Human germline genome editing: On the nature of our reasons to genome edit

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Abstract: Ever since the publication of Derek Parfit's *Reasons and Persons,* bioethicists have tended to distinguish between two different ways in which reproductive technologies may have implications for the welfare of future persons. Some interventions harm or benefit particular individuals: they are "person affecting". Other interventions determine which individual, of a number of possible individuals, comes into existence: they are "identity affecting" and raise the famous "non-identity problem". For the past several decades, bioethical debate has, for the most part, proceeded on the assumption that direct genetic modification of human embryos would be person affecting. In this paper, I argue that that genome editing is highly unlikely to be person affecting for the foreseeable future and, as a result, will neither benefit nor harm edited individuals.

Keywords: ethics; gene editing; genome editing; harm; human enhancement; non-identity problem.

Introduction

Ever since the publication of Derek Parfit's influential *Reasons and Persons,* bioethicists have tended to distinguish between two different ways in which reproductive technologies may have implications for the welfare of future persons. Some interventions harm or benefit particular individuals: they are "person affecting". Other interventions determine which individual, of a number of possible individuals, comes into existence: they are "identity

affecting" and raise the famous "non-identity problem". For the past several decades, bioethical debate has, for the most part, proceeded on the assumption that direct genetic modification of human embryos would be person affecting. However, now that such "genome editing" is a realistic scientific possibility, support for the idea that it is person affecting appears to be eroding. In this paper, I offer some thoughts on the substantive matter of whether genome editing would be person affecting and how this might matter for its ethics, as well as some speculations as to why bioethicists are revisiting this question at this particular historical juncture.

The structure of my discussion is as follows. In section I, I briefly gloss the history of discussions of the ethics of altering the human genome as well as the distinctive features of recent technological breakthroughs and suggest that the strongest use-case for germline genome editing in human beings relates to enhancement rather than therapy. Section II outlines the difference between person-affecting and identity-affecting interventions in reproduction, the nature of the reasons we have regarding each, and the standard "Parfitian" account of the ethics of genetic modification of human beings that has developed over the last four decades or so. In Section III, I turn to the science and explore what would be involved in bringing a genome-edited individual into existence: I consider a number of different processes, including some that assume further technological breakthroughs. Section IV discusses the implications of the science of genome editing for our understanding of its nature, arguing that genome editing is highly unlikely to be person affecting for the foreseeable future and, as a result, will, on the Parfitian account, neither benefit nor harm edited individuals. In section V, I observe that, were we to instead reach the conclusion that genome editing was person affecting, this would imply that it was morally obligatory for parents to genome edit their children and might even justify a legal requirement to do so. I conclude, in section VI, by suggesting that the idea of person-affecting genetic modifications functions mostly as a contrast case to facilitate philosophers' discussions of the more interesting — and less politically fraught — category of identity-affecting interventions. If we want to discuss the ethics of person-affecting interventions, we need to do more work to identify the counterfactuals that allow us to determine whether a reproductive intervention modifies a particular individual or brings another individual into existence.

I. Genome editing

Discussions of the possibility — and ethics of — altering the genetic make-up of human beings commenced as soon as genes were discovered (Kevles 1995; Mukherjee 2016).[1] Advances in assisted reproductive technology, as well as the prospect of recombinant DNA technologies, sparked serious engagement with "the ethics of genetic control" by philosophers and theologians from the 1970s onwards (Fletcher 1974; Jonas 1974; Ramsey 1970). These debates bubbled along at a steady pace until they were reinvigorated by the invention of the CRISPR/Cas9 "genome editing" system in 2012. Where previous generations of tools for producing genetically modified organisms inserted new genes into the organism's genome at more-or-less random locations the CRISPR/Cas9 system held out the prospect of extremely precise "edits" of the genome at locations of the users' choosing. Possibilities that had previously mostly been in the realm of science fiction suddenly looked realistically available.[2]

Perhaps because scientists have been keen to draw a distinction between the old "primitive" techniques of genetic modification and the new "precise" methods of genome editing, discussion of the ethics of the latter has not been sufficiently informed by the history of discussions of the former as one might have hoped. This is a shame because the relative precision of the new techniques is only relevant to some of the ethical issues raised by the prospect of alterations to the human genome. Whether the current generation has the right to shape the biology of future generations, what sorts of interventions are compatible with affected individuals' right to an "open future", concerns about the social consequences of the widespread uptake of this technology, or about the justice of only

[1] While much of this discussion concerned genetic selection, the possibility of direct genetic manipulation was also canvassed. Hermann Muller showed that it was possible to induce mutations in fruit flies in 1927 (Carlson 1981). Almost immediately thereafter, people — including Muller himself — began writing and speaking about the possibility of genetic manipulation of human beings and the ethics thereof.

