Is Germline Genome Editing Identity-Affecting?

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ABSTRACT

This article deals with the contentious problem whether He Jiankui's GGE is an identity-affecting action and therefore whether it arises the non-identity problem. Differently from some leading authors in current debate, the author argues that GGE cannot be considered an identity-affecting intervention because it does not produce an unavoidable bad effect and does not eliminate the time gap between selection and modification, which could allow the doctor to change his mind and not modify the selected embryos.

1. GGE and the non-identity problem

In Bioethical debate[1] on Germline Genome Editing (GGE) has arisen after doctor He Jiankui's experiment, made in China in 2018, on two embryos twins, whose genome was modified through CRISPR procedure in order to get immunity to HIV. So far, on the ground of the limited data available, in He Jiankui case no apparent bad effects on the health of two generated twins, Lulu and Nana, seem to have been caused[2]. Nonetheless, for the sake of the argument, I will assume that some bad effects will be caused in the next future, and that for this reason such an experiment is morally problematic.

In this debate there is an interesting disagreement about how GGE should be understood. Namely, about whether such a genetic modification should be considered an identity-affecting action and therefore whether it rises the non-identity problem. Such a problem arises when actions that cause bad, or good, effects to future individuals determine, at the same time, their identity: no harms, or benefit, could be identified for these individuals, because otherwise they would not have been existed and the actions cannot worsen off, or better off, their condition (Parfit 1984, pp. 351 ff).

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[1] Many thanks to Davide Battisti and to two anonymous reviewers for helpful comments on a first draft of this article.

[2] See https://www.theguardian.com/science/2024/apr/01/crispr-cas9-he-jiankui-genome-gene-editing-babies-scientist-back-in-lab.

The point is relevant, because it carries on important implications regarding the moral evaluation of GGE. According to the standard (comparative to counterfactual) notion of harm (Boonin 2014, p. 54), if GGE is not an identity-affecting action, any bad, or good, effects caused by GGE on the health of the genetically modified person can be considered a harm, or a benefit, made to her, because the same person would have existed even in the case GGE would not have been made, and GGE worsens off, or better off, her condition. And according to many normative theories, when GGE harms the person, it wrongs the person, and it is morally wrong. When GGE benefit the person, it is morally right.

On the contrary, if GGE is an identity-affecting action, according to the standard (comparative to counterfactual) notion of harm, it is impossible to identify harms, or benefits, done to the person, because the same person would not have existed otherwise, and GGE cannot worsen off, or better off, her condition. GGE should be considered harmless. This conclusion seems to be problematic because counterintuitive: it is the non-identity problem. Such a problem is implied by the traditional normative views, which states that an action can be right or wrong only if there is a person affected by it (and therefore called 'person-affecting views'). On the contrary, this problem is solved by other normative theories, which states that an action can be right, or wrong, if the world is made a better, or a worse, place, increasing or decreasing the amount of impersonal good (and therefore called 'impersonal views'). This is how the difference between the two views is proposed by Parfit:

> "We should do what is in the best interest of those concerned. [...] Such a principle can take different forms. We need only look at a single difference. The principle can take what I call an "impersonal" form: for example it can run: 1) We should do what most reduces misery and increases happiness. It can instead take a "person-affecting" form: for example 2) We should do what harms people the least and benefit them most. When we can only affect actual people, those who do or will exist, the difference between these forms of the principles makes, in practice, no difference. But when we can affect *who* exist, it can make a great difference" (Parfit 1976, p. 109).

Some authors believe that Jiankui's GGE is not an identity-affecting action (Feeney&Rakić 2021, Battisti 2021), but some others believe that it is. In what follows, I will try to argue why the first are right and the second are wrong. In Jiankui's case, and indeed in many other cases, GGE cannot be considered an identity-affecting action.

2. GGE considered as an identity-affecting procedure

As said before, some relevant authors consider GGE an identity-affecting procedure. Alonso&Savulescu, for example, consider He Jiankui GGE as a case of PRIA: a way of altering the person's identity related to a particular policy (Policy-Related Identity Alteration).

> "He Jiankui employed antiretrovirals to lower the viral load of the father. He also organized and paid for the sperm to be washed clean of HIV. So a different child was born, who was free of the risk of HIV. Therefore, in one sense, He Jiankui's funding of an experiment to create embryos by IVF (and protect them from HIV by sperm washing) was identity-altering. We can call this Policy-Related Identity Alteration (PRIA)'" (Alonso & Savulescu 2021 p. 556).

