

**OPINION N°122**

**The Use of Biomedical Techniques for “Neuroenhancement” in Healthy Individuals: Ethical Issues**

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## INTRODUCTION

The National Consultative Ethics Committee, in compliance with the ethical watch mandate over neuroscientific advances assigned to it by the July 27th 2011 Law on Bioethics, having previously considered the ethical issues arising out of functional MRI<sup>1</sup>, decided to devote some thought to neuroenhancement.

Human beings have always attempted to improve their performance or their well-being by the process of learning, through mastering the use of tools or resorting to substances such as coffee, alcohol or hashish, to quote but a few examples. The possibilities for healthy human beings to improve themselves (*human enhancement*) have been singularly increased by progress in the medical, surgical and pharmaceutical sciences. Broadly speaking, such improvements can be related to physical appearance (for instance, hair transplants, tattoos, plastic surgery, etc.), physical performance (drugs in sports, sexual stimulants, etc.), or to achieve what is now called “*brain enhancement*” or “*neuroenhancement*”. The reason why brain- or neuroenhancement is singled out within general “*human enhancement*” is due to the brain’s preponderant role in human psycho-cognitive performance and to the explosion of knowledge concerning cerebral function, as well as to an exponential development of techniques capable of modifying this cerebral function.

The English expressions “*brain enhancement*” and “*neuro enhancement*” have been respectively translated into French as “*augmentation cérébrale*”, “*amélioration cérébrale*”, “*optimisation cérébrale*”, “*dopage cérébral*”, “*botox pour le cerveau*” (botox for the brain), or “*neuro-augmentation*”, “*neuro-amélioration*”, “*neuro-optimisation*”, etc. referring respectively to augmentation, improvement, optimisation, doping, etc. of brain function. This abundance of different versions is evidence of the difficulty of adequately conveying in French the dual dimension — both quantitative (augmentation) and qualitative (amelioration, improvement) — of the English word “enhancement”. The French words “*augmentation*” and “*amélioration*”, however, are not synonymous and for that matter do not always go hand in hand. For instance, psychoaffective and cognitive function can be improved by a reduction in anxiety or by the attenuation of the emotional burden of certain traumatic memories. Although the French expressions “*homme augmenté*” or “*cerveau augmenté*” are in widespread use, in this Opinion we have chosen to use “**neuro-amélioration**” as meaning “neuroenhancement”. Furthermore, in this way we can avoid using the French words for “brain” and for “optimisation”, the former having excessively anatomical connotations and the latter being beyond any possibility of evaluation. It also reflects the object of the process, i.e. “psychocognitive amelioration”, without the use of such instantly negative wordings as “doping” and “botox” applied to the brain.

Throughout the history of human maturation, the means for psychological and cognitive development have abounded within family and social environments, if only through nutrition and education. These, however, are not the subject of this Opinion which will be concerned with ethical issues arising out of the use of **biomedical neuroenhancement**, i.e. involving the use of techniques capable of modifying cerebral activity (neuro-modulating techniques). Initially developed to study or treat pathological conditions, these techniques are increasingly used in healthy individuals primarily for purposes of cognitive research, but sometimes also for the enhancement of cerebral performance. They are no longer restricted to consuming pharmaceutical products; they currently call on various kinds of external electrical or magnetic stimulation through which subjects control their own cerebral activity, either to modify it for their own benefit (feedback), or to control an external appliance (artificial limbs, targets, robots, etc.). Tools capable of neuromodulation are constantly being newly

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<sup>1</sup> CCNE’s Opinion n°116 dated February 23rd, 2012.

developed (video games, Google Glass, etc.) but will not be entering the scope of this Opinion since they are not, strictly speaking, biomedical techniques.

**The expression “neuroenhancement”** could give the impression that the phenomenon it describes is established. In point of fact, it is **ambivalent**: it describes a problematic situation that needs to be evaluated, not directly established results considered to be self-evident. Moreover, it reflects two entirely distinct situations: one the one hand, modulation in the form of an increase of cerebral activity through biomedical techniques and, on the other hand the use of such techniques by certain people whose health is in no way impaired. As a result, the concept covered by this expression includes the effects induced by such modulation and also the supposed intent to enhance.

The study of neuroenhancement is fraught with **considerable methodological difficulty**, so that the results of the great number of enquiries and research efforts that have been undertaken on the subject must be approached with an open, but critical, mind and extreme caution.

The decision to “enhance oneself” is an individual decision, but its underlying motivations and, to a lesser degree, its consequences, are essentially societal. **The biomedical neuroenhancement phenomenon can only be considered in relation to a given socio-cultural and economic context.** Currently, it mainly concerns affluent countries. **This Opinion will therefore be considering the ethical issues arising out of the use of biomedical techniques for the purpose of neuroenhancement in this context.**

The issues are numerous:

Is there a dividing line between “normal” and “pathological” in psycho-cognitive terms?

What biomedical techniques are being used?

Is there an enhancement or a deterioration of cerebral function, in both the short and the long term?

Why should people want to enhance their brains, or someone else’s brain, and who is entitled to decide on the need to enhance?

Is there such a thing as a ‘medical enhancement’ discipline and who will be carrying its cost? What is the status of research on this subject?

Are there limits to neuroenhancement?

## **I FROM NORMAL TO PATHOLOGICAL, PUT TO THE TEST OF NEUROENHANCEMENT**

Historically, over the last two centuries, normality has received the closest degree of attention in two domains, public health and education. **Pedagogical and health prototypes** were the outcome, in particular as regards rules of hygiene. (Canguilhem, 1966<sup>2</sup>). In Latin, “*norma*” means “carpenter’s square” and “*normalis*” means “perpendicular”. In fact, the word “normal” only came quite late into French usage, first appearing in 1759. To rectify something which is tortuous and twisted, to make it normal, presupposes that the thing is not straight (*idem*). The possibility of a norm stems from a norm experienced. Norms are not given *a priori* and are not pre-established. When taking into consideration the person experiencing the norm, the question becomes: what behaviour is sufficiently privileged for it to appear as being normal? This behaviour is not necessarily the most frequent, since while frequency expresses the norm, it is not inferred from the norm. Frequency does not reveal anything of the capacity to institute norms, nor of normality in relation to a maximum capacity. There is always a preferred choice that we call “normal” and a depreciated rejection cast as “pathological”.

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<sup>2</sup> Canguilhem, G., *Le normal et le pathologique*, Puf, Quadrige, 1966<sub>1</sub>. (On the normal and the pathological).

**The dividing line between normal and pathological** seems easy enough to draw when it is based on a measurement such as glycaemia for diabetes or arterial blood pressure for hypertension, although even with such disorders, the borderline tends to change. Systolic arterial blood pressure defining hypertension has moved from 160 to 140 mmHg and expressions such as “prehypertension” or “prediabetes” are now in use. **In psycho-cognitive matters**, where there is no such thing as a norm or a measurement despite the existence of a host of scales, **it is impossible to define a dividing line**; expert consensus conferences have to be convened to formulate pathological entities and define diagnostic criteria. In psychiatry, the renowned American diagnostic classification manuals (DSM<sup>3</sup>), the fifth edition of which was published very recently, are moving in the direction of revisiting the major frameworks of classic psychopathology which, until now, had defined the boundaries between normal and pathological, and replacing them with sets of observable items. These developments intended to favour diagnostic reliability may be achievable to the detriment of pertinence regarding the definition of these entities. Phenomena, hitherto considered to be within the bounds of normality, end up on the list of pathological disorders and are treated as such. Controversies over grief and childhood anger are an example: grief turns into depression and antidepressants are prescribed; a turbulent child suffers from “attention deficit hyperactivity disorder” (ADHD) and is treated with methylphenidate, etc. Borderlines between normality and pathology have become blurred and fluctuant, and are frequently unsupported by research-based data. At the same time, they are the subject of heated debate influenced by pressure groups and lobbies. When DSM-5 was published in May 2013, Thomas Insel, Director of the National Institute of Mental Health, was sharply critical and suggested a confrontation with a new project, the Research Domain Criteria (RDoC), which relies on new paradigms for the understanding of mental disorders, based on endophenotypes linking clinical data to biological, genetic and imaging criteria so as to escape from the constraints of definitions which have become blurred and inflationist. Furthermore, thanks to recent neural plasticity and epigenetic studies, certain vulnerabilities and individual case histories can be mapped, thus breaking out of the classic categories of psychopathology and psychiatric nosology.

**For some, neuroenhancement extends beyond normality**, to quote Rothman, S&D, 2003<sup>4</sup>: “Cure seeks to restore health by applying a remedy... By contrast, enhancement seeks to **surpass the normal**, aiming to situate individuals at the far end of the curve”. The object is to maximise a function or to provide the function with “above-species typical capacities” (Harris, 2007)<sup>5</sup>, not forgetting that the departure from normal may in turn become the norm. And so we arrive at a range of normality, with a “high normal” and a “low normal”. The question at issue is whether the boundary is really clear between restoring health and improving certain functions, itself related to the issue of the distinction between normality and pathology. By opting for the “above normal”, neuroenhancement distances itself from the duality between normality and pathology. The spectrum of its applications is gradually broadened and thereby disconnected from the pathological. Technical action can easily displace boundaries. For example, how do we know whether Ritalin is prescribed to treat attention disorders or to make a potential hypertrophic? (Hughes, 2004)<sup>6</sup>. We now observe that the line separating the pathological from the normal has shifted.

**Substances such as beta blockers, melatonin, caffeine just make healthy people feel “good”**, like they always should have been, as it is argued in some quarters. Are they enhanced? Are

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<sup>3</sup> DSM-5. Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition. American Psychiatric Association. 2013 <http://www.dsm5.org>

<sup>4</sup> S.Rothman and D.Rothman, *The Pursuit of Perfection*, New York, 2003, p. XIII.

<sup>5</sup> Harris J., *Enhancing Evolution*, quoted by J Y Goffi, « Thérapie, augmentation et finalité de la médecine, in « Enhancement » Ethique et philosophie de la médecine de l'amélioration, Vrin, 2009, p. 114.

<sup>6</sup> Hughes J., *Citizen Cyborg*, Westview Press, 2004, p.37.

they drugged? The debate is not a scientific one since this grey area in the normal to pathological continuum obviously points to the WHO definition of health and how a given society wishes to be endowed with it.

**This difficult problem, the hazy frontier between normality and pathology, is aggravated by the very existence of neuroenhancement techniques.** Even though subjective suffering is not in itself a criterion sufficient for classifying a condition as pathological— some forms of suffering are said to be “normal” and there are pain-free pathological conditions that do not give rise to any subjective complaint — subjective suffering does nevertheless enter into the definition of the pathological domain. As a result, a person’s belief in the possibility of improving psychocognitive capacity, be it genuine or illusory, displaces the frontier even further as it reduces the pain tolerance threshold. Not being neuroenhanced would be exacerbating a new kind of deprivation. Such a process could lead to the creation of new pathological categories, or in the event that the DSM’s particular classification process continues to be in use.

**The frontier is blurred between enhancement on the one hand, restoration and treatment on the other.** Moreover, it fluctuates along with what is proposed as the dividing line at a given time, to differentiate between normal and pathological. Nor can there be a clear frontier between therapeutic research involving a sick person and cognitive research involving a healthy person, even though methodological imperatives make it necessary to use highly restrictive criteria to try and define “certainly sick” and “probably normal”. Frequently, research on healthy subjects develops as a result of the findings of research on people who are sick. Similarly, although the purpose of cognitive research in healthy subjects may not be neuroenhancement, it is essentially on the basis of data acquired by cognitive research that neuroenhancement developed.

