Special Section: Technology and the Body: Linking Life and Technology

Neurosurgical Implants: Clinical Protocol Considerations

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As neural implants transition from engineering design and testing into human subjects research, careful consideration must be paid to the ethical elements in developing research protocols. Although these ethical aspects may be framed by the design choices of the engineering, a number of challenging choices arise. In spite of many ethical considerations for neural implant technologies being shared with generic research ethics questions, there are subsets needing special attention. Even in considerations requiring increased attention, substantial overlap can be found with research ethics questions for general medical implants and for psychiatric pharmaceuticals.[1] The special attention to specific ethical questions in neural implants exists because of the value placed on preserving cognition and control as well as our continued memory of significant past research abuses in neurosurgery. This paper focuses on three issues of particular saliency to neural implant testing: inclusion/exclusion of subjects with psychiatric conditions, consent withdrawal of research subjects, and enhancement as a goal.

Past ethical missteps in the development of functional neurosurgery must be taken into account when developing any new protocol in the area of neural implants.[2] The 20th century psychiatric interventions of electroconvulsive therapy and frontal lobotomy continue to negatively influence popular thought concerning interventions on the brain.[3] Of course the history is not limited to these two therapies. Lesser known studies involving brain implants for the study of epilepsy, psychiatric illness, and pleasure, such as the Tulane experiments conducted by R.G. Heath, also provide a rich backdrop.[4] The various missteps and poorly conceived innovative approaches in the history of neurosurgical interventions in human patients provide increased incentive to provide particularly robust development and review of clinical trials for neural implants. The development of new treatments through research relies on the trust and cooperation of subject communities, general society, and industry that provide subjects, authorization, and funding. This trust can only be maintained if we recognize the obligation to study technologies in an organized, scientifically robust, transparent, and collaborative fashion.

The overwhelming majority of brain implants under study aim to provide an improved quality of life rather than an increase in survival. This provides an important element in considering the framework of appropriate risks for human subjects and applies to mortality as well as significant morbidity risks. Quality of life goals imply that outcomes must be measured in functional

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improvements rather than by simple statistical significance or physiological change. These considerations of the goals of neural implants should influence all aspects of protocol development.

Consideration One: Psychiatric Illness Exclusion

The first ethical consideration in neural implant research focuses on appropriate subject selection criteria. There are many interesting ethical issues to consider related to benefits, harms, justice, and so forth, when discussing inclusion and exclusion criteria. Although this general topic of inclusion criteria interfaces with the second and third considerations discussed below, the issue of inclusion of those with psychiatric conditions unrelated to the research question is of particular interest. To exclude all patients with psychiatric illnesses that are unrelated to the research question may sound inviting for researchers, given that it potentially reduces the complexity of patient mix as well as avoids consideration of which psychiatric illnesses could either negatively affect research results or could pose an increased risk to a subject. However, all populations should have the opportunity to both share in the risks and benefits of clinical research unless there exist good scientific or moral reasons to the contrary. Rebecca Dresser nicely uses the example of HIV research in the 1980s to emphasize the importance of inclusion and consultation with interested parties in deciding selection criteria and protocol development.[5] Not only should individuals have the potential to be included in clinical trials where benefit is likely, common stereotypes around psychiatric illnesses must be avoided. In this realm, researchers should be particularly careful to avoid assuming too much about a patient's ability to consent based simply on being labeled as having a "psychiatric illness." An important example countering this stereotype can be found in the study by Appelbaum et al. that demonstrates a retained capacity to consent among those with major depression.[6] Clearly, neural implants will have some affect on the brain, and careful reflection needs to be undertaken to identify which neural implants have the highest risk for exacerbating which psychiatric conditions. The simple message here is that, as a matter of justice, those who have a psychiatric illness label should not be categorically excluded from neural implant research. In recognizing the potential of coercion for some patients with psychiatric illness and the past abuses of neurosurgery, increased protections should be considered, such as multidisciplinary review or subject advocates within the protocol in order to avoid injustices as well as maintain trust with the public and other medical subspecialties.[7] This should be extended to review of protocols.

Consideration Two: Consent Revocation

Neural implants become part of the subject's body and have potential to influence cognition and judgment. Consent can be revoked very easily in general research. A simple request to withdraw from a study is respected. Regulations and guidelines emphasize the need for voluntariness of a research subject's participation. The question of consent revocation can be more complex with neural implants, when the removal of the implant may pose some risk, the implant may be very expensive, and the implant may affect cognition. A

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distinction may be important between "revocation of informed consent" and "informed revocation of consent." In the first case, the emphasis is placed on an ease of revocation after a very arduous process of informed consent. The voluntariness to continue is given priority. In the second case, the emphasis is placed on a more arduous process of informed revocation in order to discontinue the research protocol. This voluntariness of discontinuing then becomes the priority. The informed revocation may be of more importance when a therapy is mature in terms of actually providing a therapeutic benefit and when the patient may have some transient device-related cognitive deficit. The revocation of informed consent may be more appropriate with risks of continued participation and no benefit to the particular subject.

In developing a research protocol, careful account needs to be taken of obligations of the subject to the research and the mechanism for revocation of consent. This involves not only the distinction mentioned above, but also the possibility of a patient refusing explant of a device when explant is part of the research protocol. For instance, is it unduly coercive to require a subject to pay for a device if the research protocol calls for the device to be explanted after a given time and there is refusal? If a physician–researcher believes that leaving the implant embedded in the patient poses a dire health risk, what measures can be taken? Can therapeutic privilege be invoked for explantation to be performed without informed consent? The refusal for explant may affect both the subject and the ability to complete the research project that could help future patients. These considerations should be addressed during the development of the protocol and contained in consent forms even at the risk of implanting the idea of revocation with the subject.

Consideration Three: Enhancement

Current research in animals has demonstrated improved learning with specific invasive brain stimulation.[8] Although helping those with autism is the intended future application of this animal research, it further raises the specter of studying neural implants for augmenting human function. If studies leading to the expected use of neural implants as enhancement technologies are developed, then researchers are faced with numerous difficult protocol considerations. For instance, I have argued elsewhere that significant risk of research should not accrue to sick patient-subjects for any component intended to later primarily benefit well persons wishing enhancement.[9] Further, the costs of purely enhancing technologies should not burden an already overburdened government funding system. Although a robust discussion continues surrounding the distinction between enhancement and treatment, these distinctions are helpful at the extreme poles. In the fuzzy middle ground, we need to make our best faith effort to properly prioritizing values and resources as well as avoiding unjustly burdening those already ill for the benefits of later unrelated populations. The choice of risk to healthy subjects for studying enhancement needs to be balanced against the objective of minimizing harm.

Conclusion

Testing neural implants in human subjects requires considerable prospective planning that includes justice issues of inclusion/exclusion criteria, revocation

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of consent, and proper study of enhancement. These considerations are deeply influenced by the initial design and engineering of the device and the ways in which the media influence research, as well as later clinical considerations. It is important to be clear of the underlying values lost and gained by any choice in developing a protocol. These considerations should be reflectively built into the protocol long before a review by an ethics board.

Notes

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