They use an argument proposed by Tina Rulli. According to her, GGE "ensures that different gametes are used, and different children will be born" (Rulli 2017, p. 371). Alonso&Savulescu write: "if Jiankui was not going to perform the gene edit, he would not have carried out the experiment: he would not have carried out the IVF", "the gene editing of Lulu and Nana was not contingent, but necessary for their existence".

The conclusion derived by the two authors is that, because GGE is identity-altering, it should be accepted when impersonally safe and beneficial, but to be refused when impersonally dangerous and harmful.

Analogously, Robert Sparrow has considered GGE an identity-affecting procedure because the very decision to modify the embryos changes, at the same time, the moment of conception, and therefore the identity of the gametes and that of the embryo:

> "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 fertilizes the ovum, with the consequence that a different person is born [...]. 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" (Sparrow 2022, p. 10).

But, according to Sparrow (and differently from Alonso&Savulescu), this is a fortunate fact: otherwise, we would have a relevant moral reason to gene-editing any embryos whenever this modification results to be safe and benefi-

cial for the same embryos. But this is not the case, and there is no moral obligation to modify embryos: "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" (Sparrow 2021, pp. 10 f).

3. How GGE could be identity-affecting

A couple of distinctions proposed by David Boonin may be useful to understand why GGE could be considered identity-affecting. The first distinction is that between two different types of cases produced by actions: *bad condition* cases and *bad event* cases. "This is – Boonin writes – the difference between cases that involve the creation of people who are already in bad conditions and cases that involve the creation of people to whom bad things subsequently happen" (Boonin 2014, p. 8). The first is the case of Wilma, a mother who has a congenital disease and decides to take the risk to have a blind child instead of waiting two months and have a sighted child. Consequently, she inevitably transmits the disease to her child, causing him a bad condition. The second is the case of a Wealthy Society's risky policy which affects the identity of future people and inevitably condemn some of them to be killed at the age of 40 because of the release of a toxic waste which causes a bad event that worsens off their life.

The second distinction is that between two different ways of affecting the identity of future individuale. The first is a *direct* way, which immediately determines the moment of conception and therefore (according to Parfit's 'Time-dependence claim'[3]) modifies person's identity. The second is an *indirect* way, which creates a complex causal connection that later determines the moment of conception: "cases in which a choice has consequences that initiate a complex chain of events that eventually have an equally decisive effect on which particular people exist after the choice is made" (Boonin 2014, p. 5).

In the light of these distinctions, Wilma's case can be considered a *direct* identity-affecting *bad condition* case and the Wealthy Society an *indirect* identity affecting *bad event* case. Applying these distinctions to He Jiankui's case,

[3] "The Time-Dependence Claim: If any particular person had not been conceived when he was in fact conceived, it is in fact true that he would never have existed" (Parfit 1984, p. 351).

GGE could be considered an intervention which produces a *direct* identity-affecting *bad event* case, because the doctor's decision to modify the embryos initiates a causal connection that brings to determine which people will exist and later will cause them a bad effect.

There is another possible way to argue that GGE is identity-affecting. Alonso&Savulescu believe that genome editing made on the brain cells can modify the person's mind and therefore her identity:

> "the change to brain effected by the gene edit is so significant as to affect the psychological trajectory of the developing person. For example, a "cure" for Down Syndrome would so profoundly change the psychological capacities, dispositions and other traits as to cause the "death" of the Down Syndrome individual and the replacement with another person with greater intellectual abilities" (Alonso&Savulescu 2022, p. 27).

This is another sense of personal identity. Parfit calls this sense "personal identity over time" (1984, p. 350). This is the sense that generates the re-identification's problem for a particular person during different periods of her life. By contrast, we are dealing with what Parfit calls "personal identity in different possible histories of the world" (1984, p. 350), which generates the non-identity problem. These two ways of affecting the person's identity can, in some cases, interact each other and partly overlaps, as stated by Alonso&Savulescu, but these cases are rare and marginal. And above all, they do not overlap in He Jankui's case, which generates only the non-identity problem.

4. Some terminological remarks

Another remark regards the terminology used by Sparrow (and many others). According to him, identity-affecting interventions are opposed to person-affecting interventions: "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'" (Sparrow 2022, p. 1). Following such a terminology, both terms, 'identity-affecting' and 'person-affecting', refer to actions: identity-affecting actions as opposed to person-affecting actions.

