Presidenza del Consiglio dei Ministri

CNB

COMITATO NAZIONALE
PER LA BIOETICA

NEUROSCIENCE AND PHARMACOLOGICAL COGNITIVE ENHANCEMENT: BIOETHICAL ASPECTS

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Presentation

In Anglo-American literature the term `*enhancement*` is now widespread to indicate intentional intervention in the alteration of the body and mind in relation to `normal` physical and psychological functioning. Think of the use of psychotropic drugs to enhance memory, to increase intellectual activity, to selectively eliminate unpleasant or traumatic memories, to control unwanted emotional states. It outlines a new sphere of bioethical reflection which calls into question the aims of medicine, the meaning of care, the boundaries between health and disease, between normal and pathological, but also the meaning of human nature and social justice.

The NBC carries forward in this opinion some thoughts already expressed in previous opinions dedicated to neuro-scientific experiments, doping and aesthetic surgery. The document, after restricting the scope of its investigation to `pharmacological neurocognitive enhancement` briefly outlines the state of the art, noting that at present the modest benefits to be gained are not such as to offset the risk of significant side effects; subsequently it focuses, in particular, on the profiles of the bioethical debate regarding the use of neurostimulators by healthy subjects. On the basis of the available data on the scientific and empirical level, the Committee finally expresses several bioethical considerations, evaluations and recommendations.

The Committee does not consider unlawful, in general terms, a wise and properly regulated use of cognitive enhancers which are safer and more effective than those currently available, emphasising at the same time that many bioethical and policy issues should also be discussed and addressed. The NBC calls for new research in the neurobiological and neuropharmacological field, it reiterates the bioethical principles of experimentation (proportionality of benefit/risk, informed consent, approval of the relevant ethics committee) as regards the experimental protocols enlisting healthy subjects, it reflects on the problems of health justice, recommending that adequate information on the risks to society of such drugs and hopes for the startup of a more general public debate on the issues of *cognitive enhancement.* The Committee also points out that cognitive function can be improved in a more long-term way through study, continuous stimulation of interests, a rich social life and relationships, healthy lifestyle (nutrition, physical activity) and highlights how exaggerated expectations regarding the enhancing effects of pharmacological neurostimulators derive from a reductive view of human intelligence.

The working group was coordinated by Profs. Vittorio Possenti and Monica Toraldo di Francia, the text was drawn up by Prof. Monica Toraldo di Francia. Written contributions were made by Profs. Antonio Da Re, Silvio Garattini, Laura Palazzani, Vittorio Possenti, Giancarlo Umani Ronchi e Grazia Zuffa. Profs. Salvatore Amato, Adriano Bompiani, Stefano Canestrari, Francesco D'Agostino, Lorenzo d'Avack, Carlo Flamigni, Marianna Gensabella, Laura Guidoni, Assunta Morresi, Demetrio Neri, Andrea Nicolussi contributed to the discussion of the text within the working group. The text makes use of the scientific contribution of Prof. Silvio Garattini, consulted during the plenary session.

The document was approved by majority vote. Profs. Luisella Battaglia, Adriano Bompiani, Bruno Dallapiccola, Lorenzo d'Avack, Riccardo Di Segni, Silvio Garattini, Marianna Gensabella, Laura Guidoni, Assunta Morresi, Andrea

Nicolussi, Laura Palazzani, Vittorio Possenti, Monica Toraldo di Francia, Giancarlo Umani Ronchi, Grazia Zuffa gave a favourable opinion. Prof. Cinzia Caporale abstained from voting. Profs. Salvatore Amato, Stefano Canestrari, Francesco D'Agostino, Antonio Da Re, Maria Luisa Di Pietro, Demetrio Neri and Lucetta Scaraffia, absent from the meeting, subsequently adhered to the document.

The President
Prof. Francesco Paolo Casavola

1. Introduction

Following the document on *Neuroscience and human experimentation: bioethical problems* (17 December 2010), the NBC continues in the examination of issues relating to so-called `applied neuroethics` by proposing some reflections on the theme of so-called cognitive `*enhancement*` of a pharmacological kind and on the bioethical questions which it raises.

As is known in the last twenty years the theme of `*enhancement*` - a conceptually ambiguous term, which will be used here in the restricted acceptation of *intentional use of knowledge and technologies for biomedical interventions on the human body in order to modify, in an ameliorative and/or potentiating way, its normal functioning*[1] - has been the focus of intense debate among philosophers, bioethicists and scientists of different orientations. This debate was stimulated initially by the encounter of genetic engineering and reproductive medicine and subsequently, subjection to the attention of so-called converging technologies (*Converging Technologies: Nano-Bio-Info-Cogno*), interweaving with the themes of bionic man the transhuman and posthuman, there has developed especially in view of possible future scenarios prefiguring an anthropological `revolution` large enough to redesign human identity and the same mechanisms of evolution of the species.

We would like to start by saying, in order to avoid misunderstanding and confusion, that when it comes to the *enhancement* of human abilities, physical and/or mental, through biomedical technology we must keep in mind at least three fundamental distinctions:

- the first between enhancement of capabilities or existing functions/creation of new organic and mental features (e.g. the ability to read the minds of others, to withstand very high temperatures or vice versa, and the like);

- the second between enhancement of capabilities or transmissible functions (e.g. those possibly obtainable by means of germ cell intervention)/non-transmissible to descendants;

- the third between enhancement of human capabilities remaining within statistical normality (e.g. aimed at improving the performance of those who are `naturally` disadvantaged compared with the average)/enhancement which strives to raise above `normal` the performance of specific individuals or the general level of the population[2].

As is easily intuitable, cognitive enhancement techniques involve complex bioethical, anthropological and social issues which drive us to further refine analysis, avoiding hasty acceptance or rejection. In this document, however, the NBC does not deal with future scenarios of humanity being radically transformed by technology, nor, as regards "cognitive function", the possibility

[1] The restricted acceptation is indeed the one which today raises the greatest bioethical problems.

[2] Cf. A. Buchanan, *Cognitive enhancement and education*, in “Theory and Research in Education”, 2011, v.9, 2, pp. 145-162. However, in other contexts, and always with reference to new technologies, it is possible to use a criterion of distinction, that is less analytical, such as the +one contrasting "improvement-optimisation" with real "enhancement" including in this "last category only those interventions that drive bio-physical capacity above the typical level of the species and beyond the statistically normal margins of functionality for individuals. Cf. *NBC Human rights, medical ethics and enhancement technologies in the military*, 13 March 2013.

still only hinted at, of using new genetic technologies or micro-electro mechanical enhancement (genetic engineering, brain computer interface, intracranial magnetic stimulation). The field of interest is limited to consideration of already existing scenarios, despite their different geographical diffusion, revealing the third of the distinctions mentioned, more specifically, here we take into account so-called pharmacological `neurocognitive enhancement` - which in fact concerns, at least for now, only modest improvements possible in some specific and limited mental performance - which poses more concrete ethical questions, which need to be considered also with a view to highlighting the different profiles and stimulate a more informed public debate on the matter.

