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Ethical Issues in Enhancement Research

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Abstract

This paper is a preliminary exploration concerning how the ethics of research on human subjects may differ when we move from the well-discussed context of research on therapies to the less-discussed context of research on enhancements. A number of differences are described. There are some features that make such research more morally problematic in certain ways, but some of the features may actually ameliorate some of the moral tensions that exist in human subjects research. It is hoped that this analysis will aid and encourage discussion of the topic that could help guide those who intend to carry out such this research.

Introduction

In the not-too-distant future, we will surely find ourselves with a variety of enhancement technologies available, ones provided through genetic alteration, pharmacology and implants of various kinds. Much has been written concerning whether or not this is to be welcomed, and about the potential social problems and ethical issues raised by making these things available. But less noted has been the need to have reliable evidence of the safety and efficacy of these interventions, which will have to be obtained through testing on human subjects.

The ethics of human experimentation concerning the safety and efficacy of *therapeutic* interventions have been discussed extensively. In the United States, for example, we have federal legislation and regulations on human subjects research and a system of institutional review boards to safeguard the rights and welfare of human subjects of medical research, and the extensive discussion has created a certain degree of consensus. But enhancement technologies differ somewhat, in their nature and purpose, from clinical therapies. Thus it is worth considering, as we begin to carry out such research, how and to what extent significant aspects of the ethical issues concerning their investigation may be importantly different.

In this short paper, I can only sketch some general aspects of this topic. I will describe a few central aspects of the ethical issues concerning research on therapies, and a few core features of enhancement interventions, and then examine briefly some of the implications of this for the ethics of enhancement

research involving human subjects. I hope thereby to encourage discussion of the topic that could help guide those who intend to carry out such this research.

Necessarily, this analysis proceeds at a rather general level. The broad features discussed do not apply fully to all cases of enhancement technologies. And I will leave out important but narrowly applicable issues, such as the problems of consent of those from future generations that arise in the case of germ-line genetic enhancements. The idea is to examine more general issues about the ethics of human subjects research on enhancement technologies *per se.*

Ethics of human subjects research (for therapy)

The central ethical issues concerning human subjects research *on therapies* are generated as follows. We want to gain maximally useful and reliable scientific results concerning the safety and efficacy of therapeutic interventions for the benefit of future patients. But at the same time, of course, we want to promote and protect the interests and rights of the present subjects of research.

To clarify the ethical tension, it is useful to note two aspects of a research trial being "experimental." It's experimental in the sense that the new intervention is new and untested, so there is (on average) greater uncertainty. But, secondly – and more significantly for our purposes – it's experimental in the sense of being designed to generate new knowledge, so the protocol requires that one's "treatment" deviates from what would be given were the sole goal the maximization of subject welfare. For instance, "treatment" (including placebo) is determined by random selection, not by clinical judgment. "Double-blinding," set dosages, and restrictions on concurrent medications limit the physician's ability to use specific knowledge in one's interest. Extra test procedures are undergone. Finally, this continues to the point of statistical significance.

Research on enhancements, analogously, will not just involve uncertainty about safety and efficacy, but, more specifically, will require protocols with double-blind, placebo-controlled experiments carried out to the point of statistical significance.

Thus, for enhancement research as well as research on therapies, there is, on average, a kind of "cost" (even if this is really "suboptimal treatment") to being in a trial (Gifford 1986). In part due to this cost, and to a consequent potential for exploitation, several broad criteria have been identified to evaluate the ethical acceptability of a trial and thereby safeguard against such exploitation. Amongst these are social value, favorable risk-benefit ratio, informed consent, and justice in subject selection.[1]

Consider first the "social value" of a trial. Human subjects should not be exposed to potential harm unless there is a good expectation of clinical, scientific or social benefit. Otherwise there is a risk of exploitation, not to mention of the unwise or unfair use of scarce resources.

This social value is also one element of the second requirement – that there be a "favorable risk-benefit ratio." Risks should be minimized, potential benefits should be enhanced, and risks to subjects should be proportionate to benefits to subject and society.