[2] CRISPR/Cas9 and related tools may be used to modify an existing individual's somatic cells or to modify cells in the early-stage embryo. However, somatic cell gene editing can only directly alter the functioning of the cells into which the new gene enters, while modifications made to the cells in the early-stage embryo have the potential to effect multiple cell lineages and thus generate larger changes in the organism's phenotype (Ishii 2015). Thus, editing the embryo has significant advantages compared to genetically modifying somatic cells. For the purposes of this paper, then, I am concerned solely with the appropriate understanding of the nature of editing that affects the DNA in the cells of the early-stage human embryo — that is to say, with germline gene editing.

some having access to it, etc, are largely unaffected by the relative accuracy of the technology of genetic modification. An accurate technique of genome editing would reduce — perhaps even eliminate — some of the risks involved in the procedure but would not fundamentally alter its ethics.

Nevertheless, the relative precision of genome editing does bring into the foreground a question that has long been discussed in the broader debate about genetic modification: whether the arguments for "therapeutic" genome editing also work to justify human enhancement (Doudna and Sternberg 2017, 230-31). In what follows I am assuming that genome editing *will* primarily be used for the purposes of human enhancement: that is, in the attempt to provide future individuals with beyond-species-typical capacities. This may seem speculative but there is already a significant constituency, in both the philosophical and scientific communities, arguing in favour of this application (de Araujo 2017; Bostrom 2003; Church and Regis 2012; Green 2007; Gyngell, Bowman-Smart, and Savulescu 2019; Gyngell and Savulescu 2016; Harris 2007; Harris 2015; Powell and Buchanan 2011; Regalado 2015; Savulescu 2005 & 2007a; Silver 1999; Smith, Chan, and Harris 2012; Stock 2003). Indeed, insofar as it was intended to provide individuals with immunity to a disease (HIV) rather than to cure an existing condition, the only use of germline genome editing in human beings to date, by He Jian Kui, was arguably an attempt at enhancement rather than therapy (Kuersten and Wexler 2019; Schaefer 2019).[3] Moreover, while it undoubtedly has utility for the purpose of garnering public support for genome editing, the therapeutic case for germline genome editing is weak (Darnovsky and Hasson 2020; Lanphier et al. 2015). In most cases where children are at risk of inheriting genes for a deleterious condition, preimplantation genetic diagnosis already allows prospective parents to select unaffected embryos. In those rare cases where it does not, prospective parents could make use of donor gametes in order to avoid transmitting particular genes to their children. Given the availability of this alternative, the "therapeutic" case for genome editing actually rests on a claim about the normative significance of prospective parents' desire to avoid the use of

[3] As John Harris (2007) observes in the context of his discussion of genetic interventions to reduce vulnerability to disease "Since vulnerability to smallpox and polio, or to measles, mumps, and rubella, is perfectly normal and natural… if we alter human beings to affect their vulnerability to these things, we are enhancing them. …Vaccinations then are not 'treatments', since individuals vaccinated are not usually ill" (p. 21).

donor gametes (Cavaliere 2018; Ranisch 2019, 62). What is really being "treated", then, is the psychological distress that prospective parents claim they would suffer if they had to raise a child conceived using donor gametes (Baylis 2019, 29-33; Sparrow 2015). The prospect of facilitating increases in the expected welfare of children by providing them with enhancements establishes a significantly stronger case for genome editing and for that reason I am assuming that this will indeed be the motivation for editing, at least in the longer term. That said, much of the argument that follows will also be valid of editing for (putatively) therapeutic purposes.

II. Two types of genetic intervention

Following the pioneering work of Derek Parfit (1984), discussions of the ethics of the use of new genetic technologies in the context of reproduction has, for the most part, been structured by a distinction between two different types of genetic intervention: technologies of genetic selection; and, technologies of genetic modification.

