Procreative Beneficence in the CRISPR World

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ABSTRACT

No argument has been proffered for the moral obligation of prospective parents to act on the principle of Procreative Beneficence. It has only been argued that there is not just cause to specifically outlaw the principle's application. The United States must act however, to mitigate risk and allow for parents to make an informed risk-benefit assessment if they elect to utilize CRISPR technology. While acting on the principle of Procreative Beneficence does not constitute child abuse per the legal ethics of intention, to not apply the principle to the selection of non-disease traits would not constitute child neglect, as it is likely the basic needs of the child are still being met. The United States must guarantee equal access to CRISPR and other gene editing technologies, thereby allowing for free selection on the part of parents, in which it is likely the heterogeneity of the United States population will be perpetuated. So long as these requirements are met, there is little risk of, or opportunity for, maleficence, so the United States should not act to ban Procreative Beneficence.

Keywords: CRISPR, gene editing, human genome, genomics

INTRODUCTION

In his influential 2001 article, "Procreative Beneficence: Why We Should Select the Best Children," Julian Savulescu defends the idea that "couples (or single reproducers) should select the child, of the possible children they could have, who is expected to have the best life, or at least as good a life as the others, based on the relevant, available information." However, Savulescu might not have entirely foreseen the tremendous advancements in gene editing made in the years since the article's publication. Clustered relatively inter-spaced short palindromic repeat (CRISPR) technology is an increasingly promising field of research that has dramatically expanded our ability to alter the human genome. There has been discussion on the appropriate changes in public policy to ensure the ethical application of these developing technologies, including the permissibility of applying Savulescu's principle. Despite the changes to the genetic selection paradigm as a result of CRISPR, passing laws to prevent the application of Procreative Beneficence would not be justified.

Savulescu's discussion centers primarily on pre-implantation genetic diagnosis (PGD), and the subsequent selection of a particular embryo for implantation. In this context, the genetic content of the "possible" child is still confined almost entirely to the genetic contributions of the parental gametes. That is of course excepting mutation events and other sources of genetic variability. However, in most cases, the number of embryos that would need to be generated and undergo PGD to identify a single embryo with the complete desired genetic profile is unfeasible compared to what can be achieved through the utilization of modern genomic engineering. As the number of traits being screened for increases, and as the number of contributory loci increases, so decreases the likelihood of the optimal embryo being generated by random fertilization. The possible permutations eventually exceed the practical constraints of time and resources, which is why the application for Procreative Beneficence discussed by Savulescu was primarily one of relative comparison – it was merely determining which of a select few embryos would likely enjoy the best life, and selecting that embryo for implantation. However, CRISPR technology has significantly altered these constraints, and subsequently, the vision. Though at this point in time, the workflow for CRISPR editing does require cumbersome downstream selection, it remains vastly more efficient than alternative methods such as PGD.[1] CRISPR holds the potential for the deletion, addition, mutation or inversion of any segment of genetic code.[2] Essentially, the genetic variability is no longer random and limited, but now, directed and infinite. In defense of Procreative

Beneficence, Savulescu refutes three common arguments against its application. Despite developments in CRISPR technology, all three common arguments against Procreative Beneficence remain invalid, though the refutations have substantively changed.

A. Direct Harm to Child

The first common concern is the risk of inadvertently selecting an embryo that ultimately has a worse life than an embryo that was not selected. In this situation, Savulescu argues, harm has not been done to the selected embryo, as the alternative was non-existence. However, when CRISPR technology is employed, there are not multiple embryos – just one. The alternative is not non-existence, but rather an alternative existence, which could constitute either a worse or better life. In the case of CRISPR, the incorporation or deletion of genetic information could result in aberrant function, and have negative health consequences. However, these risks do not pose a philosophical objection to Procreative Beneficence as a principle, but merely advocate for proper risk-benefit considerations – as is the case with all technological advances. Just because there is a risk of death and injury each time a human drives a motor vehicle, we do not categorically object to the concept of rapid transit. Rather, we take immense precautions to mitigate risk and ensure safety. The same should be applied to CRISPR engineering. To that end, in recent years, there has been progress in improving the specificity of endonucleases to the extent that they can now discriminate between single nucleotide differences, thereby significantly reducing the potential for unintended outcomes.[3]

Another form of potential harm to the child is as an unforeseen consequence of the addition or removal of a trait. It is important to recall that Savulescu's principle is one of expectation. The moral requirement is to choose the child "expected to have the best life." While Savulescu uses intelligence as a non-disease trait that most people believe to be conducive to an enjoyable life, very few people have not heard the phrase "ignorance is bliss." Even if there is a consensus that increased intelligence is expected to increase the quality of life, it is impossible to predict with certainty. Suppose the augmented intelligence allows an individual to perceive a great injustice in the world – an injustice of which the individual would not have otherwise been cognizant. And suppose that injustice is so grave that the individual develops depression and ultimately commits suicide. While we may believe this scenario unlikely, few would argue that it is impossible. Does this mean we should not proceed with the use of such technology? A principle based on expectation cannot be adequately addressed without discussing the ethics of intention. The question being considered is whether or not laws should be passed to prevent adherence to the principle of Procreative Beneficence in reproductive decision-making. In many domains of the American legal system, intent plays a significant role – consider manslaughter versus murder, or Good Samaritan laws. With regard to child abuse law, which is perhaps most appropriate when considering the potential damage done by parental decision making to an unborn child, the US Department of Health & Human Services, Children's Bureau reports that in almost all states the harm to the child must be "nonaccidental."[4] Therefore, in the case of parental care, intention is considered relevant. While the Hippocratic Oath does indeed state to first do no harm, no medical procedure is without some degree of risk. In the case of genome editing, as long as the potential reward has been justified relative to the risk, the application of Reproductive Beneficence appears permissible to the extent that it should not be outlawed.

