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GENETIC ENHANCEMENT OF THE HUMAN BEING - BETWEEN REALITY AND FICTION, BETWEEN RISKS AND BENEFITS

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Abstract.

Since ancient times, man has been searching for ways to improve life, often striving for perfection, and the many advances in technology are the proof of this continuous search. Whether it is meant to prevent or cure diseases, to increase physical, mental and intellectual performance or to increase resistance to various external agents, the enhancement of the human being is a central point of interest in research. Nevertheless, the possibility of making these improvements does not automatically mean their ethical acceptance. One of the most socially and ethically challenging issues related to human enhancement and one of the most current research topic in this field is genetic enhancement of the human being. As such, the purpose of this paper is to identify the challenges that the reality of genetic enhancement of the human being may bring, weighing its benefits and risks. Interventions aimed at genetic enhancement can target both the somatic characters and the germline genome, the changes made to the latter being passed to the future generations. Although currently still classified as fiction, the rapid progress in technology brings closer and closer the reality of genetic human enhancement on large scale, assuming the interventions and the outcomes will be socially and ethically accepted. The authors of this article show that such interventions should respect the autonomy and dignity of the individual, they should ensure protection and justice, and their expected benefits should always outweigh the potential risks.

Key words: genetic human enhancement, ethics, autonomy, risk-benefit balance, equity

Introduction.

In general terms, enhancement refers to going beyond the normal/natural or transforming an existing state into a superior one, referring either to the entire human population or to an individual or group of individuals. The definition of normal is a subject of continuous debate, and the differentiation of normal from pathological is often difficult, the line between them being very fine. In the context of genetic enhancement, the notion of "normal" includes the existence of a spectrum of variants that frame certain traits (e.g., visual acuity, stature, body mass) and not just something that is typical for the human species (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

The purpose of advances in science is to bring improvements in the daily lives of people - whether they are ordinary people or scientists, and the evidence of these improvements is manifold. In the biomedical field, for example, scientific progress has allowed the manufacture of numerous devices to improve or restore lost or diminished functions - mobility, vision, hearing (Almeida & Diogo, 2019; Bouton et al., 2016; Pham et al., 2013) or development of synthetic blood substitutes (Moradi et al., 2016). In this context, it is important to distinguish between the improvement or restoration of a diminished/disabled function and the improvement of a function beyond the usual or therapeutic needs, exceeding the limits of the natural (Almeida & Diogo, 2019; Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017). A specific example in this sense

is the intervention on the skeletal muscles, to improve them. Such an intervention has a therapeutic purpose if it is provided to patients with muscular dystrophy, and an enhancement purpose if it is applied to an individual in a healthy state, placing it at a higher level than other individuals with the same state of health and providing it an advantage in sports competitions (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017). There are also situations where the line between therapy-prevention-enhancement is difficult to draw. An example of this is genetic editing to lower cholesterol levels: in a patient with advanced coronary disease it is considered therapy; for the sibling of such a patient, who has risk factors for coronary heart disease is considered prevention; in a young person who has no coronary heart disease and no risk factors, but who wants to reduce the risk below that of the general population is considered enhancement (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Currently there are many possibilities to enhance the body's normal functions beyond its normal physical or cognitive capabilities or to enhance aesthetic features: supplements to boost brain power, hormones to increase height, technologies to stimulate the brain, to name a few (Almeida & Diogo, 2019). These can be achieved both by means of biotechnologies (e.g., the use of devices such as bionic limbs, infrared vision glasses, artificial retina implant, connecting the human brain to a chip attached to a computer) and chemical compounds (e.g., pharmaceuticals or blood substitutes such as dextrans), biological (NAD⁺ and umbilical cord plasma for delaying body degradation and prolonging life) or genetic (e.g., germline interventions) (Giubilini & Sanyal, 2016; Lima & Belk, 2022).