As the name suggests, technologies of genetic selection, which include sperm sorting, selective termination after fetal imaging and/or prenatal testing, and Preimplantation Genetic Diagnosis (PGD), involve determining which individual, of a number of possible persons, comes into existence. For example, in PGD, doctors select one or more embryos from a number of embryos created using in vitro fertilisation on the basis of information determined about the genetics of those embryos in order to ensure that any child born as a result of the procedure will not have genes associated with deleterious conditions.

By contrast, technologies of genetic modification, such as recombinant DNA technology and genome editing, are typically held not to change which individual comes into existence but rather to alter the genetics – and thus the eventual phenotype – of the individual that develops from the modified embryo (Buchanan 1996; Buchanan et al. 2000, 274-275; Chadwick 1987, 116; Delaney 2011; Gyngell and Savulescu 2016; Persson 1995; Smolensky 2008).[4]

[4] While I believe it is fair to say, as I have argued here, that majority opinion in the philosophical and bioethical literature held that genome editing would be person affecting, this belief was not held universally. In particular, Noam Zohar (1991) argued that genetic modification of embryos would be identity affecting, while

Philosophers have usually insisted on the distinction between these two types of technology because, as Parfit argued, there appears to be a marked difference between them when it comes to whether – and, if so, how - they harm or benefit the person born as a result of the intervention. In ordinary circumstances, we determine whether an event harms or benefits someone by asking what that person's situation would have been like (a "counter-factual") had the event not occurred. It has typically been held that while, in practice, such a comparison may be difficult to make, and its results uncertain, there is no especial problem about making this assessment in the case of technologies of genetic modification. When we are concerned with harm or benefit, we know where to look to try to resolve the counterfactual. In Parfit's terms, these technologies are "person affecting" (Parfit 1984, 351-379). However, in the case of technologies of genetic selection, the counterfactual approach to determining harm or benefit fails. In Parfit's terms, these technologies are "identity affecting": they affect the numerical identity of the person that comes into existence (Parfit 1984, 356-359). Consequently, asking what the life of the person born as a result of the technology would have been like had another choice been made involves a comparison with what their life would have been like if they did not exist and another person existed in their place. In cases where a choice leads to someone being born with negative welfare – with a life, as the literature (Feinberg 1987) says, "not worth living" – it is plausible to hold that this harms them. That is, where life is a constant misery, we might say that it is better not to exist (Buchanan et al. 2000. Glannon 1998; Robertson 1994, 75; Steinbock and McClamrock, 1994; Strong, 2005). However, as long as someone has a life that brings them more joy than suffering, it hard to see how they can have been harmed by being brought into existence given that the alternative would mean that they would not have existed at all. Conversely, insofar as only those who exist have welfare, it is unclear whether we should think of coming into existence, with positive welfare, as being better than not existing at all. Finally, as Parfit famously demonstrated (1984, 381-390), if bringing people into existence benefits them, then it seems as though we may have an obligation to bring as many people into existence as possible, which in turn has exceedingly counterintuitive implications for population ethics. For these reasons, many people writing

Robert Elliot (1993) argued that it might be either identity affecting or person affecting depending on the detail and extent of the modification.

on the topic have concluded that, with the possible exception of cases involving negative welfare, identity-affecting choices do not harm or benefit the person who comes into existence as a result of the choice (Brock 1995; Glover 2006, 50; Robertson 1994, 76; Savulescu 2002; Strong 2005).[5]

The difference between these two sorts of interventions generates a difference in the nature of the reasons we have to perform them.

In the case of technologies of genetic modification, it seems we have obligations regarding the welfare of the future person that are just as strong, and of the same nature, as those that we have to existing persons. Once we have decided to bring someone into existence, we are obligated to the particular person the embryo will become not to harm them and, where possible, to benefit them. Unless we are willing to place sufficient normative weight on the distinction between acts and omissions, failure to provide a welfare-enhancing intervention will harm the person who develops from the embryo.

When it comes to genetic selection, though, it seems that whatever reasons we have cannot derive from the interests of the person who will be brought into existence — who will neither be harmed nor benefited by our choice (Glover 2001; Glover 2006, 50; Savulescu 2002). At the same time, it seems implausible to think that, all other things being equal, we have no reason to bring a person with a higher expected welfare into existence rather than a person with lower expected welfare when we can do so (Savulescu 2001). Reasons of "impersonal beneficence" — a concern with the amount of well-being in the world — suggest that we should prefer to bring people into existence with higher, rather than lower, welfare (Brock 1995; Parfit 1984, 369). Alternatively, we might say that we have reason to produce "non-comparative benefits" by selecting embryos with higher expected welfare (Bykvist 2007; McMahan 2013). Even so, doing the "wrong" thing doesn't make anyone worse off in the case of selection, where it does in the case of modification. For this reason, it is hard to avoid the thought that the reasons we have to select embryos are weaker than

