

ETHICAL CONSIDERATIONS REGARDING GENETIC DISCRIMINATION IN THE CASE OF HUNTINGTON'S DISEASE

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Abstract

Huntington's is a genetic neurodegenerative disease with dominant autosomal transmission, and high penetrance. This transmission model represents a high recurrence risk (50%) in case of the descendants of affected individuals. This disease can have its debut during adulthood, 40-50 years old or, in case of its juvenile form, during childhood or adolescence. The disease evolves with dystonia, choric movements, rigidity and dementia. Genetic testing for HD mutation is performed through molecular techniques and is possible at any age, independent of whether the person is symptomatic or asymptomatic. The genetic testing allows the identification of those individuals who are carriers of mutations on certain genes, these mutations being the underlying cause for some genetic diseases. At the present moment there are 3 types of genetic testing: diagnostic, carrier and predictive. The predictive tests identify whether an individual is a carrier for a certain specific genetic mutation and whether the possibility exists for him to develop certain health issues later on. Being aware of the carrier status for a certain genetic mutation for Huntington's represents an element with major impact on the individual and on their family and can lead to discrimination from the side of the insurance companies, employers as well as others.

Keywords: Huntington's disease [HD], genetic discrimination, predictive tests, medical ethics

Introduction

Huntington's disease is a rare genetic malady, neurodegenerative, which presents with a prevalence of 5-10 cases at 100.000 people among the

Caucasian population (Bates, 2002). This disease usually has its debut at middle age, after 35-40 years, and has a slow progression. In general, after 5 to 10 years from its onset most of the patients are significantly affected and only a small part of the diagnosed individuals are capable of working a stable job after this period of time.

In terms of genetics, Huntington's disease is inherited in an autosomal dominant manner, meaning that individuals that have one affected parent have 50% chances of inheriting the mutant gene and developing the disease at one point in their lives. The risk depends on the age of the individual and the length of the CAG sequence taken into consideration. Therefore, a 25 year old person with an affected parent will have 7.5% risk of developing HD during the next 10 years and 21% risk during the next 20 years (Harper, 1992). Changes in the sequence that determine the pathological phenotype are found on exon 1 of the gene where the triple nucleotide CAG can be found. The gene to which the mutations responsible for Huntington's belong is localized on chromosome 4p16.3. While the gene is transmitted from generation to generation the length of the trinucleotide increases. If the onset of Huntington's disease manifests during adulthood, the individual would present on the HTT gene around 40-50 repetitive CAG trinucleotides, while persons who have the disease since childhood or adolescence have over 60 CAG nucleotides. Normally the CAG segment is only repeated 10 to 35 times. In the case of HD patients the CAG segment appears for 36-120 times. In case of individuals who present only 36 to 39 repetitive CAG they could or could not manifest signs and symptoms for Huntington's, in comparison to those with over 40 repetitive units in the sequence who will develop the disease.

In case of Huntington's the ways to determine the genetic mutation have been known since 1993, leading to a predictive genetic test with a 100% sensitivity and specificity (Meiser, 2000). A specific feature for Huntington's is the "genetic anticipation" phenomenon, meaning that symptoms which should appear at younger ages, during childhood or adolescence, have a greater severity when transmitted throughout generations. It was proven that genetic anticipation is caused by the instability of the repetitive trinucleotide sequence CAG throughout generations. Together with the transgenerational transmission of the sequence, the number of trinucleotide sequences increases, leading to the juvenile onset which presents with a worsened evolution than the one with adult onset.

It was proven that there is an inverse relation between age of onset for HD and the length of the CAG sequence (The Huntington's Disease Collaborative Research Group, 1993).

Although the CAG sequence presents both with instability and variability, these are not independent from maternal or paternal inheritance. Studies have shown that these expansions are more frequent in case of paternal inheritance (Duyao,1993).The fact that longer CAG sequences tend to appear in case of the inheritance on a paternal line, and adding the fact that the age of onset is in an inverse relation with the length of the CAG sequence, offers an explanation of the fact that 75% of the patients with juvenile Huntington's disease inherit the gene from their fathers (Ranen , 1995).