## II NEUROMODULATING BIOMEDICAL TECHNIQUES

There are two types of biomedical techniques capable of modifying cerebral activity for the purpose of neuroenhancement: 1) medications diverted from their therapeutic indications, a subject of numerous studies and the major thrust of current debate on neuroenhancement; 2) technical devices applied to the brain, essentially for cognitive or therapeutic research. In the current brain research funding context, these techniques are undergoing rapid development. New substances (ampakines, oxytocin, new serotonin re-uptake inhibitors, etc.) and new instruments such as transcranial pulsed ultrasound are being developed, but this Opinion will only refer to substances and techniques which are already in widespread clinical use.

### IIa – Medication taken orally

**Drugs used for neuroenhancement** belong to various pharmacological categories and are prescribed to treat a variety of pathological indications. The first group is made up of **anxiolytics, mainly benzodiazepines**, first and foremost among them being Diazepam (Valium). In the 1970s, this particular medication was incredibly popular (Valium mania) and came to be used not just for anxiety disorders but also for coping with all the commonplace upsets of everyday life until the time when its adverse side effects came under closer scrutiny: attention deficits, drowsiness causing road accidents, dependence followed by addiction (Pieters 2009)<sup>7</sup>.

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<sup>7</sup> Pieters T et al. Psychotropic drug use: between healing and enhancing the mind. *Neuroethics* 2009 ; 2 : 63-73.

A second class of drugs is made up of **antidepressants**, in particular those increasing cerebral serotonin levels such as Fluoxetine (Prozac) which was put on the market in 1989 and swiftly became known, mainly by the media, as a “miracle drug”, a “personal optimiser”, able — even for people who were not depressed — to reduce selectively negative feelings, lower social inhibitions, induce a general state of psychic well-being and improve social performance (Elliott 2000)<sup>8</sup>. A “Prozac mania” ensued so that in 1994, Prozac was the second most sold drug in the world until consumption declined due on the one hand to the appearance on the market of new antidepressants, and to increased awareness of the risks of tolerance, addiction and above all, suicide, particularly in adolescents. We need not look any further than Prozac for an illustration of the difficulty in defining a borderline between normal and pathological since some people use the drug regularly for as much as ten or fifteen years for no therapeutic indication, but because they feel that their wellbeing is impeded by minor dysfunctions which remain scientifically unexplored: here the effect is observed before the process is fully understood. Some medications, which to be precise are neither anxiolytic nor antidepressant, may be taken occasionally, among them Propranolol, a treatment for hypertension, which is also indicated for post-traumatic stress disorder as it can dampen the emotional impact of certain traumatic memories (Pitman 2002)<sup>9</sup>. It is also in frequent demand as an anxiolytic for limited periods of time by, for example, students before taking an examination or performers to prevent stage fright.

**Cholinesterase inhibitors** are a third group of drugs. Their indication is to treat Alzheimer’s disease but they are increasingly used in restoration attempts to deal with age-related memory loss. Their still largely unexplored effects on healthy individuals could include performance improvement in some very specialised tasks: in response to emergencies, pilots involved in flight simulation activities who had been taking a 5mg dose of Donepezil for the past month, performed better than pilots taking placebos (Yesavage et al. 2002)<sup>10</sup>.

Currently, these first three groups of drugs (anxiolytics, antidepressants and cholinesterase inhibitors) are considerably less in use for neuroenhancement than are substances of a fourth group, **cognitive enhancers or stimulants**, such as **methylphenidate**, **modafinil** and **amphetamines** on which most neuroenhancement studies were based. Methylphenidate (Ritalin, ConcertaLP, Quasym, etc.) is used to treat attention deficit hyperactivity disorder (ADHD) in children and adolescents (a disorder for which diagnostic criteria have been considerably extended along with successive editions of DSM). Modafinil (Modiodal, Provigil, Alertec, Modasomil, etc.) was approved for the treatment of daytime hypersomnia in narcolepsy.

**The effects of these cognitive stimulants** as observed in individual studies with healthy subjects, are often divergent or even contradictory. They have been the subject of several **systematic reviews** and **meta-analyses** (Repantis 2010<sup>11</sup>, Smith and Farah<sup>12</sup> 2011, Ragan 2013<sup>13</sup>). Methylphenidate seems to have a positive effect on long-term memory consolidation, particularly when the time lapse between learning and retrieval phases is lengthy. However, in a meta-analysis

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<sup>8</sup> Elliott C. Pursued by happiness and beaten senseless. Hastings Center Report 2000; 30: 7-12.

<sup>9</sup> Pitman R et al. Pilot study of secondary prevention of posttraumatic stress disorder with propranolol. Biol Psychiatry 2002; 51: 189-192

<sup>10</sup> Yesavage J et al. Donepezil and flight simulator performance : effects on retention of complex skills. Neurology 2001; 59: 123-125.

<sup>11</sup> Repantis D et al. Modafinil and methylphenidate for neuroenhancement in healthy individuals: a systematic review. Pharmacol.Res. 2010; 62: 187-206.

<sup>12</sup> Smith MF et al. Are prescription stimulants “smart pills”? The epidemiology and cognitive neuroscience of prescription stimulant use by normal healthy individuals. Psychol.Bull. 2011; 137: 717-741.

<sup>13</sup> Ragan CI et al. What should we do about student use of cognitive enhancers? An analysis of current evidence. Neuropharmacology 2013; 64: 588-595.

covering 46 studies, it did not seem to have an effect on attention, mood or executive functions. The author's conclusion was that there was insufficient objective evidence of positive effects in healthy individuals (Repantis 2010<sup>14</sup>). Modafinil would seem to be more effective: it improved attention and was found to perform better than placebo in maintaining wakefulness, memory and executive functions in sleep-deprived individuals, according to a meta-analysis of 45 studies. (Smith and Farah<sup>15</sup> 2011). A positive effect on working memory, cognitive flexibility, planning speed and non verbal creativity was observed independently of any wakefulness effect, but mainly in subjects whose basic cognitive level was below average (Muller 2013)<sup>16</sup>. In all of the studies, there was a high degree of individual response variability: large doses of methylphenidate are required to achieve a positive effect in poor-performing subjects, whereas small doses are sufficient with high-performing participants (Finke 2010)<sup>17</sup>. In several studies, amphetamines were shown to have significant positive effects on memory and executive functions, but this was not confirmed in a large recent double-blind placebo-controlled study using a very large number of tests in 46 young adults of both sexes (Ilieva et al 2013)<sup>18</sup>.

## **Iib - Techniques used**

**Iib1 - Non invasive transcranial brain stimulation techniques** are used to focus stimulation to target a modification of cerebral activity. They include transcranial magnetic stimulation (TMS), developed some fifteen years ago and, more recently, transcranial direct current stimulation (tDCS). TMS involves delivering, through a coil placed on the skull, a magnetic current generating a current sufficient to influence neuronal activity in cortical regions: down regulating excitability after low-frequency stimulation and up regulating excitability with high frequencies. As for tDCS, weak electrical currents are applied through two surface electrodes (anode and cathode) placed on the skull. The effect varies with current polarisation: neuronal excitability increases with anode stimulation and decreases with cathode stimulation. TMS has greater spatial and temporal resolution but is not convenient for placebo stimulation. It is relatively difficult to use, there is a risk (very low) of epilepsy, and it is expensive. The tDCS method is used increasingly because it is more comfortable, more mobile and not as costly. These techniques are beginning to have therapeutic applications in psychiatry, for ADHD and depression for example, as well as in neurology for instance for the recovery of motor or cognitive function after a stroke (Hamilton 2011<sup>19</sup>, Thibaut 2013). It is worth noting that both techniques can also be combined with cognitive stimulation software so as to involve the subject in very specific cognitive tasks (attention, memory, arithmetic, visual perception, etc.) while certain cerebral regions or networks are being stimulated with TMS or tDCS<sup>20</sup>.

**For healthy individuals**, data is being accumulated (over 200 studies to date) suggesting the possibility of enhancing cognitive performance and emotional status: for cognitive capacities, facilitation of motor, somatosensory, visual perception and language learning processes have been observed, as well as enhanced verbal, visuospatial or emotional memory processing; attention, numeracy, graphic capacities and executive functions. Somewhat less simple tasks, such as statistical classification learning, solving complex problems, decision making in difficult circumstances, have

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<sup>14</sup> Cf note 11.

<sup>15</sup> Cf note 12.

<sup>16</sup> Müller U et al. Effects of modafinil on non-verbal cognition, task enjoyment and creative thinking in healthy volunteers. *Neuropharmacology* 2013; 64: 490-495.

<sup>17</sup> Finke K et al. Effects of modafinil and methylphenidate on visual attention capacity: a TVA-based study. *Psychopharmacology* 2010; 210: 317-329.

<sup>18</sup> Ilieva I et al. Objective and subjective cognitive enhancing effects of mixed amphetamine salts in healthy people. *Neuropharmacology* 2013; 64: 496-505.

<sup>19</sup> Hamilton R et al. Rethinking the thinking cap. Ethics of neural enhancement using noninvasive brain stimulation. *Neurology* 2011; 76: 187-193.

<sup>20</sup> See for example a U.S. clinical trial on Alzheimer's disease: <http://clinicaltrials.gov/show/NCT01504958>.

also been modulated. Emotional status and mood can also be modified, in particular by pre-frontal cortex stimulation. Various aspects of social cognition have been open to modification, for instance moral judgement and intentionality<sup>21</sup>, discernment, altruism, feelings of injustice or the propensity to lie or to deceive which can be facilitated or repressed depending on the prefrontal cortex stimulation parameters<sup>22</sup>. The observed effects are temporary and stimulation is applied just before the task to be performed or while it is being performed, but effects persisting over several weeks can be obtained with “repetitive” TMS or by prolonging tDCS application.

## **Ib2 - Neurofeedback**

**Neurofeedback differs from the two techniques above in that it is the subjects themselves who learn how to self-regulate in real time their own brain activity**, in response to information on this activity, imparted visually more often than not, but also through auditory or sensorial channels. The oldest and most frequently studied technique uses electroencephalography (EEG biofeedback). Electrodes placed on the scalp record cortical neuronal activity in the form of waves of various frequencies and amplitudes which are retransmitted immediately to the subject *via* a computer. Subjects then become aware of their own cerebral activity and can learn through successive biofeedback sessions to modify it, for example by increasing the production of very fast gamma waves connected with extreme attention, or the more ample and slower alpha waves associated with relaxation (Hammond 2011)<sup>23</sup>. A number of other techniques have been developed; they either use the EEG itself (low frequency neurofeedback for passive regulation) or other ways of reflecting brain function, such as infrared spectroscopy (Mihara 2012)<sup>24</sup>, but mainly functional magnetic resonance imaging (fMRI) which has the advantage, unlike EEG, of showing activity in all cerebral regions, including subcortical (Weiskopf 2012<sup>25</sup>). Clinical indications under study include mainly ADHD, learning and developmental disorders, as well as a number of other psychiatric or neurological conditions: brain damage after a stroke, Parkinson’s disease, epilepsy, alcoholism, drug addictions, chronic pain, tinnitus, etc. (Hammond 2011, Weiskopf 2012<sup>26</sup>, Mihara 2013<sup>27</sup>).

**Studies involving healthy subjects** have shown that some four people out of five are capable of learning, more or less rapidly, to modify their brain activity with the possibility of enhancing certain cognitive capacities, in particular short term and working memory (Angelakis 2007)<sup>28</sup>, learning,

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21 Stimulation of the right temporoparietal junction renders a subject more sensitive to the action than to the intention, even when the intention is to do harm, unless the action itself is dangerous, (Young 2010: Young L et al. Disruption of the right temporoparietal junction with transcranial magnetic stimulation reduces the role of beliefs in moral judgements. Proc Natl Acad Sci USA 2010; 107: 6753-6758.)

22 In one study, subjects must accept or refuse to share out a sum of money. If they refuse, no one gets the money. Generally subjects refuse to share when the division is considered to be particularly unfair. However, if an area in the right prefrontal cortex is inhibited, subjects accept an invidious sharing out suggesting that motivation for gain, however small, has taken precedence over a feeling of injustice (Knoch 2006: Knoch D et al. Diminishing reciprocal fairness by disruption of the right prefrontal cortex. Science 2006; 314: 829-832).