In the first part of the document it was considered appropriate, at the outset, to return to the controversial issue of the distinction between `normal`/`pathological` to highlight how it assumes an even more problematic nature in the sphere of neuropsychology, where the boundary between therapeutic/ameliorative becomes especially difficult to trace. Following on we deal with the `state of the art,` emphasising how pharmacological enhancement of `cognitive abilities` is, in fact, currently limited to use of `*off label* 'medicines , developed especially for the treatment of psychiatric and neurological syndromes or diseases, by healthy individuals. The second part discusses the developments of bioethical debate around this issue, starting from the publishing in "Nature"[3] (2008) of an article, written by a group of scholars from various disciplines in favour of a responsible and controlled use of drugs for cognitive enhancement (henceforth PCE) if aimed at improving memory performance and learning in the scholastic-academic sphere. Reference to the developments of this debate will allow both to clarify, on the basis of the most recent empirical data, some of the misunderstandings that have made the discussion conceptually unsatisfactory, as well as permitting to draw distinctions concerning the underlying reasons for the consumption of non-medical `neurostimulators`, helpful to the more precise delineation of the issue in question and the problems it raises. The third part is devoted to bioethical evaluations and recommendations and distinguishes what is currently under discussion from the problems which may arise, in relation to this specific field, in the relatively near future.

2. The controversial boundary between therapeutic/ameliorative

Not being able, in this opinion, to enter into the merits of a dispute that has a long history and which pertains to the philosophy and epistemology of medicine, one can mention here that - while the fundamental opposition between `naturalists` and `normativists`[4] remains - today it is generally given

[3] H. Greely, B. Sahakian, J. Harris, R.C. Kessler, M. Gazzaniga, P. Campbell & M.J. Farah, *Towards responsible use of cognitive-enhancing drugs by the healthy*, in ”Nature”, 2008, v. 456, n. 7223, pp.702-705.

[4] `Naturalists` think that we can give an objective scientific description that is value-free, of the distinction using statistical methods: the existence or absence of a deviation from the norms regulating the physiological functions typical of human organisms constitutes a universalisable criterion of distinction. `Normativists` by contrast, consider that what is classed, in different eras and societies as `disease` is always the result of a particular social context and cultural values that inform them, insisting on the aspects of social construction inherent to the definition of 'health' and 'disease', they believe that the two concepts are always permeated by value judgments determined historically and culturally. Cf. A. Pagnini (a.c.), *Filosofia della medicina.*

that the line of demarcation between therapeutic-reparative/*enhancement* of functions and abilities can, at times, be faint and presupposes, however, a prior agreement regarding what is 'normal'/'abnormal'. In this regard, for example, even the document of the European Group of Ethics in Science and New Technologies (EGE), *Ethical aspects of ICT implants in the human body,* cites as an exemplary `case` which challenges the concept of the existence of a general standard of human capabilities - functions, the case of cochlear implants for deaf children, the particular concept of `normality` that underlies the promotion of therapeutic purposes of such implants has, in fact, been challenged by the same deaf community that refuses to consider their condition as being deficient[5].

This issue becomes even more problematic when it is then faced in the relevant area of neuropsychology, where the boundary between therapeutic/ameliorative becomes particularly difficult to determine for several reasons, which it seems appropriate to mention briefly.

a. The first reason may be identified in the process of progressive medicalisation that, since the nineteenth century, has affected the emotional sphere. Those which were once considered as normal emotional reactions of living beings to the circumstances of life (bereavement, frustration, stress) have been gradually converted into pathological states, legitimising, in this sense, their medicalisation and the increasingly widespread use of the medical-psychiatric prescription of psychotropic drugs[6]. The moment these emotional reactions are medicalised and classified in psychiatric language (depression, affective disorder, etc.). and treated pharmacologically, it so happens that people are more likely to seek medical attention to be helped to overcome with pharmacological assistance any state perceived as psychological distress. In this way, it becomes much more difficult to distinguish between those who take these drugs to restore a compromised mental balance and order to lead a 'normal' life and those who possibly make use of them to `improve`, or optimise their psychological well-being and performance in the sphere of education and work. In addition, medicalisation, by focusing on the biological aspect of distress tends to underestimate, if not disregard, the social causes and family/relationship linked causes which can be the very origin of the malaise.

It should also be kept in mind, when considering this aspect , that the classifications of syndromes and psychiatric disorders are still, in large part, merely based on symptomatology, without there being a knowledge of the

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epistemologia, ontologia, etica, diritto, Carocci, 2010 (in particular: *Salute e malattia*, by Giovanni Federspil, Pierdaniele Giarretta, Nadia Oprandi).

[5] *Ethical aspects of ICT implants in the human body*, Opinion presented to the Commission by the European Group on Ethics, Brussels, 17 March 2005.

[6] B. Fantini, *An historical sketch of changing vocabularies of emotions,* Humana.Mente – Issue 9, 2009. On the trend toward medicalisation of life events and emotions, cf. also the report of the Canadian Commission on the Ethics of Science and Technology (CEST), *Psychotropic Drugs and Expanded Uses: An Ethical Perspective*, 2009.

The document of the Canadian Commission is one of the few official documents - addressed to public authorities and professional groups working within health care, as well as the pharmaceutical industry - which makes a broad examination of the various aspects related to the expanded use of psychotropic drugs in the population and, in particular, to their non-medical use (especially prevalent in Canada and Quebec), and then goes on to conclude with a series of recommendations directed to all the parties involved.

http://www.ethique.gouv.qc.ca/INDEX.PHP?OPTION=COM_DOCMAN&ITEMID=22&LANG=FR%20PUBLICATIONS).

possible biological roots of the disorder; an example being, the inclusion among psychiatric disorders of the new syndrome of attention deficit and hyperactivity[7] (ADHD: Attention Deficit Hyperactivity Disorder), which has aroused much controversy over the years and to which we shall return later.

b. A second reason lies in the possibility of making use, in order to justify the prescription and/or taking of medication to improve mood (mood enhancers) as well as cognitive performance, of the broad definition of health proposed by the World Health Organisation (the WHO, in its charter defines the concept of health as `*a state of complete physical, mental and social well-being*'). Such a definition inhibits the ability to make a clear distinction between disease and mental suffering, with all the effects, not only positive, resulting from an interpretation that emphasises the subjective dimension of suffering.

c. A third reason is that, even for the reasons mentioned, it is increasingly difficult to distinguish between treatment of affective disorders and mood, on the one hand, and cognitive *enhancement* on the other, since their relationship can prove to be circular: biomedical intervention that improves the state of mind may have positive effects on cognitive function, calming anxiety and strengthening motivation, similarly, an improvement of certain mental performance may have positive effects on the levels of mood and self-esteem.

