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Ethical, Legal, and Social Dimensions of Epilepsy Genetics

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Summary

Purpose— Emerging genetic information and the availability of genetic testing has the potential to increase understanding of the disease and improve clinical management of some types of epilepsy. However, genetic testing is also likely to raise significant ethical, legal, and social issues for people with epilepsy, their family members, and their health care providers. We review the genetic and social dimensions of epilepsy relevant to understanding the complex questions raised by epilepsy genetics.

Methods— We reviewed two literatures: (a) research on the genetics of epilepsy, and (b) social science research on the social experience and social consequences of epilepsy. For each, we note key empiric findings and discuss their implications with regard to the consequences of emerging genetic information about epilepsy. We also briefly review available principles and guidelines from professional and advocacy groups that might help to direct efforts to ascertain and address the ethical, legal, and social dimensions of genetic testing for epilepsy.

Results— Genetic information about epilepsy may pose significant challenges for people with epilepsy and their family members. Although some general resources are available for navigating this complex new terrain, no guidelines specific to epilepsy have yet been developed to assist people with epilepsy, their family members, or their health care providers.

Conclusions— Research is needed on the ethical, legal, and social concerns raised by genetic research on epilepsy and the advent of genetic testing. This research should include the perspectives of people with epilepsy and their family members, as well as those of health care professionals, policymakers, and bioethicists.

Keywords

Epilepsy; Genetics; Genetic testing; Stigma; Discrimination

The conceptualization of epilepsy as an inherited condition dates at least to 400 B.C., the approximate date of *On the Sacred Disease*, attributed to Hippocrates (Temkin, 1971). In the many centuries following, clinicians and scientists have articulated varying notions of its heritability (Temkin, 1971; Schneider and Conrad, 1983). Currently, genetic researchers are attempting to identify both genes that cause epilepsy via monogenic inheritance and genes associated with increased susceptibilities to epilepsy, including possible genetic predispositions to developing epilepsy after central nervous system trauma. Pharmacogenetic research also is being done to ascertain the genetic bases for differential responses to medications used to treat epilepsy.

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Advances in research on epilepsy genetics have the potential to improve the quality of life of people in families affected by epilepsy by offering new means of preventing, controlling, and curing the disease, its symptoms, and its sequelae. At the same time, the ethical, legal, and social dimensions of genetic information about epilepsy require careful consideration. Some aspects of the experience of having epilepsy, as documented in social scientific research, are particularly important to understanding the ethical, legal, and social dimensions of genetic testing for epilepsy. Therefore this review considers the current state of the field of epilepsy genetics alongside social scientific analyses of the experience of having epilepsy. It draws on these two literatures as a means of highlighting areas for future empirical research and for efforts to develop guidelines for genetic testing.

GENETICS AND EPILEPSY

In the last decade, substantial progress has been made in the identification of genes that influence risk for some forms of epilepsy. To date, almost all of this progress has come from analysis of rare families with autosomal dominant patterns of transmission. As of August 2005, 12 genes have been identified in autosomal dominant forms of eight nonsymptomatic epilepsy syndromes. All but two of these genes encode voltage-gated or ligand-gated ion channels. In families with autosomal dominant nocturnal lobe epilepsy, mutations have been found in the genes encoding two subunits of the neuronal nicotinic acetylcholine receptor (*CHRNA4* and *CHRNB2*) (Steinlein et al., 1995; De Fusco et al., 2000). In families with benign familial neonatal seizures, mutations have been found in the potassium channel genes *KCNQ2* and *KCNQ3* (Charlier et al., 1998; Singh et al., 1998). Mutations in the genes encoding three sodium channel subunits, *SCN1A*, *SCN1B*, and *SCN2A*, have been found in different families with generalized epilepsy with febrile seizures plus (GEFS+) (Wallace et al., 1998; Singh et al., 1999; Escayg et al., 2000; Sugawara et al., 2001a; Sugawara et al., 2001b), and mutations in *SCN2A* have been found in families with a different phenotype, benign familial neonatal–infantile seizures (Heron et al., 2002). Mutations in *GABRG2*, the gene encoding the gamma 2 subunit of the γ-aminobutyric acid subtype A ($GABA_A$) receptor, have been found in families with GEFS+ (Baulac et al., 2001; Harkin et al., 2002) and in families with childhood absence epilepsy with febrile seizures (Scheffer et al., 2001; Kananura et al., 2002). In a large French Canadian family with an autosomal dominant form of juvenile myoclonic epilepsy (JME), a mutation was identified in *GABRA1*, encoding the α1 subunit of the $GABA_A$ receptor (Cossette et al., 2002). Mutations in *EFHC1*, encoding a protein with an EF-hand motif that appears to influence calcium currents, were identified in another set of families with JME (Suzuki et al., 2004). In three families with an autosomal dominant form of idiopathic generalized epilepsy (IGE) with a range of different syndromes, mutations were identified in the chloride channel gene *CLCN2* (Haug et al., 2003). In families with autosomal dominant partial epilepsy with auditory features (ADPEAF), mutations have been found in the leucine-rich glioma inactivated 1 gene (*LGI1*), which encodes a leucine-rich repeat protein (Kalachikov et al., 2002; Morante-Redolat et al., 2002; Ottman et al., 2004). The mechanism by which *LGI1* influences epilepsy risk is still not well understood, but based on protein homology, it appears likely to be involved in development of the central nervous system (Kalachikov et al., 2002).