<sup>23</sup> Hammond DC. What is neurofeedback: an update, Journal of Neurotherapy: investigations in Neuromodulation, Neurofeedback and Applied Neuroscience 2011; 15: 305-336.

<sup>24</sup> Mihara M et al. Neurofeedback using real-time near-infrared spectroscopy enhances motor imagery related cortical activation. Plos one 2012; 7: 232-234.

<sup>25</sup> Weiskopf N. Real-time fMRI and its application to neurofeedback. Neuroimage 2012; 62: 682-692.

<sup>26</sup> Cf note 24.

<sup>27</sup> Mihara M et al. Near-infrared spectroscopy-mediated Neurofeedback enhances efficacy of motor imagery-based training in poststroke victims. A pilot study. Stroke 2013; 44: 1091-1098.

<sup>28</sup> Angelakis E et al. EEG neurofeedback: A brief overview and an example of peak alpha frequency training for cognitive enhancement in the elderly. The Clinical Neuropsychologist 2007; 21: 110-129.

reaction time and visuospatial capacities as well as executive functions (Enriquez Geppert<sup>29</sup>, 2013). Enhancement has also been reported for other types of activity, such as artistic performance (dancing, instrumental music, singing, etc.) sports (golf, archery, etc.) and even surgery (Hammond 2011)<sup>30</sup>.

### **Ib3 – Deep brain stimulation**

Deep brain stimulation (DBS) is an invasive neurosurgical procedure involving the implantation of microelectrodes in very specific target areas, varying with indications, deep inside the brain. They are connected to an adjustable stimulator, placed under the skin. It was first used successfully from 1987 onwards to treat abnormal movement, initially in Parkinson's disease and later in other disorders such as essential tremor, dystonia and the tics in Tourette syndrome. DBS was then used experimentally for treatment-resistant epilepsy or chronic pain (Benabid 2012<sup>31</sup>, Lozano<sup>32</sup> 2012). Unexpected psycho-cognitive effects were observed so that the DBS scope of investigation was very swiftly extended to psychiatric disorders with successful outcomes reported for extreme cases of major depression resistant to all previous treatments (Mayberg<sup>33</sup> 2005), for severe obsessive-compulsive disorder (Mallet<sup>34</sup> et al 2008) and *anorexia nervosa* (Lipsman<sup>35</sup> 2013). Research was then further extended to a broad variety (over 200 trials under way), ranging from persistent vegetative states to addictions (to alcohol, morphine, opium, etc.), obesity, bulimia, aggressiveness and even hypertension or memory loss in Alzheimer's disease (Laxton<sup>36</sup> 2010).

The use of an invasive procedure such as DBS for neuroenhancement would appear to be unimaginable, presenting as it does, *inter alia*, a 2 to 5% risk of infection or stroke. However, in view of the very circumscribed nature of its outcome, the potential reversibility of its effects and the current exponential expansion of its investigative spectrum are such that this possibility is no longer beyond belief (Johansson 2011)<sup>37</sup>.

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<sup>29</sup> Enriquez-Geppert S et al. Boosting brain functions : improving executive functions with behavioral training, neurostimulation and neurofeedback. International Journal of Psychophysiology 2013; <http://dx.doi.org/10.1016/j.ijpsycho.2013.02.001>

<sup>30</sup> A study on ophthalmologists' training for microsurgical techniques revealed that those who completed 8 EEG neurofeedback sessions were quicker to learn, less anxious and managed to reduce the length of time of their surgical procedures by 26%. Ros T et al : Optimizing micro surgical skills with EEG neurofeedback. BMC neurosciences 2009; 10: 10-87.

<sup>31</sup> Benabid AL et al. *De la stimulation cérébrale profonde aux interfaces cerveau-machine : l'apport des micro-nanotechnologies*. Nanosciences en médecine 1 vol. Springer science 2012 ; 85-95. (From deep brain stimulation to brain-machine interfaces: the contribution of micro-nano technology. Nanosciences and medicine.)

<sup>32</sup> Lozano AM. Deep brain stimulation therapy. Effectively treats movement disorders and could work in neuropsychiatric conditions. BMJ 2012; 344: e1100.

<sup>33</sup> Mayberg HS et al. Deep brain stimulation for treatment-resistant depression. Neuron 2005; 45: 651-660.

<sup>34</sup> Mallet L et al. Subthalamic nucleus stimulation in severe obsessive-compulsive disorder. N Engl J Med 2008; 359: 2121-2134.

<sup>35</sup> Lipsman et al. Subcallosal cingulate deep brain stimulation for treatment refractory anorexia nervosa. A phase 1 pilot trial. Lancet 2013;381:1361-1370.

<sup>36</sup> Laxton AW et al. A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease. Ann Neurol 2010; 68: 521-534.

<sup>37</sup> Johansson V et al. Beyond blind optimism and unfounded fears: deep brain stimulation for treatment resistant depression. Neuroethics 2011. DOI 10.1007/s 12152-011-9112-x. In an enquiry directed at 299 American neurosurgeons, members of the World Society for Stereotactic and Functional Neurosurgery, 54% of responders were convinced that DBS would be used for neuroenhancement in future; only 48.6% considered DBS to be unethical for the purpose of improving memory; 56.8% considered it ethically justifiable to use the technique for reducing the sexual urges of sexual predators who requested this to be done (Lipsman 2011: Lipsman N et al. The contemporary practice of psychiatric surgery: results of a survey of North American neurosurgeons. Stereotact Funct Neurosurg 2011; 89: 103-110.). In another study,

**To sum up**, neuromodulating drugs and devices are essentially studied and used, with an ever-broadening range of indications, for the symptomatic treatment of certain neurological and psychiatric disorders. The fact that certain unexpected psychocognitive effects have been observed, together with the very rapid development of non invasive techniques, has led to an explosion in the number of cognitive research studies involving healthy subjects, with effects being observed on memory, alertness, arithmetic, power of reasoning, mood, emotional status and social cognition. **Such fragmentation is far removed from reflecting the global psychocognitive function of human beings.** Furthermore, these effects are **labile, limited, partial** and short-lived. And yet, it is observation based on these effects that has led to the development of the biomedical neuroenhancement phenomenon.

### III – BENEFITS AND RISKS?

It should be emphasised from the outset that **the risk-benefit ratio of the biomedical techniques used for neuroenhancement cannot be evaluated** at the present time. This is because the short-term studies referred to above address cognitive research and not neuroenhancement and they are hindered by major methodological bias. As for long-term data, there are none due to the fact that these techniques have only recently emerged and that neuroenhancement epidemiological follow-up studies are difficult to set up.

#### III a – The short term

The major **methodological difficulties** in the above mentioned studies are such that an interpretation of their results is of questionable value: the subjects are volunteers, which necessarily introduces a selection bias; numbers recruited are small which is a curb on statistic validity; mandatory experimental conditions as regards diet, sleep or coffee consumption do not reflect real-life situations; tests are carried out after a single dose of medication or a single brief focal stimulation, so that there is no way of knowing whether a benefit would be lasting after long term repeated use; studies are rarely double-blinded and placebo-controlled; individual results vary with the cognitive performance baseline level, the metabolic characteristics of the substances being tested, the genotype of the enzymes involved and the response to placebo; the studies are using a battery of tests with the risk that, in view of the great number of tests performed, finding a positive test result could be solely due to chance.

On the debit side, despite the beneficial psychocognitive effects described above, there are some negative effects: decreased improvement after methylphenidate administration with high cognitive baseline subjects (Finke 2010<sup>38</sup>); non linear (U-shaped) dose-response relationship, with zero effects, or even detrimental effects with certain doses (de Jongh<sup>39</sup> 2008); inhibition of the activity of a cortical area close to the one being stimulated during focal brain stimulation; paradoxical effect depending on the type of EEG neurofeedback with, for example, enhancement of working memory to the detriment of cognitive processing speed, and *vice versa* (Angelakis 2007<sup>40</sup>). Such negative effects are rare, so that on the whole the balance seems to be in favour of positive effects, but on the one hand,

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neurosurgeons were agreeable to using DBS for violent or antisocial patients. (Fumagalli 2012 : Fumagalli M et al. Functional and clinical neuroanatomy of morality. Brain 2012; 135: 2006-2021).

<sup>38</sup> Cf note 17.

<sup>39</sup> De Jongh R: Botox for the brain: enhancement of cognition, mood and prosocial behavior and blunting of unwanted memories. Neuroscience and Biobehavioral Reviews 2008; 32: 760-776.

<sup>40</sup> Cf note 28.

there is always a publication bias to the advantage of positive studies and, on the other hand, is it truly of benefit to the person concerned if, for example, memory improvement brings back to mind painful episodes in the past or prevents their being committed to oblivion? And how should the globally improved function of the subject be quantified and not just the improved results of a given specific test? Current studies cannot supply the answers to these questions.

**People using neuroenhancement techniques have a highly favourable opinion of their effects**, contrasting with the relatively modest outcomes of studies. **This gap between perceived benefit and results observed** yawns even wider in real-life conditions: 70% of methylphenidate users allege a positive or very positive effect and the highest consumers are those whose satisfaction scores are highest. They do not hesitate to claim, in the media or over social networks, spectacular improvements in their intellectual performances, like a Harvard student who stated in the Washington Post that: “In all honesty, I haven’t written a paper without Ritalin since my junior year in high school.” (Rabiner 2009<sup>41</sup>, Laurance<sup>42</sup> 2003 quoted by Outram<sup>43</sup> 2012). The same discrepancy was also observed, for instance, for omega-3 polyunsaturated fatty acids supplementation, which is perceived as being beneficial for cognition whereas double blind studies and their meta-analysis have produced no evidence whatsoever of enhanced cognitive test performance (Luchtman<sup>44</sup> 2013). Several theories have been put forward to explain the impact of the perceived individual benefit: placebo effect with all its still mystifying characteristics, the ripple effect due to the proximity of other enthusiastic users of “smart pills”, “study tools” and “brain steroids”, the self-image enhancement effect, illusion owing to excessive self-confidence, alertness effect in people who do not get enough sleep, a genuine pharmacological effect on people with undiagnosed ADHD, other pharmacological effects undetected with the tests used but which might explain, for instance, the fact that in a doubled-blind placebo-controlled study on amphetamines, subjects felt they were performing better when using amphetamines, whereas objective results for all the tests were actually negative (Ilieva et al 2013<sup>45</sup>).

### IIIb The long term

The most scientific and objective way of assessing the **risk-benefit ratio in the long term of using neuroenhancement techniques** would be to carry out double-blind randomly assigned, placebo controlled prospective studies. However, while such studies are justified and even essential in pathological conditions, deliberate and *a fortiori* prolonged administration of potentially dangerous brain activity modifiers to healthy subjects would be unacceptable (Heinz<sup>46</sup> 2012). The only acceptable studies would be the so-called “observation” (“case/control studies” or “cohorts”) epidemiological studies, such as the “Monitoring the Future (MTF)” longitudinal study, which evaluates the use of psycho-stimulating drugs such as amphetamines and methylphenidate by children and adolescents, be they prescribed or taken without medical supervision (Johnston<sup>47</sup> et al., 2009). These observation studies however are difficult to implement and subject to major methodological bias, such as, as regards neuroenhancement, under-reported consumption or the impossibility of

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<sup>41</sup> Rabiner DL et al. Motives and perceived consequences of nonmedical ADHD medication use by college students. *Journal of Attention Disorders* 2009; 13: 259-270.

<sup>42</sup> Laurance J. Ritalin abuse hits students looking for an exam kick. Available at: <http://www.independent.co.uk/news/education-news/ritalin-abuse-hits-students-looking-for-an-exam-kick-537088.html> 2003. [accessed 13 June 2011].

<sup>43</sup> Outram SM. Ethical considerations in the framing of the cognitive enhancement debate. *Neuroethics* 2012; 5: 173-184.