Third, each research subject must give voluntary, informed consent. Barriers to such consent must be identified and addressed.

Fourth, even if each of informed consent, social value, and a favorable risk/benefit ratio obtain, there are also issues concerning justice in subject selection. Those who bear the burdens of research should be able to have the benefits. Researchers shouldn't target the vulnerable for risky research or favor the advantaged for beneficial research.

Having identified these as the central ethical criteria, our question here is: How might these issues change as we move to the context of testing the safety and efficacy of enhancement regimens?

Scope of "Enhancement technologies"

Of course, we must say something about what this class of enhancement technologies is that we are concerned to evaluate here. On the face of it, enhancements alter the features of individuals in a way that doesn't (just) restore health, but that goes beyond the standard of health; on one view of the definition of health, that means doing more than just curing and responding to disease. Put otherwise, enhancements raise individuals above the species-typical norm (as opposed to only bringing them up to that norm).

As a result, enhancement is sometimes said to go beyond what medicine can (objectively) justify. It's less objectively important; indeed it is optional, in a way that addressing illness is not. Relatedly, value judgments are required to determine what direction counts as enhancement. Nor, unlike the case of therapy, is there an objective answer concerning what natural stopping point there might be to the enhancement. In addition, it's said that it goes beyond human nature.

The attempt to make such generalizations raises various important issues: First, the kinds of things that fall under the category "enhancement technologies" are quite varied: genetic enhancement of physical and mental abilities; increasing the human life span; inserting chips into one's brain; drugs to enhance physical and mental performance or one's personality characteristics. These might not all fit the above characterizations. Relatedly, there is controversy over whether a line can meaningfully and usefully be drawn between therapy and enhancement.

These are important issues, but I will not pursue this further here. I don't take my project here to be to draw sharp lines, or to capture the essence of enhancement technologies. More specifically, I do not claim that the analysis provided here applies across the board to all instances of enhancement research, or certainly that the issues would be serious in every case; there is much variation and also many countervailing factors. Still, the intent here is to identify issues that are not just incidental, but that arise often and because of enhancement in the above senses. Thus these are things that those embarking on such research need specifically to keep in mind as research trials are planned and executed.

So what are some of the features of research on enhancements which may potentially alter the ethics of research? I will outline a number of them, using the taxonomy described above: social value, risk-benefit ratio, informed consent, and subject selection.

(1) Social Value

Let us first consider social value. What features are there that affect the extent to which enhancement research is objectively important and socially valuable?

One position would be to claim that these enhancements, by being outside of the natural or the bounds of human nature, are in fact inherently a bad idea. But such appeals are notoriously vague and there is reason to be skeptical about them. I will leave this aside here.

Instead, I propose to focus on the fact that enhancements, by not being about bringing one up to the level of health, but going beyond that, will typically be optional. This may suggest their being not as objectively important to the individual as life or health. But there is another implication of their being optional and not a matter of addressing ill-health: it also means that insurance is less likely to cover them, and this has several implications. The knowledge resulting from such investigation doesn't do as much

good, for it doesn't help as many people. It also can give unfair advantage to those already advantaged, thus exacerbating the gap between haves and have-nots. Leaving aside the insurance coverage question and returning to the lack of grounding in a standard of health, other points are often made: given the competitive advantage and no obvious stopping point, going down this road could give rise to a spiraling arms-race, as people strive to get ahead with respect to increasingly demanding norms.

Some have appealed to such considerations to argue that we simply should not pursue these things; their conclusion concerning research would simply be that we should not do it. What I want to focus on here is the more modest claim that this affects the assessment of the social value of the research, one of the components in evaluating particular trials. This then impacts, for instance, the degree of risk that could acceptably be imposed.

Of course, while much more modest than the claim that these factors argue against allowing the provision of these enhancements, this is still a controversial line of thought, and a number of potential objections come to mind.

