

The therapeutic principle facing cognitive enhancement by drugs

El principio terapéutico frente al potenciamiento cognitivo mediante fármacos

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Abstract

This qualitative research uses a methodology of literature review, analysis and phenomenological analysis. Currently, there are reports of non-prescribed use, by healthy people, of drugs for the treatment of cognitive ailments. Such intake has been carried out for the purpose of enhancing specific cognitive abilities such as memory, concentration and reaction capacity. This non-recommended use of drugs has been documented through a series of research and surveys that find an upward trend in the consumption of these drugs, especially in specific sectors of the population, such as university students in developed countries. The potentiating character of these drugs when consumed by healthy people leads to the need to contrast their use with the bioethical principle of totality or “therapeutic”. Therefore, the present work aims to analyze whether or not the

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use of these substances can be justified from a bioethical perspective in the light of the interpretation of the principle of totality.

It is concluded that the use of cognitive enhancers may be allowed in people without specific pathology but who report a low performance in certain cognitive areas or a detriment in such capacities derived from advanced age and not from a diagnosed disease. This is if safety criteria are met and that serious and continuous research is carried out on its benefits in the aforementioned populations.

Keywords: potentiation, principle of totality, therapeutic, potentiating drugs, transhumanism.

Introduction

The accelerated progress of neurosciences has allowed various groups to glimpse the possibility of improving or enhancing some cognitive capacities of the human being. This trend is also manifested in the intake, without medical prescription, of drugs originally intended for the treatment of specific pathologies, especially drugs for attention deficit/hyperactivity disorder (ADHD) such as RitalinVR (methylphenidate) and AdderallVR (mixed salts of amphetamines), as well as the drug that promotes wakefulness, ProvigilVR (modafinil) and is used for the treatment of narcolepsy or the treatment of Alzheimer's disease (donepezil). Modafinil and methylphenidate specifically are two drugs widely used to treat disorders related to concentration and wakefulness. Methylphenidate was first developed in the 1940s by a Swiss chemist named Leandro Panizzon. Panizzon was looking for a substance that could improve concentration and attention in people and discovered that this substance had that effect. The FDA first approved the drug in 1955 as a treatment for ADHD. Since then, methylphenidate has been used to treat ADHD, as well as narcolepsy and other sleep disorders.

Modafinil, on the other hand, was developed much later, in the 1970s, by French chemist Michel Jouvét. Jouvét was looking for a drug that could help keep soldiers awake for long periods of time

without affecting their cognitive performance. Modafinil proved to be a very effective substance for this purpose and was used extensively in the French military during the Gulf War in the 1990s. Subsequently, the drug was approved by the FDA in 1998 to treat narcolepsy and other sleep disorders.

Although both modafinil and methylphenidate are primarily used to treat disorders related to concentration and wakefulness, their mechanisms of action are different. Methylphenidate works by increasing levels of dopamine and noradrenaline in the brain, while modafinil acts on a number of neurotransmitters, including dopamine, noradrenaline and GABA.

Today, both modafinil and methylphenidate are widely used outside of their FDA-approved indications. Many people use them as “cognitive enhancers” to improve their performance at work or school (1).

This non-recommended use of drugs has been detected through a series of investigations and surveys that find an upward trend in the consumption of these drugs, especially in very specific sectors of the population such as university students in highly developed countries. However, the analysis of this phenomenon does not seem to be reduced solely to the treatment of a possible drug addiction, since the addictive effects of these substances are not duly documented. And the populations that occupy them refer to not doing it regularly but for specific situations in which they do not seek recreation but the increase of various faculties such as attention, the empowerment. The foregoing denotes a different nature of use on other types of substances.

The research, development and use of substances with fine enhancers in the human being must be analyzed from the perspective of ethics, taking into account the various implications in some aspects of the person. A general or different analysis runs the risk of reflecting only a partial vision of the implementation of said pharmacological technologies. In the literature, you can find examples of the general analysis that various authors make about any attempt to “improve” human abilities. Although these analyzes shed light on

this new trend, it is considered that the challenge consists in the bio-ethical review of each of the technological possibilities. Only a casuistic review of the possible indications in the person of each of the emerging technologies in this field will be able to fully reflect a line of action that moves away from immobility but at the same time does not fall into the blind faith of progress, in terms of Grace. (2).

Within the specialized literature, the phenomenon of the use of drugs to obtain cognitive improvements is analyzed from three main perspectives: a) use as a health problem and an addiction (1,3,4); b) “empowerment” as an emerging phenomenon within medicine (5) and 3) the so-called *lifestyle drugs* (6,7) from the analysis of a liberal perspective against drug use and self-determination of personality.

From the first perspective, the study of the use of enhancing drugs focuses on the current non-recommended off-label use of drugs for the treatment of various pathologies and that seems to have spread among students and some professionals in first world countries. The focus of this type of approach envisions the phenomenon as a medical problem that must be analyzed from the perspective of drug addiction and the safety in the use of these medications (6,7,8,9). However, while it is true that safety and the possibility of addiction are indeed related and relevant issues for the analysis of the phenomenon, it is not equivalent to the problem of opioids (10). The various surveys have shown that the majority of healthy users of this type of drugs have not developed dependence, have used them occasionally, consume them exclusively in specific situations, and show reasons for their use that are very different from recreational ones (1,11,12,13,14,15), so this approach, although adequate since it analyzes the consequences and safety of drugs, seems not to cover the phenomenon in all its complexity and dimension.