But it is better to follow Parfit's original use of these notions. The term 'person-affecting' is used by Parfit to refer to (evaluative) terms like moral views, principles, reasons, harm and benefit etc., and is opposed to 'imperson-

al' views, principles, reasons, harm and benefit etc. By contrast, the term 'identity affecting' is used by Parfit to refer to (descriptive) terms, like actions, choices, cases, outcomes etc., and is opposed to actions, choices, cases, outcomes etc., that are not identity-affecting.

What are the problems in calling 'person-affecting' an action that is not identity-affecting? A first problem is that such an action can *affect* the person for the better (benefiting her and being morally right, for example the action of saving her from drawing) or for the worse (harming her and being morally wrong, for example the action of punching her in the nose), but it could also have no effect on her (for example the action of playing football with our friends in the park): in this case it does *not affect* the person for the better or for the worse (being morally permitted). But it is odd to call *'person-affecting'* an action that does not affect the person, while it is not odd to say that this action is not identity-affecting.

A second problem is that, if we call person-affecting any action that is not identity-affecting, it seems to follow from this terminology that person-affecting normative principles should be limited to evaluate these actions (called 'person-affecting actions') and cannot be extended to evaluate identity-affecting actions, which should be evaluated only by impersonal principles. But this is exactly the point in discussion between person-affecting and impersonal views and such a terminology looks like a verbal trick to solve the disagreement.

This problem is evident in the way in which Alonso&Savulescu (2022, p. 23) put together the two terminologies: "the identity altering interventions generate what [has] been called impersonal reasons and the person affecting interventions generate person-affecting reasons". Yet, this is wrong. Identity-affecting actions generate *different people* cases, and these cases can be evaluated both by person-affecting views and impersonal views (but Parfit adds *wide person-affecting* views as well). By contrast, actions that are not identity-affecting generate *same people* cases and these cases can be evaluated only by person-affecting views. In these latter cases, the distinction between person-affecting and impersonal views does not arise.

Therefore, if GGE is an identity-affecting action, it can be evaluated by person-affecting and impersonal views as well. On the one hand, according to person-affecting views, a bad health condition caused to genetically modified a person cannot be considered a harm made to her, because this person would not have existed otherwise and GGE does not worse off her condition. There-

fore, even if GGE had these bad effects, it would be morally permitted. (Many believe that such a conclusion is implausible because counter-intuitive, and this fact arises the non-identity problem). On the other hand, according to impersonal views, a bad health condition caused to genetically modified a person can be considered an impersonal harm, because GGE makes the world a worse place. Therefore, if GGE had these bad effects, it would be morally wrong. (Such a conclusion is not counter-intuitive, and the non-identity problem does not arise). On the contrary, if GGE is not an identity-affecting action, any bad effects caused by GGE on the person can be considered a harm made to her, and there is no difference in the evaluation made by person-affecting and impersonal views: if GGE had these bad effects, it would be considered morally wrong by both views.

5. Why GGE is not identity-affecting

In what follows I want to show why He Jiankui's GGE is not an identity-affecting action. The comparison with two examples made by Derek Parfit can be helpful to clarify why Jiankui's GGE is not an identity-affecting intervention. The first is the case of Ruth, a woman who have a congenital disease and decides to have a child immediately, instead of making a paid IVF to avoid the transmission of a disease which will kill her son at the age of forty.

> Ruth′s Choice. [...] Her congenital disease kills only males. If Ruth pays for the new technique of in vitro fertilization, she would be certain to have a daughter whom this disease would not kill. She decides to save this expense and takes a risk. Unluckily, she has a son, whose inherited disease will kill him at about the age of 40 (Parfit 1984, p. 374).

The second is the case of Ann, who does not have any congenital disease but decides to carry on a risky cure for infertility which infects her and her son with a rare disease and will kill him at the age of forty:

> Ann cannot have a child unless she takes a certain treatment. If she takes this treatment, she will have a son, who will be healthy. But there is a risk of one in two that this treatment will give Ann a rare disease. This disease has the following features. It remains dormant for twenty years, is undetectable, kills men but does not harm women, and is infectious. The following is therefore true. If Ann takes this treatment and has a healthy son, there is a chance of one in two that in twenty years she will infect her son with a disease that will kill him twenty years later, or when he is about forty. Ann chooses to take this

treatment, and she does later infect her son with this fatal disease (pp. 375 s).

One of the differences between these two cases is about how close the causal connections that determine the disease are. According to Parfit, in Ruth's case the causal connection is closer ("more close" Parfit writes), because the mother's disease is congenital and does not depend on her choice. On the other hand, in Ann's case the causal connection is less close, because the disease is not congenital and depends on the mother's choice to carry out a risky cure for infertility. In this case (like in the risky policy case) "the causal connections take the same form. Each choice produces a side-effect which later kills people who owe their existence to this choice" (Parfit 1984, p. 376).