[5] Although, inevitably, several authors have defended the claim that it *is* better to exist than not to exist and therefore that bringing people into existence benefits them. See, for instance, Holtug (2001) and Persson (1995).

the reasons we have to modify them (Gyngell, Douglas, and Savulescu 2017; Zohar 1991, 276-8).[6]

Thus far, I have just been providing an account of the intellectual landscape surrounding the ethics of interventions designed to shape the genomes of future human beings. While inevitably, each and every aspect of this account is contested by one author or another (Roberts and Wasserman 2009), it is, I believe, fair to say that the account I have provided is the "standard" account. The philosophical literature on the non-identity problem is both voluminous and notoriously difficult and I have no ambition to make a substantive contribution to this literature here. Nor do I wish to imply that the standard account is necessarily the correct – let alone the only available – one. I have chosen to focus here on the person/identity affecting distinction, and its normative significance for those influenced by Parfit, because of the extent of Parfit's influence in the literature on the ethics of reproduction. What I wish to highlight for current purposes is the assumption in the standard account that genetic modification, unlike genetic selection, would be person affecting.

What is striking now that genetic modification, in the form of genome editing, is actually possible is the fragility of the grounds for this belief. While some contemporary writers have continued to maintain that genome editing would be person affecting (Cavaliere 2018; Gyngell and Savulescu 2016; Gyngell, Douglas, and Savulescu 2017; Powell, Kahane, and Savulescu 2012), Tom Douglas and Katrien Devolder have recently called this claim into question (Douglas and Devolder 2019). In order to understand why, we need both a better understanding of the science of genome editing and a willingness to confront some difficult philosophical — and perhaps even metaphysical — questions.

III. The science of genome editing

The first experimental attempts to edit the human genome involved editing early-stage human embryos. A team of researchers lead by Junjiu Huang at Sun Yat-sen University edited non-viable "tripronuclear" human embryos formed by the fusion of two sperms with

[6] The difficulties involved in characterising the nature and force of the reasons that we have relating to the welfare of individuals in the identity-affecting cases are, in a large part, what makes the non-identity problem a problem.

each oocyte (Liang et al. 2015). Because the zygotes each consisted of multiple cells and because the CRISPR/Cas9 construct was not 100% efficient in performing the desired genetic modification many of the modified embryos exhibited “mosaicism” and consisted of a mixture of edited and un-edited cells. Subsequent attempts to edit human embryos have also produced mosaic embryos (Kang, He, Huang et al. 2016; Tang et al 2017). Because PGD only reveals information about the genetics of the particular cell or cells taken from the early-stage embryo and because it is impossible to know which cells will develop into which tissues, mosaicism makes it difficult to predict the phenotype of the individual that might develop from the embryo (Adashi and Cohen 2020; National Academies of Sciences, Engineering, and Medicine 2017, 237). For this reason, the possibility of mosaicism stands as a significant barrier to an ethical practice of human germline genome editing of embryos (Harper and Schatten 2019; Lea and Niakan. 2019; Mehravar et al. 2019).

It is, however, possible that improvements in the science of genome editing will increase its efficiency and thus decrease the risk of mosaicism in modified embryos (Davies 2019). Already, Ma, Marti-Gutierrez, Park, et al. (2017) have shown that co-injecting the sperm and CRISPR/Cas9 construct into the oocyte at the point of fertilisation greatly reduces the percentage of the embryos produced that are mosaic. However, this experiment also suggested that introducing new genetic sequences into human embryos was more difficult than scientists had anticipated, with the embryos repairing the break introduced into the chromosome by the CRISPR/Cas9 construct using a maternal gene rather than the “repair” sequence carried by the construct as the researchers anticipated. If this proves to be the case, it may limit the potential of this technique for human enhancement in so far as enhancement may require introducing novel genes into the human genome. Whether it is the case or not, scientists will almost certainly have to check whether their genome editing has been successful by means of preimplantation genetic diagnosis before proceeding to implant a modified embryo into the womb of a woman. They will also need to check that the editing hasn’t produced “on-target” or “off-target” effects that might prevent the embryo from developing normally and/or be deleterious for the well-being of the person who would develop from the embryo (Adashi and Cohen 2020; Ormond *et al.* 2017). In all likelihood, then, genome editing embryos will involve modifying multiple embryos before choosing one or more to implant.