It is also based on these findings that some bioethicists have questioned not only the possibility of drawing, in different circumstances, a convincing distinction between therapeutic/ameliorative, but also the value of this distinction as a criterion for making judgments on the lawful-ness/unlawfulness of the different practices made possible, or even just thinkable, by biotechnological development[8]. In other words, equivalence between what is therapeutic and allowed, ameliorative-potentiating and not allowed, does not seem to be convincing and therefore of help as regards bioethical assessment.

3. Pharmacological "enhancement" of cognitive abilities: current issues and prospects

Returning to the theme of increasing individual cognitive abilities, there is a distinction, preceding all others, and should not be forgotten: that is between the `conventional`, `classic` methods, for improvement - which are culturally accepted and that, in most cases, have been practiced for thousands of years:

[7] Attention Deficit Hyperactivity Disorder is a neuropsychological developmental disorder in children and teenagers, characterised, according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III, DSM-IIIR, DSM-IV), by inattention and impulsivity and/or hyperactivity all of these symptoms, which are not caused by cognitive impairment (mental retardation), but by objective difficulties in self-control and the ability to plan, are persistent in all contexts and situations of life of the child resulting in significant limitation of daily activities (source: National Institute of Health http://www.iss.it/adhd/cosa/cont.php?id=231&lang=1&tipo=1).

[8] Of this opinion are some of the most famous protagonists of bioethical debate, for that matter, positioned on opposite sides, as, e.g. L. Kass, *Report of the President's Council on Bioethics, Beyond Therapy. Biotechnology and the Pursuit of Happiness* and Dana Press, New York 2003 and N. Bostrom & A. Sandberg, *Cognitive enhancement: Methods, ethics, regulatory challenges,* in "Science & Engineering Ethics", 2009, 15, 3, pp. 311-41. As noted by Kass, the ethically pertinent questions not so much about "whether or not a certain bio-medical practice is or is not aimed at care or enhancement, but rather those who ask themselves "*what are the good/bad uses of bio-technical power*?", "*what makes utilization [of this power] good or at least acceptable?".*

education, mental exercise, mnemonic techniques, and more recently use of electronic technologies etc… - and methods that can be defined as `non-conventional` and still at the experimental stage, although at different stages of development, such as genetic engineering, neural implants, the deliberate creation of nootropics (from the Greek *noos*, mind, and *tropein*, monitor) etc.[9]. As mentioned, it is with regard to the second that complex philosophical, anthropological, ethical and social problems have been raised, within the field of neuroscience. However, also included, as part of the second, is the more modest practice of cerebral stimulation through drugs.

The use of substances of various kinds (caffeine, nicotine, amphetamines etc...) to improve resistance to fatigue and intellectual performance has, as is known, a long history; the `novelty` today is, rather, in the availability of more sophisticated pharmacopeia, developed for the treatment of psychiatric and neurological syndromes and diseases (Alzheimer's, Parkinson's, dementia syndrome, attention deficit and hyperactivity, narcolepsy, autism, etc.) whose use by `healthy` individuals would seem to increase to some extent - albeit with conflicting results -short-term memory[10], the capacity for concentration and learning, cognitive control (which represent, it should be pointed out, only a few aspects of our mental processes)[11]. In the last decade for this category of `neuroenhancers`, or `nootropics`, multiple labels have been coined, depending on an implicit positive/negative judgement on their non-medical use, as well as the intention to suggest analogies with other types of interventions on the body regarded as lawful/unlawful: *smart drugs*, lifestyle drugs (substances intended to alter lifestyle), viagra for the brain, cosmetic neurology, brain doping, etc.[12].

Among the molecules in question, whose continuative consumption seems to be especially prevalent among the students of Colleges and Universities in

[9] Cf. N. Bostrom and A. Sandberg, *Cognitive enhancement* cit; S.M. Outram, *Ethical Considerations in the framing of the cognitive enhancement debate,* in "Neuroethics", 2011, 5, Issue 2, pp.173-184.

[10] Cf. M.J. Farah, J. Illes, R. Cook-Deegan, H. Gardner, E. Kandel, P. King, E. Parens, B. Sahakian & P.R. Wolpe, *Neurocognitive enhancement: what can we do and what should we do?,* in "Nature Reviews Neuroscience", 2004, 5, Issue 5,pp.421-425. The pursuit of control over the mechanisms of memory, however, is not just about the search for substances that can help to increase memory in the short and long term, but also that of agents that may prevent the consolidation of undesirable memories in the case of traumatic events. The use of drugs that can block unpleasant memories by those not the victim of trauma would be another way of alteration of the neural basis of memory in order to improve its normal functioning. On this last aspect and on the unilateralism of this approach to the conception of the functioning of `memory` cf. N. Levy, *Changing one's mind. The ethics of memory erasure in eternal sunshine of the spotless mind*, in "S & F", 2011, n.5, online magazine: www.scienzaefilosofia.it.

[11] Needless to say, at least as regards the media reports of the debate on this type of cognitive potentiator, a reductive view of human intelligence tends to prevail, its being represented as a set of separate functions-performances, each of which can be acted on autonomously and effectively with a pill, without taking into account the environmental, emotional, and relational influences, affecting them.