<sup>44</sup> Luchtman DW et al. Cognitive enhancement by omega-3 fatty acids from child-hood to old age: Findings from animal and clinical studies. *Neuropharmacology* 2013; 64: 550-565.

<sup>45</sup> Cf note 18.

<sup>46</sup> Heinz A et al. Cognitive neuroenhancement: false assumptions in the ethical debate. *J Med Ethics* 2012; 38: 372-375.

<sup>47</sup> Johnston LD et al. Monitoring the future national survey results on drug use, 1975-2008. Volume I: secondary school students (NIH publication n° 09-7402). Bethesda: National Institute on Drug Abuse; 2009.

differentiating between recreational use and neuroenhancement purposes (Wilens<sup>48</sup> 2008). Such studies should address homogeneous groups of subjects, taking into account very specifically educational and socio-cultural levels, nutritional parameters and, above all age, since neuroenhancing effects on the brain are bound to be different for the developing brain of a child, the mature brain of a young adult or the declining brain of an elderly person. The studies should continue over a very long period of time to take account of possible tardy adverse effects, similar to those described for psychotropic drugs. They should be evaluating not only psycho-cognitive functions, but also quality of life and more generally social integration. At this time, there are no studies available on the long term effects of recent techniques used by healthy individuals for their neuroenhancement, but it is to be feared in any event that when they are used without any medical supervision their users will be less inclined to respect contra-indications (precautions for use, dosage and supervisory conditions) so that there would be an increase in the occurrence of unwanted side effects and a risk of overdosing. There would also be cause to worry about non invasive brain stimulation techniques since in practice they are marketed with no other pre-condition than having an EC marking and are therefore not nearly as regulated as medications are. They are also the object of unsupervised direct and frequently misleading advertising. Users therefore incur psychocognitive risks such as agitation, insomnia, lack of concentration, or even epileptic seizures if there is a departure from proper stimulation parameters.

**The long-term risk-benefit ratio of neuroenhancement techniques is unknown and may well to continue to be so for a long time in view of the difficulties outlined above.** There is no way of knowing if the therapeutic benefit found for pathological indications would persist in the long term for the psychocognitive enhancement of healthy subjects or if tolerance might not set in with consequent “wearing off” of the effect. The benefits that users of neuroenhancement techniques are seeking are clear and explicit: generally, become more intelligent, happier, more efficient and higher performers. But do not these benefits themselves contain an element of risk: could not overestimation of their actual capacities by the individuals concerned become dangerous as suggested by accidents occurring when repetitive tasks are demanded of sleep-deprived subjects using Modafinil (Repantis 2010<sup>49</sup>)? Could the paradoxical effect of enhancing one cognitive function to the detriment of another one as described in the short term (enhancement of working memory to the detriment of the speed of cognitive processing, and *vice versa*) (Angelakis 2007, de Jongh 2008) persist in the long term with, for example, development of hyperamnesia but a deterioration of intelligence and social cognition?

**Would such adverse side effects be reversible?** Would neuroplasticity, that is the brain’s capacity to modify its functional connectivity on a continuing basis, on which are founded cognition, memory and learning, be initially stimulated by neuroenhancement only to gradually fade away in the long run to the extent of arriving at an inversion of effects, (De Jongh 2008)? Could regular medication with methylphenidate taken by young people lead to premature cognitive decline? Could the imperfectly reversible or even irreversible side effects — such as the abnormal movements developing in 5% of patients treated with antipsychotics — appear after ingesting various drugs which were meant to have an enhancing effect?

One of the major potential risks is drug abuse, a habit which may remain recreational but can also lead to dependence and **addiction** with vulnerable subjects. For some individuals, the risk of addiction could even be inherent to any neuroenhancement, since the modulation of memory capacities and of learning processes involves, *inter alia*, the dopaminergic neurotransmitter systems which are the root of dependence and addiction (Heinz 2012). But while the activation of the dopaminergic system and the release of dopamine remain moderate (50 to 100% increase) during the form of brain

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<sup>48</sup>Wilens TE et al. Misuse and diversion of stimulants prescribed for ADHD : A systematic review of the literature. Journal of the American Academy of Child and Adolescent Psychiatry 2008; 47: 21-31.

<sup>49</sup>Cf note 11.

stimulation associated with intellectual activity, the ingestion of coffee and food or in the course of sexual activity, they are greatly increased, indeed by as much as 1000%, with the use of substances for neuroenhancement, be they classic addictive substances such as cocaine and amphetamines, or new products such as methylphenidate or Modafinil. Repeated use of these substances stimulates dopamine release which in turn increases appetite for the substances, thus creating the vicious circle of dependence and addiction with all its consequences for the individual and for the community (Heinz 2012). Another form of addiction could be induced by neurofeedback techniques because they are conducive to enjoyment.

**To sum up**, in healthy subjects, major methodological difficulties impede an evaluation of the benefits and risks of using biomedical neuroenhancement techniques. In the short term, there is a considerable disproportion between the moderately positive effects observed in experimental cognitive research conditions and the scale of the benefit perceived by users in real life. In the long term, the risk-benefit ratio is totally unknown as regards the persistence (real or perceived) of the benefit and the possibility of persisting harmful effects, amongst which the most probable if one takes into account past experience (with amphetamines), is addiction.

#### **IV – USE OF BIOMEDICAL NEUROENHANCEMENT TECHNIQUES: BY WHOM, FOR WHOM?**

After describing biomedical techniques used for neuroenhancement, we must assess what could be called **“the societal phenomenon of neuroenhancement”**, that is the fact that certain healthy individuals use these techniques for the supposed purpose of neuroenhancement. The cult value of performance in modern society, the “cosmetic” recourse to such techniques, the “off-label” diversion of medications developed for specific pathologies, the military and financial considerations: this set of factors demands an analysis of neuroenhancement from the point of view of its social implications.

##### **IVa- The scale of the phenomenon**

**The scale of the societal phenomenon known as neuroenhancement** is not well known because, more often than not, it is assessed using data on the consumption of stimulant drugs used without medical prescription instead of using questionnaires targeting neuroenhancement specifically. It is therefore not possible to differentiate between recreational or occasional use, for example to stay awake throughout a particular night or fight the effects of jet lag, and more regular use for neuroenhancement (Ragan 2013<sup>50</sup>). Furthermore, medically justified prescriptions can be used off-label for instance through “loans” from young patients to their “chums” — this being a practice that prevails for one adolescent out of every five using Ritalin to treat ADHD, as reported in a study carried out in Michigan (Boyd 2007<sup>51</sup>) — or fraudulent drug procurement. Using medications for neuroenhancement could involve 8 to 25% of American students, mostly methylphenidate users, and among these 4 to 10% would be using the drug at least once a year, 2 to 5% at least once a month and 1 to 3% once a week (Outram 2010<sup>52</sup>). Neurostimulant drug use is all the more common with low-performing students (Rainer 2009) enrolled in universities with high standards, since the aim is to

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<sup>50</sup> Cf note 13.

<sup>51</sup> Boyd CJ et al. Prescription drug abuse and diversion among adolescents in a southeast Michigan school district. Archives of Pediatrics Adolescent Medicine 2007; 161: 276-281.

<sup>52</sup> Outram SM. The use of methylphenidate among students: The future of enhancement? Journal of Medical Ethics; 36: 198-202, 2010

enhance performance to prepare for examinations or the submission of papers (White<sup>53</sup> 2006, Outram 2012). Not only students are involved: a poll by the journal Nature, directed at its readership, reports on the use of neuroenhancers by 20% of them (Maher 2008<sup>54</sup>) and in a German study covering 3000 employees, involvement was observed in 5% of men and 1.9% of women (Dak<sup>55</sup> 2009).

Despite the unknown quantities in the individual risk-benefit ratio of biomedical neuroenhancement techniques, it is likely that **such use will continue to develop** in view of the current socio-economic context and the combination of several different factors: the relentless pursuit of performance, media infatuation and considerable financial stakes. The ginkgo biloba industry, despite its minimal effect on cognition, is worth billions of dollars (Solomon<sup>56</sup>, JAMA 2002). The pharmaceutical industry involved in research on neuropsychiatric disorders is beginning to evaluate purely symptomatic effects on certain psychocognitive parameters (memory, concentration, swiftness in task performance, etc.) with an enormous potential market in their sights. It is highly probable that any medication or technique with a potential for enhancing psychological status or cognitive function will be gradually slipping from medicinal use by patients to consumption by healthy subjects; already transcranial direct current stimulation (tDCS) and neurofeedback machines for home use are on offer on the Internet together with the assistance of neuroenhancement “counsellors”.

Contrary to the case in the United States and Germany, in France there is no data available on the use of biomedical neuroenhancement techniques. It would seem advisable to organise **observation studies** (cf supra IIIb) in various socio-professional categories to attempt an assessment of the scale and evolution of the neuroenhancement phenomenon on the one hand, and to analyse the reasons motivating people who try to “enhance” themselves with biomedical techniques, on the other hand. This would serve to generate quantitative and qualitative data which could be used as a basis for reflection on the possible creation of preventive, or even regulatory, measures (Lücke 2012).

**To sum up:** The social neuroenhancement phenomenon, although difficult to evaluate in quantitative terms, is still fairly limited, but is very likely to expand in the current socio-economic climate. This is justification enough for the launching of observation studies.

#### **IVb-Autonomy**

**Hypothesising the existence of biomedical neuroenhancement processes for which the risk-benefit ratio would be known and judged “acceptable”, one of the major issues to be dealt with is autonomy** and, to be more specific, discovering whether there might be circumstances in which their use would be implicitly mandatory — i.e. the individuals concerned considering themselves obliged to do so — or explicitly, i.e. administered by others without the subject being consulted or even without the subject’s consent.

Users of biomedical neuroenhancement techniques vigorously claim for themselves the right to freedom of choice for their own lifestyle, but do not realise that their sense of freedom more often than not is the product of an environment. **Implicit coercion** is a clear fact, as evidenced by the above mentioned studies of American students showing that the main motivation for using psychostimulants is to achieve peak performance when passing exams and that poorly performing students in

<sup>53</sup> White BP et al. Stimulant medication use, misuse, and abuse in an undergraduate and graduate student sample. *Journal of American College Health* 2006; 54: 261-268.

<sup>54</sup> Maher B. Poll results: Look who’s doping. *Nature* 2008; 452: 674-675.

<sup>55</sup> Dak 2009. Gesundheitsreport. DAKForschung. <http://www.dak.de/content/filesopen/Gesundheitsreport-2009.pdf>

<sup>56</sup> Solomon P et al. Ginkgo for memory enhancement: A randomized controlled trial. *JAMA* 2002; 288: 835-840.

universities with stringent academic standards are more likely to be users. In a competitive society, a similar situation is to be observed in various professions or companies in which people are under constantly increasing pressure to be more efficient and productive. Those in favour of using neuroenhancing techniques consider that they are putting things into perspective when they claim that this loss of autonomy is compensated by the benefits of psychostimulants which, since they increase alertness and concentration, might well bring about a reduction in sometimes fatal accidents in the workplace (Greely<sup>57</sup> 2008). They fail, however, to consider the number of accidents that could be related to mistakes made through being overconfident or sleep-deprived, nor do they probe the reasons why people decided to use these drugs nor, therefore, do they consider the benefits that could be derived from improving working conditions and making goals more flexible. Other forms of implicit coercion are those arising out of market pressure. Is advertising for the “smart pill” or “turbo-charging the intellect” irresistible? It is true that advertising, in particular for medications, is strictly regulated, but in varying fashion from one country to the other: methylphenidate for medical indications is authorised in the United States but not in Europe. Advertising for “off label” use (meaning for purposes that were not approved by regulatory authorities) is prohibited everywhere and liable to huge fines. Nor would it make economic sense according to the pharmaceutical industry’s representatives, but the authors of a major Swiss study on human optimisation (TA-SWISS 2011) believe that the very size of the fines is indicative of the degree in which illegal marketing is not just a fact, but also probably a very lucrative one.