According to the second perspective, that of enhancement, the phenomenon must be analyzed from a more general approach, since the use of drugs that enhance cognitive functions has the capacity to transform society and the individual, as it is one more step towards improving in general (3,6,16,17). Unlike the first perspective, this

one is broader than the phenomenon itself, since it affirms that the discussion questions medicine and its role in the life of man, leading him towards the medicalization of daily life (6, 18, 19). This analysis rules out whether the problem is exclusively a health problem, and questions the effect it will have on society as a whole and not so much individually, thus taking on a more panoramic character that sometimes resorts to speculation, but which poses very plausible social problems against the use of drugs for non-therapeutic purposes.

Finally, the third approach makes use of the term *lifestyle drugs* and views the dilemma of the use of enhancing drugs from an individual perspective. Although it does deal with the problem of the possible medicalization of society, its approach to the term seems to be influenced by liberal thinking that supports the use of all kinds of methods to determine the personality of the specific individual. From this perspective, more focused on the individual than on the community, the possibility of using this type of drugs is submitted for consideration as a personal decision that responds to social and cultural factors to a greater or lesser extent chosen by the subject who uses them. In this way, the use of lifestyle drugs is similar to plastic surgery and other non-therapeutic body modifications that are the sole decision of the person undergoing them (20,21,22,23,24). From this perspective, although the social implications in terms of justice, security and medicalization of society are recognized, the focus falls more directly on the individual and his lifestyle, which is why those who have emerged from this analysis fight for review of the application of freedoms in the choice of pharmacological means. Therefore, from the perspective of “lifestyle drugs”, some advocate the express recognition of the cognitive freedom in which it is included, the use of these substances for personal purposes of those who wish to use them, and the recognition of the right to refuse to use them (20,21,22,23,24,25,26,27).

Although it is true that each of the three approaches through which the phenomenon of the current and future use of drugs with

enhancing effects is analyzed, they point out relevant and essential issues in its review, each one separately seems to be incomplete. The use of enhancing drugs must be analyzed both from the current situation (health problem) and with a more or less prospective vision of the possibilities of science in the development of increasingly effective substances with fewer side effects. In addition, although it is true that the phenomenon must be seen from the perspective of security and precaution in the current user, it must be understood as an incipient situation in which the issue of empowerment is in question. Therefore, the discussion should not only focus on the individual use but on the possible collective consequences of it, in all kinds of countries and cultures. For its part, it can be accepted that the use of these drugs may be a derivative of individual freedom and the free development of personality in accordance with the decisions of each user. Therefore, it is impossible to deny its relevance in the collective and social situation, both of a determined community as of a society in a country with its own social and economic reality. Therefore, the review of this topic must be done from the three perspectives proposed so that its result is that of an understanding of a complex phenomenon of large dimensions without losing sight of the particularities of the individual and of the culture in which it develops.

Additionally, it is considered that the phenomenon of the development and use of enhancing drugs from bioethics should be reviewed, using the three aforementioned perspectives, but in light of the contrast with the fundamental bioethical principle with which it generates the greatest controversy: that of totality or “therapeutic principle”. This principle seems to be the most relevant and, in turn, the least explored in terms of cognitive enhancement, even though its possible transgression is the most evident in the subject to be discussed. This does not presuppose that the analysis of the phenomenon cannot be carried out by contrasting it with other principles. In addition, the present work also recognizes that freedom and autonomy as differentiated concepts must be fully analyzed in

pharmacological enhancement, but after determining the ethics of the intervention itself in light of the totality of the human being.

2. The therapeutic or totality principle in the possible use of drugs with cognition-enhancing effects

Health has been defined throughout history in many ways, from the absence of disease to the state of absolute well-being (28,29,30). All definitions of health determine its opposite: disease and, in turn, determine excesses in medical interventions, which would be classified as “non-therapeutic” and therefore “enhancing”. However, each definition encounters problems when faced with a more complex analysis and especially when contrasted with particular situations of patients at the limits of normality curves (16, 31,32,33).

Health understood as the absence of disease is one of the criteria taken by most detractors of the position that promotes the possibility of improvement or empowerment. However, even the WHO no longer accepts this definition because it is considered reductionist (29). In the view of critics of the dichotomous definition, it leaves the task of population health exclusively in the hands of the physician and the health care system. In addition, it does not recognize that the health of the human being must be analyzed from an integral vision of the person and not simply the biological one. In addition, even from a purely biological perspective, it is stated that the definition is not sustainable since living organisms go from health to disease progressively and not sharply, as might be assumed from reading the aforementioned concept. Therefore, every living being can be in the process of acquiring a disease without actually having it or manifesting it externally. Additionally, it is stated, there are populations that, without being in the assumption of the disease, are found at the extremes of the pattern measurement curves, so it is impossible to treat them from this perspective (for example, prediabetes).

From the opposite point of view, there are people with disabilities who often do not pose a risk to their lives. In terms of the above definition, disability must be understood as a disease (because it is on the spectrum) and therefore must be treated. However, critics of this dichotomous vision affirm that disability should not be treated as a disease, and they say it constitutes the clearest example against the aforementioned definition (34). The foregoing by virtue of the fact that disability should not be understood exclusively as a disease but as a characteristic that cannot be treated, but that must seek adaptation. Considering everyone who suffers from a disability as “sick” is not necessarily the most appropriate vision for their integration into public life and their individual development.