[12] Cf. For example. J. Harris, *Chemical cognitive enhancement: Is it unfair, unjust, discriminatory, or cheating for healthy adults to use smart drugs?*, in "Oxford Handbook of Neuroethics", J. Illes, B.J. Sahakian (eds), Oxford Univ. Press, 2011; R. Langreth, *Viagra for the Brain*, in "Forbes", 4 February 2002; *I doping della mente,* in "La Repubblica Salute", 12/02/2009, p. 8; A. Chatterjee, *Cosmetic neurology - The controversy over enhancing movement, mentation, and mood*, in "Neurology", 2004, 63, pp.968-974; A. Chatterje, *The promise and predicament of cosmetic neurology*, in "Journal of Medical Ethics", 2006, 32, pp.110-13. Chatterjee, e.g., while highlighting the ethical and social issues currently causing concerns and uncertainties, there are no doubts that `cosmetic neurology` will become in the near future, as acceptable as aesthetic surgery.

the United States and Canada, there are e.g. Ampakines[13], which promise to enhance brain activity in memory and attention disorders, and others put on the market for the treatment of ADHD, such as methylphenidate[14], or for the treatment of narcolepsy and sleep apnea, such as modafinil, a substance that, by acting on sleep-wake mechanisms, enables `healthy` individuals to stay awake for many more hours than normal in terms lucidity and concentration[15].

According to the data found in the English literature concerned with the phenomenon of the consumption of PCE, the estimate, regarding North American Colleges and Universities, is approximately 7% - 8% of students, with peaks up to 25% or even 37%, but also among teachers, professionals and managers, the phenomenon seems to be in expansion. It is not surprising then that this literature tends to present the university campus as a kind of laboratory for nootropic testing, where every day young students carry out experiments on their brains using substances to improve their scholastic performance and feel

[13] The Ampakines are substances that interact with the AMPA receptor, potentiating the activity of glutamate, a neurotransmitter involved in learning processes and codification of memories.

[14] The molecule that is effective in the treatment of ADHD is methylphenidate that is basically an amphetamine. In recent years the controversy about administering to children and adolescents diagnosed as suffering from ADHD drugs based on methylphenidate (marketed with the names of Ritalin, Adderall etc). has been fierce and criticism has been directed so much to the increasing number of these diagnosis, not substantiated by reliable tests, with regard to the side effects, even very serious ones, of the drugs themselves - the unspoken effects by the great pharmaceutical companies that market them making huge profits - and not least to the addiction that they can create. In Italy Ritalin was registered by AIFA in 2007; to avoid its being used unjustifiably there was established at the same time - at the Department of Medicine of the National Institute of Health - the National Registry for ADHD, whose protocols are described in the ISTISAN Report 09/20. The registry is the instrument to prevent misuse of the medication, by providing support for the diagnosis - which can only be made at an authorised Centre for mental health and neuropsychiatry afferent to the registry - as well as the choice of treatment, which may not be pharmacological. This means that medication is under control and children who are subjected to therapy (today around 1700) are about ten times fewer than those of other countries. Adderall, instead, has not yet been registered in Italy.

[15] Modafinil is used to treat excessive daytime sleepiness in patients with narcolepsy, a neurological disorder originating from an alteration of the central nervous system mechanisms that regulate our sleep-wake rhythms. Its precise operational mechanisms are not yet fully known although - as explained by Cristina Colombo who is in charge of the Centre for Mood Disorders at the Hospital San Raffaele Turro - "We know that it stimulates the production of dopamine, substances responsible for the acceleration of the heartbeat and a rise in blood pressure, setting in motion a series of functions such as concentration and alertness." non-medical use of modafinil may be dangerous to health as it tends to be misused, by exceeding the recommended doses: By continuing to stimulate the production of dopamine, for example, increases the burden on the heart and increases the risk of heart attack. In addition, sleep is a necessary function to the brain and psyche, and it is "essential for the reorganisation of cognitive functions such as memory and learnign". Since 2000, Modafinil has become available in Italy, but its use restricted to two criteria: the first is that the drug can only be prescribed by specialists for narcolepsy (by neurologists and pneumologists when it comes to patients suffering from obstructive sleep apnea, for which the drug has proved an effective aid), the second criterion is linked to the accurate estimation of epidemiological data in order to understand the level consistent with appropriate use.
(http://d.repubblica.it/dmemory/2007/03/10/attualita/attualita/120sci539120.html).
In a recent intervention Nora Volkow, director of the National Institute on Drug Abuse (U.S.), recalled that in the UK, unlike the U.S., the use of neurostimulants by the military was banned after the discovery that they could lead to paranoid disorders: cf. S. Hyman, N. Volkow, D. Nutt, *Pharmachological cognitive enhancement in healthy people: Potential and concerns,* in "Neuropharmachology", 2013, 64, pp. 8-12. As for the more general *off-label* use of these substances in the military field, refer to NBC, *Human rights, medical ethics and enhancement technologies in the military*, 13 march 2013.

more competitive with less stress. As for 'where' to obtain PCE, according to a recent study, 52% of those using them make use of a medical prescription (even faking ADHD symptoms), 14% turn to compliant pharmacies, while the remaining 34% buy them through the Internet, where there is an abundance of so-called cyberpharmacies, or on the black market on campuses, regardless of the additional risk that this may entail[16].

However, one should add that the neuroenhancers currently in circulation all have "very limited effectiveness, but raise quite a few problems with regard to their `safety`, however, since pharmaceutical companies are investing a lot of money and time in the development of molecules aimed at the treatment of cognitive decline (both physiological and pathological), many people think that it will soon be joined by a safer and more effective pharmacopoeia[17]. It is said that there is strong request from an aging population which can not bear to lose its memory, parents determined to stimulate their children by whatever means, students and professors busy competing with each other in the academic arena, professionals stressed by an unsustainable pace of work. There are those who believe therefore that in the very near future neuroscience will make significant progress as to the understanding of our complex brain mechanisms and that more valid cognitive enhancers than those available today will be developed: some people will use them as therapy, others because their requirement is `borderline` and others simply to have an advantage in competition[18]. But there are also those who sustain - based on a highly biologistic conception of mental functioning - that the democratic values underlying our public education systems militate in favour of the institutionalisation of pharmacological cognitive enhancement in the education sector, and more generally in the educational process, if they came to develop PCE that in addition to being safer, were also able to ensure the better functioning of normal cognitive processes. According to proponents of this conception[19] (widely criticised from many sides) the institutionalisation of cognitive enhancement, under the conditions described above instead of inciting new inequalities, could mitigate existing ones and, at the same time,

[16] S.M. Outram, *Ethical consideration in the framing* cit.

[17] But there are also scientists, engaged in this field of research who consider such a forecast too optimistic, e.g., Gary Stix, one of the most well-known collaborators of ` Scientific American, believes that it is highly unlikely - given our little knowledge of various aspects of neuropsychopharmacology - that in the near future we will be able to develop a drug, that does not produce serious health risks, capable of improving memory, attention and the speed of learning.
http:**//**blogs.scientificamerican.com/observations/2011/12/07/are-we-as-smart-or-dumb-as-we-can-get.