One might object that if an enhancement is genuinely not so important, then it is not such an injustice that those with less resources will not have access to it. Note that one important response to this is that, actually, these are just the things (many of them) that can provide great social and economic advantages to individuals, even if they don't technically count as "medical" needs that are thus deemed to warrant insurance coverage.

It might also be objected that these problems are not unique to enhancement. After all, if a given therapeutic regimen has substantial cost but is covered by most insurance plans, then a crucial inequality occurs between those with and without (adequate) insurance. One might be tempted to respond that the fault here lies with the lack of universal access to health care, and not with medical research into therapies. But of course, then one might make a similar appeal in the case of enhancements: that research on enhancements shouldn't be hindered because the insurance system fails to cover these truly important enhancement interventions.

In any case, if one really ensures that these enhancements are available for all and not just the rich, then this indeed would address the problem here. (One question that arises is whether it is enough to charge that the blame lies elsewhere in this manner, or whether one must in fact pledge to change the insurance system as a condition of being able to do the research.)

A different line of thought would be to argue directly that in the long run these enhancements will indeed actually be deeply socially important for the future of humanity, due to the great, almost unlimited potential benefit that these things could bring. (All this raises some questions about how and to what extent such an assessment ought to take into account inequality, and to what extent need we focus our attention on the near future and to what extent on the distant future.)

I cannot begin to resolve all the questions, empirical and normative, that can be seen to arise. What's true is that such features concerning inequality won't apply equally across the board of enhancements. And many cases will be complex: drugs for enhanced attention might, due to expense and thus differential availability, exacerbate inequality, but also serve as an important public good in their use by physicians, pilots and air-traffic controllers.

Still, as a trend, I think that this feature, of diminished social value due to lack of access and inequality, is to be taken seriously as a central issue for those embarking on enhancement research. We should explore its consequences further for the ethics of human subject research in this area, and researchers have a responsibility to look out for and assess such factors.

(2) Costs and Benefits of Being a Subject

The second locus of assessment involves consideration of the costs and benefits for the individual subject in such a trial, and the comparison of this with the social value of the research.

The benefits being optional is again relevant. One implication of this is that these benefits are not so objectively important for the individual, especially when compared to any countervailing medical risks. Thus this fact will lower the benefit and hence the benefit/risk ratio. But note at the same time that another implication of its being optional (and viewing the optional as less valuable) is that being in the placebo group and forgoing the benefit is not such a high cost. This would tend to diminish the moral difficulties with clinical trials of enhancement interventions.

This illustrates that we cannot provide here some overall judgment about research on enhancement technologies being more (or less) morally problematic; rather, we can only identify factors that have to be attended to because they tend to alter the structure of the risk/benefit assessment.

For a more specific example bearing on enhancements and the risk-benefit ratio, consider research on therapies where it appears that participation is not in the medical best interest of the patient, and we wonder whether the subject is being rational in entering the trial. It is sometimes said that part of why entering a given trial may not be such a bad choice (despite its downsides) is that participants get special medical attention from expert clinicians – or even that they get access to doctors, which they might not have gotten it otherwise. But in the enhancement case, this won't be a factor, so there will be an important difference.

Again, like other differences between the therapy and enhancement contexts, this cuts both ways: On the one hand, there isn't the added benefit that makes being in the trial more valuable to the subjects (thus making the enhancement research case more problematic). But on the other, there isn't the worry of subjects being vulnerable to coercion or manipulation by this sort of "perk" (thus *reducing* the moral worries about the trials).

(3) Informed Consent

The next locus of assessment is the requirement of voluntary informed consent of all participants. Much has been said about the details of what is required, and what dilemmas exist concerning what counts as competent or informed, etc. How might the move from therapy to enhancement affect these matters?

There are many questions one could explore here: Is the information more complicated (or less so)? More (or less) liable to misunderstanding? Is the population different with respect to their ability to understand, or with respect to their motives or vulnerabilities? To explore this systematically, it would be important to consider (and obtain empirical information concerning) who the subjects of such experiments will in fact be and what characteristics they will have. This is a large task and must be left for another occasion.