Now, the use of this statement (health as the absence of disease) necessarily implies the definition of the concept of disease. This definition is not obvious either, since to clarify it, it is necessary to resort to other concepts such as statistical normality and functionality. Although it is true, in most cases, the disease is easily determinable through clinical analysis and observation of symptoms, on many occasions it is necessary to make use of statistics and their normal patterns. These patterns of normality have not only been questioned from the sociological field (in the case of homosexuality or menopause) but have also been criticized for their variability over time in the face of progress in research and their comparison between specific groups of populations. Although statistics is a great ally to the medical field, its generalization in specific issues of normality has been questioned in some areas. In addition, in the specific issue that concerns this work, the statistical parameters have also been criticized due to the fact that there will always be individuals who are placed at the extremes of the curve (below the average). This type of case close to “abnormality” in statistical terms, but intractable from a medical point of view since they are not found in the concept of disease, justify the possibility of a new definition of the norm.

Due to the above, the use of the definition of health as the absence of disease does not seem to adequately answer all the ques-

tions currently raised in terms of diagnosis, nor does it resolve particular situations in which individuals are disadvantaged, but do not suffer from any kind of illness. In addition, the use of this dichotomous definition could mean an intervention when the person does not require it (disability) and a non-intervention when the person could benefit from it, as is the case of those who are at the extremes of the curves or of secondary preventive medicine in general.

Contrary to the definition previously exposed is the broad definition of the WHO in which reference is made to “complete well-being”. This vision of health has also been widely questioned and applauded in equal measure. It is recognized as a non-reductionist vision that refers to various spheres of the human person and that also removes the absolute responsibility of the doctor and the health systems for the condition of the population. However, on the other hand, the use of the concept of well-being is affirmed with the qualifier of total, it is too broad and subjective since there is no definition by the organism of what should be understood by it. From the above derive the arguments that affirm the use of this definition can lead to the medicalization of the society that does not present it as such a disease. In addition to justifying all kinds of interventions from cosmetic surgery to enhancement.

With regard to the concept of normality, medicine and philosophy of science have given many definitions to this concept, as well as criticisms of them. One of the central objections to the concept of normality lies in the definition of disability, and the treatment that Western societies give to those who fall outside the agreed normality parameters. In this sense, various authors question the existing dichotomy and affirm that the concept of normality has led to the equating of “difference” with “disease” (35). Questions to this sharp dichotomy (normality-abnormality=disease) are made from the review of specific cases in mental health issues and through the review of “abnormal” behaviors (36). In addition, a strong criticism is made from the perspective of disability in people who, although with limitations, enjoy a full life and whose “suffering” is not compatible

with life. Added to the above is the fact that the parameters of statistical normality have varied and do vary over time, and the various scientific discoveries, as well as the numbers indicating normality in height, body mass, or even cholesterol or glucose levels have been modified over the years (29,36). It is argued that facts such as the increase in life expectancy, the advances in malnutrition in some countries and the increasingly advanced treatment of various chronic diseases that would previously have been fatal should be taken into account (29,37), in order to constantly adjust the values of normality. The presence of these variations in the normality parameters due to demographic conditions constitute an argument against the perennial nature of the concept and for many authors they represent the logical reason for not accepting it. Additionally, transhumanists find in this variation the possibility of framing the concept of improvement within the natural evolution of “normality”, thus creating ever-greater ranges of acceptability. The sharp line created between the normal and the disease has led to problems not only in the treatment that societies have given to diversity, but it has even come to pose problems in the definition of empowerment and the limitation of the doctor’s actions in the face of disability. In a desperate attempt to cure and reverse the difference, the doctor loses sight of the possibility of a different way of life for the “patient” (36,38).

Normality as a concept is also criticized from a homogenizing cultural perspective. The foregoing by virtue of the fact that:

In any case, among human beings who are classified as normal, there are biological and social variations that generate diverse situations in such a way that what is considered normal in one place may be abnormal in another. Therefore, health is also a relative concept, both in the spatial and temporal dimension, varying from one culture to another depending on the specific context (29).

From this perspective, issues such as autism, ADHD, the way of teaching deaf children, psychological disorders, menopause, treatable

chronic diseases, disability and even old age pose problems for the general definition of statistical normality.

However, leaving aside the parameters of normality, the concept of comprehensive health expounded by the WHO has also been criticized for its absolute nature by including the concept of well-being. This statement leads to the conclusion that most of the time people are in a state of illness (more precisely *unhealthy*) (1,34,37). This complete welfare state is, for critics, unfeasible, unquantifiable and impractical. This is due precisely to the lack of review of the concept in light of advances in science. Currently, various diagnostic processes detect abnormalities at levels that would be imperceptible and that will not immediately generate disease or symptoms. Additionally, the development of genetics makes it possible to detect propensities that may or may not be actualized and become pathologies (37). Huber affirms that a determining factor for rethinking the definition of health is demographic changes and life expectancy, as well as the emergence of new treatments for chronic diseases. These advances allow many people to reach advanced ages with this type of disease without seeing their life especially limited (1,39). In accordance with this author and his co-investigators, the WHO definition considers all types of people with a disability or chronic condition to be sick, even if they are treatable. For what he proposes, the concept of adaptability should be included in the definition of health and thus limit a set that he supposes is too broad (37). The previous criticism brings us back to the absolute concept of health, within which so many situations can fit that there is a risk of interpreting any discomfort as a disease and resorting to treatment. The medicalization of society is not only a concept that could put State coffers at risk, but also the individual himself, who, constantly feeling sick, abnormal or inadequate, will resort to all kinds of interventions. Nevertheless, at the same time, returning to the health-disease binomial would lead to a backwardness in public health issues that, moreover, does not conform to the reality of medicine.