In 2011, in the Human Genetics Commission Report on the concept of Genetic Discrimination, it was stated that: together with the new genetic sequencing techniques of the human genome and with the reduced costs for genetic testing, the possibility will exist that genetics will be used for new purposes that will not be easy to predict (Modell, 2002).

There are 3 types of genetic testing: diagnostic, carrier and predictive.

a) Diagnostic genetic testing: identify the current status of the individuals. The most well-known test are the prenatal screening tests and screening tests applied on newborns.

b) Genetic testing for carriers: used in order to identify individuals with genetic conditions.

c) Predictive genetic testing: give information on the fact that a person presents with a certain genetic mutation which in time leads to the development of a certain condition. The test is used in the case of healthy individuals who have a medical history for a certain conditions but do not present with symptoms.

The most frequent diseases that get tested using predictive tests are: Huntington's disease, breast cancer, Down syndrome, cystic fibrosis and phenylketonuria (Human Genetics Commission-Report on The Concept of Genetic Discrimination, 2011).

Candidates for predictive testing are asymptomatic persons, who want to find out if they are susceptible to developing a genetic condition in the future. The information has personal value but, in addition to that it affects the family members. The potential for genetic discrimination – especially in the case of medical insurance, life insurance and employment – represents a major concern for patients in predictive testing programs.

Genetic discrimination is defined as difference in attitude towards the individual in regard to rights, privileges and opportunities, based only on genetic information, including a medical history (Billings, 1992).Introducing predictive genetic testing has certain consequences such as social, political, economic and psychological. In regard to this aspect the following should be taken into account: a) Firstly, genetic information is family related, and the test results for one individual have direct health implications for other

genetically related persons; b) Secondly, the risks of genetic testing cannot be obvious as they are psychological, social and financial risks. The psychosocial risks include feelings like guilt, anxiety, self-respect, social stigma, and discrimination in regard to insurance and employment. c) Thirdly, genetic information often has a limited predictive power.

An example for genetic discrimination in case of patients with risk for developing Huntington's disease is that of a young teacher in Germany, who was refused the employment in a school because some of her family members had HD, therefore she presented with a 50% risk of developing the condition later on in life. The examining physician reported her employable but she also presented with a higher risk for absenteeism in the future (Burgermeister, 2003).

Another example is that of a social worker in the United States of America, who was working for an agency caring for chronic patients. During a workshop on the topic of care in case of disabled patients, she told a story of the first person she ever cared for – her mother that died because of Huntington's. The fact that her mother had Huntington's suggested that she presented with a 50% risk for developing this condition, for which reason after one week from making this statement the company that used to hire her a social worker, terminated her employment contract (<http://www.geneticalliance.org/advocacy/policyissues/geneticdiscrimination>)

The recent case of the teacher in Germany who was refused a job because she presented with a high risk for HD (Burgermeister, 2003) and that of the social worker who got her employment contract terminated, rise the concern in regard to discrimination by employers based on genetic testing. This attitude introduces additional ethical considerations.

It is right to deny access to a work place based on predictive genetic information from a genetic test or from other source or based on a family history of a certain disorder? That question (and a similar one regarding private health insurances) have been on the public agenda for 20 years and have been debated upon at large on both international and European level, in the USA and in other parts of the world.

There are three main reasons for which using genetic information in the employment framework is so controversial. Firstly, in the nowadays society, to be employed is a crucial fact when it comes to income, social rank and social safety; selection of personnel based on genetic criteria can easily lead to social exclusion for large groups of people because of dubious reasons – “a genetic subclass”. Secondly, collecting genetic information deals with the right for a private life, especially when workers are requested a genetic testing. Thirdly, being aware of the fact that knowledge regarding future health risks can have a negative impact on a person's work place or

insurance opportunities, discouraging people from taking these genetic tests, deterring from the health benefits they, their relatives, and children could have from these test (Feldman ,2011).

