

Alzheimer's and the Ethical Issues of Genetic Testing

When I was given the assignment to write a paper about Genomics, my mind was flooded with ideas. I am generally more interested in the ethical controversies that arise concerning Genomics, but I also wanted to research something that relates to my family- specifically the fact that my grandma has Alzheimer's disease. First I decided to research the genetics of Alzheimer's to better understand to what extent it is an inherited disease. But as I proceeded with my research, I stumbled upon many interesting articles about the ethical issues concerning possible and future genetic testing for Alzheimer's. So my paper has now developed into a commentary on the general issue of genetic testing presented through the specific context of Alzheimer's disease.

Alzheimer's disease is characterized by a gradual, irreversible deterioration in mental abilities such as memory and reasoning. It can be divided into two main forms- early onset and late onset (early-onset generally occurs before the age of 40). Late-onset Alzheimer's is by far the more common form, but early onset is currently more related to genetic testing. Three genes have been associated with early-onset. About 15 families in the world have a genetic fault on chromosome 21 in the amyloid precursor protein that affects the production of the protein amyloid (associated with Alzheimer's when it builds up in the brain). Several more families have a fault on chromosome 14 in presenilin-1. A smaller group of families have a fault on chromosome 1, called presenilin-2. On average, half the children of a person with one of these genetic defaults inherits the disease.

A genetic link has also been discovered in the late-onset form, but it is not confined to a few families. The link is with a protein found in the blood and the brain

called ApoE. There are three forms- ApoE2m ApoE3 and ApoE4- and each person has two copies of the gene. About one fourth of the population inherits the ApoE4 gene, and this increases the risk of developing the disease by up to four times. Two percent of the population inherits an ApoE4 gene from each parent, and their risk is increased by ten times. Sixty percent of the population inherits two ApoE3 genes, and about half of these develop Alzheimer's by their late eighties. Only one in six people carry the ApoE2 gene and it is the least associated with Alzheimer's. People with one ApoE2 gene and one ApoE3 gene have to live into their late nineties before the risk reaches fifty percent. One in 200 people inherit two copies of the ApoE2 gene and are at lower risk.

The main difference between the genetic links associated with early and late onset forms is that the ApoE risk increases the chances of disease, but does not make it certain, whereas the rare familial form of Alzheimer's is certainly caused by genetic faults. In fact, some researchers think that Apoe4 does not even affect whether a person gets the disease, but more when they might get it. Other genes will probably be found that contribute to Alzheimer's, but the degree of risk involved is likely to be small. Therefore familial Alzheimer's is much more relevant to the controversy of genetic testing.

This brings me to the introduction of the pros and cons of genetic testing. Although I am first going to specifically discuss these in relation to Alzheimer's, it is important to note that this discussion relates to all genetic testing. The issue at hand is whether genetic testing should be available, and to what extent.

For members of families who carry the genes for familial early-onset Alzheimer's, a genetic test could indicate whether an individual carries the gene mutation and will eventually develop the disease. The mutations in genes associated with this

form of Alzheimer's are considered "highly penetrant", which means they correlate strongly with the occurrence of the disease. A commercial test is currently available for the gene presenlin-1.

On the other hand, tests for the ApoE gene would be of no use to an individual because it has no reliable value for predicting Alzheimer's, and it is medically useless with regard to treatment. Presently, genetic tests to determine susceptibility to late-onset would only be of value in a research setting that is investigating the role of genes in the onset and progression of the disease. Therefore, I have established that genetic testing is only relevant if it can reliably predict the onset of disease. I do not see why anyone would want to be tested for the ApoE gene if it really does not reveal any conclusive or certain results about the possibility of developing Alzheimer's. But the fact that I do not believe genetic testing is relevant unless it is definite does not mean I believe it is wrong if it is not conclusive. I believe the technology of testing should be available to any individual or group who wish to use it for either personal or professional reasons.

For example, right now there is no known cure or treatment for Alzheimer's. So is it worth it for a person to find out if they have a genetic mutation that will definitely cause the disease? Some people might argue that this knowledge will only cause unnecessary grief, but I believe that each individual has the right to know his/her medical future, regardless of the outcome. This goes back to the idea of the individual's right. "Worth" is a word that can be interpreted very differently by different people. Therefore the question "is it worth it?" can only be answered at an individual level.