An alternative method of genome editing, which would avoid the difficulties associated with the possibility of mosaicism — although not of "off target" or "on target" effects — would be to directly edit sperm or oocytes prior to fertilisation. As it would not be possible to check the success of the editing in the gamete without destroying it, preimplantation genetic diagnosis of the embryo created using modified gametes would be required in order to determine whether the editing had been successful or not and to screen for deleterious genetic changes as a result of the editing (National Academies of Sciences, Engineering, and Medicine 2017, 241-242).

There are, moreover, several other ways that genome editing might be carried out, albeit on the assumption that other reproductive technologies will soon come to fruition (National Academies of Sciences, Engineering, and Medicine 2017, 242-245).

When researchers want to edit cells, they usually edit stem cells, which can be maintained in culture indefinitely and (perhaps) differentiated into other cell types as required (Hockemeyer and Jaenisch 2016). Beginning with stem cells also allows researchers to attempt to edit multiple cells and then identify, and proceed to work with, those where the editing has been successful. This in turn makes it easier to make multiple edits to the genomes of the cell line.

Pluripotent stem cells have the potential to develop into any cell in the organism's body - including gametes (sperm and oocytes). This means that if scientists can discover the appropriate sequence of molecular signals and environmental conditions it should be possible for them to derive gametes from pluripotent stem cells (Mathews, Donovan, Harris, et al. 2009; Whittaker 2007). Researchers have already succeeded in producing sperm (Nayernia, Nolte, Michelmann et al. 2006; Hayashi, Ohta, Kurimoto et al. 2011) and oocytes (Hayashi, Ogushi, Kurimoto et al. 2012; Hubner, Fuhrmann, Christenson *et al.* 2003) from mouse stem cells and a number of teams are working to achieve this feat using human induced pluripotent stem cells (Panula, Medrano, Kee et al. 2011; Irie, Weinberger, Tang et al. 2015; Yamashiro, Sasaki, Yokobayashi et al. 2020). Once this ("*in vitro* gametogenesis") is possible then scientist will be able to bring a genome-edited human being into existence by editing stem cells, and then deriving gametes from these cells that would transmit the modification to embryos created using these gametes, which could then be implanted into the womb of a woman (National Academies of Sciences, Engineering, and Medicine 2017,

243-245). If an individual wanted to edit the genome of their child then that individual could serve as the donor of somatic cells that would be induced to become pluripotent: the child born of gametes derived from these cells after they were genome edited would be the genetic offspring of the donor.

One disadvantage of this technique is that it would struggle to achieve phenotypic modifications that require an individual to have some particular combination of different genes. The reshuffling of genes that occurs during the formation of gametes would mean that only some sperm (or oocytes) would carry the desired combination of genes. Securing phenotypes that required an individual to be homozygous would require scientists to modify cells in the paternal and maternal line and derive both sperm and oocytes. Again, scientists would need to create multiple embryos and then choose between them to select embryos that had all and only the desired modifications.

These difficulties could be avoided if scientists were willing (and able) to carry out "nuclear transfer" to create human embryos from pluripotent stem cells.[7] Scientists could then perform multiple modifications of the genome of stem cells, checking at each stage to see if their modification has been successful by means of a genetic assay of a cell derived from the modified line, before transferring the nucleus of one of the modified cells into an enucleated ovum, and implanting it into the womb of a willing woman, in order to bring a genome-edited individual into existence. This procedure has previously been used to generate genetically modified animals of a number of different species (Lai and Prather 2003; McCreath, Howcroft, Campbell et al. 2000; Shimozawa, Ono, Muguruma, et al. 2002). Editing a stem cell line derived from the somatic cells of an existing individual would allow scientists to create a genome-edited clone of that individual. Editing an embryonic stem cell line derived from an embryo created using donated gametes would allow scientists to create embryos that would develop into the genetic offspring of the donors of the gametes. That is to say, this procedure would allow couples to genome edit their children. Once more, it seems likely that scientists would need to employ PGD to check that the modified embryos contained the desired genes and that no deleterious genes had been introduced

[7] Most discussions of nuclear transfer concern the transfer of the nuclear material from a *somatic* cell into an enucleated ovum, as *per* the procedure that generated "Dolly" the sheep. In this case, the procedure would involve the transfer of nuclear material from a pluripotent stem cell into an enucleated ovum.

via off-target effects, although, importantly, in both these scenarios, in the best case, all the embryos would be genetically identical.