In addition to these gene discoveries in nonsymptomatic epilepsies, genes have been identified in a number of Mendelian symptomatic epilepsy syndromes. These include progressive myoclonic epilepsies [e.g., Unverricht–Lundborg disease, Lafora disease, and the neuronal ceroid lipofuscinoses (Shahwan et al., 2005)], X-linked myoclonic epilepsy with mental retardation (Stromme et al., 2002), and cortical malformation syndromes such as polymicrogyria, pachygyria, and periventricular nodular heterotopia (Guerrini, 2005; Mochida, 2005). In addition, mutations in *SCN1A* have been identified in many patients with severe myoclonic epilepsy of infancy (SMEI) (Claes et al., 2001; Ohmori et al., 2002; Sugawara et al., 2002; Wallace et al., 2003).

These gene discoveries are very exciting because they lead the way to research on basic pathophysiologic mechanisms that could someday be used to develop new treatments, or even to ways of preventing epileptogenesis. However, most people with epilepsy have no affected relatives, and only a tiny fraction of all epilepsies are consistent with Mendelian modes of inheritance. In the large group of people with non-Mendelian forms of epilepsy, the genetic influences on risk probably consist mainly of "complex" disease genes—that is, genes with only a small effect, which act additively to increase risk, possibly in combination with environmental factors (Ottman, 2005). Research is under way to identify these complex epilepsy genes, but progress has been slow, and few findings have been confirmed (Tan et al., 2004).

Given that most of the genes identified in families with Mendelian inheritance so far have encoded voltage-gated or ligand-gated ion channels, variants in ion channel genes also may well contribute to risk for genetically complex epilepsies. Two other types of genetic effects may also play a role in some cases. First, some "sporadic" epilepsies (i.e., those occurring in the absence of a family history) may be caused by de novo mutations. This mechanism is important in SMEI, in which many of the mutations identified in *SCN1A* have been de novo (Claes et al., 2001; Ohmori et al., 2002; Sugawara et al., 2002; Wallace et al., 2003). Second, some epilepsies may be caused by somatic mutations occurring in critical brain regions.

The relations between genotype and phenotype in the epilepsies are not at all straightforward. As discussed later, these complexities have important implications for genetic testing. *Locus heterogeneity*, in which a single syndrome is caused by different genes in different families, is well documented. Multiple autosomal dominant susceptibility genes have been identified in four syndromes: benign familial neonatal seizures (*KCNQ2* and *KCNQ3*), autosomal dominant nocturnal frontal lobe epilepsy (*CHRNA4* and *CHRNB2*), GEFS+ (*SCN1A*, *SCN1B*, *SCN2A*, and *GABRG2*), and autosomal dominant JME (*GABRA1* and *EFHC1*). Moreover, different genetic mechanisms—single gene versus complex—can produce the same syndrome in different families, making it impossible to classify syndromes according to genetic mechanisms. For example, the IGEs are genetically complex in most cases, but some families have autosomal dominant inheritance (Cossette et al., 2002; Haug et al., 2003; Suzuki et al., 2004). Although mutations in *LGI1* have been found in 50% of families containing two or more subjects with temporal lobe epilepsy with ictal auditory symptoms (Ottman et al., 2004), most patients with these symptoms are sporadic and do not have *LGI1* mutations (Bisulli et al., 2004; Flex et al., 2005).