**Explicit coercion** implies, in the biomedical neuroenhancing context, that people are made to use such techniques by others, whether they want to or not, without their consent or even against their will. This is perhaps the case for instance with **children** (Graf 2013<sup>58</sup>) whose parents are themselves under pressure to enhance performance or are victims of social inequalities and who give their children methylphenidate, without any therapeutic indication, in some cases so that they can be top of their class in school and in other instances to try and smooth out social inequalities (Singh 2007<sup>59</sup>, 2010). In such circumstances, the drug is obtained illegally or even by faked allegations of ADHD symptoms (Harrison<sup>60</sup> 2007).

Another sector in which explicit coercion could prevail would be the **justice** system if brain stimulation or neurofeedback techniques — which, as we have seen, seem able to modify mendacious or deceptive attitudes (§ Ia) — were used to assist in lie detection (Hamilton 2011), in the same way as functional MRI which has been recently authorised for use in the judicial system in the latest revision of the July 7, 2011 bioethics law.

**Coercion by decision of society**, for instance targeting aggressive or antisocial people, could be readily considered in the case of non invasive techniques since, as we have seen, some American neurosurgeons did not reject even using invasive deep brain stimulation in such cases.

Another environment where the development of neuroenhancement techniques would be of particular interest, indeed where such developments were pioneered, is the **armed services and intelligence community** which has considerable research funding available to it for such purposes, in

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<sup>57</sup> Greely H et al. Towards responsible use of cognitive-enhancing drugs by the healthy. *Nature* 2008; 456: 702-705.

<sup>58</sup> Graf WD et al. Pediatric neuroenhancement. Ethical, legal, social, and neurodevelopmental implications. *Neurology* 2013; 80: 1251-1260.

<sup>59</sup> Singh I. Clinical implications of ethical concepts : moral self-understandings in children taking methylphenidate for ADHD. *Clin Child Psychol Psychiatry* 2007; 12: 167-182.

<sup>60</sup> Harrison AG et al. Identifying students faking ADHD: Preliminary findings and strategies for detection. *Archives of Clinical Neuropsychology* 2007; 22: 577-588.

the United States at least<sup>61</sup>. An example of this is DARPA's (Defense Advanced Research Projects Agency) cognition enhancement programme which arrived, among other things, at the development of a "cognitive cockpit" giving pilots the possibility of optimising all their tasks in real time, ranging from the selection of the most readily available sensory organ for data transmission to prioritising requirements and eliminating sources of distraction. DARPA is also working on new techniques, such as individual warfighter helmets featuring transcranial pulsed ultrasound technology even more effective than transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS), or new substances able to boost alertness or relieve fatigue, emotional stress and empathy. One such substance is oxytocin, a hormone which could, we are told, augment the expression of certain "virtues", such as loyalty, generosity or a spirit of self-sacrifice (Basl<sup>62</sup> 2010, Tennison 2012, Nuffield Council 2012<sup>63</sup>). In the American armed forces, in a combat situation, it is the commanding officer on the ground who decides on the benefits and risks for the soldiers under his command of taking a particular drug to neutralise feelings such as fear. Reducing empathy is particularly sought after for drone pilots for whom killing someone, a child specially, using a screen while they themselves are safely removed from any threat of injury is sometimes experienced as psychologically less acceptable than killing an enemy soldier on the battlefield (Tennison<sup>64</sup> 2012).

Apart from these special groups, what is going to happen if implicit or explicit coercion lead to the general use of medication or of a biomedical technique for neuroenhancement: What will happen if tomorrow, we all use Ritalin (Zarifian<sup>65</sup>, 1996)? *"Future psychotropic substances stimulating vigilance, memory, sexuality, will have the status of a medication. Individual differences will be abolished and social orthopedias based on chemical crutches will no longer be called into question"*.

**To sum up, the ethical issue of autonomy is critically endangered by neuroenhancement.**

Individuals believe themselves to be free of any constraint, but in point of fact they are driven by a compulsion to perform. "We must always be aware that the fervent quest for performance driven by an imperious desire to make progress, can mask the most constraining of alienations." (CCNE's Opinion n° 81). For certain special groups, such as children, people under accusation of a crime or an offence, soldiers, individuals whose behaviour is judged to be antisocial, there is a risk of dominion and manipulation. The "gradual shift from benevolence to manipulation, from 'doing something for' to 'doing something to' someone could be almost imperceptible (Chneiweiss, 2012<sup>66</sup>)."

#### **IVc – Social justice, equitable allocation of resources**

In the replies to all the enquiries into the use of biomedical techniques for neuroenhancement in various socio-professional categories, almost every one considered that it was up to individual preferences and responsibility. And yet the consequences of such decisions do not affect only the person concerned; others are also involved. Furthermore, there is reason to wonder to what extent individual decision is abstracted from social reality. Using neuroenhancement — assuming that it is successful — **eliminates equality of opportunity and of success**. The American student who is using methylphenidate does so "to be the best", meaning better than anyone else, and it is no coincidence

<sup>61</sup> Current state-of-the-art neurosciences, including new forms of brain scanning, brain-computer interfaces (BCIs), and neuromodulation, is being tapped for warfighter enhancement, deception detection, and other cutting-edge military applications to serve national security interests (Tennison 2012).

<sup>62</sup> Basl J. State Neutrality and the Ethics of Human Enhancement Technologies. *AJOB Neuroscience* 2010; 1: 2: 41-48.

<sup>63</sup> Nuffield Council on Bioethics. Novel neurotechnologies: Intervening in the brain. A guide to the report 2012.

<sup>64</sup> Tennison Mn et al. Neuroscience, Ethics, and National Security: The state of the art. *PLoS Biology* 2012; 10: e1001289.

<sup>65</sup> Zarifian E., Ethics of the use of psychotropic drugs, in *Cerveau et psychisme humain, quelle éthique ?* assoc.Descartes John Libbey, 1996, Vol.1 under the direction of Gérard Huber, p.196-197

<sup>66</sup> Chneiweiss, H., *L'homme réparé*, Plon, 2012, p.33. (The repair of man).

that he is more inclined to use the drug before a competitive, rather than a non competitive, examination. He says that he wants to be the best because “you want to get into the best grad school...into the best program after and get the best job” (Forlini<sup>67</sup> 2009), which presupposes that this student has sufficient funds to support his plan of action. The real or perceived disadvantaged circumstances in which other students find themselves, following on from the implicit coercion mechanism mentioned above, could lead some of them to using psychostimulants although they would prefer not to or are downright opposed to their use. Such consequences related to individual differences, slipping towards inequality, also exist in other performance-related contexts, for both children and adults<sup>68</sup>.

**Furthermore, the consequences do not only have an individual impact;** there is a serious risk of arriving at an “**enhanced**” **social class** made up of a minority of well-informed individuals whose financial circumstances are sufficiently comfortable to give them access to it. The outcome would be an enlargement of the ever-growing gap between rich and poor, with the rich becoming not only richer, but also more powerful, more intelligent, and even happier than others, with the obvious danger of discrimination and possibly dominance (Chatterjee<sup>69</sup> 2004). Even the perception that this “enhanced” social class might have of the parameters defining good psychocognitive health could be modified to the extent that they view the “non enhanced”, the “diminished”, as handicapped. It is sometimes argued that the existence at the very top of the pyramid of this “enhanced” social class, would have a knock-on effect on the less privileged classes, but this argument — valid perhaps in economic and absolute terms — ignores the complexity of factors governing cognitive levels and modulating psychological well-being. It is also contradicted as far as education is concerned by research demonstrating that focusing on the best pupils in a class is not the best way of improving the general level of the class as a whole (Baudelot<sup>70</sup> et al, 2009). As for the idea of seeking “by appropriate measures to prevent human enhancement from becoming the prerogative of wealthy users” (Académie Suisse, 2012<sup>71</sup>), it seems very utopian if the factual situation is considered realistically as regards for example inequality of access to education, food, hygiene and health. It is also argued by those in favour of neuroenhancement that because it would increase intelligence quotients, it could help to improve productivity and reduce unemployment since intelligence quotients have an impact on productivity and social achievement. This argument, apart from the fact that it presumes that access to neuroenhancement would be fairly allocated, is based on the assumption of a direct link between an increased intelligence quotient and a reduction of unemployment. The existence of such a link is contradicted by facts (Heinz 2012).

On a global scale, the risk is just as great of widening the gap between countries that can avail themselves of neuroenhancement techniques and the financial resources to implement them, and those countries that are unable to do so, with the same danger of being subjected to dominance and manipulation.

**To sum up,** neuroenhancement techniques (supposing them to be effective) would have a harmful effect on equality of opportunity and success for individual citizens and would represent a risk

<sup>67</sup> Forlini C et al. Autonomy and coercion in academic “cognitive enhancement” using methylphenidate: Perspectives of key stakeholders. *Neuroethics* 2009; 2: 163-177.

<sup>68</sup> See CCNE’s Opinion n° 81, “Performance and Health”, November 17th 2003.

<sup>69</sup> Chatterjee A. Cosmetic neurology. The controversy over enhancing movement, mentation, and mood. *Neurology* 2004; 63: 968-974.

<sup>70</sup> Baudelot C et al. *Pour une synthèse des résultats du PISA* (Programme for International Student Assessment) 2009. (Summary of results)

<sup>71</sup> *Académies Suisses des Sciences. Une médecine pour les personnes en bonne santé? Analyse et recommandations concernant le human enhancement. 2012.* (Swiss Academy of Science. Medicine for people in good health? Analysis and recommendations concerning human enhancement).

of bringing about the emergence of an “enhanced” social class, thus contributing to a further widening of the gap between rich and poor.

#### **IVd – The physician’s role and medical involvement**

**Doctors cannot simply ignore the use of biomedical techniques for neuroenhancement and their possible consequences on individual and public health.** Although they are not therapeutic, it cannot be denied that they have an effect on the body and for that reason are of concern to doctors.

At first sight, it could be argued that in France doctors have little reason for concern on this subject and that their position must be straightforward since the only medical prescriptions which the social services support are those complying with indications approved for marketing by the regulatory authorities (AMM - Autorisation de mise sur le marché). For the substances under discussion, the only authorised indications are for the treatment of pathologies. The situation is not so clear with technical devices for which, as we have already seen, marketing authorisation is not nearly so strictly enforced and indications are less well defined. In any case, be they medications or devices, their theoretical restriction for use only in pathological indications is now completely illusory since they can be purchased on the Internet.

As a social phenomenon, neuroenhancement is still largely unknown in France, so that there have been no **enquiries into doctors’ thoughts** on neuroenhancement and their reactions in practice to requests for the use of biomedical neuroenhancing techniques. In contrast, surveys were organised in the United States and in Switzerland. Response varied widely, often reflecting the physicians’ personal beliefs and attitudes to medical practice. Some go so far as to reject out of hand the very principle of biomedical enhancement, while others are more receptive, along the same lines as their attitude to cosmetic surgery. Most of the doctors responding held rather less categorical views, stating that they more inclined to prescribe neuroenhancing medications to the elderly than to young patients because more benefit might be expected with advancing age (restoration plus augmentation?) and there could be a higher risk for younger people (Banjo 2010<sup>72</sup>). NEpA (Ott<sup>73</sup>, 2012), a Swiss study involving both psychiatrists and general practitioners returned fairly similar results: 49% of responders would be open to the possibility of using neuroenhancing techniques, on a case by case basis; 10% would comply with requests and 41% were unable to make up their minds whether they would accept or refuse.