For the moment, neither artificial gametogenesis nor live birth after nuclear transfer has yet been demonstrated in humans. However, as noted above, artificial gametogenesis has been achieved in mice and is widely expected to eventually be possible in humans. Nuclear transfer is already used to produce genetically modified non-human animals and related procedures are employed in human cells in the context of mitochondrial replacement techniques (Craven et al. 2010). It is therefore not unreasonable to expect these technologies to be developed in the not-too-distant future. It is true that both of these technologies would raise a host of other ethical issues should they ever come to fruition. Nuclear transfer, in particular, is likely to be highly controversial insofar as it would make it possible to clone existing — or deceased — human beings. Nevertheless, the potential of these technologies to facilitate genome editing is itself likely to be an important consideration in the case for developing them.

IV. The nature of genome editing in the light of the science

What this brief survey of the science of genome editing shows is that, while the literature has tended to treat modification as an alternative to selection, in reality the process of modification will usually involve selection. Genome editing would require IVF or related manipulations (such as nuclear transfer) of embryos *in vitro* and will almost certainly involve preimplantation genetic diagnosis before the modified embryo is implanted in the gestational mother's womb. Given that not all implantations lead to a successful pregnancy, it would also often require creating multiple edited embryos. Whether these procedures are person affecting or not, according to Parfit's schema, then, seems to depend on how we conceptualise the relationship between the embryo selection stage and gene-editing stage.

If we focus on the history *of the particular embryo* that developed into the genome-edited individual, then it seems natural to say that this individual would have had a different phenotype if the embryo were not edited. That is to say, on this line of thought, the editing *is person affecting* according to the Parfitian account. Presuming that the edit constitutes an enhancement – or is, at least, therapeutic — this would mean that the individual has benefited from the genome editing. This line of thought may appear especially plausible if

the editing procedure involves nuclear transfer from genetically modified stem cells because in this case any selection that did occur will not have affected the genome of the individual that was eventually brought into existence.[8]

If, instead, we focus on the history *of the events* that led to the birth of a genome-edited individual, then – with the possible exception of the case where the editing proceeded via nuclear transfer from modified pluripotent stem cells – genome editing looks *identity* affecting. Because the process of genome editing includes selection, if it were not for the editing another person would have come into existence. This line of thought looks especially compelling if modification proceeded via the derivation of gametes because it is clear that if this procedure were not performed a different pair of gametes would have fused and created a person with a different genome. However, given that, in practice, in order to check the accuracy of the editing, genome editing will involve creation of, and selection from amongst, multiple embryos, it seems likely that in almost all cases where (prospective) parents choose to edit their child a different child would come into existence if they decided not to pursue genome editing. This in turn means that, on the Parfitian account, genome editing will neither harm nor benefit those born as a result of the procedure.

Up until this point I have been focusing on the implications of the modification and selection that occurs *in the course of* the process of genome editing. However, as Tom Douglas and Katrien Devolder (2019) have pointed out, parental decisions around genome editing themselves exert a powerful influence on the identity of the person who is brought into the world.

In their paper, Douglas and Devolder are concerned to determine whether therapeutic genome editing might, as a number of authors have argued, be morally preferable to genetic selection because it conveys a benefit on the individual who is born as a result (Cavaliere 2018; Gyngell and Savulescu 2016; Gyngell, Douglas, and Savulescu 2017). Douglas and Devolder suggest that whether genome editing benefits the child born as a

[8] Whether such interventions will be person affecting or identity affecting will depend on the identity conditions for human beings. If human beings are fundamentally organisms, then selection amongst clone embryos will involve choosing between individuals. However, insofar as the inner cell mass of the embryo, from which the future individual will develop, can develop out of any of the genetically identical cells in the zygote, it might be argued that substituting one clone embryo for another does not affect the identity of the person who is brought into existence.

result will depend on what the parents would have done if they had decided not to pursue genome editing. They consider a (hypothetical) scenario where scientists identify a particular embryo as containing genes associated with a genetic disorder, via PGD, and the prospective parents then proceed to request that that embryo be genome edited. They argue that, in such a case, what the prospective parents would do if they decided instead not to genome edit would depend on the seriousness of the condition they were trying to treat. In cases where the condition is likely to be serious, they suggest that prospective parents would most likely discard the embryo and seek an alternative route to having a child (for instance, by using donor gametes). However, in cases where the condition is unlikely to have much of an impact on the welfare or opportunities available to the future child, they might decide to proceed to request that the embryo is implanted "as is". As Douglas and Devolder note, this (plausible) reading of the relevant counterfactuals has the surprising implication that, at least if we accept the Parfitian account, we would have stronger reasons to pursue genome editing for trivial conditions on the grounds that genome editing for serious conditions would not be person affecting.