This also opens the door to the initial premise of empowerment/enhancement in transhumanism. The thin and even blurred line

between health and disease is an argument against the ethical premise of some bioconservatives who affirm that only intervention for therapeutic purposes will be morally acceptable. If we add to this the absoluteness of the WHO definition, a number of interventions in the human body can be justified, even based on the bioconservative argument, in order to achieve the so-called “absolute state of well-being”. Determining which ethical line is impossible to cross at present is usually complicated. Will the initial proposal to determine what is therapeutic and prohibit what transcends it be the solution to the ethical dilemma? Is it possible for sure to use this criterion in all circumstances?

It can be affirmed without fear of being mistaken that the insertion of lenses that allow man to see in the dark is undoubtedly an enhancing technology that under no circumstances could be therapeutic, for this is a capacity that is lacking in the human species as a whole. (16). These kinds of functions, non-existent in man naturally, can easily be outlawed by arguing that they openly violate his nature. However, there are modifications or “improvements” whose application necessarily alludes to the concept of normality or average. In this way, its absolute prohibition is more difficult, since many have been created, initially, for the treatment of diseases and later its possible enhancing effect has been discovered (16,40,41,42,43,44).

If an in-depth analysis is carried out, the scope of preventive medicine today transgresses somewhat the limits of the therapeutic concept and there are many who argue against the dichotomy posed by bioconservatives as an ethical criterion. They even go so far as to raise doubts about issues such as vaccines whose function is by definition to strengthen the immune system of the recipient. In such a way that, the detractors of the dichotomy raise the question of whether the inoculation is evidently therapeutic or borders on an improvement that protects man against the environment, also increasing his life expectancy (2,16,36,45). In this sense, both the definition of health and the absence of disease and the absolute definition of the WHO present epistemological problems when confronting the concept of improvement and certain particular cases (16).

While the clearest concepts of body-machine hybridization can be immediately outlawed by applying the distinction between therapy and enhancement, at present, some examples are presented that escape this distinction. The insertion of technology for health monitoring can constitute an efficient method of diagnosis, which would even reinforce the difficult distinction between the sick and the healthy, but: Is this an example of *improvement* or just one more advance in preventive medicine?

From the point of view of the concept of normality, examples can also be found whose therapeutic limit is unclear. A clear example is that of height, whose variations over time have been significant (36,46). When is the use of growth hormone justifiable from a therapeutic perspective, if the height range has varied over the years? Can its use be therapeutic in some cases, but enhancer in others? (16) Who and under what criteria will determine the legitimacy of the intervention? From the point of view of well-being, no one will argue that short stature can cause self-esteem problems in the individual, while in someone else in equal circumstances it may be irrelevant. Is it a personal decision or should it rest with the treating physician?

In the specific field of cognition, the definition of health and disease becomes even more complex due to the difficulty in measuring it and the various factors that must be taken into account. Additionally, the complexity presented in the analysis of what constitutes normality and health (well-being) directs the discussion to an obvious path. What is best? Can it really be said that one intervention or another always constitutes an improvement for every individual? Not always what is “more is better” (47,48,49). The qualification of what modification in the human body would constitute an improvement, even in the cases of science fiction, is far from being a perpetual and general concept. The specific cultural, social and individual situations of each person could determine and modify what each of them understood by improving themselves (50). In this sense, some might think that it would be more appropriate to speak of empowerment, however, the exploration of possibilities that is being

proposed not only describes the increase in already existing capacities in man, but also the possibility of adding new ones to the human catalog (51,52). But it is not only the modification or increase in the amount of man's abilities that would represent a problem in terms of determining their goodness and therefore qualifying them as improvements. Empowerment of already existing capabilities may not be desirable for some individuals in certain cases, even if they are in favor of empowerment in general. While some people would find an increase in their memory capacity attractive, others would see no use in this same increase, and other groups might consider the option aberrational because their ability to forget unpleasant events that tend to fade over time is diminished. Would everyone opt for the same "improvements"? It is unlikely. In addition, if this were the case: Can the same improvements be considered then?

In this sense, the very concept of improvement can be affirmed, even though it could be clearly distinguished from therapeutic intervention, it is difficult to define. Well, we lose sight of the fact that not always what is more is what is best. Above all, he fails to glimpse the individuality of the human being, his tastes, needs and hobbies. Thinking about improvements that everyone requires does not understand the human race with its differences on an individual, cultural, social and spiritual level.

With regard to drugs with enhancing effects, their mode of action, effectiveness and possible side effects in the medium and long term of their use in healthy people have not been widely studied, and some groups are constantly fighting for their review (1,8,17,44). This type of research should determine the actual efficiency in cognitive terms of existing drugs, when taken by people without a specific condition, as well as adverse side effects. However, there is some evidence of a moderate benefit in the use of these, which varies by a number of circumstances, but the data is still scarce and the scientific community has paused in its ethical deliberation until medical science reveals more certain results. (53,54,55,56,57). Additionally, science is advancing in the development of new drugs, whose therapeutic purpose seems hopefully effective against conditions

such as Alzheimer's, ADHD, among others, but whose use can easily lead to a new, more effective option for enhancing capacities in healthy people. (7,8,17,58,59,60,61). The foregoing coupled with the enormous effort applied to the development of the various BRAIN projects existing in various parts of the world, to fully understand the functioning of the human brain and the interactions between the multiple cognitive functions, with their respective ethical dilemmas, may entail research in this field is just around the corner, but it has not been developed yet (5).

