movements and cardiovascular function. J Psychopharmacol 2003; 17(3):283-92.
52. Ferré S. Role of the central ascending neurotransmitter systems in the psychostimulant effects of caffeine. J Alzheimers Dis 2010; 20(Suppl 1):S35–49.
53. Hewlett P, Smith A. Effects of repeated doses of caffeine on performance and alertness: new data and secondary analyses. Hum Psychopharmacol 2007; 22(6):339–50.
54. Reyner LA, Horne JA. Suppression of sleepiness in drivers: combination of caffeine with a short nap. Psychophysiology 1997; 34(6):721–5.
55. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ 2006; 174(6):801–9.
56. Riedel BW, Lichstein KL, Dwyer WO. Sleep compression and sleep education for older insomniacs: self-help versus therapist guidance. Psychol Aging 1995; 10(1):54–63.
57. Heatherley SV, Hayward RC, Seers HE, Rogers PJ. Cognitive and psychomotor performance, mood, and pressor effects of caffeine after 4, 6 and 8 h caffeine abstinence. Psychopharmacology (Berl) 2005; 178(4):461–70.
58. Rogers PJ, Dernoncourt C. Regular caffeine consumption: a balance of adverse and beneficial effects for mood and psychomotor performance. Pharmacol Biochem Behav 1998; 59(4):1039–45.
59. Nehlig A. Is caffeine a cognitive enhancer?. J Alzheimers Dis 2010; 20(Suppl 1):S85–94.
60. Evans SM, Griffiths RR. Caffeine tolerance and choice in humans. Psychopharmacology (Berl) 1992; 108(1-2):51–9.
61. Juliano LM, Griffiths RR. A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. Psychopharmacology (Berl) 2004; 176(1):1–29.

62. Schuh K, Griffiths R. Caffeine reinforcement: the role of withdrawal. Psychopharmacology (Berl) 1997; 130(4):320–6.
63. Dews PB, O'Brien CP, Bergman J. Caffeine: behavioral effects of withdrawal and related issues. Food Chem Toxicol 2002; 40(9):1257–61.
64. Fillmore MT, Mulvihill LE, Vogel-Sprott M. The expected drug and its expected effect interact to determine placebo responses to alcohol and caffeine. Psychopharmacology (Berl) 1994; 115(3):383–8.
65. Smit H, Rogers P. Effects of low doses of caffeine on cognitive performance, mood and thirst in low and higher caffeine consumers. Psychopharmacology (Berl) 2000; 152(2): 167–73.
66. Addicott MA, Laurienti PJ. A comparison of the effects of caffeine following abstinence and normal caffeine use. Psychopharmacology (Berl) 2009; 207(3):423–31.
67. Owens DS, Benton D. The impact of raising blood glucose on reaction times. Neuropsychobiology 1994; 30(2-3):106–13.
68. Benton D, Owens DS, Parker PY. Blood glucose influences memory and attention in young adults. Neuropsychologia 1994; 32(5):595–607.
69. Scholey AB, Harper S, Kennedy DO. Cognitive demand and blood glucose. Physiol Behav 2001; 73(4):585–92.
70. Owen L, Scholey AB, Finnegan Y, Hu H, Sünram-Lea SI. The effect of glucose dose and fasting interval on cognitive function: a double-blind, placebo-controlled, six-way crossover study. Psychopharmacology (Berl) 2012; 220(3):577–89.
71. Messier C. Glucose improvement of memory: a review. Eur J Pharmacol 2004; 490(1-3):33–57.
72. Smith MA, Riby LM, Eekelen JA, Foster JK. Glucose enhancement of human memory: a comprehensive research review of the glucose memory facilitation effect. Neurosci Biobehav Rev 2011; 35(3):770–83.
73. Sünram-Lea SI, Foster JK, Durlach P, Perez C. Investigation into the significance of task difficulty and divided allocation of resources on the glucose memory facilitation effect. Psychopharmacology (Berl) 2002; 160(4):387–97.
74. Meikle A, Riby LM, Stollery B. The impact of glucose ingestion and gluco-regulatory control on cognitive performance: a comparison of younger and middle aged adults. Hum. Psychopharmacol Clin Exp 2004;19:523–35.
75. Manning CA, Hall JL, Gold PE. (1990). Glucose Effects on Memory and Other Neuropsychological Tests in Elderly Humans. Psychological Science 1990; 1(5):307–11.
76. Serra-Grabulosa JM, Adan A, Falcón C, Bargalló N. Glucose and caffeine effects on sustained attention: an exploratory fMRI study. Hum Psychopharmacol 2010; 25(7-8): 543–52.
77. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: exercise effects on brain and cognition. Nat Rev Neurosci 2008; 9(1):58–65.