In some respect, Jiankui's case is like Ann's case. In Ann's case the son's identity and his disease are determined by her choice, which produces a complex causal connection that later will kill him. Similarly, in Jiankui's case the choice to carry on GGE determines the identity of the two twins and will produce side-effects which later could worsen off them. But there is a fundamental difference: in Ann case the bad effect produced by the choice is fatal and *unavoidable*. Ann cannot interrupt its actualization: she can initiate it, but she cannot stop it. The same is true for the risky policy case. In these cases, there are no alternative: the causal connection is close enough to determine the conception of a particular person and to produce the future bad effect.

On the contrary, after the initial decision, Jiankui could have acted otherwise and could have not edited the two embryos, thus avoiding the production of the bed effect. Such a production depends on his other subsequent choices, and there is a time gap between the decision of modifying the two embryos, their selection trough IVF and the effective modification: a gap that allows the doctor to act otherwise. The doctor knew the potential risks for the future children and, after having selected Lulu and Nana, he could have changed his mind, not modifying them. Thus, Lulu and Nana could have existed without modification and no harm would have been produced. In addition, after modification, the doctor could have not implanted them into the womb, and they could not have existed at all. In Jiankui's case, there are some alternatives, and the future bad event is not unavoidable.

It is true that whether the decision of GGE had not been taken, different people would have been conceived: to achieve his decision to modify an embryo, the doctor selects some gametes and, for example, produces the embryo A, instead of some other gametes which could have produced the embryo B. But, even in this case, the modification is on the very embryo A: once selected,

the embryo A can grow with or without modification. It depends on the choice of the doctor. The same person could have existed without modification.

Thus, in Jiankui's case, the doctor's initial *decision* to gene-edit two prospective children is (indirectly) identity-affecting, because it initiates the causal connection that brings to select the embryos, but the subsequent *action* of modifying the two selected embryos using CRISPR technique, presupposes the prior existence of these embryos[4]. Therefore, Jiankui's GGE cannot be considered an identity-affecting action, and it does not arise the non-identity problem.

6. Jimmy's case

In order to better illustrate Jiankui case, Alonso&Savulescu imagine the case of Jimmy, who is a child born with a genetic mutation which will be lethal in his later childhood. Such a mutation is caused by a mistake made by the doctor during a radiography to his mother ovaries. This intervention brings the mother, called June, to postpone of one day the timing of conception with the consequence of changing the identity of her child:

> Did irradiating June's eggs harm Jimmy? [...] According to the identity altering policy argument, the decision to X-ray June meant she arrived home late. If it hadn't been for the X-ray procedure, another completely different sperm would have entered the egg, and a different individual created, not Jimmy (Alonso&Savulescu 2022, p. 26)

Yet, such a case is different from Jiankui's. In Jimmy's case the causal connections are close enough not to permit any alternative. Because the mother does not know the mistake made by the doctor during X-rays and her potential risk, there was no reason for her to change her mind and not conceive the child.

[4] See also Battisti (2021, p. 8): "regardless of the parents' intentions or motivation, if they are already in the IVF process, the embryo still exists and, thanks to GGE, there is the possibility to treat it, then the moral considerations change. In the post-conception context, we appreciate the existence of an embryo that is numerically identical to the future individual. Treating the embryo with GGE will affect the future child: in this context, the parents' decision no longer creates a brand-new numerical identity, as in the pre-conception context, but affects the child only in a qualitative way. As the context has changed (before the designated embryo did not exist, now it does), our moral obligations towards the future individual also arise, regardless of whether or not the designated embryo was created to be treated with GGE".

Therefore, Jimmy could not have existed otherwise (no child would have been born) and there is no person-affecting harm made on him. On the contrary, Jiankui, knew very well the potential risk of GGE: he could have acted otherwise and could have not modified the embryos once selected, breaking the causal connections that expose Lulu and Nana to future harms.

In order to have a more careful analogy with Jiankui's case, Jimmy's example needs to be modified: we have to imagine that after one week the doctor informs the mother about the mistake he made during the radiography and prescribes her some pills to eliminate any X-rays' bad effect on the genome of the already conceived embryo, but the mother decides to save her money and not to take the pills. In this case, it seems plausible to say that a person-affecting harm is made on Jimmy: he could have existed otherwise, and the mother could have prevented the future bad event.