In this sense, research aimed at testing the efficacy of existing drugs on the market, as well as that, which will be developed in the future, must be analyzed from the perspective of ethics rather than legality. Well, in this type of research you can find various factors to take into account to determine the implications that both research and development would have for the person from the individual as well as the collective.

The principle of totality or therapeutic principle maintains that the person is a unitary whole. It recognizes the inviolability of life and the human body. Therefore, intervention in the human body can only be done to save the whole. If for this it is necessary to mutilate, part of the organism, said intervention will be justified (62).

In order to comply with this principle, the following precise conditions are required:

- a) The intervention must be on the direct cause of the evil;
- b) There must be informed consent of the person;
- c) There should be no other ways or means to deal with the disease (impossibility of curing the entirety without intervention); and,
- d) There must be a good, proportionately high chance of success (62).

In addition, it is important to point out that the therapeutic principle necessarily implies a judgment of proportionality, which includes

quantitative and qualitative aspects (63). These aspects refer to the means and the end sought, but not from a general and abstract point of view, but from an individual perspective specific to the circumstances of each case (64).

Regarding the weighting of the means, it is stated that it must review several elements: a) The security of scientific suitability, b) proportionality, c) the risk-benefit and; d) quality of life. Not only the doctor affirms Casas, must evaluate the latter unilaterally, but mainly by the patient given the individual characteristics and values that each one manifests (64).

Traditionally, the therapeutic and totality principle refers to the classification of means as “ordinary” or “extraordinary”. This classification does not respond to a predetermined catalog of media but to statements that seek to facilitate the distinction in specific cases. In such a way that ordinary means are considered those that:

- a) Have a reasonable expectation of benefit to the patient;
- b) They are supposed to be of common use and of easy access and implementation; and,
- c) They do not have significant burdens for the patient (65, 66,67).

Therefore, a *contrario sensu*, it is said that extraordinary means have opposite characteristics and do not imply a real or significant benefit for the patient. In addition, they represent an excessive burden for the patient or a significant cost (68,69). However, it is important to affirm that these situations may vary over time, and from patient to patient in accordance with the advances of science, its access and the individual characteristics of each person (65). That is why the personalist literature agrees that this proportionality of means in the therapeutic principle must be reviewed in the light of the human being understood as a totality. In other words, it must take into account the social, economic and spiritual aspects that surround it, and not only consider it from the merely biological aspect (69).

On the other hand, the principle of totality in the literature is usually analyzed from a negative perspective of action. That is to say, its statement is in contrast to therapeutic determination and there are few references that analyze it in the light of improvement (64,65,66,67,70). This is because when this principle was enunciated in bioethics, little was said about the possibility of improvement and its contrast with it was not relevant. However, current analysis may well focus on the application of this principle to all types of non-therapeutic technology, as Marín and Gómez Tatay do in their guide to the ethical assessment of transhumanism. This guide uses the various personalist principles for the analysis of all types of interventions with transhumanist overtones (non-therapeutic). And although little is mentioned in it on the specific topic of drugs and the principle of totality, they do conclude that each intervention has particular characteristics that must be contrasted with the principles without generalizations and taking into account the person as a whole (social, cultural and physical). Therefore, in order to analyze each of the technologies, the authors propose that the following questions directly related to the implicit proportionality in the statement of the therapeutic principle must be answered.

- ...P0.3. What are the alternatives available to get the results you expect?
- P0.4. What is the scientific evidence on the effectiveness of the technique?
- P0.5. What risks or unintended consequences are involved in taking the action?
- P0.6. Have you lived, up to now, in clear conditions of inferiority in some area for not having carried out the procedure that is proposed? (Evaluate the difference it would make to do it)
- P0.7. What would be the impact on society and the environment if the use of the technique were extended or generalized?...
- ...P0.10. What sectors of the world population currently have access to the technique? ... (71).

Additionally, the authors continue, in order to adequately contrast the principle of totality with some improvement technique, it must

be questioned whether the intervention involves serious damage (such as amputation or disfigurement) or if it alters the normal physiology of the human person. Only if its physical integrity is not seriously altered, could its analysis continue according to the aforementioned ethical guide. This next step of assessment, he affirms, must be carried out in light of the person's goals, his freedom exercised consciously, and responsibly (71). However, this analysis, as well as many others, is made on the global phenomenon of transhumanist empowerment and not on facts of pharmacological enhancement in certain populations.

The largest amount of literature that contrasts empowerment with the principles of personalism carries out a global analysis where topics from machine-body hybridization to gene editing are discussed (72,73,74,75). Therefore, their conclusions contribute little to the review of the phenomenon in the specific area of cognition in particular individuals such as those mentioned in this paper. Moreover, they fall into the speculative generalization that this paper tries to avoid.