78. Sibley BA, Etnier JL. (2003). The Relationship between Physical Activity and Cognition in Children: A Meta-Analysis. Pediatr Exerc Sci 2003; 15(3):243–56.
79. Richards M, James SN, Sizer A, et al. Identifying the lifetime cognitive and socioeconomic antecedents of cognitive state: seven decades of follow-up in a British birth cohort study. BMJ Open 2019; 9(4):e024404.
80. van Uffelen JG, Chin A Paw MJ, Hopman-Rock M, van Mechelen W. The effects of exercise on cognition in older adults with and without cognitive decline: a systematic review. Clin J Sport Med 2008; 18(6):486–500.
81. Smith PJ, Blumenthal JA, Hoffman BM, et a. Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. Psychosom Med 2010; 72(3):239–52.
82. Coles K, Tomporowski PD. Effects of acute exercise on executive processing, short-term and long-term memory. J Sports Sci 2008; 26(3):333–44.
83. Winter B, Breitenstein C, Mooren FC, et al. High impact running improves learning. Neurobiol Learn Mem 2007; 87(4):597–609.
84. Lambourne K, Tomporowski P. The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. Brain Res 2010; 1341:12–24.
85. Brisswalter J, Collardeau M, René A. Effects of acute physical exercise characteristics on cognitive performance. Sports Med 2002; 32(9):555–66.
86. Voss MW, Kramer AF, Basak C, Prakash RS, Roberts B. Are expert athletes 'expert' in the cognitive laboratory? A meta-analytic review of cognition and sport expertise. Appl Cogn Psychol 2010; 24(6):812–26.
87. Colcombe SJ, Kramer AF, Erickson KI, et al. Cardiovascular fitness, cortical plasticity, and aging. Proc Natl Acad Sci USA 2004; 101(9):3316–21.
88. Burdette JH, Laurienti PJ, Espeland MA, et al. Using network science to evaluate exercise-associated brain changes in older adults. Front Aging Neurosci 2010; 2:23.
89. Gordon GR, Choi HB, Rungta RL, Ellis-Davies GC, MacVicar BA. Brain metabolism dictates the polarity of astrocyte control over arterioles. Nature 2008; 456(7223):745–9.
90. Neeper SA, Gómez-Pinilla F, Choi J, Cotman C. Exercise and brain neurotrophins. Nature 1995; 373(6510):109.
91. Vaynman S, Gomez-Pinilla F. Revenge of the 'sit': How lifestyle impacts neuronal and cognitive health through molecular systems that interface energy metabolism with neuronal plasticity. J Neurosci Res 2006; 84(4):699–715.
92. Erickson KI, Raji CA, Lopez OL, et al. Physical activity predicts gray matter volume in late adulthood: the Cardiovascular Health Study. Neurology 2010; 75(16):1415–22.
93. Pereira AC, Huddleston DE, Brickman AM, et al. An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. Proc Natl Acad Sci USA 2007; 104(13): 5638–43.
94. Diekelmann S, Born J. The memory function of sleep. Nat Rev Neurosci 2010;11(2):114–26.
95. Fischer S, Hallschmid M, Elsner AL, Born J. Sleep forms memory for finger skills. Proc Natl Acad Sci USA 2002; 99(18):11987–91.
96. Walker MP, Brakefield T, Morgan A, Hobson JA, Stickgold R. Practice with sleep makes perfect: sleep-dependent motor skill learning. Neuron 2002; 35(1):205–11.

97. Mednick S, Nakayama K, Stickgold R. Sleep-dependent learning: a nap is as good as a night. Nat Neurosci 2003; 6(7):697–8.
98. Lahl O, Wispel C, Willigens B, Pietrowsky R. An ultra short episode of sleep is sufficient to promote declarative memory performance. J Sleep Res 2008; 17(1):3–10.
99. Censor N, Karni A, Sagi D. A link between perceptual learning, adaptation and sleep. Vision Res 2006; 46(23): 4071–4.
100. Tsunematsu T. What are the neural mechanisms and physiological functions of dreams? Neurosci Res 2023; 189:54–9.
101. Ji D, Wilson MA. Coordinated memory replay in the visual cortex and hippocampus during sleep. Nat Neurosci 2007; 10(1):100–7.
102. Rasch B, Büchel C, Gais S, Born J. Odor cues during slow-wave sleep prompt declarative memory consolidation. Science 2007; 315(5817):1426–9.
103. Mölle M, Born J. Slow oscillations orchestrating fast oscillations and memory consolidation. Prog Brain Res 2011; 193:93–110.
104. Wagner U, Gais S, Haider H, Verleger R, Born J. Sleep inspires insight. Nature 2004; 427(6972):352–5.
105. Cai DJ, Mednick SA, Harrison EM, Kanady JC, Mednick SC. REM, not incubation, improves creativity by priming associative networks. Proc Natl Acad Sci USA 2009; 106(25):10130–4.