Alonso&Savulescu refuse the argument of taking into consideration the doctor's decisions in the moment before gene editing took place and the possibility for him to change his mind. Following Rulli, they say that this argument "is a specious move and brings 'an artificially contrived scenario'" (2021, p. 571). Yet, on the contrary, such an argument seems to be a common philosophical counterfactual hypothesis, which can be helpful to clarify the claim.

7. Selection and modification of gametes

In Jiankui' case CRISPR technique operated on *embryos* and not on *gametes*, and we have argued that, in this case, GGE is not identity-affecting. This argument seems to hold even in some cases of gene-editing made on gametes. Sparrow considers gametes' modification as the main reason to argue that GGE is identity-affecting:

> 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 (Sparrow 2022, p. 10).

Yet, in some cases, the implication between gametes' selection and their modification is less close than Sparrow believes. Even in cases of gametes' modification, there are some alternatives: the doctor, or the parents, could change their mind and decide not to modify the gametes once selected. The time gap be-

tween the initial decision, selection and modification is short but not reduced to zero and there is room for the possibility of not modifying the selected gametes. In some cases of gametes' GGE, the causal connection is closer, but not so close to make always fatal the future bad event.

There are cases where there is no time gap between gametes' selection and their modification, or where modification precedes selection. In these cases, selection really implies modification and the person conceived could not have existed otherwise. In these cases, there is no possibility for the doctor, or the parents, of changing their mind: there is no alternative, and the conception of the edited person is unavoidable. This may to be the case of the 'derivation of gametes' quoted by Sparrow, where gametes are generated in laboratory, using pluripotent stem cells ("in vitro gametogenesis", IVG), and if the doctors had decided not to perform genome editing, they would not have employed IVG. Consequently, different gametes would have been used and different individuals would have been conceived. In such a sort of cases, modification seems to precede selection.

But other cases seem to be different. Some examples, derived by Wringley *et alii* (2015) and discussed by Alonso&Savulescu (2021, p. 571), can illustrate this difference. These examples regard different types of 'mitochondrial replacement techniques' (MRT), which allow prospective parents who are at risk of passing on mitochondrial disorders to have healthy children.

A first type is 'maternal spindle transfer' (MST), which removes maternal chromosomes from the mother's egg and places them in an enucleated donor egg. This reconstructed egg contains the mother's nuclear DNA and a donor's healthy mitochondria. In such a case "the very process of manipulating the maternal gamete takes time, the sperm used to fertilize it (in standard cases) will be different from the sperm that would have fertilized it if the maternal gamete had not undergone manipulation" (Wringley *et alii* 2015, p. 634). In MST case, there seems to be no alternative: the embryo produced by GGE cannot be produced by gametes selected without modification.

A second type of mitochondrial replacement technique is 'pro-nuclear transfer' (PNT).

> PNT begins with two eggs: one from the mother, which contains diseased mitochondria, and a donor egg with healthy mitochondria. Both are fertilized and the two pronuclei (i.e. the respective genetic contributions from both the egg and sperm) are removed from each zygote. The enucleated zygote produced by the mother's egg and the father's sperm is then discarded. The two

> pronuclei that were created using the donor's egg and the father's sperm are also discarded. Next, the two pronuclei taken from the parents' embryo are injected into the enucleated 'donor' embryo. At the end of the procedure, the embryo produced contains the parents' nuclear DNA and the donor's healthy mitochondria (Wringley et alii, p. 632)

The case of PNT seems to be different: in such a case the manipulation is applied to an egg post-fertilization, and there is a time-gap between selection and modification and the possibility, for doctors and parents, of changing their minds. In the first case, selection seems to be inextricably entangled with modification, but in the second case it can be disentangled.

8. Conclusion

If these considerations are sound, in He Jiankui's case GGE is not an identity-affecting procedure (it is not 'person-affecting', in Sparrow's terminology), and its evaluation does not arise the non-identity problem. And the same may be true for many other cases of GGE.

This conclusion can be relevant for our moral evaluation of such cases of GGE. If this practice is not identity-affecting it should be evaluated only from a person-affecting point of view (in this case, the distinction between person-affecting and impersonal perspective does not arise, as we have seen). Therefore, the evaluation of such a practice depends on whether GGE benefits or harms the modified individuals.

Thus, the moral conclusion to be derived is that, according to many perspective[5], we have moral reasons to gene-edit embryos whenever safe and beneficial and not to gene-edit them whenever dangerous and harmful. At the end, we are less lucky than Sparrow believes.

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[5] For example, according to a parson-affecting principle of beneficence (see Magni 2021).

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