In the United States, off-label prescribing for neuroenhancement, meaning that the medication is being used in a manner not specified by the FDA, is left to the appreciation of the physician. The AAN’s Ethics Committee (American Academy of Neurology, Ethics, Law and Humanities Committee) produced a kind of **Guide of Best Practices** for doctors faced with a request for biomedical neuroenhancement, which included mainly the following advice: 1) View all requests as appropriate and requiring medical evaluation; 2) Assess the reasons for making the request: underlying pathology?, restoration or augmentation?, anxiety?, low self-esteem? coercion? etc.; 3) Specify that the prescription is off-label; 4) Provide information on the short term risk-benefit ratio and the relatively unknown value of this ratio in the long term, together with the potential risk of addiction and of irreversible brain damage; 5) Verify contraindications, provide information on conditions of use, dosage, supervision; 6) Explain possible alternatives, in particular life style changes; 7) Explain, while carefully avoiding any element of moral judgement, the reasons for accepting or refusing to prescribe

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<sup>72</sup> Banjo OC et al. Physician attitudes towards pharmacological cognitive enhancement: Safety concerns are paramount. PLoS One 2010; 5: e14322.

<sup>73</sup> Ott R et al. Doping the human brain: Swiss psychiatrists’ and general practitioners’ views on neuro enhancement practices. Swiss Med Wkly 2012; 142: W13707.

(Larrivière 2009). All the above recommendations emphasise the importance of the physician-patient **clinical relationship**.

The Swiss Academies' Working Group (2012) also made some recommendations on the subject, while abstaining from any positive or negative pronouncement on the subject of neuroenhancement, but nevertheless advising against any active promotion. They insisted, among other things, on the importance of circumspection in respect to individual requests and their underlying motivations, of protecting children in particular and other vulnerable individuals from possible risks, of suggesting, in the event of a health-harming lifestyle, psychosocial counselling with the aim of helping the person concerned to become more self-sufficient and better able to resist the urge to conform at whatever the price to pre-ordained performance criteria and standards.

**In the United States, specific recommendations were formulated for children and teenagers: neuroenhancement techniques are definitely not recommended**, in particular because 1) of how difficult it is to draw a dividing line between normal and pathological psychocognitive development, 2) concern over the possible harmful effects on a developing brain and 3) uncertainties regarding the autonomy of judgement and decision in children and adolescents<sup>74</sup>.

While physicians are in the front line in responding to requests for biomedical neuroenhancement techniques, and while it is important that they should consider these issues with care, **it is the very concept of medicine that is being called into question**: should medicine keep to its traditional roles, i.e. prevention, diagnosis and treatment of diseases, or should it broaden its mandate to increasing the well being of people who are not in ill health? The FDA (Food and Drug Administration) seems to be thinking along the lines of an extension of responsibilities, as evidenced by its statement that it considered as being health-related and therefore subject to FDA regulation, any product or device claiming to enhance the cognitive functions of healthy subjects (Larrivière<sup>75</sup> 2009). This possible extension of medical competence to neuroenhancement **raises public health issues, in particular those relating to health priorities and to cost management**. The impossibility of drawing a clear dividing line between treatment and enhancement in the psychocognitive domain, the ever more insistent social and professional demand for heightened performance, the medicalisation of conditions hitherto classified as normal and the economic importance of potential markets, are all factors converging to promote the neuroenhancement sector to the detriment of traditional prevention and treatment sectors — which are even now far from being entirely satisfied — and this at a time when available resources are scarce. Were the cost of neuroenhancement borne entirely by users and only a small minority of wealthy people were able to afford it, the health system would still generally be under threat (in addition to the fact that social justice would be denied). For example, should employment in this sector become more attractive than in traditional branches of medicine, there could be a drain on personnel resources, particularly harmful at a time when there is a shortage. In the same way, national health insurance financial resources would be strained if adverse effects on the health of those concerned or on the health of others were to emerge, raising the issue of who would be absorbing the extra expenditure, as happened recently for taking on the cost of surgical removal of defective mammary implants. When the implant had been required for a pathological indication (breast cancer for instance), it was decided that for reasons of collective solidarity, the cost should be taken up by the health system, but not in the case of surgery for cosmetic reasons. A similar logic would seem appropriate for biomedical techniques to “enhance your brain” and plastic surgery to “improve your body”: in either case, what of the actual significance of these “enhancements”?

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<sup>74</sup> Graf. 2013.

<sup>75</sup> Larrivière D et al. Responding to requests from adult patients for neuroenhancements. Guidance of the Ethics, Law and Humanities Committee. *Neurology* 2009; 73: 1406-1412.

**To sum up**, reflection on the physician's role when responding to a request by a healthy person for biomedical techniques in pursuit of neuroenhancement cannot be dissociated from the community's reflection on the kind of health system it wishes to have. If medical objectives were to extend to the neuroenhancement of healthy subjects, would there not be **a risk of major distortion in health priorities, the risk being inevitably aggravated if public resources were involved?**

#### **IVe—The role of research**

While current investment<sup>76</sup> in neurological research in order to gain a better understanding of neuropsychiatric disorders and how to treat them or to elucidate cerebral function is neither disputable nor disputed, **research on neuroenhancement is the subject of controversy**. And yet, is there really any clear distinction between therapeutic research on sick patients, cognitive research on healthy subjects and research on neuroenhancement?

The absence of a sharp dividing line between therapeutic research on patients and cognitive research on healthy subjects is illustrated by President Obama's justification for the 100 million dollar financial request to finance the BRAIN project: "Today our scientists are mapping the human brain to unlock the answers to Alzheimer's".

The issue is infinitely more problematic if the possible dividing line is between cognitive research and research on neuroenhancement (cf II and IIIa) with a healthy subject. When people in good health receive medication or non invasive brain stimulation to study their memory, reasoning power, speed of computation, etc. and an improved score compared to previous testing results is observed, is this fundamental cognitive research or research on neuroenhancement? Even when the **object is cognitive research**, there is a grave risk, given the public's and the media's infatuation with anything to do with the brain, that the outcome will be transformed, amplified, exaggerated, so that for instance a slightly increased score for a memory test becomes "memory enhancement" and the underlying technique described as "*the* memory pill" or "*the* memory helmet". The dividing line is particularly blurred in the field of military research, even when the objective put forward is repair, as in the REMIND and REPAIR programmes in DARPA, aiming respectively at developing "a hippocampus to serve as a neural prosthesis in the event of memory impairment" and "to model brain-machine interface to facilitate rehabilitation following brain injury and remote control of external systems".

In France, the boundary is just as nebulous since the law which became applicable in 1988<sup>77</sup> concerns "research organised and applied to human beings in view of developing biological or medical knowledge"<sup>78</sup>. The law is intended to provide the greatest degree of protection to people accepting participation in a biomedical research project, through the implementation of an *a priori* assessment of the project before it starts, involving an opinion delivered by a committee for personal protection together with official administrative approval. The prior examination of a research project provides future participants (sick or in good health) with guarantees on the project's pertinence (*inter alia*, an

<sup>76</sup> On April 2nd 2013, President Obama launched his most ambitious scientific project to date: "The BRAIN initiative (Brain Research through Advancing Innovative Neurotechnology)" "Today our scientists are mapping the human brain to unlock the answers to Alzheimer's". He requested 100 million of Federal financing for this project to be conducted by the National Institute of Health, the Defense Advanced Research Projects Agency and the National Science Foundation. The European counterpart is the Human Brain Project which is even more ambitious since its aim is to build a supercomputer integrating everything known about the brain, up to and including the structure of the neuronal membrane ion channels.

<sup>77</sup> Law n° 88-1138 dated December 20, 1988 (modified) on the protection of individuals accepting to participate in biomedical research. Law n°2012-300 dated March 5, 2012 on research involving human beings will be replacing it (as stated in article 11) "and enter into force upon adoption and publication in the *Journal Officiel* of the implementing decrees mentioned in articles L. 1121-17 et L. 1123-14 of the Code of Public Health and in article 8 of this law".

<sup>78</sup> Article L. 1121-1 al.1 of the Code of Public Health.

evaluation of the quality of the study considering, in particular, the end-purpose of the research as a determining factor) as well as on the acceptability of risks and potential injury. The law provides for reinforced protection of vulnerable people. This is the case in particular when those concerned are under legal age or adults under legal protection or unable to express consent<sup>79</sup>.

So it is that, although its object was not neuroenhancement, **cognitive research** involving healthy subjects has yielded a body of data from which biomedical neuroenhancement developed. This implies that any **cognitive research**, over and beyond strict enforcement of legislation on the subject, must be conducted with the greatest degree of methodological stringency in view of the high potential for bias (IIIa) and with the utmost **caution in the interpretation, use and communication of results**. The inclination to elucidate must not be satisfied to the detriment of scientific accuracy; the incitement to justify research by its potential applications must not be allowed to generate an escalation in the presentation of results and their potential scope. Total transparency must be the norm, with full access to all data, both negative and positive.

Would it not be appropriate, in parallel with the development of cognitive research, to push for more action in favour of **building up the basic foundations of psychocognitive development**, first and foremost among them being education and nourishment, advantages which are still so inequitably distributed? At the current time, worldwide, 200 million children are not developing normally because of defective care during pregnancy and post-partum, of exposure during the first 1000 days of life to malnutrition and infection and finally because they are not receiving enough attention and stimulation<sup>80</sup>. Moreover, a great many children — mostly girls — do not even have access to the most basic form of schooling. Should there not also be more efforts made to encourage physical exercise at a time when children are becoming increasingly sedentary, although it has been amply demonstrated that regular physical activity improves not only the health of the body but also health of the mind, cognition, academic performance, that it reduces anxiety and depression and constitutes a favourable factor in terms of quality of life and socialisation? (Editorial Lancet 8th June 2013<sup>81</sup>). Should we not be fearful that the development of new biomedical instruments with the potential for enhancing brain function — particularly if they are reported with sensationalist intentions — will contribute even more to turning the population at large away from the basic resources mentioned above, i.e. nutrition, education, learning, physical activity, etc.? (Lücke<sup>82</sup> et al 2011, 2012) ?

**To sum up**, cognitive research involving healthy subjects, although it does not aim specifically at neuroenhancement, raises important issues, in particular the pertinence of questions asked, as well as the interpretation and communication of results. There is a risk that the development of new so-called neuroenhancement techniques could be pursued, particularly when funds are scarce, to the detriment of developing basic resources such as nutrition, education, learning and regular physical activity.

## V Neuroenhancement: the issue of limits

**A general overview of recent progress in prevailing scientific thinking on cerebral physiology** is required to understand biomedical developments for the purpose of neuroenhancement. If these concepts are taken into account, it becomes possible to provide a non caricatural representation of

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79 Article L. 1121-7 et 1121-8 of the Code of Public Health. Such research projects are to conform, at the very least, to the Helsinki Declaration (2008) protecting incompetent individuals, those under legal age in particular.

<sup>80</sup>Lancet, April 13th 2013.

<sup>81</sup>Editorial. "Ready, set, go for physical activity". Lancet 2013;381:1960

<sup>82</sup> cf note 76.

brain function and to move on to the subject of brain/machine interaction. New concepts, such as transhumanism and posthumanism have emerged, based on such interaction.

## V.1. Towards a cognitive function physiology

Immediately after the Second World War, a rapid succession of scientific, medical and technological advances overturned completely our existing understanding of mental processes and their cerebral foundation. Five main components are identifiable in this fertile scientific narrative.

### **The computational metaphor of neuron and brain**

The idea that the neuron could be viewed as a machine for the procession of information has been the basis for cybernetics, artificial intelligence and the cognitive sciences (founding works by von Neuman, Wiener<sup>83</sup>, Pitts & Mc Culloch). This fundamental idea is based on the possibility of describing elementary neuronal activity as a coding activity (the binary principle: resting potential state versus the action potential state) as a result of the integration of the excitatory and inhibitory signals that the brain is receiving continually. The spatial arrangement of neurons into networks interconnected by synapses therefore defines the **neural networks** able to perform a very large number of fundamental logical operations and of representing informational states.