106. Killgore WD. Effects of sleep deprivation on cognition. Prog Brain Res 2010; 185:105–29.
107. Hobson JA. Sleep is of the brain, by the brain and for the brain. Nature 2005;437(7063):1254–6.
108. Hobson JA, Pace-Schott EF. The cognitive neuroscience of sleep: neuronal systems, consciousness and learning. Nat Rev Neurosci 2002; 3(9):679–93.
109. Lutz A, Brefczynski-Lewis J, Johnstone T, Davidson RJ. Regulation of the neural circuitry of emotion by compassion meditation: effects of meditative expertise. PLoS One 2008;3(3):e1897.
110. Leung MK, Chan CC, Yin J, Lee CF, So KF, Lee TM. Increased gray matter volume in the right angular and posterior parahippocampal gyri in loving-kindness meditators. Soc Cogn Affect Neurosci 2013; 8(1):34–9.
111. Moore A, Malinowski P. Meditation, mindfulness and cognitive flexibility. Conscious Cogn 2009; 18(1):176–86.
112. Hodgins HS, Adair KC. Attentional processes and meditation. Conscious Cogn 2010; 19(4):872–8.
113. Chiesa A, Calati R, Serretti A. Does mindfulness training improve cognitive abilities? A systematic review of neuropsychological findings. Clin Psychol Rev 2011; 31(3): 449–64.
114. Sumantry D, Stewart KE. Meditation, Mindfulness, and Attention: a Meta-analysis. Mindfulness (NY) 2021; 12(6):1332–49.
115. Lodha S, Gupta R. Mindfulness, Attentional Networks, and Executive Functioning: a Review of Interventions and Long-Term Meditation Practice. Journal of Cognitive Enhancement 2022; 6(4):531–48.
116. Kasamatsu A, Hirai T. An electroencephalographic study on the zen meditation (Zazen). Folia Psychiatr Neurol Jpn 1966; 20(4):315–36.
117. Murata T, Koshino Y, Omori M, et al. Quantitative EEG Study on Zen Meditation (Zazen). Psychiatry Clin Neurosci 1993; 48(4):881–90.
118. Hölzel BK, Ott U, Gard T, et al. Investigation of mindfulness meditation practitioners with voxel-based morphometry. Soc Cogn Affect Neurosci 2008; 3(1):55–61.
119. Davidson RJ, Kabat-Zinn J, Schumacher J, et al. Alterations in brain and immune function produced by mindfulness meditation. Psychosom Med 2003; 65(4):564–70.
120. Lutz A, Slagter HA, Dunne JD, Davidson RJ. Attention regulation and monitoring in meditation. Trends Cogn Sci 2008; 12(4):163–9.
121. Pagnoni G, Cekic M, Guo Y. "Thinking about not-thinking": neural correlates of conceptual processing during Zen meditation. PLoS One 2008; 3(9):e3083.
122. Kozasa EH, Sato JR, Lacerda SS, et al. Meditation training increases brain efficiency in an attention task. Neuroimage 2012; 59(1):745–9.
123. Kjaer TW, Bertelsen C, Piccini P, Brooks D, Alving J, Lou HC. Increased dopamine tone during meditation-induced change of consciousness. Brain Res Cogn Brain Res 2002; 13(2):255–9.
124. Luders E, Toga AW, Lepore N, Gaser C. The underlying anatomical correlates of long-term meditation: larger hippocampal and frontal volumes of gray matter. Neuroimage 2009; 45(3):672–8.
125. Lazar SW, Kerr CE, Wasserman RH, et al. Meditation experience is associated with increased cortical thickness. Neuroreport 2005; 16(17):1893–7.
126. Hölzel BK, Carmody J, Vangel M, et al. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Res 2011; 191(1):36–43.
127. Zrenner C, Ziemann U. Closed-Loop Brain Stimulation. Biol Psychiatry 2024; 95(6):545–52.
128. Vassallo M, Picozzi M. Managing brain-hype: Understanding and discriminating overemphasized brain-based allegations. Med Histor 2023; 7(3): e2023053.
129. Bublitz F, Almeida H, Luiz SOD, Perkusich A. Pervasive advertising: An approach for consumers and advertisers. Proceedings 2013 IEEE 3rd International Conference on Consumer Electronics; 2013 Sep 09-11: Berlin, DE. Berlin: IEEE; 2013.
130. van den Anker J, Reed MD, Allegaert K, Kearns GL. Developmental Changes in Pharmacokinetics and Pharmacodynamics. J Clin Pharmacol 2018; 58 Suppl 10:S10–S25.
131. Tully JL, Bridge O, Rennie J, Krecké J, Stevens T. The rising use of cognitive enhancement drugs and predictors of use during COVID-19: findings from a cross-sectional survey of students and university staff in the UK. Front Psychol 2024; 15:1356496.

