Ethical Considerations on Gene Therapy for Color-Deficient People

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ABSTRACT

In 2009, a procedure for creating trichromacy in dichromatic monkeys has been proposed by Mancuso *et al*. The treatment could be used to "cure" color deficiency in human observers in the future, but to-date the method has not been adjusted and tested on humans yet. I believe that from an ethical view point the proposed method should be adjusted for humans and allowed for clinical trials, as long as the risks and harms are minimized, the treatment and its long-term benefits and risks have successfully been studied on animal trials, and as long as possible human trials follow certain international standards like for example the informed consent etc. Since color deficiency does not qualify as "real" disability, however, only somatic gene therapy as opposed to germ line therapy should be allowed, and private actors and the patients themselves should carry the main costs of development and application. From a social view point, other image improvement methods, like for example daltonization, should be prioritized for public funding in order to increase usability in general resulting in better navigation and communication for not only color-deficient people but other groups of people who have issues distinguishing color due to age, etc. as well.

1. INTRODUCTION AND BACKGROUND

The majority of people can differentiate between millions of different colors. Most scientists agree on that the perception of color leads to behavioral advantages connected to the attentional system, object recognition, and possibly detection of emotional states, as I discussed in a previous paper (Simon-Liedtke, Farup and Laeng 2015). Also, color has been used more and more in our modern world for communication in arts, navigation, traffic, and education. Color-deficient people are people that have difficulties distinguishing certain colors, however, most color-deficient people are not in fact color-*blind*. De Valois and De Valois (1993) explain that information from our eyes is processed in three distinctive pathways representing color attributes of intensity, red–green opponency and blue–yellow opponency. Most color-deficient people only have a reduced or missing perception along the red–green axis, but perceive fairly good color perception along the blue–yellow axis. In natural settings, color-deficient people might face discomfort (f.ex. collecting berries in the forest) but they are not in immediate threat of danger. It is especially in social contexts that color-deficient people are confronted with problems (Flatla and Gutwin 2012). Luckily, there are computational solutions in image processing to simulate color-deficient vision or daltonization methods that improve images for color-deficient people, as listed in a previous paper (Simon-Liedtke, Farup and Laeng 2015).

Mancuso *et al.* (2009) have proposed a procedure – aka the Mancuso-Neitz method – based on somatic gene therapy for creating trichromacy in dichromatic squirrel monkeys by injecting the missing cone pigment in the retina of dichromatic males. The procedure is

implemented as somatic gene therapy, i.e. the genes are affected only in the treated cells directly (Anderson 1985), in opposite to germ line therapy, where the specific gene is modified in the genome as a whole (ebid.). Although this procedure might also be used to "cure" color deficiency in human observers, the method has not been adapted for humans to-date, and thus is not permitted for clinical trials on humans yet. Prior to approving clinical trials, there are certain international standards for these kind of clinical trials, like the Declaration of Helsinki (WMA 2013) that lists certain guidelines to ensure ethical conduct for test on humans like the right of informed consent, right to withdraw, privacy etc. On a national level, institutions and branches of government like the US Department of Health and Human Services (HHS) (1997) provide detailed guidelines about what can and cannot be done, and how it should be done, like for example that all trials have to be supervised. Therefore HHS introduces Institutional Review Boards (IRB) for monitoring trials. Furthermore, Anderson (1985) argues that the aspect of delivery, expression, and safety[1] has to be successfully fulfilled in animal studies as requirement before proceeding to clinical trials on humans. One main factor in the ethical debate about gene therapy for - people is whether this type of gene therapy would be defined either as somatic gene therapy to correct a genetic defect or as enhancement genetic engineering. In other words, whether color deficiency is defined as disability or as non-harmful anomaly. In this paper, I present arguments for and against allowing gene therapy for human observers, before I conclude with the proposition that gene therapy for color deficiency should indeed be allowed for humans under certain restrictions.

2. DISCUSSION

The ethical problem of gene therapy for color-deficient people gravitates around the two questions of if gene therapy for color deficiency should be allowed at all, and if yes, if the introduced Mancuso-Neitz therapy should be allowed for clinical trials on humans. The evaluation depends strongly on whether or not the nature of color deficiency is defined as natural variation, i.e. anomaly, or as mild disability. I argue for somatic cell gene therapy on a case-by-case analysis because it might facilitate color-deficient people to fulfill their life goals, and clinical trials have to follow certain international standards.