The European Council established a Convention for Human Rights and Biomedicine (1996), in order to cope with genetic discrimination (Lemmens, 2000) which provides that genetic testing can only be carried out for medical purposes or for scientific research related to medical purposes, and not for selective purposes for activity and insurance. The most recent moratorium regarding genetic testing in Great Britain (Secretary of State for Health, 2003) protects against insurance related discrimination for those with risk for HD.

In May 2008, the US Congress voted an act known as the Genetic Information Non-Discrimination Act (GINA) that enacts and gives protection for persons in regard to genetic discrimination, through the regulation of genetic information usage upon employment, in the work place or in the health insurance sector (Office for Human Research Protections (OHRP) 2009).

There are people in Canada with a family history of HD who were refused life insurance coverage and were informed that they could be subject to predictive genetic testing in order to qualify for insurance (Lemmens,2000). Such a constraint threatens basic autonomy, including intimacy and confidentiality rights. In this manner, people are bound to obtain information that they maybe would not want to know, and the potential adverse reactions that could appear (depression, psychiatric admission, suicide attempts)(Almqvist, 2003)are significant. In the case of persons with Huntington's, suicide is more frequently present in the general population and is the third most common cause of death(Ranen ,1995).

In Australia, from 2002 until 2005 was carried out the Australian Project for Genetic Discrimination, with the purpose of gathering information regarding genetic discrimination in the case of individuals with risk for HD or that could develop the disease (Otlowski, 2002; Taylor ,2007).

The results of this study presented with similar discrimination cases in case of healthy individuals, which appeared because of health services, employers and insurance companies. Furthermore, within this study the person with Huntington's reported discrimination actions or social stigmatization from the aforementioned institutions (Taylor, 2008).

Studies were carried out that presented many genetic discrimination cases when it came to people with HD. A couple was refused application for adoption because they presented with a high risk for Huntington's (Billings, 1992).

In a study carried out by Bombard et al in Canada, on 233 asymptomatic persons, genetically tested for high risk for Huntington's, a

40% of the people reported a risen concern regarding genetic discrimination (Bombard , 2009).

In North America, in a study carried out on 1001 individuals with risk for Huntington's, these people reported that their biggest concern was losing their health insurance, and from this reason alone 41.6% pay for the test or other medical services themselves, trying to hide from the employer or insurer their risk for HD (Oster, 2008).

The sole ability of looking at someone's future through predictive genetic testing brings with it the potential of personal and family overthrowing. The majority of the people choose not to obtain this information; at world level the absorption for genetic testing is low, from 5% to 24% in case of persons with risk (Creighton, 2003). It is a personal and complicated decision. With this aim, numerous protocols were developed in order to explore the pro and con arguments for the candidates for genetic testing. Most of the people experiment a significant increase in psychological stress levels, no matter whether they are proven to have a high or low risk for developing HD (Almqvist,2003).

Numerous protocols and international guidelines were published, conceived by members of scientific groups such as: International Huntington Association (IHA) and Working Group on Huntington disease of the World Federation of Neurology (WFN), which assure that people with a high risk for Huntington's understand and accept the implications of this diagnosis.

Conclusion:

Lack of policy decisions and educational campaigns meant to inform the population regarding Huntington's disease, led to discriminative practices from the employers and insurance companies to individuals diagnosed with this disease or being at risk for developing it.

Furthermore, there is an urgent need for prioritization of efforts for legislative improvement of the medical services addressed to individuals with Huntington, such as:

1. Ensuring patients' access to quality health care, including diagnosis through genetic tests and appropriate treatments;
2. Involvement and participation of the patients and their representatives in developing health policies;
3. Promotion and involvement of patients' activities in population educational activities about this disorder;
4. Achievement of National Program for familial screening regarding early detection of individuals at risk of developing Huntington's disease.

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