Douglas and DeVolder's argument is fascinating and well-made. However, it assumes that it would be ethically defensible to genome edit, and then to proceed to implant, a single, already existing, embryo, which, as I have argued here, is highly unlikely for the foreseeable future. In all likelihood, genome editing will involve creating and editing multiple embryos before selecting the "best child possible". Moreover, where prospective parents are motivated by a desire to enhance their children rather than to avoid a genetic disorder, which, I have suggested, is a more plausible motivation for the project in the longer term, the decision to genome edit will almost certainly be identity affecting, as a couple (or individual) will usually make it before they have created any embryos and the process itself will, at the very least, alter the timing of conception. This is itself usually sufficient to bring it about that a different sperm fertilises the ovum, with the consequence that a different person is born (Parfit 1984, 351-352). Thus, if we include the decision to edit in our deliberations about the relevant counterfactual for assessing harm or benefit, then genome editing will be identity affecting and the children born as a result of the procedure will neither be harmed or benefited by it.

V. What if genome editing is person affecting?

At the very least then, for the foreseeable future, it will be plausible to hold that genome editing is not person affecting and — at least according to the standard Parfitian account — fails to benefit the genome-edited individual. In some ways this is fortunate, because the conclusion that genome editing is person affecting would have radical — and controversial – implications in the context of the debate about parental obligations arising from the purported principle of "procreative beneficence" (Savulescu and Kahane 2009).

According to its proponents (Savulescu 2001), the principle of procreative beneficence requires 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.

Although the principle is formulated in relation to selection, in so far as it is derived from a purported parental duty of beneficence more generally, it is clear that it is intended to apply to decisions about modification as well. The reference to selection is a historical artefact owing to the fact that technologies of genetic modification were not realistically available when it was formulated.

Once it becomes possible to improve a child's expected welfare by means of genome editing, procreative beneficence will imply that we are obligated to genome edit whenever we are bringing people into existence (de Araujo 2017; Harris 2007, 3; Gyngell, Bowman-Smart, and Savulescu 2019).[9] Moreover, if genome editing is person affecting, this will be a "real" obligation and not merely a "*pro tanto* reason" of the sort that allows advocates of procreative beneficence to duck the counter-intuitive implications of their account of parental obligations in cases involving selection (Sparrow 2007; 2011). That is to say, while it is perhaps plausible to claim that in cases where failure to act on one's obligations does not harm anyone (as in cases of selection, according to Parfit) agents do nothing wrong if they

[9] Here and below, I am going proceed as if the relevant metric in discussions about what sort of children we should have is "expected welfare" (or "welfare" for short). However, an equally plausible, more liberal, measure is "openness of future" (Sparrow 2011).

choose to ignore their *pro tanto* reasons and act instead on the basis of other reasons they have, in cases where failure to enhance would harm the child, those who are bring a child into existence have a *prima facie* obligation (and not merely a *pro tanto* reason) to enhance. If they are to act otherwise, prospective parents must act on the basis of other obligations and not mere preferences.

Even without postulating a distinct duty of procreative beneficence, duties of beneficence more generally suggest we will be obligated to genome edit once we've decided to bring people into existence. By definition, enhancement will promote the welfare of children, and so we have reason to pursue it (Chan and Harris 2007). Unless one places a good deal of weight on the moral significance of the distinction between acts and omissions, failure to enhance will harm the child and thus nonmaleficence will also require us to pursue enhancement (Savulescu 2005).

