



Online Ethics Center
FOR ENGINEERING AND SCIENCE

Gene Therapy For Alzheimer's Disease

Author(s)

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2000

Description

A scenario about research with patients who have dementia meant to stimulate discussion about the ethical issues that arise in this type of research.

Body

Basal forebrain cholinergic neurons deteriorate severely in AD. Nerve growth factor (NGF) prevents deterioration of these neurons in mice, rats, and large primates. When administered to aged rats with lesions in the basal forebrain, NGF actually reverses memory deficits. By gene therapy, aged primates show a reversal of deterioration of cholinergic neurons. The effects of NFG have been widely replicated but never applied to humans before gene therapy became available in the research context.

In this study, a Phase I safety trial of ex vivo NFG gene therapy is proposed. The AD patient's fibroblasts will be genetically modified (using virus vectors) to produce NFG in vitro and then grafted into the brain. Based on pre-clinical primate studies, five injections of cells will be performed on each side of the brain. Greater numbers of injection grafts might compromise safety, while fewer will likely prove inadequate.

Over the course of the year, post-operative patients/subjects will be monitored

monthly for safety and for cognitive function using various cognitive scales as well as scales measuring activities of daily living. Because this protocol involves surgery and some risk, these patients/subjects will be in the early stages of AD so as to still be competent to provide informed consent. Additionally, early-stage patients/subjects have the most to gain by prevention of neuronal deterioration and improved function of remaining neurons. Each patient/subject will be accompanied to all clinic visits by an informant (usually the primary family caregiver), who will also make daily observations for adverse events. A condition of entering this study is that current anti-dementia drugs like donepezil, which in some AD patients can mitigate certain symptoms like word finding difficulties and inattentiveness to tasks for a period of six months to a year, cannot be prescribed during the first year of the study.

- If donepezil is considered standard therapy, how would you design a control study?
- Would you allow surrogate consent for participation in this study? Why or why not?
- Would you accept an advance directive for research as providing informed consent for patients in more advanced stages of AD to enter this study? Why or why not?
- How do you present the study to potential subjects and how neutral do you attempt to be in this presentation?
- A recent fatality in gene therapy involving an adolescent has been reported. Would this impact your presentation of the study?

Notes

Caroline Whitbeck introduced methods and modules for discussing numerous issues in responsible conduct of research at a Sigma Xi Forum in 2000. Partial funding for the development of this material came from an NIH grant.

You can find the entire sequence on the OEC at [Scenarios for Ethics Modules in the Responsible Conduct of Research](#). Some information in these historical modules may be out-of-date; for instance, there may be a new edition of the professional society's code that is referred to in an item. If you have suggestions for updates, please contact the OEC.

Contributor(s)

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