[18] M. Talbot, *Brain Gain,* New Yorker, April 27 2009. Italian translation: *Con un poco di pillole il cervello va su e diventiamo più efficienti, lucidi, creativi, wow! o è solo doping cerebrale*?, http://mag.wired.it/rivista/storie/con-un-poco-di-pillole-il-cervello-va-su.html.

[19] Cf. A. Buchanan, *Cognitive enhancement and education*, cit. It should be noted that in the ranks of so-called `technophiles`, there are also those who believe that cognitive "enhancement" is not desirable, because it is too dangerous for the survival of the human race, unless it is accompanied by a corresponding moral "enhancement of human beings, obtainable by the development of new biomedical and genetic technologies": cf. I. Persson & J. Savulescu, *The perils of cognitive enhancement and the urgent imperative to enhance the moral character of humani*ty, in "Journal of Applied Philosophy", 2008, 25, (3), pp.162-177.

help to correct biochemically those cognitive defects that come under human `normality` and impede optimal functioning of our mental abilities[20].

4. Profiles of the debate on the use of neuroenhancing drugs by the healthy

In the context of bioethical debate on pharmacological cognitive *enhancement* - firstly in the Anglo-American area and later also in other countries, including Italy - there was a defining moment with the publication in "Nature" of a deliberately provocative article written by many people together and entitled *Towards responsible use of cognitive-enhancing drugs by the healthy*[21]. But in previous years several essays on neurocognitive enhancement had come out which had taken into account, above all, the pharmacological phenomenon and outlining the subsequent bioethical debate on the subject[22] All authors started with the assumption that the phenomenon of the non-intermittent consumption of PCE was a phenomenon in constant expansion - a "fact of life" already for many people - which, like it or not, had to be acknowledged.

In the article in " Nature" Henry Greely and the other signatories were, on the whole, in favour of a controlled and responsible consumption of neurostimolants designed to improve concentration, speed of response, short-term memory, etc. Assuming that the use of these neuroenhancers by the "healthy" (i.e. those not in need of the drug for therapeutic purposes) is largely dictated by the desire to have higher marks and to improve one's capacity for

[20] According to Allen Buchanan the institutionalisation not only has a positive impact on individual development (the *individual's flourishing*) and social well-being as a whole, but would also contribute to overcoming the stigma against those who are diagnosed as suffering from specific learning disorders, such as, for example, ADHD. Next, as regards "normal" cognitive defects of the species he does not ignore that they may be, or have been functional to our relationship with the outside world and with others, nevertheless, he believes that, in the near future, they may prove harmful faced with the challenges that will arise. In his view, therefore, the objective should be not only to improve the condition of those at the lowest end during the `natural` distribution of mental abilities, but it should also include the improvement of normal cognitive functions of the average person and increment our ability to absorb and integrate information.
In contrast, the advantages of functioning by means of not perfectly logical mental patterns have been the subject of numerous studies (cf. e.g. E. Boncinelli, *Il cervello la mente e l'anima. Le straordinarie scoperte sull'intelligenza umana*, Mondadori, 1999, chapter VII).
More recently, Gary Stix has insisted on the paradoxical and undesirable consequences that may occur with the non-medical use of stimulants to increase certain cognitive performances such as, for example, the ability to focus attention: to be mentally fixed on a single task may in fact be of hindrance rather than of help to the flexibility of thought needed to address a very significant intellectual challenge. Furthermore, according to Stix, "the complex mix of chemical signals,enzymes and proteins that collaborate to form a memory creates a self-regulating balance that resists tinkering unless disrupted by disease":
http://blogs.scientificamerican.com/observations/2011/12/07/are-we-as-smart-or-dumb-as-we-can-get.

[21] H. Greely, B. Sahakian, J. Harris, R.C. Kessler, M. Gazzaniga, P. Campbell & M.J. Farah, *Towards responsible use of cognitive-enhancing drugs by the healthy* cit.

[22] Among them: A. Chatterjee, *Cosmetic neurology* cit. And by the same Author, considered one of the most knowledgeable scholars of the subject, *The promise and predicament of cosmetic neurology* cit; Martha J. Farah *et al.*, *Neurocognitive enhancement: what can we do and what should we do?* cit; B. Sahakian and S. Morein-Zamir, *Professor's little helper*, in "Nature", 2007, pp. 1157–1159.

study and learning, they wondered whether it would be better to make consumption lawful rather than leaving the demand to the black market, that is to say, illegal and uncontrollable. It was also pointed out how the strong social pressure that drove people to seek to raise the level of their performance in education and work could trigger some real mental illness (performance and competition anxiety), which would have been better prevented, even allowing the use of pharmacological aids of the kind mentioned[23].

The discussion opened by "Nature" was then further enhanced thanks to a series of contributions that focused attention, especially on two ethically important issues: the relationship between the expected benefits and risks to health and the possibility that the various access opportunities to these substances generate socially discriminatory situations. What however should be emphasised here is that the same approach to the problem, as outlined by Greely and his companions, has the object of criticism of some recent publications[24], particularly with regard to two central aspects of their premise: the first concerns the distinction between subjects considered as healthy according to a standard of statistical normality/individuals with cognitive difficulties, and the second concerns instead the reasons underlying the consumption of neuroenhancers by the student population.

For the first aspect, new empirical studies have highlighted how some of the so-called "healthy individuals" included in the estimates of consumers of PCE for scholastic- academic purposes, in fact, show symptoms very similar to those identified with the syndrome of attention deficit and hyperactivity disorder (ADHD), or at least revelatory of specific undiagnosed cognitive difficulties. In these cases, the "use of the substances in question could be regarded as a kind of "self-treatment" and not as the search for a real enhancement of `normal` cognitive abilities[25] (`normal` is used here as a statistical concept in correspondence to a standard). If this is true, it follows that either we review the belief that the non-medical use of stimulants for scholastic--academic reasons is necessarily a form of "*cognitive enhancement"*, or we acknowledge the difficulty of separating the self-treatment of cognitive disorders from *enhancement*, with the consequence of making even more difficult and confusing the abstract distinction between enhancement and therapy. The condition of ambiguity, in this case (as in others), is in fact accentuated by the

[23] In the wake of these interventions "Nature Network" has also carried out, in April 2008, an informal online survey, which asked readers-scientists if they had tried to improve "attention, concentration or memory" through the use of drugs such as Ritalin (methylphenidate), or Provigil (generic name: modafinil). Responses were prompt: a reader in five responded affirmatively. The majority of the 1,400 respondents - of 60 different nationalities - also claimed to be in favour of adults being allowed to decide for themselves whether to take nootropics or not. 69% considered any side effects to be an acceptable risk, while a third of the readers admitted they would feel impelled to give their children these so-called smart drugs if they come to know that this practice was being adopted by other parents.

