« With the increasing number and performance of instruments related to brain imaging technologies (e.g., EEG, fMRI), there is a growing risk that the protection of one’s private life and personal information will be challenged. »

« Further tangible future applications include adapting advertisements to consumers’ preferences after reading their minds and gaining access to and taking advantage of health data and intimate thoughts. »
Scientific research on the brain has traditionally incorporated biochemical, electrophysiological and psychological methods to discern the molecular, electrical and behavioral bases of the brain’s function. The main goal was – and remains – to understand brain physiology and pathology to prevent or treat diseases. To that end, a wide range of pharmaceutical drugs, brain stimulation technologies and even gene technologies have been developed.

**Ultimately, it is predicted that the applications developed from such technologies may extend well beyond therapy and participate in human neuroenhancement.**

In a futuristic perspective, some of the novel brain interventions developed in recent decades might even result in the engineering of “super-brains” that might, for example, possess pseudo-telepathic powers to remotely control machines or other humans. Thus, the cognitive abilities of our brains are a central preoccupation of “transhumanism” a concept coined by the biologist Julian Huxley in 1957 that describes how human capacities might be extended beyond what would be considered the “normal functioning” of body and mind (Bostrom 2005). Although such a scenario today resembles a view of the future in a science fiction novel, the potential of using emerging technologies to enhance human beings has already raised a panoply
of concerns that stimulated scientific and socio-ethical debates.

The first part of this chapter explores traditional and modern strategies that enhance our cognition and our psychology (which we refer to as “neuroenhancement”) and that range from substances as common as coffee to today’s “smart drugs”, brain stimulation technologies and genetic or epigenetic engineering. The second part of this chapter consists of a discussion of the risk-benefit perspective of neuroenhancement, with an emphasis on why implementing such innovations in our society can be ethically sensitive.

**DRUGS AS ENHANCERS**

It seems that human beings have always searched for ways to render themselves “better” and “smarter”. Broad-spectrum plant-derived natural compounds for increasing neuro-functioning – such as Ginseng, Passion Flower, Hippophae and coffee – have been a full part of medical practice in various cultures for centuries. The effectiveness of these neuro-enhancing herbs in improving concentration and alertness was confirmed from a scientific perspective many years ago, and they have come to be collectively known as “adaptogens” (Brekhman and Dardymov 1969).

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**ADAPTOGENS ARE BOTH SOCIAIALLY AND ETHICALLY ACCEPTED ACROSS THE GLOBE. DESPITE THE FACT THAT MANY OF THEM, WHEN MISUSED, CAN HAVE SEVERE AND HARMFUL SIDE EFFECTS.**

With the emergence of modern science, we are able to isolate and purify natural substances – and synthesize new substances with neuro-enhancing properties. Stimulatory compounds that modulate perception, mood, consciousness, alertness and behavior include substances such as cocaine and amphetamines. Cocaine was first isolated in 1855 from the leaves of the coca plant and had become a frequently used stimulant in some countries, including the United States, by the beginning of the 20th century. For instance, it was used in the formulation of the early version of Coca-Cola. Amphetamines were chemically synthesized in 1927 and were initially used to treat asthma. Their stimulatory effect was soon noticed, and their use ranged from diet pills to anti-fatigue drugs, popular
in treating narcolepsy and in lengthening the attention span of soldiers during World War II.

In the late 1960s, the potential for the abuse of amphetamines and cocaine was recognized, which fostered further research that aimed to replace both substances and that led to the development of the first generation of synthetic psychotropics, including neuroepileptics, antidepressants and anxiolytics. However, those psychotropics were soon abandoned due to their unpleasant side effects, and were replaced by second-generation drugs known as “smart drugs” or “nootropics” – from the Greek words noos (mind) and trepein (turn, change) (Giurgea 1972). Nootropics are a class of psychotropic drugs that affect learning ability, concentration and memory. They protect the brain from injuries (both physical and chemical) and have no sedative or toxic effects. The first nootropic drug, Piracetam, was synthesized in 1964 by Dr. Cornelius E. Giurgea with the intention of enhancing brain function (Giurgea 1982). By advocating that:

"MAN IS NOT GOING TO WAIT PASSIVELY FOR MILLIONS OF YEARS BEFORE EVOLUTION OFFERS HIM A BETTER BRAIN”.

Giurgea paved the way for the development and increasing acceptance of neuro-enhancing drugs (Rose 2006).