But I do want to focus our attention on one especially important topic. One of the most serious difficulties concerning the ethics of clinical research, and which ties specifically to the adequacy of consent, concerns the "*therapeutic misconception*" – the mistaken belief that the research protocol is designed to advance the patient's interests. Research shows that subjects tend not to understand, or take seriously, how research is different from therapy (Appelbaum, et al. 1987). They don't understand concepts like placebo, randomization, or double-blinding. Despite being told otherwise, they very often believe their treatments are chosen specifically on the basis of what is medically best for them. It is clear that we must

work much harder to make informed consent effective, and also that informed consent cannot stand on its own as a sufficient justification of trials.

Now surely, it will be said, research on enhancement technologies will raise considerably less moral difficulties in this crucial respect. Those entering enhancement trials will surely know that the goal is enhancement, not therapy. So, potentially, here is a way in which enhancement trials could be substantially less morally worrisome than trials of therapies.

I think there is something to this, but I also think that simply to accept it at face value would constitute an understandable but profound mistake. The contrast between therapy and enhancement is a different contrast from that between research and therapy; indeed, the latter should really be termed "research vs. *practice*," where practice can be either therapy or enhancement. The "therapeutic misconception" involves confusing therapy in the sense of "we are doing this for you (the patient or subject)" (that is, practice) with research in the sense of "we are doing this for the greater good (or future patients)." This confusion is caused, amongst other things, by the subjects' intense need to believe they are being helped.

But subjects of enhancement research could also be confused (or in denial) about the likelihood that the intervention given to them (in the study) will help them, and whether they are being given that which is thought most likely to help them.

The outcome of experimental enhancement intervention, if "successful," could well be a benefit for the research subject (and these benefits might well be hoped for, longed for or even desperately and perhaps irrationally sought after). People can certainly want desperately to gain what they take to be a bit of social and economic advantage. And yet, because of risks due to increased uncertainty and (more importantly) failure of benefit due to the requirement of study design, the potential subjects can well – in exactly the same way as with clinical research – think that they are expected to receive benefit when they are not (or, overestimate the degree of expected benefit). So the therapeutic misconception problem, as a profound challenge to the adequacy of informed consent, cannot be ruled out in this way.

On the other hand, it does seem that this would not tend to be the rather extreme kind of situation sometimes faced in the "therapeutic" context. It won't come at the end of a long line of attempts at experimental treatments, where a patient has run out of alternatives and may be facing death. The subject is less likely to think specifically that their doctor has chosen this for them (despite explanations of randomization, etc.). For one thing, their personal physician is less likely even to be involved.

Still, the degree to which a strong desire to have these enhancements could come to be a source of irrationality, hindering informed judgment, is an empirical question, one related to the psychology of individuals and the social forces that make such enhancements attractive. The issue is worthy of further investigation.

(4) Fair Selection of Subjects

Fair selection of subjects requires, amongst other things, that those populations who bear the burdens of research should have the potential to share in the benefits. I will consider here just a couple of issues.

The first relates to the point discussed earlier: some populations will be unlikely to benefit from research on interventions not covered by insurance, and this, along with exacerbation of inequality, would negatively affect the "social benefit" component of whether a trial is ethical (and hence the benefit/risk ratio).

But here the point is different – that it lessens the moral legitimacy of enrolling particular subjects in the trials, because some groups that bear trial burdens will not share the benefits. The point is often made in terms of the especially egregious practice of *singling out* such groups – which is not going on here – but it has moral force more generally. Indeed, at least in some circumstances, it seems plausible that those who will volunteer for such trials will often be just those who will not be able to afford getting the "treatment" "on their own", once it is deemed safe and effective and put on the market. Participation in research would be their only shot at getting whatever benefits might come from this.

Again, there is a variety of responses to this. We could exclude such individuals from such trials, but this would be difficult and perhaps not desirable. We might take all this to be a reason not to pursue such trials because they cannot be carried out fairly. Or we might infer instead that this generates a special obligation to ensure that all benefit from the knowledge, by making access not dependent on insurance.