In order to carry out the contrast between pharmacological cognitive enhancement and the therapeutic principle, it is necessary to emphasize that the sharp distinction between therapeutic and enhancement is not evident in concrete cases. That is why even the report made by the European Parliament on *Human enhancement* in 2009 (76) recognizes from the beginning that the limits between the therapeutic and the enhancer are quite blurred, so it affirms that it is essential to stop basing the notion of the improvement in conceptualizations such as "normality" or "disability".

Even so, in the review of the enhancing phenomenon, authors can be found whose ethical judgment on an intervention is based exclusively on the determination of its therapeutic function (77,78). Therefore, they state that only those measures taken to restore health are ethically valid and those that do not have this intention, but exceed it, are ethically reprehensible. In the 2001 report of the President's Council on Bioethics of the United States of America, Kass, among others, defines the following terms:

Therapy: is the use of biotechnological power to treat people with known diseases, disabilities or impairments in an attempt to restore them to a normal state of health and physical condition.

Enhancement is described as the directed use of biotechnical power to alter, by direct intervention, not disease processes but the “normal” functioning of the human body and psyche, to increase or improve its native capacities and performances (78).

In this way, for the aforementioned authors, therapy is always ethical, while improvement, as they define it, is ethically reprehensible.

In the specific case of cognitive enhancement through drugs, current research seems to focus correctly on obtaining substances that specifically improve cognitive abilities in specific pathologies, but with special emphasis on old age (8,15,17,79,80,81). Cognitive deterioration because of the passing of the years (and not attributable to a specific pathology) can easily be considered both as a disease and as a normal process attributable to the passing of the years (82). Old age and the deterioration that it brings with it are not considered pathological in current medicine and the adaptation capacity of the elderly has shown to be important in the perception of their reality and their quality of life (34). However, the possibility of prolonging the optimal functioning of some cognitive abilities in the last years of older adults is being studied from neuroscience and pharmacology, not necessarily from the therapeutic perspective of the treatment of conditions such as Alzheimer’s, but from it, but for application in adult populations without diagnosed disease. The possibility of enhancing cognitive abilities that naturally suffer deterioration in the elderly raises a change in the therapeutic paradigm, but with an ethical view towards improving the quality of life of a growing sector of the population and with more life expectancy.

Additionally, it is important to affirm that the future of enhancing drugs is most likely generated precisely in the investigation of the use of substances for therapeutic purposes and that it is the non-prescribed use (*off label*) that attributes to them the ability to enhance some aspects in healthy people (58). Therefore, subsequent

research in this regard is expected to focus on the effects of existing drugs in people without any disease and the new drugs start at first as therapies for specific pathologies such as Alzheimer's and lead to an enhancing use with the passage of time and the evolution of its results (8,17,58).

Even so, it seems essential to determine the ethics of the possible investigation of the use of drugs in healthy people for potentiating purposes, either from the review of the effects of the already existing ones or those that may be developed, regardless of their therapeutic destination or not. In this sense, it is important to point out that opening the possibility of this type of research for non-therapeutic purposes, can only be carried out after a study of the various aspects that it entails. At the same time, it constitutes a necessity since an increase in the use of these is observed, especially in universities and in some sectors of the population (9,11,12,13,14,15,83) for which risk assessment is essential.

In order to evaluate the ethicality of research on pharmacological enhancement, although it may be contradictory, it seems necessary to evaluate the results obtained so far in the little research that seems to abandon the therapeutic principle. It is especially enlightening to review the results obtained, since everything seems to indicate that the use of enhancing drugs (modafinil and methylphenidate) has better results when people whose normal levels of memory, attention or concentration are at the lowest levels of the curves established for them (1). This revelation (still in its infancy) seems to collapse the image currently associated with the use of smart drugs (*smart pills*). In the collective imagination, these enhancers are used by the so-called *High achievers*¹ to further improve their performance in various tasks. The few clinical studies that have studied the effect of these enhancers reveal that the greatest quantifiable benefit can be seen in those individuals whose performance is lower in areas

¹ A term that is difficult to translate into Spanish but refers to a person who achieves more than the average person on a given task, for a variety of reasons, its equivalent in Spanish would be high performance students.

such as memory, attention and concentration (*low performing subjects*) (1,3,7,8,12,15,17,59,60,61). In other words, the studies seem to reveal that the use of drugs is more beneficial in people who are in the lower limits of the normal curves but who do not have a specific pathology. In an experiment on the working memory effects of drugs in healthy young individuals, the amount of benefit was inversely proportional to the working memory capacity of the volunteers. That is, those individuals with lower levels of performance seemed more likely to benefit from improvement than those with higher levels (59, 81). The foregoing, although it has not been widely reported due to the scarcity of studies on enhancement, constitutes relevant data for analysis, since the use of this type of technology could mean reducing the ranges in the normality curves (17).

On the other hand, it has been proven that the slowing down of some cognitive processes is normal in old age, such as memory, so there is experimentation with the possibility of stopping this cognitive deterioration in people over 60 years of age. The deterioration of age does not necessarily constitute a pathology but is the natural process of aging. Certain limitations in working memory (*prospective memory*) have been observed in “normal” older adults, without any pathology, in these cases it is not necessarily in the presence of senile dementia or its beginnings, but rather it is a natural process associated with aging (17,82). Advances in neuroscience and pharmaceuticals can considerably improve the quality of life of the elderly (45,61). The implications from the point of view of well-being in old age would certainly be great and would meet the well-being requirements of the definition of the OMS. However, some could argue that old age itself is treated as a pathology, thus denying a natural process (84) and inevitably falling into transhumanist postulates and improvement. Therefore, from the point of view of ethics, it must be determined if it is justifiable to deny this possibility to the elderly based on the previous argument.