People have pursued the improvement of the human being and human life in general, since ancient times, first as part of the process of civilization, then from the desire to strive for perfection, in forms adapted to the times in which they lived (Almeida & Diogo 2019; The Nuffield Council on Bioethics, 2016), even in the absence of illness, in order to increase mood, capabilities and well-being. Sometimes influenced by the transposition of rich imaginations in stories and illustrations with heroes with supernatural powers, in works of art or in philosophical musings, ideas for improvement gradually took shape in reality (Almeida & Diogo, 2019). Humans have always wanted to preserve as long as possible or improve the features and characteristics that induce their well-being or that help them integrate more easily into society: beauty, intelligence, strength or endurance (MU School of Medicine, 2023).

Genetic engineering through genome editing techniques involves the modification of genetic material (DNA or RNA), both in structure and function, by insertion, deletion or replacement (Gaj et al., 2013; The Nuffield Council on Bioethics, 2016).

Genetic enhancement is oriented towards two types of changes: limited to the individual on whom the intervention was made (e.g., editing of muscle cells to develop stronger muscles) and transmissible to the next generations (e.g., editing of cell receptors) (Almeida & Diogo, 2019).

Reality versus fiction.

Proponents of human enhancement aspire to create individuals with a higher degree of intelligence, a higher life span and a higher level of well-being, the ultimate goal being to overcome the current human biological frailty (Pearce, 2012). Although at present such interventions seem to be part of the realm of fiction, their gradual fulfillment is becoming closer, given the speed of technological progress and the wealth of those willing to invest in this type of research (Lima & Belk, 2022).

In the past researchers have applied genetic engineering techniques to enhance plants (e.g., diversifying flower colors, increasing the number of buds that will produce flowers,

disease resistance) and animals (e.g., disease resistance, superior wool quality to sheep) (The Nuffield Council on Bioethics, 2016). The technological progress in recent years brings the reality of using genetic engineering for the enhancement of the human being ever closer (Almeida & Diogo, 2019). This is especially true since the completion of the Human Genome Project, which allowed the knowledge of changes/disorders associated with different genetic variants (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017). This reality requires the adaptation of the principles of bioethics to technological progress, so that the human being is protected from any direct harm, resulting from the enhancement intervention itself, or indirectly, by unfairly placing an individual in a lower position than another who benefits from artificial enhancement (Almeida & Diogo, 2019).

Some of the attempts at genetic engineering recorded so far have led to undesirable, unexpected, unforeseen outcomes, sometimes endangering the individual, results that could not be explained and for the occurrence of which it could not be determined to what extent the factors that were involved were related to genetic intervention or to the body's pre-existing condition. These side effects highlight the lack of sufficient knowledge currently for researchers to venture further and apply genetic engineering techniques to the human body.

In the field of gene therapy, concerns are related to the alteration of other cells in addition to the target cells, the aggressiveness of viruses which are supposed to be harmless, the insertion of genes in a place different from the targeted place in the cell nucleus, the possibility of failure with the need to repeat the procedure, the possibility that some of the side effects will be observed too late, after the modified genetic character has already been transmitted to the descending generations (MU School of Medicine, 2023).

Genetic enhancement raises concerns about the possibility of generating changes against nature or the possible dehumanizing nature of the changes. Also of concern is the similarity of genetic enhancement interventions to the 20th century eugenics abuses in the USA and Nazi Germany (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017; Lima & Belk, 2022; MU School of Medicine, 2023).

On the one hand, in the case of gene therapy, intended to restore the individual to a normal state, acceptance seems closer to reality. On the other hand, accepting the enhancement of the human being in the absence of a disability or a defect that places it below the threshold of normality is much further from becoming a reality (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Genetic editing of the germline cannot yet be applied on a large scale - both for therapeutic/preventive purposes (in clinical trials), and for the purpose of improvement in the absence of a disease. However, taking into account the rapid technological evolution, this reality cannot be considered too far, which is why public consultation is recommended regarding the potential risks and benefits of such a reality (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Risks versus benefits.

Interventions aimed at genetic enhancement can target somatic traits, non-heritable by future generations (Almeida & Diogo, 2019; Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017), but also interventions on the germlines-gametes, the fertilized egg and the first stages of embryonic division (Baltimore et al., 2015; Ishii, 2015), which will be passed on to future generations.