Here is a second, more profound issue. It is partly about whether it is fair to involve certain subjects in a trial. But it crosses categories and involves as well whether subjects will have adequate knowledge for informed consent, or, if they do, will in fact volunteer. The issue involves taking seriously a particular motivation for subject participation (altruism) and the way different goals can be intertwined in research.

A central part of the reason people volunteer to be subjects in human experimentation is altruism. They may want to give back to the medical enterprise which has benefited them in the past; they may have taken on the general goal of finding a cure for a given disease. But surely such prospective volunteers will normally assume that the benefit potentially produced by their participation would be to the therapeutic enterprise, not to the enhancement enterprise, so if in fact it instead went to the enhancement enterprise (indeed, if that was a significant part of the motivation of the research), this would not respect those subjects but instead exploit them. On the one hand, this argues against the moral fairness and thus legitimacy of enrolling such patients. But note that it also has implications for the practical matters of future trust, cooperation and recruitment.

Of course, a subject might potentially be altruistic in this broader way – for instance, having the goal of "giving back" *to society as a whole*, not just *to the therapeutic enterprise*. This fact reminds us that we need to have a better understanding of what the reasons are for agreeing to be part of human research, and whether this might be different in the case of enhancement research. (And this again calls for some empirical research.) But I do take the narrower sort of altruism to be more likely – that a subject would be less likely to go along in the hope of contributing to enhancement capabilities rather than therapeutic capabilities – and so this poses the above problem for enhancement research.

This is an especially thorny issue because research will often serve a dual purpose – partly for knowledge about therapy and partly for knowledge about enhancements – and it will be difficult or perhaps impossible to tease apart the actual benefits, let alone the intended benefits and motivations for the research (and, relatedly, the potential subjects' perceptions of all this). This will be more so in the case of more basic research that will have widely applicable results, but it might be hard ever to separate it out completely. And of course the more enhancement treatments "take off" and become especially prominent and profitable, the more it could come to take up (and be perceived as taking up) a significant portion of the driving force of research.

Again, part of the response could be to ensure that various classes of society do indeed benefit from the technologies generated. But note that the issue here is partly a matter of whether benefits go to the wealthy or to all, but also partly a matter of identification with the therapeutic enterprise or the enhancement enterprise. Hence the problem is not completely resolved even by ensuring that the resultant interventions will be made available to all.

Conclusion

Much of the ethics of *enhancement* research on human subjects will be the same as that concerning *therapy* research on human subjects. But I have identified various relevant differences within each of the categories of social value, risk/benefit ratio, informed consent, and subject selection. The basic claim is that those pursuing and evaluating this research must take note of these differences, and not just proceed on the assumption that we have already addressed these questions with our experience with research on therapies (or, worse, that such issues don't even arise because this is not clinical research).

The assessment here doesn't all go in one direction; it is not that overall there are moral reasons making research on enhancement more morally difficult. Rather, some of the features make such research more morally problematic in certain ways (and hence these things might be used in arguments against pursuing enhancement). But some of the features may actually ameliorate some of the moral tensions that exist in human subjects research.

Relatedly, these are not the kind of considerations that apply across the board. Much depends on the particular features of a given case. For example, I have focused on aspects arising from inequality. But if one can identify enhancements that really will be affordable and helpful to all, then for those cases, these concerns don't apply. Still, something's being an enhancement technology should heighten our awareness of the possibilities of this concern.

Again, we are reminded throughout this discussion that, in order to adequately address the set of ethical issues concerning this research, we really need more empirical information about a number of matters (how the subjects of such experiments might be different, why subjects in fact decide to participate, the likelihood of actually making various enhancements widely available after testing, etc.). So there is also more of this sort of research to be done before we can be confident of our judgments here.

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Notes

1. These four are amongst a group of seven kinds of considerations determining the ethical acceptability of research on medical therapies identified by Emanuel, et. al. (2000), who also include scientific validity, independent review, and respect for enrolled subjects.