Although “stimulants” are the most well-known nootropics, broad spectrums of substances are classified under the same term. This classification currently includes metabolic agents (e.g., creatine, carnitine), herbs and plant extracts (e.g., Bacopa Monnieri, St. John’s Wort), dopaminergics (e.g., Modafinil, Ritalin, Adderall), nutrients (e.g., choline, creatine), eugeroics (e.g., Modafinil, Adrafinil, Nuvigil) and racetams (Garnock-Jones and Keating 2009; Sulzer 2005). Despite their usefulness in treating disorders such as narcolepsy, Alzheimer’s and Parkinson’s diseases, in addition to attention deficit hyperactivity disorder (ADHD), the mode of action of many nootropics remains elusive (Mondadori 1994; Mondadori 1993).

Substances such as the narcolepsy drug Modafinil (Provigil®) – also called “Brain Viagra” – were so effective that they became popular within certain work communities (for instance, night-shift workers and students) (McCabe 2005; Gerrard and Malcolm 2007). Even Hollywood has
recognized their “usefulness” and expanded the possible scenarios of “future generation” drugs. Built on the urban myth that we commonly use only a small portion of our brain capacity, films such as Limitless (2011) or more recently Lucy (2014) have taken the possible effects of magic pills to an entirely new level. Both movies portray neuroenhancement as alluring, creating “super humans” with outstanding cognitive abilities.

**HOWEVER. THESE MOVIES ALSO RAISE IMPORTANT SOCIO-ETHICAL ISSUES. INCLUDING THE ABUSE OF POWER IN LIMITLESS AND THE FEAR OF LOSING WHAT MAKES US HUMAN IN LUCY.**

**BRAIN STIMULATION TECHNOLOGY**

Neuroenhancement strategies are not limited to “magic pills”.

**CUTTING-EDGE TECHNOLOGY ALSO INCLUDES BOTH INVASIVE AND NON-INVASIVE BRAIN-CONTROLLED MACHINES.**

Until recently, the actual implementation of these technologies was considered too futuristic and/or beyond the scope of realistic deliberations into their possible applications. However, in the movie Transcendence (2014), Hollywood has recently picked up on scenarios that might arguably be possible, challenging our perception of where human beings end and machines begin.

The significance of this field, which aims at understanding the neural connectivity of the brain, is also highlighted in the array of consortiums and projects on the topic launched in recent years. Between 2012 and 2014, the Human Connectome Project, the Human Brain Project and the BRAIN initiative were launched. The objective of the first project is to provide a network map of the normal brain. The second project uses computer simulations to increase our understanding of brain function. Building on previous knowledge, the third and newest project aims at “accelerating the development and application of innovative technologies” related to the brain (Bargmann and Nesome 2014).

**THE NON-INVASIVE TECHNOLOGIES USED TODAY ARE REPRESENTED BY “TRANS-CRANIAL MAGNETIC STIMULATION” AND “TRANS-CRANIAL DIRECT CURRENT STIMULATION”.**

They consist essentially of
non-invasive techniques (electrodes on the scalp) that transmit small magnetic fields and electrical currents to specific regions of the brain to increase or decrease neuronal activity in the stimulated area. These techniques are used to treat psychiatric disorders, depression, post-traumatic stress disorder or schizophrenia, Parkinson’s disease, and epilepsy (Rossi 2009). In addition to their therapeutic use, they have been shown to enhance cognition, selective attention (Gladwin, den Uyl, and Wiers 2012) and working memory (Fregni 2005). Other techniques, including “deep brain stimulation” and “neural prosthetics”, involve technological implants inserted into the brain and are therefore more invasive. Deep brain stimulation requires the implantation of an electronic device into the brain in combination with medication to provide curative or palliative solutions to severe disorders, such as obsessive-compulsive disorder, Tourette syndrome, Alzheimer’s or Parkinson’s diseases (Rabins et al. 2009). The most promising methods may be the so-called “brain-machine interfaces” (BMI), which typically do not require deep surgical implantation into the brain. BMIs are based on brain activity recording techniques, such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). These interfaces are mainly used for brain-computer communication and, to date, have come to play an important role in neurological rehabilitation (Dalv and Wolpaw 2008).

One of the most mature – and largely known – brain stimulation technologies is the Cochlear implant, which transforms sound waves into electronic signals and stimulates the auditory nerve to transfer information into the brain. Various artificial retinas have also been developed. Typically, these are connected to a small external computer (an “exocortex”) that processes the electronic information captured by the artificial retina and sends it to the visual cortex of the brain for detection. Further applications of the technology involve neural implants that relay voluntary motor signals to prosthetics or computers to correct movement disorders (Collinger 2013; Yanagisawa 2011).

During the last decade, the production of safer and more efficient brain implants, improved surgical procedures that render the insertion of deep brain stimulation devices
reversible, and a number of successful therapeutic trials have fostered the potential to apply this type of technology, for example, to memory enhancement (Bell, Mathieu, and Racine 2009). Much like the “magic pills” are becoming the norm in certain communities, we anticipate similar success for these brain-stimulating technologies.