Interventions for the genetic enhancement of the human being are associated with both risks and benefits, with concerns related to autonomy, but also related to justice. Before these become an easily achievable reality, it is important to weigh them and ensure that the benefits outweigh the risks so that interventions “do no harm” the beneficiaries (Almeida & Diogo, 2019).

Interventions on the human genome for therapeutic purposes have become increasingly morally accepted by society (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017). An example of accepted gene therapy is the treatment of “bubble boy” disease (De Ravin et al., 2016).

In the case of genetic interventions aimed at enhancement beyond the limits of normal and therapy, their moral acceptability is still a matter of debate, given the various concerns such as those related to informed consent, safety and efficacy. Acceptance of gene therapy is dependent on acceptance of progress in science and trust in modern medicine, enhancement interventions being more easily accepted by those who generally accept progress in medicine (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Transhumanists - supporters of the use of last-generation technologies for the enhancement of the human being (Lima & Belk, 2022), argue their support through the positive purpose of these technologies, such as the possibility of a longer life, in the best health and the greatest happiness, with enhancement of cognitive (e.g., memory, intelligence) or somatic (e.g., muscle strength) capabilities, compared to what can be achieved within the normal human limits (Harris, 2010).

Achieving longevity has been and it still is the goal of many research studies. Currently, cosmetic dermatological or plastic surgery interventions can delay the aging or aging appearance of the skin by an insignificant number of years, while with the help of technologies it is hoped to a lifespan of at least 150 years (Lima & Belk, 2022).

In the field of reproduction, transhumanists claim that the use of genetic engineering is similar to the option of choosing a partner who possesses certain qualities, in order to pass them on to the offspring (MU School of Medicine, 2023), but also as a method of protection for the offspring, by removing the risk of being born with a genetic disease inherited from parents (Chan et al., 2017; Quinn et al., 2010).

Likewise, transhumanists place on the same scale genetic engineering and the other ways in which the individual can improve physically, intellectually or cognitively: either through personal effort (e.g., education, practice/perseverance, diet, exercise, coffee consumption), or through external support (e.g., vaccination, plastic surgery, cosmetic interventions), reasoning that the final goal is the same (MU School of Medicine, 2023).

Bioconservatives, who support the maintenance and protection of the intrinsic values of the human being, framed by some authors in “human essence” (Sandel, 2007), campaign against the use of the enhancement technologies. For example, bioconservatives separate the social or competitive advantage conferred by improvement achieved by one's own efforts or due to innate characteristics and that achieved by artificial genetic modifications, showing that the latter can undermine, for example, the goals of a competition (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Bioconservatives raise the issue of social equity in the context of the use of genetic enhancement methods. An example is the enhancement of cognitive functions with the help of modern technologies, which gives enhanced individuals advantages over non-enhanced individuals in various situations where these super-cognitive functions constitute a competitive advantage - such as in a job competition (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Changes inflicted by the germline interventions raise a number of concerns that must be carefully analyzed before they are accepted. These changes are permanent and involve more than the individual in the embryo/fertilized egg/gamete stage, being transmitted to the next generations (Almeida & Diogo, 2019; Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017) and generating cultural and social changes in long term, including social inequities (Committee on Human Gene Editing: Scientific,

Medical, and Ethical Considerations et al., 2017). Another debatable issue is the extent to which parents have the right to decide on the future of their children. Through the use of genetic enhancement technologies, children are considered by their parents to be beings that can be designed and manipulated according to their own desires and ambitions and not as a gift that must be accepted in the form that is received (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017; Sandel, 2007). As traits that will be passed on to offspring are modified, questions are raised regarding the influence of these changes in the evolutionary process of the human species, if these techniques will be applied on a large scale (Almeida & Diogo, 2019). In the case of application on a smaller scale, the question arises of the use of the benefits obtained from genetic modifications by some individuals at the expense of other individuals, a situation that brings into discussion the issue of equity and the risk of discrimination, both in terms of access to such technologies, as well as the competitive advantages provided by enhancement (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

Some authors bring up the issue of using resources for genetic manipulation to improve the human being, related to the prioritization of needs: to what extent are resources such as money, time, and energy worth investing for such purposes, compared to other emergencies present in the current society or from the near future (Almeida & Diogo, 2019).