This computational representation has its limits, but it was the point of departure for many an important discovery. Thus, the neural information processing concept contains the idea of a “code”: the search for a code or for **neuronal codes** — in the same perspective as that of the genetic code — forms the basis for computational neurosciences. Possibly the most telling example in this field is the discovery by Hubel and Wiesel (Nobel prize winners 1981) of the anatomic and functional cortical cell columnar architecture of the primary visual cortex and, in particular, a demonstration of the codes used by the neurons in these structures to represent the visual contrast transmitted by the retina. This rich (and fertile) informational metaphor was the source of the **comparison between the functioning of brains and computers**.

This metaphor however can be taken only so far and some of the limits were raised at the outset (e.g. considerations on analog and digital processing in J. von Neumann’s “The Computer and the Brain, 1958. The massively parallel organisation of cerebral connections, the permanent modifications to the brain’s structure (“hardware”), in particular as related to its activity, render a comparison between brain and computer remarkably complex and also questionable. We can no longer, therefore, if we wish to avoid making a caricatural representation of the way in which the brain processes information, continue to consider the informational metaphor in simplistic terms. Furthermore, alternative theoretical models suggest that **the nature of the representations constructed by the neural networks is not disconnected from the outside world but, on the contrary, in direct relationship to it**.

### **From neurons to cerebral areas and then to neural networks**

At an early stage, anatomical and electrophysiological developments explored the way in which neurons could handle complex processing and varied representations due to their spatial organisation into cerebral areas and more particularly into networks connecting separate cerebral areas. The detailed description of cerebral specialisation (Sperry, Nobel Prize 1981) led: 1) to a reactivation of Gall’s nineteenth century theories. Leaving aside his “phrenological” misconceptions, he was the first to suggest the idea of a functional specialisation of the various regions of the brain, and 2), it had the effect of making this concept more complex by introducing a more dynamic and interactive dimension.

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<sup>83</sup> Wiener N., *The Human Use of Human Beings, Cybernetics and Society*, 1950, Da Capo Press, Inc, USA.

The theory of a patchwork of areas of the cortex specialising in reading, language or arithmetic, as supposed by the phrenology concept, has been replaced by the idea of complex networks connecting several cerebral areas. This is the basis for a large number of recent studies using **structural anatomic connectivity techniques with MRI**. The concept of connectivity between activities in various regions was the background for fertile developments in the cognitive sciences, along the lines of Norman Geschwind's pioneering work.

### **The intricate relationships between cognition, motivation and emotion**

The study of patients with brain lesions, particularly in the frontal lobe, has contributed to reconsidering the functional independence between rational cognitive processes (voluntary decision-making based on explicit reasoning) and processes based on emotions or motivations (the Damasio<sup>84</sup> school). These discoveries, in particular those bearing on **the importance of the limbic system**, the basal ganglia and the orbitofrontal cortex in the genesis of appropriate decisions and behaviours are central to a great many studies, in psychopathology particularly.

### **Different forms of cerebral plasticity**

Various clinical and experimental situations have given rise to the general concept of “**cerebral plasticity**” which in fact covers a whole range of different phenomena. Plasticity, first of all, includes the living and changing characteristics of the neural networks' structure, in particular as it relates to a number of epigenetic factors (environment, social interaction, cerebral activity, stimulation, diet, etc.). The recovery of functions after brain injury is another example. The plasticity concept is also used to emphasise the possibility, for a brain genetically programmed for given activities, to be “recycled so as to carry out other functions”. In the same way, the demonstration that social concepts such as pain or social humiliation give rise to the activation of the cerebral networks of physical pain, reinforces the concept of **neuronal recycling** (model by Stanislas Dehaene).

### **Beyond adult neurons...**

Finally, the brain is not solely made up of non dividing adult neurons. Several other constituents (glial cells, stem cells, blood vessels, etc.) seem to be playing an increasingly understood role in cerebral activity.

**V.2. Brain-machine interaction:** In the 1980s, artificial intelligence (AI) brought cybernetics back into the limelight: the project's intention was to translate cognitive processes into a machine in order to better assess their scope and improve their performance. This translation has been made easy with the use of techniques to record electrical and biochemical activities (Michel Imbert, 1992): detecting a stimulus, a sound, etc. Artificial intelligence led to the development of expert systems. It highlights the thought that tasks assumed to be simple in fact suppose an immense body of knowledge that we have difficulty in formulating (Daniel Kayser, 1992).

The idea underlying the AI project is the following: the more a problem is **fragmented**, the more cerebral functions are separated, and the more we are able to increase them. Separation induces augmentation and augmentation induces separation. The separation of functions is the basis of **robotics** which supposes a breakdown of tasks. Tasks are no longer considered as for humans or machines, they are first and foremost tasks recognised as such and that either man or machine can accomplish.

One example of interaction between brain and machine is to be found in the brain computer interface techniques (BCI), as they are named, through which it is possible to restore certain capacities for functional communication, or even action, to conscious but paralysed patients. For example, using

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<sup>84</sup> A.Damasio, Descartes' Error. French translation: Odile Jacob, 1995.

EEG or ocular movement recordings it is possible to decode in real time certain motor intentions or certain choices. These techniques are already in use to allow paralysed patients to move an object (such as a cursor on a screen or a wheelchair) or to compose a verbal message. The techniques were essentially designed to compensate for motor impairment (severe motor disorders as in the advanced stages of ALS (amyotrophic lateral sclerosis)<sup>85</sup>, or for locked-in syndrome sufferers, but are also gaining ground in developments for transport system safety<sup>86</sup> and in new generation video games (e.g. Kinect consoles and BCI systems based on EEGs).

The development of virtual techniques based on man/machine interaction “*radically changes the world’s criteria for objectivity and rationality*” (Jouvent<sup>87</sup>, 2009). We should note that access to the virtual is real for the brain (Sirigu<sup>88</sup>, 2011): “*When an individual is plunged into virtual reality and simulation, he is wearing headphones and is in a complex environment. But even while that environment may be unreal, it may be real enough for the brain*”.

It was in the framework of this man/machine interaction that **cyborgs** were first mentioned: hybrid beings, part organic and part electronic. “*By substituting bionic devices stuffed with electronics and other mechanical contrivances for parts of our bodies, humanity is gradually acquiring the capacity to replace Homo sapiens with another human species*” (Ferone<sup>89</sup> et Al., 2011). The name took hold with progress in the conquest of space. It represents the coupling between astronauts and their cybernetic attire; it is part of a strategy for augmenting a human agent’s capacities. Taking it from there, should we ask: Is there a limit to turning nature into artifice? How is the dividing line between natural and artificial blurred by cyborgs and bionic prostheses?

**To sum up**, the fragmentation of cognitive functions reflects neither the brain’s plasticity, nor the entirety of how it functions. Are brain/machine interaction and cyborgs new forms of neuroenhancement?

### V.3. Beyond man/beyond human?

#### V.3.1. Position and modification of self.

Long-term neuroenhancement raises the issue of a **possible modification** of the self. What do we mean by: “I am no longer the same?”, or: “He or she is no longer the same person”? Such questions are asked after taking medications or after using other so-called neuroenhancement techniques.

Do the changes brought about by these techniques go together with a personal change? The answer would be positive if, for example, ingesting medication were to lead to a change in how we see ourselves. When do such things happen? It would seem to be the case whenever customary correlations, human habits — all that enables people to adapt to their environment — are suspended. When Alice in Lewis Carroll’s famous story, takes a drink she grows taller or shorter by several centimetres. This is sufficient to introduce a break with what she was before, so that she no longer can “explain herself to herself”. Self-awareness is therefore modified for Alice, when a less familiar world

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<sup>85</sup> For example: “A P300-based brain–computer interface: Initial tests by ALS patients” by Sellers and Donchin, *Clinical Neurophysiology* 2006).

<sup>86</sup> For example, continuous monitoring of EEG vigilance levels.

<sup>87</sup> Jouvent, R., *Le cerveau magicien*, Odile Jacob, 2009, p. 24.

<sup>88</sup> Sirigu A., OPECST, 2011, report n°4469, p.148

<sup>89</sup> Ferone, G. et Vincent J-D, *Bienvenue en Transhumanie*, Grasset, 2011, p. 243.

replaces her customary world<sup>90</sup>. Although it may seem naive to think that sense of self depends on some increase or reduction, it cannot be denied that this feeling may be modified when some technical threshold is breached by the regular and prolonged consumption of, in particular, medications. It is therefore important to take into account of the modifications in a person's behaviour when evaluating the "internal" processes connected to sense of self<sup>91</sup>.

Because of the lack of long term observation studies on neuroenhancement (IIIb) the question remains unanswered regarding the potential risk in modifying primary capacities, relating to self, in human beings, such as "*being in good health, living a long life, having a good memory, being even-tempered, not being perpetually afflicted by incapacitating emotions such as timidity or fear*" (B.Baertschi, 2011). Practising endurance, concentration, attention and patience, has been the hallmark of mankind's progress throughout its history and has paved the way for great achievements. Those who did so were durably changed, albeit imperceptibly. If the same outcomes can be arrived at using medications and in a shorter time, the "self" will also be modified, but not in the same way as with a learning process, for instance. What is at issue here is the way in which self-modification takes place.

**To sum up**, the use of medication and of biomedical techniques raises the issue of a **possible modification of the sense of self** and of self-acceptance. Such use puts into question the permanent nature of each person's relationship with self. What might be this self we are to believe is modified?

### V.3.2. Humanism, transhumanism, posthumanism

The sense of self involves our conception of mankind. Three major directions in modern humanism are apparent (from F. Bacon to R. Descartes): cure diseases, improve capacities, prolong life. In the context of this Opinion, it is the second of these directions that is the problem here, since defining a maximum for capacities is no easy task. Stretching our limitations is one of "mankind's eternal projects" (Baetschi, 2009)<sup>92</sup>. We are "constantly in need of improvement", because we are "indigent and needy within ourselves" (Montaigne, 1588)<sup>93</sup>. Sporting activities are part of this search. But in what way would such humanism appear incomplete or insufficient?

The posthumanist movement, which emerged in the 1980s, is based on the contention that there is no such thing as an intrinsic standard for human nature, nor any stability of that nature (Anders<sup>94</sup>, G. 2002). This movement expressed a severe critique of classical humanism, incapable they contend, of translating its claims into facts. Posthumanism sees itself as the heir of enlightenment, in so far as it seeks more autonomy for human beings, viewed as indefinitely perfectible. It wishes, as described by Anne Fagot-Largeault at the CCNE's annual Ethics Event in 2012, to "take charge of our evolution, direct it so that it is favourable for us", as though the unpredictability of the human species were an obstacle instead of the necessary condition of all bids for freedom. The challenge is, through continuing maximisation of human capacities, to extend ever further the limits of human evolution: age and its failings, pain and even death itself.

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<sup>90</sup> "The out of the way things".

<sup>91</sup> Yves Agid, *L'homme subconscient, le cerveau et ses erreurs*, Robert Laffont, 2013, p.36-39.

<sup>92</sup> Baertschi B., "*Devenir un être humain accompli : idéal ou cauchemar ?*" ("Become an Accomplished Human Being: Ideal or Nightmare" in "*Enhancement*", *éthique et philosophie de la médecine d'amélioration*, (Ethics and Philosophy of Medical Enhancement" directed by Jean-Noël Missa and Laurence Perbal, Vrin, 2009, p.80.

<sup>93</sup> Montaigne, M., *Essais*, Puf, Quadrige, II, 16, p.618

<sup>94</sup> Anders G., *L'obsolescence de l'homme*, tome II, trad.franç. 2002. (The Obsolescence of Human Beings).