[24] See in part S.M. Outram, *Ethical considerations in the framing...* cit. and the extensive bibliography that accompanies this essay; D. Repantis, P. Schlattmann, O. Laisney and I. Heuser, *Modafinil and methylphenidate for neuroenhancement in healthy individuals: a systematic review*, in "Pharmacol. Res", 2010, 62, pp.187-206.

[25] S.M. Outram, *Ethical considerations in the framing* cit. On the difficulty of establishing a reference standard for cognitive functions, given the diversity of human beings, cf. *Commission on the Ethics of Science and Technology* (CEST) Canada, *Psychotropic Drugs and Expanded Uses: An Ethical Perspective, cit*; in this regard, the Commission notes that in reality any definition of "normality" cannot but be complex, and of a subjective and evolutionary nature.

fact that the same molecule is associated with both the concept of `therapy` and that of `enhancement`.

With regard to the second aspect, many parties have highlighted the need to collect a larger number of data on the frequency of consumption and the reasons underlying the "use of nootropics, also to avoid the risk of an overestimation of the current phenomenon of the search for intellectual enhancement, confusing what, in actual fact, are "recreational aims" with the desire to improve one's cognitive performance [26].

The most recent research, taken as a whole, allows for some generalobservations to be made, that are useful to set in a more analytically accurate manner related bioethical assessments.

a) A first observation concerns the difficulty of gathering information about epidemiologically significant effects on 'healthy' individuals - in terms of the effectiveness and safety - of various neurostimolants.

This difficulty is due to the fact that the data reported in the studies in question (still very little) vary considerably for two reasons: because of the differences in the methods applied in the experimental protocols[27]; because, dealing with illegal practices, the collection of data on their diffusion is anything but simple. There is, indeed, an understandable resistance to come out into the open and, also, those who let themselves be interviewed, by admitting to make use of these drugs, are often brought , more or less consciously, to accentuate the benefits and minimise any adverse effects. More specifically, with regard to the effectiveness of these neuroenhancers in general, it turns out to be very low and very variable, according to the most recent reviews of experimental studies.

Resulting from this is the general recognition by the scientific community, of the need for better coordination of research, with standardisation of methodologies, together with the need to `increase knowledge` of the delicate balance of the brain with which it is interfering and the complex mechanisms that modulate the diversity of individual responses when taking nootropics, of one kind or another (not coincidentally a substantial part of neuropharmacological and neurobiological research is currently directed precisely to the identification of the factors, biological or otherwise, which may affect this variability).

As regards, more particularly, the risks to health of PCE - whose long-term effects are, however, still almost unknown - it should be noted that even on this aspect there is no agreement, apart from the fact that their non- intermittent use can have very serious and/or long-term side effects and that there is a need to carry out further studies in this regard. You may however consider that the

[26] It is estimated, very approximately, that in the list of motives in first place there is the desire to improve attention and in second place "recreational aims", the "enjoyment of" free time (but the two motives are often combined), followed by the desire to acquire a different style of studying, to get higher marks and the need to reduce hyperactivity. However, for an accurate estimate of the true motives, the data available is still conflicting and insufficient: cf. C.A. Ragan, I. Bard, I. Singh, *What should we do about student use of cognitive enhancers? An analysis of current evidence*, in “Neuropharmachology”, 2013, vol. 64 (*Cognitive Enhancers: molecules, mechanisms and minds 22nd Neuropharmacology Conference*), pp. 588-595.

[27] With reference to both the different levels of difficulty of the tests to which recruited subjects in the research are subjected, as well as to the different methods of measuring the results. Cf. M. Husain and M.A. Mehta, *Cognitive enhancement by drugs in health and disease*, in “Trends Cogn. Sci.”, January 2011, 15(1), pp. 28–36.

modest benefits possibly obtainable do not seem, at present, able to balance the risk of significant side effects for those who take them for non-medical purposes[28].

b) More importantly, from the perspective of cognitive neuroscience, is the aired possibility, supported by some empirical data, that these drugs - taken by healthy persons and those who are not in good health - while improving individual aspects of cognitive functioning depress others. With regard to those 'healthy' individuals, some researchers that have long been dealing with the issue[29] have asked themselves whether neuroenhancers that heighten attention may not at the same time blunt creativity and/or other mental functions. In support of this prestigious studies in cognitive psychology are cited, which claim that there is an inversely proportional relationship between concentration and creativity.

c) Also pointed out is that there is now much evidence also in favour of the thesis by which the PCE available today (for the three mental domains of short-term memory, of attention-learning ability, cognitive control) work on average but in descending order, i.e. in an inversely proportional way to the so-called `IQ` of those who use it[30].

d) Lastly, it must be emphasised that many of the considerations in the bioethical debate are still of a speculative nature and projected towards the future, as for now, there are no drugs available that demonstrate a favourable benefit-risk ratio. The effects of enhancement recorded at the moment are of little importance as they are limited to specific experimental situations that have little significance for the improvement of functions linked to the cognitive process[31].

5. Evaluations and recommendations

As we have seen, issues related to the use of PCE have been for some years the subject of a vivacious scientific, bioethical and biopolitical debate seeing English scholars in the front line. The issues raised by non-medical use of nootropics, intertwine with questions of great complexity, of a more philosophical-gnoseological nature which however do not come into or only indirectly fall within the context of this document, e.g. the question of determining the meaning and content of the notions of `knowledge` and `cognitive` - which are not reducible to a sum of individual performances - or the question of whether what is being `enhanced` is the brain or the mind,

[28] The problem of "safety" concerns, of course, all drugs, none of which is devoid of side effects, but tolerance to the possible risks cannot but be much lower when there is no necessity to treat a disease.

[29] M. Farah, C. Haimm, G. Sankoorikal, and A. Chatterjee, *When we enhance cognition with adderall, do we sacrifice creativity? A preliminary study,* in “Psychopharmacology”, 2009, 202, 1, pp. 541-7.

[30] Martha Farah hypothesises that this is due to the fact that people with naturally low levels of dopamine are those that can benefit more from an artificial boost.

[31] Cf. *Cognitive enhancers: molecules, mechanisms and minds 22nd Neuropharmacology Conference*: *Cognitive enhancers*, in “Neuropharmachology”, v. 64, 2013, in part. *ivi* C.A. Ragan, I. Bard, I. Singh, *What should we do about student use of cognitive enhancers? An analysis of current evidence* cit.

which refers to the more general discussion on the relationship between mind and brain and their related themes and issues[32].