132. Heinz A, Müller S. Exaggerating the benefits and downplaying the risks in the bioethical debate on cognitive neuroenhancement. Rethinking Cognitive Enhancement 2017; pp. 69–86.
133. Schelle KJ, Olthof BM, Reintjes W, Bundt C, Gusman-Vermeer J, van Mil AC. A survey of substance use for cognitive enhancement by university students in the Netherlands. Front Syst Neurosci 2015; 9:10.
134. Beauchamp TL, Childress JF. Principles of Biomedical Ethics (Principles of Biomedical Ethics. Oxford: Oxford University Press; 2008.
135. Gordon EC. Cognitive enhancement and authenticity: moving beyond the Impasse. Med Health Care Philos 2022; 25(2):281–8.
136. Leuenberger M. Authenticity in the Ethics of Human Enhancement. In Jotterand F, Ienca M, editors. The Routledge Handbook of the Ethics of Human Enhancement. London: Routledge; 2023. p. 131–40.
137. Tomažič T, Čelofiga AK. Ethical aspects of the abuse of pharmaceutical enhancements by healthy people in the context of improving cognitive functions. Philos Ethics Humanit Med 2019; 14(1):1–6.
138. Hendriks L, Mihalopoulos C, Le LK, Loo C, Chatterton ML. Cost-utility analysis of rTMS as add-on therapy to standard care for the treatment of hallucinations in schizophrenia. Eur Psychiatry 2022; 65(1):1–32.
139. McMaughan DJ, Oloruntoba O, Smith ML. Socioeconomic Status and Access to Healthcare: Interrelated Drivers for Healthy Aging. Front Public Health 2020; 8:231.
140. Dunlop C, Howe A, Li D, Allen LN. The coronavirus outbreak: the central role of primary care in emergency preparedness and response. BJGP Open 2020; 4(1):bjgpopen 20X101041.
141. Patel V, Saxena S, Lund C, et al. The Lancet Commission on global mental health and sustainable development. Lancet 2018; 392(10157):1553–98.
142. Cohen Kadosh R, Levy N, O'Shea J, Shea N, Savulescu J. The neuroethics of non-invasive brain stimulation. Curr Biol 2012; 22(4):R108–11.
143. Wardrope A. Authenticity and autonomy in deep-brain stimulation. J Med Ethics 2014; 40(8):563–6.
144. Bublitz JC, Merkel R. Autonomy and authenticity of enhanced personality traits. Bioethics 2009; 23(6):360–74.
145. Di Stefano N. The Idea of Beauty and Its Biases: Critical Notes on the Aesthetics of Plastic Surgery. Plast Reconstr Surg Glob Open 2017; 5(10):e1523.
146. Wexler A. The Social Context of "Do-It-Yourself" Brain Stimulation: Neurohackers, Biohackers, and Lifehackers. Front Hum Neurosci 2017; 11:224.
147. Goyal M, Singh S, Sibinga EM, et al. Meditation programs for psychological stress and well-being: a systematic review and meta-analysis. JAMA Intern Med 2014; 174(3):357–68.
148. Schulte-Frankenfeld PM, Trautwein FM. App-based mindfulness meditation reduces perceived stress and improves self-regulation in working university students: A randomised controlled trial. Appl Psychol Health Well Being 2022; 14(4):1151–71.
149. Segall S. Equality of Opportunity for Health. In: Eyal N, Hurst SA, Norheim OF, Wikler D, editors. Inequalities in Health. Oxford: Oxford Academic; 2013. p. 147–63.
150. Marmot M, Allen JJ. Social determinants of health equity. Am J Public Health 2014; 104 Suppl 4(Suppl 4): S517–9.
151. Wasserman J, Palmer RC, Gomez MM, Berzon R, Ibrahim SA, Ayanian JZ. Advancing Health Services Research to Eliminate Health Care Disparities. Am J Public Health 2019;109(S1):S64–S69.
152. Maslen H, Douglas T, Cohen Kadosh R, Levy N, Savulescu J. The regulation of cognitive enhancement devices: refining Maslen et al.'s model. J Law Biosci 2015; 2(3):754–67.
153. Cabrera LY, Fitz NS, Reiner PB. Empirical Support for the Moral Salience of the Therapy-Enhancement Distinction in the Debate Over Cognitive, Affective and Social Enhancement. Neuroethics 2014; (3):243–56.
154. Zheng J. Ethical Implications of Biohacking as Activism: Democratized Health Care, Danger, or What?. Aresty Rutgers Undergraduate Research Journal 2021; 1(3). Accessed: Nov. 13, 2024. [Online]. Available: https://www.academia.edu/70580628/Ethical_Implications_of_Biohacking_as_Activism_Democratized_Health_Care_Danger_or_What

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