With this introduction to the ethics of genetic testing, I want to introduce some formal pros and cons specifically related to Alzheimer's. I'll start with a pro: a genetic

test for Alzheimer's could identify people who might benefit from new drugs to delay symptoms in the early stages of Alzheimer's. This is probably the most important and beneficial aspect of genetic testing. As new drugs and technologies are developed to prevent or even delay Alzheimer's, people who are aware of their risk will be better able to capitalize on the existence of these methods. This "pro" is especially strong for diseases that already have known cures. Obviously if a person can utilize genetic testing to find out if they will develop a treatable disease, the benefits of this testing are very great.

On the other hand, for diseases with no known treatments, a "con" can be raised against genetic testing. This "con" would be that "a genetic defect cannot be repaired, and effective treatment is not yet available, so a test could raise anxiety without offering a clear course of action". This is true, but here again I revert back to the decision of the individual. If a person wants to find something out about themselves, I believe they have a right to do this, even if grief and anxiety result.

Unfortunately, the Stanford ethics panel on genetic testing for Alzheimer's disease disagrees with me. They concluded that in most cases, the tests do not provide enough information to be useful except in research. But I would have to argue that although the tests might not be useful, it is not unethical for them to be available.

The panel does bring up several very important cons against testing: first, the greater social impact resulting from individuals knowing their genetic susceptibility to incurable diseases. This relates back to the idea of grief and anxiety resulting from the test outcome. Although I think the individual has the right to choose to risk feeling the resulting emotions that come with testing, I do understand the idea of a greater social

harm, and I feel this is the most valid argument against genetic testing. I do understand that people could become depressed or even dangerous if they find out they have an incurable disease. But the idea of genetic counseling, which I will introduce later, could help alleviate this potential societal harm.

Another issue broached by the panel is the potential for discrimination, primarily in access to long-term care, but also in other areas such as employment. This is a very valid concern, but I believe it could be avoided if proper guidelines for testing are developed. For example, the Alzheimer's association has six principles intended to prevent genetic discrimination. These apply to current tests for early-onset genes, and to reliable tests that may eventually be developed to predict late-onset Alzheimer's. The second principle states that "the presence of a gene is not a basis for underwriting insurance premiums for health-care, long-term care, or life insurance". Principle three continues with "genes should not be used to deny access to housing, employment, health care, or any other goods and services". Number four states "genes should not qualify an individual for disability-related benefits".

All these principles are extremely vital to protecting the individual's rights, and in assuring that genetic testing is used solely for determining disease in a confidential manner intended only for treatment purposes. Principle five adds that "anonymous testing should be available, making the fact of and results of genetic testing for Alzheimer's disease invisible on an individual's record". With all these principles in place, it seems that genetic testing can be conducted in a safe and confidential way.

Principle number six brings up a very important concern also raised by the Stanford ethics panel: the availability of skilled genetic counselors. There are few trained

genetic counselors in the U.S. and demand for them is likely to increase as scientists learn more about the genetics of disease. Number six states, “genetic testing for Alzheimer’s should be done with pre and post test counseling, which includes a full discussion of the implication of the test and provides the individual with all the information necessary to make an informed decision. All genetic information and counseling should be provided in culturally and linguistically appropriate formats and should take into account an individual’s literacy level”. This principle embodies the idea that genetic testing should only be conducted in an educated and well-informed setting, so that the individuals who choose to take the tests will be aware of their situation and all their options.

The Stanford panel eventually concluded that genetic testing for Alzheimer’s disease is currently not appropriate for most people. My conclusion is that although the tests may not necessarily be relevant for all people, they are still appropriate for anyone who wants to discover something about their personal genetics. Therefore I do not believe the genetic tests should be limited, but I do believe that they should be conducted under strictly enforced guidelines such as the ones drafted by the Alzheimer’s association. This way, genetic testing can continue freely, not only on an individual level to assess risk, but also at a professional level to develop a more comprehensive idea of what causes certain diseases, and what cures can be developed to treat them.

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