In short, at present it is difficult to make a univocal bioethical judgment about PCE which could be developed in the near or distant future, for the many reasons already mentioned: research still in its initial stages together with its remarkable acceleration that does not allow adequate moments for adjustment, the still partial knowledge of how PCE works and the complex brain mechanisms which they affect, etc. With the caution mentioned above - and with the realistic expectation that not even in years to come will there be a "magic" pill capable of improving our cognitive performance[33] replacing the usual processes of education and training, study and learning - it can be assumed that in future a `wise` and properly regulated use of cognitive enhancement of a pharmacological kind, is not, in principle, in itself morally reprehensible, once its effectiveness and its not being harmful has been ascertained. Its not being abstractly unlawful, however, does not eliminate the numerous problems regarding bioethics and policy - already explored in literature - that the possible development of safer and more effective PCE raises and which it is appropriate to mention here, these particularly include:

1) coercion (direct and indirect) and freedom: discussion - in the hypothesis of legalisation - on the possibility that this practice could, even if it weren't compulsory , nevertheless become coercive for the population in general or for specific categories (both in the public and private sector) in terms of the penalisation-marginalisation of those refusing to use it;

2) equality: also cause for concern is the possibility that, leaving the regulation of distribution to the free market, only wealthy people could, however, afford access to PCE that is effective and likely to be very expensive, resulting in further accentuation of the already existing `natural` and social inequalities. This problem is the subject of animated discussion in the context of different models of *distributive justice* that have queried the criteria which is most suitable for a `fair` allocation of resources for enhancement[34];

3) fairness and merit: moreover the question arises as to how one could ensure fairness in competition and the principle of merit should the liberalisation of PCE be accepted;

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[32] Intertwined to this issue are the questions raised by Neil Levy on the limits of acceptability of practices that relate to the functioning of the mind and the problematic nature of the significance, for ethical judgment, of the distinction between the changes and enhancements concerning the manipulation of "external" mental resources (notebooks, lists, computer etc.) and those which apply to the manipulation of internal resources with interventions on brain mechanisms: N. Levy, *Neuroethics and the extended mind*, in J. Illes and B. Sahakian (eds), *The Oxford handbook of neuroethics* cit.; to *Oxford handbooks of neuroethics* see also N. Levy, *Neuroethics and the extended mind* in J. Illes and B. Sahakian (eds) The Oxford Handbook of Neuroethics cit.; see also *Oxford handbooks of neuroethics* for a comprehensive and updated view of the themes central to the debate on the present and future of neuroscience and related gnoseological, ethical, legal and political issues (consciousness and intentionality, responsibility and determinism, mind and body, neurotechnologies aging and dementia, legislation and public policy, science, society, and international perspectives).

[33] Cf. the call to scale down expectations by N. Volkow (Director of the National Institute on Drug Abuse - NIDA - at the National Institutes of Health), in S. Hyman, N. Volkow, D. Nutt, *Pharmachological cognitive enhancement in healthy people: potential and concerns,* 2013 cit.

[34] There seems no doubt that the more ethically appropriate criterion is that of distribution according to need especially in the event of cognitive deficits and related "aids" that compensate for disadvantage and reconstitute some kind of equality of opportunity.

4) self-perception and perception of the social bond: with regard to this it has been pointed out that there is the risk that the spread of the use of PCE may favour a view of one's actions directed more to one's immediate performance rather than to one's commitment to self formation and that this is likely to affect self-perception and the sense of one's `value` and, at the same time, accentuate the tendency to compete rather than to cooperate.

Having said this, with reference to the current state of empirical research, scientific knowledge, the pluralistic bioethical debate on the use of PCE and certain trends found within the individual and social context - but also warning that the picture is continuously complicated by the difficulty, repeatedly underlined, in establishing an unequivocal boundary between therapeutic purposes and enhancement purposes – the NBC makes the following general evaluations:

1) the issue of cognitive enhancement presents numerous innovative elements, which are still in need of adequate and continuous investigation; this aspect is further exacerbated by the general lack of empirical data and statistical results. The international debate on PCE has reached to date rather inhomogeneous results, given the general scarcity of empirical data and statistical results with respect to their possible effectiveness, their harmfulness, the methods of their use and distribution. Still almost nothing certain is known about the short-term and long-term effects and, on the phenomena of dependency that may be associated;

2) Therefore further research is important, in the field of neuroscience and brain functioning, directed at identifying more accurately and in detail effectiveness and side effects of these drugs on sick individuals, even in order to better determine whether possible use for enhancement purposes of a specific function does not lead to the (possible) decline or impoverishment - temporary or irreversible - of other functions[35] with possible irreversible damage and dependency. And it is, at the same time, hoped that there will be an increase in the pre-clinical research on the subject. As for the testing of these molecules on healthy subjects the same recommendations on ethical requirements apply as expressed in the previous opinion of the NBC *Neuroscience and human experimentation: bioethical problems*[36]: benefit/risk ratio proportionate informed consent preceded by adequate counselling, utility of the research and approval by the appropriate ethics committee;

3) A delicate problem concerns the distribution and allocation of resources to the field of cognitive enhancement that may be at the expense of those intended to cure (therapy) and prevention (prophylaxis). On the other hand it is a fair assumption that much research aimed at enhancement will not be developed for a considerable time but rather research to fight debilitating and degenerative diseases or conditions, it cannot be ruled out that, sooner or later, there will be research started aimed only at enhancement, with the correlative

[35] On the state, still in its initial stages of research on the neural basis of highly complicated functions such as attention, memory, executive functions, etc.. cf. podcast brought by the 22nd Neuropharmacology Conference on Cognitive Enhancers, moderated by T. Insel, *Director, National Institute of Mental Health, NIH, USA*, with the participation of J. Krystal, M. Ehlers, *New drugs development for cognitive enhancement in mental health: challenges and opportunities,* 2012.
http://www.journals.elsevier.com/neuropharmacology/podcast/free-podcast-on-new-drug development/.