B. Psychological Burden

The second potential consequence addressed by Savulescu is the psychological burden on the parent and child due to expectation. For the parent, should the child lead a tragic life by the parent's measure, the parent could feel responsible. Or perhaps, the parent could feel disappointment if the child does not develop as anticipated or intended. The child could experience pressure to be exceptional, or to meet specific expectations. Or perhaps, the child could be impacted by an altered sense of free agency. Savulescu argued that such psychological effects could be well managed with proper therapy. Whether the applied technique is PGD or CRISPR, the role of the environment remains the genetic scapegoat. With regard to expectation, for traits that are indeed deterministic, there is no concern because the gene will certainly be expressed and the trait will indeed be manifest. For those traits that are multi-factorial, and for which the environment is demonstrated to play a role, that fact can be a refuge for the

mind. Both the child and the parent can place the child's development externally, on environmental forces outside their control. However, should techniques for epigenetic modifications develop to eliminate the role of the environment in genetic expression, such developments would need to be considered. Thus, the application of Procreative Beneficence poses no imminent threat to the psyche of the individual stakeholders.

C. Societal Ramifications

Adopting a larger scope, some have suggested Procreative Beneficence would have a detrimental effect on society as a whole. Savulescu argued that the risk of increased or maintained social inequality is not a valid objection, arguing that alternative avenues should be pursued to address such issues. With the aforementioned expansion of possible children, it seems unlikely that Procreative Beneficence would substantially alter societal equity, provided access is readily available to all strata of society. And it is worth mentioning that this is not entirely unrealistic considering the rapid decrease in cost observed for these technologies.[5] If CRISPR engineering continues along its trajectory, every prospective parent could theoretically choose to create the exact same child. At which point, equality is a nonissue because every individual is quite literally identical. Is it likely for society to progress towards that end?

As members of a society, there are values shared in common by most individuals. However, overall, American society at present is largely heterogeneous. Savulescu mentions that Procreative Beneficence will be weighed along with Procreative Autonomy. If the autonomy of the parents is respected, it is not likely all parents will select the same non-disease traits. It is more likely that the parents will project their biases and personal values onto their potential offspring during the selection process. For example, someone who feels that athletic prowess is essential to well-being will likely select a different body type than someone who places musical talent as paramount. Hands suited to palming basketballs are not suited to manipulating violin strings. Similarly, selfishness runs counter to altruism, independence to socialability, etc. And the notion of which of these values, at the expense of its counterpart, is conducive to well-being varies greatly over time and space. In some sense, this projection of parental values onto offspring already occurs, through environment manipulation. This process is usually termed "instilling" values, as parents attempt to encourage behaviors, while discouraging others. The inclusion of genomics into the equation merely constitutes an extension within the DNA-environment interplay. To ban the selection of genetically based linguistic skills would be akin to banning a parent from reading to their child at night.

It is also important to recognize that many traits only contribute positively to well-being insofar as their superiority relative to the general population. This is especially true in American society, which historically has emphasized competition to a certain extent, as well as a need for social mobility based on merit. An unfortunate reality of a society with finite resources is that often satisfaction of one's desires requires that someone else's not be satisfied. Considering that CRISPR has opened the potential for equality of capability, should everyone pursue those traits, they are no longer conducive to well-being, and thusly no longer contribute to Procreative Beneficence. This runs parallel to Savulescu's discussion of sex selection in a society that discriminates against women. In that example, sex functioned as a trait homogeneous in nature, in that the status of "male" was uniform and treated uniformly by society. CRISPR has the potential to make other traits such as intelligence or height, equally uniform. It is worth noting that in some cases this also alleviates the aforementioned burden of expectation. If the expectation is one of superiority, provided equal access, that superiority is not realistic.

CONCLUSION

No argument has been proffered for the moral obligation of prospective parents to act on the principle of Procreative Beneficence. It has only been argued that there is not just cause to specifically outlaw the principle's application. The United States must act however, to mitigate risk and allow for parents to make an informed risk-benefit assessment if they elect to utilize CRISPR technology. While acting on the principle of Procreative Beneficence does not constitute child abuse per the legal ethics of intention, to not apply the principle to the selection of non-disease traits

would not constitute child neglect, as it is likely the basic needs of the child are still being met. Similarly, structures must be in place to allow for the counseling of both the child and parent throughout life, particularly to ensure all parties understand the intricacies of gene-environment interactions. Additionally, the United States must guarantee equal access to CRISPR and other gene editing technologies, thereby allowing for free selection on the part of parents, in which it is likely the heterogeneity of the United States population will be perpetuated. So long as these requirements are met, there is little risk of, or opportunity for, maleficence, so the United States should not act to ban Procreative Beneficence.

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