2.1 Is gene therapy for color deficiency ethical justifiable in general?

I argue that color-deficient people would benefit from gene therapy on a personal level but that most color-deficient people could function perfectly in society without it as well. On the one hand, banning gene therapy for color deficiency would lead to minor personal distress and discomfort for color-deficient people when navigating in social contexts, and it would manifest the exclusion of color-deficient people from certain professions like becoming a pilot, train conductor etc. Although, color-deficient people have indeed slight empirical measurable disadvantages to normal-sighted observers, I do not believe that color deficiency justifies as mild disability. Firstly, it does not lead to immediate danger or harm of the color-deficient person's life. In opposite to other disabilities, where people would suffer a notable decrease in quality of life, and exclusion from central aspects of daily life, color-deficient people manage most important tasks without difficulties since they learned to compensate for their deficiency when growing up. Exclusion occurs only in

[1] In other words, only the targeted cells should be affected, the exogeneous gene does lead to the creation of the additional pigment, and it does not harm the cell or the whole animal.

some peripheral aspects like mentioned professions, and society as a whole can usually compensate very well for a color-deficient person who is excluded from those professions. The benefit for color-deficient level on a personal level, on the other hand, can be huge, ranking from facilitating navigation in traffic to fulfilling lifetime professions. Inclusion and self-realization of all their citizens is an important goal in many Western democracies including Norway, the USA etc. Last but not least, the Mancuso-Neitz method could lead to development of tetracromacy in trichromatic people (Jordan 2010).

In conclusion, the resulting benefit for society as a whole from curing color deficiency is not very high, and, in my opinion, would not justify heavily public funding of development of such a therapy. Moreover, I want to underline that most problems for color-deficient people occur in a society that only focus on the needs of normal-sighted, i.e. trichromatic, people. Most problems can easily be solved by implementing guidelines known from universal design and usability, i.e. making all media that use color as communication more accessible for the color-deficient and other "visually disadvantaged" interest groups, like for example the elderly, as well. For this purpose, image processing provides the possibility of daltonization, i.e. the automatic image enhancement for the color-deficient, and other image enhancement methods. Also, I argue that it is unjustified to realize the treatment as a germ line therapy, meaning to change the genetic code in the genome such as to extinguish color deficiency altogether, since the effects of changing the gene pool are firstly hard to comprehend and do not justify the means, similar to the arguments about germ line therapy by Anderson (1985) in general. However, I do believe that gene therapy for color deficiency should be allowed as somatic gene therapy, if funded privately, since the presented therapy could help many color-deficient people to increase their personal quality of life, enable democratic inclusion and help them to fulfill lifetime professions.

2.2 Is the Mancuso-Neitz color deficiency gene therapy ready for clinical trials?

General ethical aspects circulate around the question of risks and harms for the health of people and animals involved in the process of developing the final treatment, and patients of the final treatment. In order to allow the presented Mancuso-Neitz method for clinical trials, we have to guarantee the integrity of health, human rights and the dignity of people and animals involved. Harms and unnecessary danger have to be averted. The current method to-date has only been tested on squirrel monkeys, on which it does not seem to have any negative effects, but the authors have not sufficiently listed long-term consequences of the treatment for the animals. If the presented results from Mancuso *et al.* (2009) are true, the results suggest sufficient integrity according to Anderson's (1985) three requirements from animal studies. Namely, only cones have been affected, the modulated genes did create the additional and intended pigment, and no other cells were harmed. However, further studies have to be conducted on animals as well to document and investigate long-term effects. If these studies, too, test satisfactorily, the method could be allowed for human clinical trials given they comply with international standards defined by for example the HHS (1997) or the Declaration of Helsinki (WMA 2013). I argue that a new chapter for clinical trials on humans could be opened given that the long-term effect of the treatment have been studied on animals, an exact overview over benefits and risks of the treatment has been documented, and as long as the trials follow international standards like the right to informed consent, and the trials are planned and monitored according to national and international standards guaranteeing the reduction of risks for the patients. Moreover, as discussed before, I believe that the financial costs of the development should not be handled by the general public but by private actors.

3. CONCLUSIONS

In conclusion, I argue for the case of gene therapy for color-deficient on an individual level if international standards are fulfilled for the treatment, the risk is reduced to a minimum for the patient, and private actors handle the costs. Public funding should better be spent on other solutions that may help both color-deficient people and other groups with color vision that differ from the majority like for example the elderly. More precisely, the focus should be put on usability and daltonization. Concerning the Mancuso-Neitz gene therapy, I argue that clinical trials should be allowed if patients of this clinical trials are treated according to guidelines of international standards like informed consent, information about the risks etc., and the research is financed by private actors or the patient him/herself.

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