Additionally, there is evidence that the use of these drugs can enhance specific functions, but at the same time slow down others,

so the enhancing effect may not be beneficial for complex tasks (3,7,8,17,59,60, and 61). This also seems to demystify some specific aspects that are debated in the literature on the inequality that the use of these drugs can generate (76,79,85,86,87,88,89). Therefore, from another faction of the specialized literature, in light of these preliminary results, they discuss the possibility that their use could “level the ground” between subjects with low performance in specific tasks and those who are at “normal” and high levels of performance (16,36,43,90).

In this sense, from the therapeutic principle of Sgreccia’s personalism and the most current interpretations that are made about it, it is linked to the proportionality of therapies, that is, the requirement of a proportion between risks and damages, and benefits. But these benefits must be understood in an assertive and unitary sense (of the person) so both the bodily good and the spiritual and moral good of the person must be considered (71,91). Therefore, the moral criterion determined exclusively in the therapeutic or not of the intervention is insufficient due to the difficulty of determining that character and due to the very concept of beneficence to the person in certain situations.

In this way, it is possible to affirm that the investigation could abandon the rigidity of the therapeutic principle from an ethical approach, if it is accepted that the sharp distinction is not a valid moral parameter for the determination or not of the development of a drug or the test of an existing one, in people without specifically diagnosed pathology. In this sense, the Code of Medical Ethics and the Italian Bioethics Committee already expressly include the medical possibility of authorizing treatments that go beyond conventional therapeutic goals. The aforementioned legal system in its article 76 recognizes this possibility and regulates both cognitive enhancement and the so-called physical enhancement (cosmetic surgery),² affirming that said treatments can be carried out as long as

² The doctor, both in research activities and when non-therapeutic services are required but aimed at improving the individual’s physiological, physical and cognitive

human dignity, identity, integrity and compliance with the principle of proportionality (risk benefit) and precaution. It also limits the granting of treatment to an adequate and thorough informed consent in which the “patient” is informed about all the risks associated with the consumption of the drug as well as the limitations of its possible effects in accordance with scientific evidence (92). The foregoing is the basis, from the perspective of the code, of the investigation on the possible empowerment so that these informed consents actually have the necessary information on the positive or negative effects of the “enhancement” treatments.

3. Analysis and Discussion

A first glance could lead us to conclude, emphatically, that the use of drugs with non-therapeutic effects should be condemned in light of the principle of totality or therapeutic. However, the determination of the concept of disease and therefore of the scope of the therapeutic, in the best of cases, is blurred. However, regardless of the difficulty of such determination, it seems probable that the use of cognition-enhancing drugs can be justified in specific cases and under specific premises.

The therapeutic principle legitimizes the intervention in the corporality of the person as long as such manipulation is exerted on an illness or disease in order to cure or save physical life. However, as Sgreccia rightly states, this principle must be analyzed not only in itself, but also in relation to the existing proportionality between

capacities, operates respecting and safeguarding their dignity in all their individual reflexes and social identity, identity and integrity of the person and their genetic peculiarities, as well as the principles of proportionality and precaution.

The doctor acquires the written informed consent taking care to verify an understanding of the risks of the processing. The doctor has the duty to deny any request that is considered disproportionate and high risk, also due to the invasiveness and potential irreversibility of the treatment compared to non-therapeutic but enhancing benefits.

damages, benefits and risks (62,93). In addition, the benefits must be interpreted from the perspective of the unitary and complex human person, not only from the point of view of corporeality, but also from its psychological, spiritual and moral spheres. Although it is true that most of the literature on this principle refers to the limitation of therapeutic effort and not the other way around, that is, empowerment, it is possible to interpret it a *contrario sensu*. The foregoing by virtue of the fact that it is affirmed that interventions in the person may be legitimized if it is understood that they support the development of this person towards the purposes for which it is ordered. The therapeutic principle does limit futile interventions in terminal, idle and non-curative illnesses, but it does not expressly oppose improvement if it is aimed at a benefit beyond the merely bodily.

Additionally, it is important to underline the fine line that separates the therapeutic from the improvement in the current state of neurosciences, which makes it difficult to strictly apply the distinction between therapy and potency. Therefore, the analysis must be done in some particular situations that precisely represent the cases found in this division.

- a) Cases and people who are located at low levels of the normality curves: The assumption refers to those people whose levels of attention, memory or other executive functions do not reach pathological levels, nor do they suffer from disorders, but are below average and close to what is considered “out of the norm”. As has been partially evidenced in some of the aforementioned studies, it seems that these individuals benefit more from the consumption of the drugs analyzed. This evidence seems to contradict the popular belief that it is the fittest individuals who use and benefit the most from these drugs. From the perspective of the therapeutic principle, intervention in these cases may not be completely denied, the foregoing by virtue of the fact that determining

whether these people are affected by a disorder is not entirely easy, since their classification depends on normative criteria more or less arbitrary and of a statistical nature. Therefore, from personalism, this sharp distinction does not seem to fit the vision of person. In such a way that, if it is indeed verified that the “enhancing” effect of the drugs is more beneficial in this population, that the risks are acceptable, and that there is no therapy that achieves the same or similar results, the intervention could be justified. The foregoing always considering the specific needs of people who are in this case. Since some individuals may find such an increase in some of their abilities desirable while others may not want or need such empowerment. Thus, these people could benefit from employment and develop a profession or trade that requires specific levels of attention, memory or etc.