But the ancestor of posthumanism is transhumanism<sup>95</sup> which considers the possibility of an evolution in which self-regulated mechanisms act on an artificial selection that is no longer entirely in the hands of Darwinian evolution (J.Proust, 2011), so that humans can surpass themselves with the assistance of genetic engineering, robotics, nanotechnologies and virtual reality. This capacity to surpass oneself is to be understood as access to transcendence (E. Regis, 2002) and is presented most frequently as a list of humanity's grievances against nature (M. More, 1999). These grievances dwell in particular on mankind's lack of instinct and perception in respect to other living creatures: the aim therefore would be to improve human faculties of perception and memory by an improvement in the integration of techniques, either those currently available or those of the future. For example, people having the advantage of wearing hearing aids would be the paradigm for creating this type of integration. Some nanorobots with an impact at cellular level will, so we are told, prolong life more successfully than natural cells are capable of doing (Maestrutti, 2011), while others will purify the blood and eliminate pathogenic agents. But the ultimate example, so far pure fiction only, is to think of the human mind in terms of downloading with the help of a very powerful computer (Goffi<sup>96</sup>, 2011). This is a dream of a brain conceived as a pure information processing system, a brain that is no longer interacting with the world and is reduced to being no more than "*a flow of information in computer networks: not in the world, certainly not of the world, but for ever more out of the world*" (Goffi<sup>97</sup>, 2011). Some thinkers choose to defend in this way the idea that by merging computer networks and human intelligence, the outcome would be a more powerful form of intelligence than either one or the other of its components (Kurtzweil, 2005). According to the upholders of transhumanism, a true cyborg has a biological brain capable of controlling robots and using the artificial extensions of its body. Some dream of converging technologies, combining nanotechnology, biotechnology and biomedicine, information technology, cognitive sciences (NBIC) so that it would "*in theory be possible to exercise almost total control, being in possession of the keys to understanding the information code of matter at every level thanks to the capacity to manipulate bits, atoms, neurons and genes*"<sup>98</sup>.

Posthumanism, together with transhumanism, would like to free mankind from the concept of finality: humans would not be a slave to any particular finality; they would learn to *generate* finality, to organise it — hence the interest in intentional systems, be they human or mechanical (feedback systems). But the ethical issue remains in its entirety: by multiplying intentional systems like individual projects, are we not losing sight of the overall aim, the social project of human development?

Posthumanism seeks to fashion the brain into an agent for remote control of the body using an electronic connection or a computer network. It would seem that for certain post humanists, the human brain's link to a body is contingent. The brain would be engaged in a dialogue with the body as though the one could be separate from the other.

Will robotics be providing a service to individuals or contributing to a form of transhumanism? Optimists would say that the more hybrid systems are remote from natural systems, the less viable they become and, on the contrary, the more they interact with natural systems, the more adaptable they

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<sup>95</sup> The word was coined by J.Huxley 1957: J. Huxley, "Transhumanism" in *New Bottles for New Wines*, Londres, Chatto & Windus, 1957.

<sup>96</sup> Goffi J-Y, *Journal international de bioéthique*, 2011, vol. 23, n: 3-4, pp.17-30.

<sup>97</sup> Cf note 99.

<sup>98</sup> Marina Mestrutti, *Posthumains, représentation du corps entre incomplétude et amélioration*, *International Journal of Bioethics* 2011, vol.23, N03-4, pp. 49-64. (Human, transhuman, posthuman. Representations of the body between incompleteness and enhancement.)

become (Weissenbach J., 2012<sup>99</sup>).

Some, one of them being the philosopher J. Habermas, for example, are concerned about the displacement of frontiers between human and animal or between natural and artificial. He fears human development may lead into using exclusively today's technical forms, leaving aside "*the symbolic (language) pathways allowing for the internalisation and discussion of norms*". How can the confrontation be avoided between a "*pre-human animal (instinctual regulation)*" and "*a mechanically regulated posthumanity*" (Hottois<sup>100</sup>, 2009)?

Other thinkers defend the view that "*from its very beginnings, the human species was 'technical', that is a species that produces artefacts, that tirelessly invents and re-invents itself*"<sup>101</sup>. From that premise, neither posthumanism nor transhumanism exist, there is only a simple and continuous variation of human neuro-plasticity and feedback, available to man for learning and improving capacities (Clark & Chalmers, 2003).

From an anthropological viewpoint, others again would argue that "humanity changes species slightly every time there is a change in both tools and institutions" (Leroi-Gourhan<sup>102</sup>, 1964). Man's humanisation interacts with man's hominization (Delmas Marty<sup>103</sup>, 2013). Humanisation relates to institutions and cultures, hominization is to be understood in the Darwinian meaning of the development of the human species. Their "interaction" is one of the challenges of civilisation.

**To sum up**, classical humanism, in particular as it stems from the Age of Enlightenment, is founded on human perfectibility. Increasingly, it is confronted with transhumanism and posthumanism, two schools of thought listing human bio-finality as forms of control.

## VI – CONCLUSIONS AND RECOMMENDATIONS

In the context of its continuing ethical watch mandate over neuroscientific advances, CCNE decided to devote some **thought to neuroenhancement, which should not be understood as meaning that any such enhancement is actually established**. The appraisal was limited to "**biomedical neuroenhancement**", that is the use, by healthy subjects, of biomedical techniques (medications and medical devices) deviated from their therapeutic indication or research purpose to achieve a supposed psychocognitive enhancement objective. Tools with which to modify psychocognitive functions have existed for a very long time, but the recent explosive development of research on the brain, the substantial implication of the military in this research and expected advances in NBIC convergence all combined to bring about **the current change in the scale and nature of neuroenhancement technologies**. With the development of new modes of perception, of remote control using brain/machine interfaces, etc., this evolution is currently under way and is no longer a figment of science fiction. But it is happening so swiftly that to a very large extent it is preceding the acquisition of knowledge.

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<sup>99</sup> Weissenbach. J, CCNE Report, 2012, Annual Ethics Event.

<sup>100</sup> Hottois, G., "*Science fiction et diète de l'imagination scientifique*", in "*Enhancement*", *éthique et philosophie de la médecine d'amélioration, sous la direction de Jean-Noël Missa et Laurence Perbal, Vrin, 2009, p.22*. ((Ethics and Philosophy of Medical Enhancement" directed by Jean-Noël Missa and Laurence Perbal, Vrin, 2009, p.22.

<sup>101</sup> G. Hottois, *Species Technica*, p.222 and 183.

<sup>102</sup> Leroi-Gourhan, A., *Le geste et la parole*, Albin Michel, 1964. (Gesture and Speech)

<sup>103</sup> Delmas Marty, M., *Organiser les interactions entre hominisation et humanisation*, (Organising the interactions between hominization and humanisation). in *La Bioéthique pour quoi faire ? Puf, 2<sup>o</sup>13, PP.131-135*.

This reflection on biomedical neuroenhancement leads to **two major lines of concern**, the one on health, research, medicine and social protection, the other on the individual and life in society.

### 1. The issue of research, health, medicine and social protection

The dividing line between ‘normal’ and ‘pathological’ being particularly imprecise and labile in the psychocognitive area, it is no easy matter to draw dividing lines between the improvement of certain functions, the restoration of health and treatment of a pathological condition. This is also true of a research environment where, frequently, cognitive research involving the healthy has grown out of findings based on an examination of the sick. In the same way, biomedical neuroenhancement evolved on the basis of data acquired by cognitive research. **In cognitive research studies on healthy subjects**, certain psychocognitive function **improvements** have been observed, but they were **unpredictable, modest, fragmentary and sporadic**. Furthermore, major methodological biases inherent to such studies, together with the risk of drifting into being instrumental to neuroenhancement, demand that **studies be conducted with the greatest degree of intellectual rigour and that results be interpreted, put to use and communicated with the greatest degree of caution**.

**The long-term risk-benefit ratio** for healthy subjects resorting to biomedical techniques for the purpose of neuroenhancement remains a total unknown, but the example of amphetamines suggests **a probable risk of addiction**. This situation, in which lack of knowledge and a potential risk co-exist, deserves to be of particular concern to institutions such as schools and universities and is reason for maintaining **a prudent attitude on the subject of these techniques and to advise in the strongest terms against their use by children, adolescents and vulnerable individuals**.

The unknown factors still shrouding the issue of biomedical neuroenhancement underline the need for long term **observation studies** to provide the quantitative and qualitative data — currently unavailable in France — that are **necessary for drawing up, if need be, preventive or even regulatory measures**. These measures would cover not only medications and medical devices already governed by regulation — less restrictive as it happens for devices which are not held to carrying out risk-benefit ratio studies — but also the transcranial cerebral stimulation instruments for non medical purposes that are the subject of a proliferation of offers on the Internet, coupled with misleading advertising regarding their so-called “neuroenhancing” virtues and which, moreover, do not afford the protection of formal regulatory approval by public health institutions.

**It is essential that everyone, and members of the medical professions in particular, be adequately informed on the various issues involved in biomedical neuroenhancement** so as to inform the debate on the role of physicians and of medicine in the face of this phenomenon. Doctors will need, on a case-by-case basis when neuroenhancement claims are made on them, find a guide for their response within the framework of the clinical relationship with their patients, based on good practices if such are drafted. The community as a whole must reflect on the type of medicine it wishes to have: should medical practice stay within the tradition rails of prevention, diagnosis and treatment of disease, or should it be extending its domain to include this new phenomenon? The stakes are potentially high as regards health priorities and the financial implications of health policies. **Enlarging the scope of medical practice to biomedical neuroenhancement for healthy subjects would imply a major risk of distorting health priorities, a risk which could only increase if public resources were to be committed**. Such a distortion would seriously endanger the principle of social justice at a time when basic methods for promoting psychocognitive development — among the most important of which are nutrition, education, learning and physical exercise — are already so inequitably distributed.

## 2. The issue of the individual and life in society

Those who use neuroenhancement techniques claim insistently for themselves the right to freedom of choice for their lifestyle, without realising that such freedom, more often than not, is the outcome of a **fiercely competitive socio-economic climate and cult of performance which encourages coercion, implicit frequently**. In its Opinion N° 81, CCNE noted that “the fervent quest for performance driven by an imperious desire to make progress, can mask the most constraining of alienations”. The wish to be ‘neuroenhanced’ may seem to be widely shared, by social conformity, but its achievement is only attainable for a few. The risk would then be high of ending up with an ‘enhanced’ social class, containing a small minority of well-informed individuals with sufficient financial resources to achieve their aims. The rush to compete, the cult of performance, or even the desire to dominate, perhaps manipulate, can also generate extremely worrying **explicit coercion** situations in which biomedical neuroenhancement techniques would be used without, or even against, the consent of those concerned.

A person’s life experience is not solely related to individual propensities or cerebral activity; it **is pre-eminently committed to forms of life within society**. Thus, normality cannot be extended independently of the relationship between individuals and their social environment. This relationship is not the outcome of a pre-established physiological state, or of ideally contrived conditions of existence, even if these two situations happen to be usefully consistent with simulations or models. They remain an abstraction compared to forms of life. To confuse model and reality amounts to a **reduction of human complexity** and a betrayal of the scientific modelling function which is to enrich the understanding of the reality under study.

**Seeking a “plus” in the order of psychocognitive functions** is founded on a fragmentation of these functions, a fragmentation presupposed by the biomedical neuroenhancement techniques. But the augmentation of certain measurable functions does not necessarily signify that the individual’s global psychocognitive functioning and relationship with others are actually improved. A scientific analysis which takes into account a cognitive function as one which is separated from other such functions cannot be deemed to comply with the requirement that an individual must always be considered as **a global person** in a given human environment. **The sense of self** cannot be diminished to measuring capacities or focusing on performance.

These conclusions are an incentive to consider neuroenhancement with a combination of moderation, open-mindedness and in a spirit of **scientific inquiry** while trying to steer clear of both the optimism displayed by “enhancers” and the pessimism of “anti-enhancers”, the most extremist of whom see on the horizon, for the former, an “enhanced” human being, surpassing even human status, and for the latter, a man diminished.

More than ever, **ethical watchfulness** is called for, consisting in putting technical rationalities to the test of human conscience, not as an impediment to the development of the techniques, but to reconcile them with their use by humans, with the debate they give birth to and with the often scant information that heralds their emergence.

Paris, 12th December 2013