**GENETIC ENGINEERING**

The interest in neuroenhancement through the use of “magic pills” or brain-machine interfaces is growing significantly. Nevertheless, as the pharmacological and technological interventions described above imply, these strategies have been developed to alter somatic and phenotypic traits, as opposed to germinal and genotypic traits. For this reason, they can typically only temporarily fix an abnormality, and frequent repetition of the treatment is often required. In other words, the neuroenhancement that is achieved by these means is not permanent over the long term and cannot be transmitted genetically to offspring.

When a permanent – and trans-heritable – neuroenhancement is intended, genetic engineering technology is necessary, at least for now and according to our best knowledge. The most recent decades of biological research have generated a large amount of information on the human genome that may indeed be of interest in developing more permanent neuroenhancement strategies in the future.

**THE GROWING KNOWLEDGE ABOUT THE GENES INVOLVED IN HUMAN COGNITION HAS LED TO NOVEL TREATMENTS TO RESTORE NEUROLOGICAL FUNCTIONS TO BE TESTED IN HUMANS.**

For instance, one of the first successful (2011) gene therapy trials in neurobiology was the treatment and cure of choroideremia, which causes successive blindness in males from childhood to middle age (Benjaminy, Macdonald, and Bubela 2014). Moreover, the human gene named rbAp48 was recently found to be involved in age-related memory loss (Pavlopoulos 2013). Notably, when this gene was knocked out in mice, the animals exhibited short-term memory loss, failing both novel object recognition tests and various maze experiments. When the gene was reintroduced, the mice
could remember new objects better and find their way out of the mazes. Such genes are foreseen as future candidates for restoring or enhancing cognitive functions.

As a complement to genetic research, epigenetics – the study of how the environment influences the expression of our genetic background without inducing any changes in the DNA sequence – has also been shown to play a key role in neurological processes and behaviors. It has been observed that maternal interaction with offspring in rats might alter the expression of a specific gene in the offspring by modulating DNA methylation – a chemical reaction that occurs in DNA strands (Weaver 2004). Different levels of methylation in this specific gene were found to influence the animals’ stress response in adulthood. Similar studies in humans have also revealed associations between early-life conditions (such as stress and social adversity) and the epigenetic programming of gene expression by DNA-reversible modifications that affect psychological health in adulthood (McGowan and Szyf 2010).

**During Embryogenesis, Fetal Development and Early Life – or by Reversing the "Epigenetic Programming" That Occurs Through DNA-Reversible Modifications – WE MIGHT HAVE FOUND NOVEL OPPORTUNITIES TO OPTIMIZE ONE’S FUTURE HEALTH.**

Despite the documented efficiency of the abovementioned trials in treating rare neurological disorders, genetic and epigenetic engineering in humans remains in its infancy. However, the increasing knowledge regarding our genome, in combination with the array of novel genome editing techniques, offers hope for the development of strategies that may possibly reverse detrimental innate genetic traits or acquired epigenetic variations programmed by adverse early-life conditions. Given that these technologies appear to be effective for therapeutic purposes, they also hold great potential for enhancing cognitive abilities in the future.

**Socio-Ethical Issues**

With these advancements in neurobiology and the potential for neuroenhancement they entail, certain ethical and social issues are
emerging. The first issue involves medical safety. It is commonly acknowledged that the clinical risks—unwanted side effects or unanticipated future outcomes to patients and research participants—must be minimized. The great complexity of the brain makes such interventions very sensitive. Before we implant an electronic device into someone’s brain, for instance, there should be no other alternative remaining, and the expected benefits should be significant and highly likely.

However a risk-benefit analysis that is grounded only in a clinical and therapeutic mindset may be insufficient in addressing:

« THE LARGER SOCIETAL RISKS THAT WE FACE WITH THE APPEARANCE OF A DIVERSITY OF NOVEL NEUROENHANCEMENT OPPORTUNITIES IN OUR LIVES. »

For instance, lowering the clinical risks of psycho-stimulants by developing smart drugs with only minimal side effects may simultaneously lower the threshold of benefits that are required for their acceptable implementation. Hence, the minimization of their clinical risks may lead to the trivialization of their use, which may lead to larger consequences for society, as we discuss below. For this reason, it is important to the subsequent regulation of their use to consider how these technologies can impact not only the health of individuals but also human life and the common good more generally.

FOR INSTANCE, PRIVACY AND CONFIDENTIALITY ISSUES ARE EMERGING AND SHOULD ALSO BE ADDRESSED.