Proponents of genetic modifications through germline interventions point out that society must accept the freedom of decision regarding their use, as a characteristic of a liberal democratic society (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017). Furthermore, they claim that people even have an obligation to look out for the welfare of those who cannot decide for them, making the best decisions on their behalf, including unborn children (Harris, 2010). Nevertheless, the question arises when the decision fits better to parents than to their future children (i.e., a child that will be

However, the ethical acceptance of gene editing technologies is conditioned by a careful analysis of the benefits and risks to demonstrate that the expected benefits outweigh the potential risks which are currently incompletely known (Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations et al., 2017).

An example in this sense is the CRISPR technology (short for “clustered regularly interspaced short palindromic repeats”) that can be used for inducing modifications of the human genome (National Human Genome Institute, 2023). The addition of the CRISPR-associated protein 9 (Cas9) in 2012 gave rise to concerns expressed both in medical journals and in the mass media (The Nuffield Council on Bioethics, 2016). This technology was used for creating a gene mutation by deleting some base pairs of the CCR5 gene in the genome of two Chinese twin girls, to provide them resistance to HIV infection that could have been transmitted from their father, who was infected. This genetic intervention has led to much controversy. Criticisms were based on the low risk of infection and the futility of such an intervention, given that the infection was kept under control and the virus titer was undetectable (Almeida & Diogo, 2019), as well as the character of enhancement rather than therapy of such an intervention (Cyranski, 2018). More than futility and consumption of resources to achieve such changes, mutation of a gene can be associated with unexpected side-effects that are beyond the current scientific knowledge. Given that a gene is usually responsible for a multitude of traits, related or not (Almeida & Diogo, 2019; Falcon et al., 2015), there is a risk of endangering the individual who owns it (Almeida & Diogo, 2019). For example, in the previously mentioned case, in which the CCR5 gene mutation was made, researchers claim that in addition to protection against HIV infection, the mutation increases the risk of severe side-effects or early death in the case of other diseases, such as influenza virus infection (Galis & Metz, 2007) or multiple sclerosis (Gade-Andavolu et al., 2004).

Another example of highly ethically debated issue in the field of CRISPR/Cas9 technology for intervention on the human germline was the work of a Chinese team, aimed at correcting the gene responsible for β -thalassaemia, a genetically inherited blood disease, whose severity depends on the type of mutation. Their work involved ‘non-viable’ (i.e., abnormal fertilized) IVF human embryos. Although the intention might serve a good purpose (i.e., finding solutions to prevent a severe disorder in the future child, fighting disease and reducing the suffering), the ways by which it is reached raise ethical issues regarding risks and benefits, as well as resource wasting. For example, the reliability of testing using abnormal fertilized embryos when information regarding mutations cannot be extrapolated. Then, given that normal fertilized embryos are rarely available for research, some researchers came with the idea to create embryos with donated eggs and sperm only for research purposes, which again raises ethical issues considered to be worse than using ‘left-overs’ from infertility treatment and morally unacceptable (Munsie & Gyngell, 2018).

Conclusions.

Although still largely in the realm of fiction, human genetic enhancement is based on the use of genetic engineering for practices such as germline gene editing, replacement of mutant genes, or biosynthesis of new substances intended to improve various traits of the individuals. Genetic enhancement of the germline, with the selection of characteristics of interest during gestation, can provide benefits related to the performance of the individuals, but at the same time raises issues regarding the risks to their health, autonomy, identity and dignity, as well as to the future of the human species. The many unknowns that currently exist mean that the application of genetic interventions for human enhancement purposes requires a careful analysis of the individual and societal risks and their weighing against the expected benefits before these interventions become a reality.

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