The content of these obligations also seems highly likely to be problematic given the implications of widespread systematic social injustice for the expected welfare of children with different phenotypes. Just as phenotype is always the product of the interactions between genes and the environment, so too is expected welfare a product of the interactions between phenotype and the environment. That is to say, whether an individual's particular phenotype, for instance, sex, race, or sexual inclination, promotes or lowers their expected welfare will depend on the society in which the individual lives. In highly patriarchal societies, for instance, women will have lower expected welfare than men, while in racist societies, skin colour will have implications for expected welfare. The impact of injustice on life prospects means that in societies such as the United States, the United Kingdom, Australia, and arguably much of Europe, the "best" baby turns out to one who will grow up to be white, male, and straight… and blonde-haired and blue-eyed (Sparrow 2011).[10] No matter how committed they are to achieving a just world, parents won't be able to change the fact that their child will grow up in a sexist, racist, and homophobic environment. However, once genome editing becomes possible, they will be able to change the extent to which their children are impacted by unjust social norms by

[10] As I have argued elsewhere, if, some for reason, we insist that parents are obligated to ignore the implications of social injustice for the welfare of their children, an obligation to maximise expected welfare seems likely to require that parents select girl children (Sparrow 2010).

modifying their children. In an unjust world, procreative beneficence will require parents to become complicit with injustice.

The idea that parents are obligated to genome edit their children to suit existing social norms is offensive enough. However, should the benefits made available by genome editing become sufficiently large, there will be a compelling argument that parents should be required by law to enhance their children. Arguments for reproductive liberty will still have some force but when failure to enhance looks like "genetic child-abuse" the balance of considerations will, at the very least, swing heavily towards a concern for the interests of the future child (Savulescu 2007b). Just as the law currently places limits on the rights of parents when it comes to actions that might harm existing children, in the future the law may restrict the liberty of parents to refuse to enhance their children (Sparrow 2011).

VI. Final political reflections

When there was no realistic prospect of genome editing, the rhetorical/institutional incentives of claiming that there would be an obligation to genome edit, once it became possible, because genome editing would be person-affecting (i.e. those benefits, especially in terms of citations and media attention, associated with being seen to advance a "radical" and "provocative" claim) outweighed the rhetorical/political costs of doing so (i.e. having to admit that coercion might be justified if parents refused to enhance their children). However now that genome editing looks more possible, the balance of rhetorical/institutional costs and benefits has arguably shifted. In particular, the toxic political implications of advertising an obligation to genome edit, which plays directly into not-entirely-unfounded public fears about coercive eugenics, loom larger.

Perhaps it is not surprising, then, that the arrival of CRISPR has moved some authors to reconsider whether genome editing is person affecting. As long as we hold that genome editing is not person affecting, it is possible — at least superficially — to insist both that enhancement is morally obligatory, and that people do nothing wrong — or at least no harm — if they fail to act on this obligation... and therefore that there is no justification for laws requiring enhancement. Advocates of enhancement can both appear to be standing for a radical claim – "we are obligated to enhance" - and deny that anyone need fear being forced

– or even required – to do anything they don't already want to do (Sparrow 2010). They can have their cake and eat it too.

What cries out for explanation, though, is why the assumption that genome editing (or "genetic modification," as it once was) would be person affecting had such currency in the literature historically. After all any choice that affects which sperm fuses with which egg will be identity affecting. As Parfit (1984, 351-361) observed, because small changes in the timing of conception will almost always have this consequence, this means that almost everything we do alters who comes into existence. It seems obvious that any reproductive technology that requires couples to undergo in vitro fertilisation rather than conceive naturally will be identity affecting.

My suspicion is that the idea of person-affecting modification served mostly as a contrast to the more philosophically interesting phenomenon of identity-affecting modifications. If one is concerned with the ethics of PGD, as most authors writing about the ethics of genetic interventions were until the advent of CRISPR, then it is tempting to counter-pose it to the (purportedly) person-affecting case of genetic modification. Moreover, as I observed above, if one is thinking about genetic modification of individuals then it is natural to focus on the history of the embryo that becomes the modified individual and compare the modified individual's welfare with what it would have been had they developed from the same embryo were it not modified. Yet, as I've also observed here, in practice, were the modification not performed, a different individual will almost always come into existence.

At the very least, then, before we can conclude that genome editing would be person affecting, we need to come to a better understanding of how to identify the relevant counterfactuals. That is, how should we determine who would come into existence if genome editing were not performed? Until we can reach consensus on this important methodological question, it will be tempting – and all too easy - for those influenced by Parfit to treat genome editing as person affecting or identity affecting as it suits their rhetorical or political purposes at the time. The issues around genome-editing are complex enough that we should be reluctant to allow them to be further muddied in this way.

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