With the increasing number and performance of instruments related to brain imaging technologies (e.g., EEG, fMRI), there is a growing risk that:

« THE PROTECTION OF ONE’S PRIVATE LIFE AND PERSONAL INFORMATION WILL BE CHALLENGED. »

For example, mind reading devices and research that aims to read intentions or the thoughts of criminals is steadily gaining interest in the justice system as a supplementary tool to assess one’s liability in a crime.

SIMILARLY, MILITARY USES OF MIND-READING TECHNOLOGY (FOR INSTANCE, TAKING INFORMATION FROM SOMEONE WITHOUT HIS CONSENT FOR
REASONS OF NATIONAL SECURITY MIGHT ALSO REPRESENT A POTENTIAL THREAT TO PRIVACY AND CONFIDENTIALITY.

Further tangible future applications include adapting advertisements to consumers’ preferences after reading their minds and gaining access to and taking advantage of health data and intimate thoughts.

With the development of “mind transferring” technologies – in which “individual knowledge” can be stored in computers – strong concerns related to the storage, processing and manipulation of such “sensitive” information are being voiced.

FOR INSTANCE, SHOULD EMPLOYERS OR INSURANCE COMPANIES HAVE ACCESS TO THIS INFORMATION? MOREOVER, MIGHT SUCH ACCESS LEAD TO DISCRIMINATION IN SOCIAL SECURITY OR EMPLOYMENT?

ADDITIONALLY, ISSUES RELATED TO INDIVIDUAL AUTONOMY AND SOCIAL JUSTICE MIGHT ALSO ARISE.

With the increasing use of nootropics to boost learning and memory capacity, we might enter into a “competition game” in which students and workers are asked to handle significantly more tasks based on their increased productivity and efficiency. Forecasting the future of previously existing trends, we may wonder whether the use of cognitive enhancers will remain a free choice.

« INDEED, THERE MIGHT BE INCREASING PRESSURE TO TAKE THESE DRUGS TO PERFORM. »

This may affect the free and voluntary decision-making process that should guide these actions. Further, if an increasing number of people use these drugs to boost their academic performance, we may wonder whether it is fair for the individuals who do not. If not everyone has access to cognitive enhancers, disparities in performance according to social status will likely be created and reinforced, further increasing the social gap between the rich and the poor. Hence, we might discuss the fairness of only certain people having the ability to enhance their human capacities, whereas others might not even have enough resources to reach their “normal” unenhanced human potential.

Further macroscopic economic issues are also at stake. Indeed, given
that the healthcare system is already cracking under the insurmountable costs of therapeutic health services:

> IS IT REASONABLE TO INVEST SO MUCH IN DEVELOPING NEURO-TECHNOLOGIES AND TO COVER THEIR NON-THERAPEUTIC USE WITH PUBLIC FUNDS WHEN WE – AS A SOCIETY – MIGHT NOT BE ABLE TO AFFORD IT?

In fact, doing so would lead not only to an undesirable extra financial burden on society but also (arguably) to another burden on the environment, given that the creation of these technologies requires substantial extra energy and materials, which are both limited resources. Inversely, the contemporary imperatives of a growing economy might be used as a rhetorical justification for increasing the required amount of productivity from individuals (e.g., workers, students) by elevating their cognitive potential. However, such a race for competition and productivity is endless. Is this how we want to live? We must be aware of both the economic constraints and the pressures of the economic model we have chosen if we aim for the ethical implementation of neuro-enhancers in our society.

With the mapping of the human brain and its connection to machines, we might increasingly perceive ourselves in mechanistic terms as being highly determined by our body, which these technologies can always “upgrade”. Following such a perspective, according to which all human behaviors may be explained by neurotransmitters and localized brain activity, which in turn might be subject to modulation to “improve” behavior, we might wonder whether concepts such as merit, motivation, courage and, above all, free will will continue to have the same value. In this context, what place would remain for individual choice and how might it modify the lived human experience?

Moreover, increasingly perceiving ourselves as mere biologically determined ‘automated machines’ – i.e., not influenced by God or any external spirit – we may well reconsider what place religion and more generally spirituality will hold in our societies.

In sum, critical questions emerge.

DO WE WANT PRIVACY AND CONFIDENTIALITY TO REMAIN IMPORTANT VALUES IN THE FUTURE?
Can we accept that our lives might be ruled by the pressure of an endlessly growing economy that keeps asking for more and more from each individual? How do we anticipate or expect to change? Will it be a bodily or a spiritual change? Will we remain ‘free creatures’? Adopting a precautionary approach to the implementation of neuroenhancement technology and finding answers to such questions is essential to appropriately prepare for its effect on our human and cultural identity and on what we think of and how we interact with other people.

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