

Ethics in the genetics of epilepsy: What are the pros and cons?

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Abstract

Genetic data and tools offer enormous potential benefits to humankind but raise significant societal concerns as well. As the impact of the new genetics grows, we can expect the society to be increasingly confronted with many novel, challenging, and sometimes disturbing issues. Genetic testing of complex disorders such as epilepsy raise even more concerns in regards to various social and ethical issues because of the associated stigma. Proper research involving all concerned should result in the formulations of guidelines for the clinicians, researchers, people with epilepsy and their families and health care planners.

INTRODUCTION

Ethics is defined as the science of morals, a treatise on morals or rules of behavior. "Ethics" is a generic term for various ways of understanding and examining the moral life and for resolving ethical problems.¹ Ethics as a science evaluates human practices by calling upon normal standards and also gives prescriptive advice on how to act morally in a specific kind of situation. The accepted principles providing for ethical practice of medicine and research on human subjects are based on recognition of the ideals of autonomy of the person and confidentiality, beneficence (to do the right thing), concerns for human dignity & human rights, non-maleficence (to avoid causing damage) and respect for national laws and international conventions.²

Ethical guidelines have been prescribed ever since the recorded history of organized medical profession many millennia ago. The most commonly recognized is the 'Hippocratic Oath' attributed to the famous Greek physician. There are specific guidelines on various aspects of ethical practices in the ancient Indian System of Medicine (Ayurveda) attributed to Carak and Susruta ~ 1000 BC.^{3,4}

Epilepsy is perhaps one of the oldest recorded medical disorders known to mankind for more than 3000-4000 years. The history of ethics is perhaps as old as the history of epilepsy itself.

THE HUMAN GENOME SEQUENCE: HOPE AND REALITY

The first draft of the Human Genome Sequence

comprising 3.2 billion base pairs is now available for analysis to help us understand ourselves and combat diseases reducing the suffering of humankind. The challenge of unraveling the functional meaning of this encrypted data is the most daunting task for the next several decades. It is too often forgotten that DNA is the 'most private possession' we have. DNA is our 'biological identity card' and should be managed very carefully. It is mandatory to establish 'rules' to be agreed upon by the scientists, patients and the civil society.

GENETICS AND OUR NEW RESPONSIBILITIES

We should be aware that the more we can get inside the genetic code, the more responsible we become towards our fellow human beings who should benefit from our scientific knowledge and not be exploited. The proper use of biological material collected for genetic research need to be rigorously defined according to ethical principles agreed upon by both scientists and patients.¹

GENETIC TESTING OF EPILEPSIES: GAINS

Recent knowledge in regards to genetics of epilepsies can help us to understand better some of the mechanisms that determine epileptogenesis, clarify a few of the unresolved issues such as mode of inheritance, and improve clinical management of some types of epilepsies.⁵ Emerging information on the genetic aspect of human epilepsies will allow the development of

better and earlier predictive tests and eventually usher in a field of prevention-based medicine and diagnostics. This knowledge is also expected to help starting to design new therapeutic strategies based on the recent concepts of pharmacogenetics and pharmacogenomics. A better understanding of how DNA variations underlie our individual responses to medical treatments will help develop drugs customized for those populations and individual patients. Drug development is expected to be faster, cheaper, and more effective with fewer adverse reactions.

The recent FDA Alert (2007) is a classical example of how the recent knowledge on pharmacogenomics could be relevant to clinical therapeutics. Dangerous or even fatal skin reactions (Stevens Johnson syndrome and toxic epidermal necrolysis), that can be caused by carbamazepine therapy, are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including South Asian Indians. Testing for HLA-B*1502 before starting therapy among those who are planned to be treated with carbamazepine can help preventing this potentially dangerous adverse reaction.⁶

GENETIC TESTING OF HUMAN EPILEPSIES - CONCERNS

Even though some current gene tests have been beneficial and their potential benefit enormous, the science is very new and dynamic. Genetic testing is also likely to raise significant ethical, legal, and social issues for people with epilepsy, their care givers and the health care planners.⁵ There is a lack of medical options to treat or prevent many of the disorders for which gene tests are used. The long lag time between linking a gene mutation with a disease and developing effective therapeutics is a major limitation. Additionally, patients who undergo gene testing face significant risks of jeopardizing their employment and insurance status. Patients face an additional burden: the psychological impact of testing can be devastating. Genetic information is shared; all these risks extend to family members as well. The current lack of available medical options for most of these diseases, uncertainties surrounding test interpretation, the potential for provoking anxiety, and the risks of discrimination and social stigmatization could outweigh the early benefits of testing.

SOCIETAL CONCERNS ARISING FROM THE NEW GENETICS

Genetic data and tools offer enormous potential benefits to humankind but pose significant risks as well. As the impact of the new genetics grows, we can expect the society to be increasingly confronted with many novel, challenging, and sometimes disturbing issues. Clinicians, Researchers and the Society need to ensure fairness in the use of genetic information by insurers, employers, courts, schools, adoption agencies, the military, and among others. We need to have guidelines on who should have access to personal genetic information, how will it be used and who owns and controls genetic information.

Privacy and confidentiality of genetic information is a must. There are many issues that need to be addressed like how does personal genetic information affect an individual and society's perceptions of that individual? How does genomic information affect members of minority communities? What is the psychological impact and stigmatization due to an individual's genetic differences? Reproductive issues including use of genetic information are another important aspect in reproductive decision making, and reproductive rights.^{2,7}

There are many other questions that need to be answered. Do healthcare personnel properly counsel parents about the risks and limitations of genetic technology? How reliable and useful is fetal genetic testing? What are the larger societal issues raised by new reproductive technologies? Besides various clinical issues, we need to provide facilities to educate the doctors and other health service providers, patients, and the general public in genetic capabilities, scientific limitations, and social risks.^{2,7}

There are many uncertainties associated with gene tests for susceptibilities and complex conditions (e.g., Epilepsies) linked to multiple genes and gene-environment interactions. Should testing be performed when no treatment is available? Should parents have the right to have their minor children tested for adult-onset diseases? Are genetic tests reliable and interpretable by the medical community? Commercialization of products including property rights (patents, copyrights, and trade secrets) and accessibility of data and materials are the other grey areas. Who owns genes and other pieces of DNA? Will patenting DNA sequences limit their accessibility and development into useful products? Another area of concern is the

implementation of standards and quality-control measures in testing procedures. How will genetic tests be evaluated and regulated for accuracy, reliability, and utility? Currently, there is little regulation at the governmental level.

ETHICS IN GENETICS OF EPILEPSY: A CAREFUL BALANCE

Scientific progress continues to advance rapidly as society scrambles to keep apace. No one can anticipate some of the ways current and ever more powerful future DNA technologies will be put to use, nor their unintended and potentially controversial or adverse effects. As we begin to realize the benefits of the new genetics, maintaining a cautious approach will help minimize the risks. Despite the availability of some general resources, no clear guidelines in regards to many complex issues involved in the genetic testing of human epilepsies are currently available for helping people with epilepsy, their family members and health care providers. The ethical, legal, and social concerns raised by genetic research on epilepsy can be a very important topic for future research that must involve those having epilepsy, their family members, health care professional, policy makers and the bioethicists.⁵

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