- b) Old age and “natural” cognitive deterioration: despite the fact that the effects of these drugs have not been adequately tested in elderly people, many of their advocates advocate their possible use in older adults with “normal” levels of cognitive impairment without specific pathology. Old age is not a disease, but a number of pathologies and detriment of capacities accompany it. Despite the fact that a healthy and active old age is possible, there is a glimpse of the possibility of using drugs to enhance attention and memory in this population and thus improve their quality of life. It is evident, in this case, there is no clear pathology, but we are in the presence of a simple deterioration due to the passage of time, so intervention from the clear view that what is not curative is immoral should be outlawed. However, from ethics and from a broader vision of Sgreccia’s therapeutic principle, non-intervention does not seem to be the appropriate solution.

It seems that these specific assumptions show that the sharp distinction between illness and health not only does not exist in many cases,

but also that it should not be the only bioethical criterion to deny the intervention. However, it is necessary to specify that the therapeutic principle is not only neither clear cut nor dichotomous but must always be analyzed in light of the risk (damage)-benefit proportionality (principle of beneficence). Therefore, from the perspective of this principle, what is beneficial must be determined from the broad concept of person, but at the same time must be weighed against the inherent risk of the intervention. In the case at hand, that of enhancer drugs, this benefit in healthy people is still in doubt since there is a need for further studies. Carrying out these studies can be justified from a bioethical perspective, since there are cases such as those mentioned above in which the intervention is not the result of an arbitrary whim of the users but a possibility of improving the quality of life of certain groups that are at a disadvantage. Additionally, the risk of employment in healthy people should also be determined by conducting specific research in the aforementioned population groups. Bioethics will only be able to justify the use of these drugs exclusively in those cases (such as those mentioned) in which the limits between therapy and improvement are not entirely clear by weighing the risk-benefit and adequate informed consent from bioethics. Said intervention can be justified precisely by the broad interpretation of the principle that concerns us and by the difficult determination of the concept of health in these cases.

Abandoning the rigidity of the therapeutic principle does not necessarily imply the medicalization of society, nor the absolute acceptance of transhumanist postulates. It does not even imply the absolute abandonment of the principle as such, only its reformulation under less rigid criteria and more adaptable to the advancement of science, not based exclusively on mathematical models of normality curves but on the acceptance of specific situations (old age, low levels of performance etc.) that from ethics can justify the intervention. In addition, whose practical realization may not necessarily be pharmacological, but comprehensive, with “traditional” or non-controversial techniques such as training and meditation. This justification can be found precisely in the intrinsic value of cognition

as a global and complex phenomenon inherent to man and that justifies intervention from the individual and community spheres, with due caution.

The dynamism of science has led us to consider that normality curves may be practical in medicine's day-to-day life, but not very precise when faced with specific situations in terms of disability and empowerment (37). These considerations become even more complex when compared to measurements such as those used in the field of cognition and the specific functions whose relationship between them has yet to be determined from the field of neuroscience (90). Added to the above, the sharp distinction becomes more and more difficult if one considers that currently the trend of medicine in the psychopathological area has abandoned the rigid concepts of pathologies. It focuses on the concept of spectrums, in addition to the fact that are increasingly discovering so-called *mild conditions* in the area of cognition and emotions (32, 33, and 90). Therefore, everything seems to indicate that the denial of intervention based exclusively on the criterion of cure (treatment) is not enough in the face of the reality of scientific discoveries and the difficulty in determining "normal patterns" in specific areas of cognition and the possibility of adaptation (15,16,31,32,33,35,90,91,94,95,96,97).

The therapeutic paradigm from a closed dichotomous perspective does not glimpse the complexity of the person, since it can deny the possibility of intervention in cases in which the quality of life of the person involved can be ethically improved.

4. Conclusions

- The idea of conducting medical research on the use of drugs with enhancing effects from a bioethical perspective can be explored precisely by the broad interpretation of the therapeutic principle if it meets the other essential ethical requirements for its realization.

- The broad interpretation of the therapeutic principle should not imply the medicalization of society, nor the acceptance of transhumanist postulates. It only means recognizing the totality of the person and in this way reformulating the expression of the principle under less rigid criteria and more adaptable to the advancement of science. In such a way that both the investigation and the possible and eventual prescription of these drugs must take into account social, economic, psychological, employment factors and other individual conditions of people.
- From ethics, the largest number of interventions that exceed the traditionally therapeutic limit in the current state of science, must be those that are intended for the blurred limits existing between the curative and the enhancing, which have been mentioned in the first part of this job (old age, low performance or low IQ, etc.).
- The exploration of the possibility of improving or enhancing cognitive abilities through drugs can be justified from bioethics as long as:
 - a) It is used in populations that, given their specific characteristics (being at the extremes of the curves or with natural cognitive impairment or others) can benefit substantially from consumption.
 - b) Rigid precautionary criteria are met in research on the effects of drugs.
 - c) The risk-benefit is adequately weighed.
 - d) Serious, extensive and long-term investigations are carried out on: the desired effects, the adverse effects and the possibility of addiction, which yield favorable results in the former and acceptable in the case of the latter and,
 - e) There are guarantees of access to reliable information, as well as public policies that guarantee the non-violation of the human rights of freedom and equality.

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