[36] Opinion of the 17th of December 2010.

question of the moral acceptability of that choice. With regard to this, the NBC believes that with the scarcity of resources, which is generally the common situation public intervention to support research on enhancement would not be advisable, if it came at the expense of research and development plans dedicated to drugs for therapeutic purposes;

4) It should also be considered that cognitive function can be improved in a more lasting manner through instruction, education and continuous training, a rich social life and from relationships, from study, learning, continuous stimulation of interests, from healthy lifestyles (nutrition, physical activity). It is a path that clearly requires a lot of time, but (perhaps) it is more respectful of the opportunities for growth and development of personal and relational identity as well as of self-esteem and the feeling of `self-fulfillment`. In addition, paradoxically, the positions of those who today say they are in favour of the liberalisation of PCE can be seen as a further attempt, with regard to the many already present, of medicalisation of everyday life and for quick and "easy" solutions, via the taking of a drug, to difficulties and problems which instead require more careful reflection as well as social and institutional management;

5) Similarly it should be emphasised that one of the factors underlying the impetus for the non-medical consumption of these "pills" is often a reductive vision, which identifies intelligence in a quantitative manner with the increase-expansion of notions-information, without considering that intelligence involves a qualitative dimension and needs a solid emotional “foundation” to be developed and exercised. The exaggerated expectations of *cognitive enhancers* may lead to a sort of `drug-centeredness` attributing to chemistry a power to shape human beings far above reality;

6) Then one should question whether the absence of a pathological condition, diagnosed as far as possible clearly and definitely justifies the use of PCE notwithstanding risks and damage even if only probable and/or possible arising from the interference of these interventions with delicate and complex brain mechanisms. Here there emerges a profile of responsibility of each individual not only towards their own health but above all of the medical specialist who must ensure the appropriacy of the prescription and therefore prevent an “improper" non-therapeutic use of these drugs[37]. It is also desirable

[37] With regard to this see: *Letter to the Editor. Better evidence for safety and efficacy is needed before neurologists prescribe drugs for neuroenhancement to healthy people,* in “Neurocase: The Neural Basis of Cognition”, 2012, v.18, Issue 3; and E. Racine, C. Forlini, *Disagreements with implications: diverging discourses on the ethics of non-medical use of methylphenidate for performance enhancement,* in “BMC Medical Ethics”, 2009: http://www.biomedcentral.com/1472-6939/10/9 which calls into question the guidelines expressed by the Ethics Law and Humanities Committee of the American Academy of Neurology, for the behaviour of neurologists in the face of a request, by healthy individuals, for drugs for the improvement of cognitive functions. Cf. D. Larriviere, M.A. Williams, M. Rizzo, R.J. Bonnie, On behalf of the AAN Ethics, Law and Humanities Committee, *Responding to requests from adult patients for neuroenhancements: guidance of the ethics, law and humanities committee*, in “Neurology”, 2009, 73, pp.1406-1412. According to the Committee of the American Academy of Neurology, the prescription of substances of this type for `*neuroenhancement* `is not - both in legal and moral terms - obligatory nor prohibited: the decision rests with the neurologist who has to take it within the doctor-patient relationship and respecting the criteria of informed consent. The criticisms raised by Eric Racine and Cynthia Forlini have shown that these guidelines do not consider adequately neither the social aspects of PCE or the particular responsibility of specialist doctors - whose purpose is the protection of the complex bio-psychological functions of the brain - and which, in addition, are based on a tacit acceptance of the safety and efficacy of the drugs in question.

to find suitable methods to prevent the purchase of PCE via the Internet, which as a tool facilitates an uncontrolled spread and without a prescription, with inevitable negative consequences at the personal and social level;

7) But the questions raised by PCE do not only concern individuals and their self-determination: they intersect numerous problems with regard to social life, the sense of belonging of citizens and their relationship with others. Undoubtedly today the phenomenon of recourse to neuroenhancers, to improve one's performance in various fields, is stimulated by strong environmental pressures accentuating competitiveness, and the present climate of growing insecurity about the future, which also has the effect of eroding the non-formal adherence to the values of personal commitment, loyalty, *fairness*, solidarity etc. There emerges here the problem of possible *feedback* which, in turn this practice, if not properly regulated, could have in consolidating a mentality set on thinking of one's actions in terms of the immediate maximisation of productivity, of efficiency - even beyond one's capabilities - or competitive record. The bioethical problem does not concern only the harmfulness to health; it also calls into question the consideration of basic social-political values such as equal opportunities, fairness, and cooperation. This applies even more strongly - as mentioned above - if one considers that in future safer and more effective nootropics could be developed. If free use of PCE was accepted, perhaps difficult to find and/or particularly expensive, this could give rise to other forms of undue advantage to the benefit of those who may have recourse to it, both in scholastic- academic and work contexts, accentuating existing inequalities and altering even more the sense of common citizenship and social solidarity;

8) Therefore the NBC does not consider - even in the presence of new safer and more effective molecules - the free market for pharmacological cognitive enhancement, managed only on the basis of the encounter between supply and demand, to be bioethically acceptable. There are areas that need to be protected from the intrusion of the market and trade, especially in a general situation in which for a long time now, the "mentality" that impels towards medicalisation, encouraging merchantilism, tends to invade areas of life traditionally managed according to a different logic. Similarly state intervention would not be acceptable, neither in the private context of work, led by the intention to favour the establishment of purported public interests nor private interests, i.e. orientated to paternalistically enhance their citizens, or its own officials or employees;

9) In conclusion, with regard to this, it is important to have a proper information and awareness on the part of public opinion regarding the expectations that the use of PCE can realistically meet and, even more, about the possible risks and damage to health, both mental and physical, that is associated. Special attention altogether must be dedicated to children, because of their particular vulnerability, the possible long-term effects (still not fully known) of this type of nootropic on a brain still in formation;

On the basis of these evaluations the NBC recommends:

1. that Italy should also intensify research into the cerebral sphere, taking account of the numerous international programs in progress;

2. that, at present, very severe constraints for the prescription of drugs with neuroenhancing effects be maintained and that these should always and

only be prescribed by specialists in the sector with specific skills in neuropharmacology;

3. that public institutions should seek suitable methods for the implementation of a campaign for prevention- information, addressed to the medical sector, schools and families, which is not limited to illustrating the harmful effects on health of these artificial aids and the highlighting of their limited effectiveness as cognitive enhancers, but it should also be directed to a better knowledge and critical consideration of the factors predisposing to their consumption by young people, in order to identify strategies to strengthen the individual, the environmental and cultural factors that may hinder the expansion of a black market;

4. that, pending further epidemiologically significant research into the short-and long-term effects of PCE (research concerning both intrinsic safety and the possible adverse effects on other mental functions, as well as social life as a whole), a public discussion on the more general issues of cognitive enhancement should be started, with the contribution of experts from the various fields involved, so as not to be unprepared if in the near future safer and more effective nootropics should become available.