Another complication is *variable expressivity*, in which a mutation in a single gene can produce different epilepsy phenotypes in different individuals. For example, in GEFS+, the seizure disorders in family members who have inherited a single mutation in *SCN1A* can include simple febrile seizures, febrile seizures plus (in which febrile seizures persist beyond age 6 years, or are accompanied by afebrile generalized tonic–clonic seizures), idiopathic generalized epilepsy, temporal lobe epilepsy, or myoclonic–astatic epilepsy (Singh et al., 1999). Further, mutations in three of the four genes found to be mutated in GEFS+ families have been found in other syndromes also: *SCN1A* mutations (many of which are de novo) in patients with SMEI (Claes et al., 2001; Ohmori et al., 2002; Sugawara et al., 2002; Wallace et al., 2003), *SCN2A* mutations in families with benign familial neonatal infantile seizures (Heron et al., 2002), and *GABRG2* mutations in families with childhood absence epilepsy with febrile seizures (Wallace et al., 2001; Kananura et al., 2002).

Pharmacogenomics is another promising research area in the epilepsies. Its goal is to define genotypes likely to predict response to antiepileptic medications (AEDs). The possibility of using genetic testing in the process of selecting treatments, although potentially advantageous to people with epilepsy, also raises complex ethical and social issues. Most important,

pharmacogenomics raises questions regarding equity in access to new testing regimens and alternative treatment modalities. However, many of the issues raised by genetic testing for genes that increase risk for the development of epilepsy differ substantially from those raised by pharmacogenomics. In this article, we focus on testing for genes associated with an increased risk for developing epilepsy, rather than genes that influence treatment response.

SOCIAL SCIENTIFIC PERSPECTIVES ON EPILEPSY

The ascendance of genetic information about epilepsy and its possible clinical applications raise a variety of ethical, legal, and social issues. Many of these issues are not unique to epilepsy. For example, ethical and legal concerns that are raised by genetic tests, generally, include appropriate informed consent, autonomy, confidentiality and privacy of genetic information, and the imperative of balancing individual, parental, and societal interests when considering genetic testing for a minor. Similarly, the potential of genetic information to contribute to psychological distress, adverse labeling, and discrimination in health insurance, life insurance, and employment is an important consideration for genetic testing for any medical condition (Billings et al., 1992; Burke et al., 2001). Equity in the availability and affordability of prophylaxis and/or treatment for identified genetic susceptibilities is another important concern raised by genetic testing in general (Burke et al., 2001). However, the social scientific literature highlights several particular dimensions of the experience of having epilepsy that are critically important to understanding the social dimensions of genetic information about and testing for epilepsy.

Sociologic inquiry indicates that "a good deal of the experience of epilepsy comes from people confronting '*what it is*,' meaning what it has come to be as a social object and the kinds of practices. . .that surround it" (Schneider and Conrad, 1983). In other words, social interactions with important others, such as doctors and family members, are tremendously consequential in shaping the experience of being diagnosed and living with epilepsy. Therefore insofar as it changes the form or content of such interactions, genetic information and genetic testing have the potential to reshape significantly the experiences of people with epilepsy.

For example, social scientific research suggests that questions about disease etiology are a focal concern of people with epilepsy (Scambler, 1994). Persons with epilepsy for whom doctors cannot identify an etiology often develop their own theories about epilepsy causation and seizure precipitants, commonly focused on "prolonged stress" as a primary etiologic factor (Scambler, 1994). People who identify stress as an etiologic agent frequently believe that alleviating stress will cure their epilepsy and/or that lifestyle or environmental modifications will control their seizures (Scambler, 1994). Therefore whereas identification of a genetic etiology could be reassuring to people with epilepsy who desire a definitive physiologic explanation, it could be disturbing for those who favor lay etiologic theories that emphasize environmental and potentially more controllable causes and/or precipitants, such as stress or diet (Scambler, 1989).

The identification of genetic etiologies of epilepsy also could affect mechanisms of stigma, discrimination, and social isolation already associated with epilepsy. For example, genetic information might make it seem as if having epilepsy is an enduring and essential part of a person with epilepsy, even if it has been many years since that person has experienced a seizure. The history of epilepsy provides many instances in which notions of heritability have been invoked as a rationale for stigma and discrimination against persons with epilepsy, including institutionalization, prohibitions on marriage and immigration, and forced sterilization (Temkin, 1971; Schneider and Conrad, 1983).

Contemporary social scientific research indicates that although stigma and discrimination have declined since WWII (at least, in the United States, Britain, and Europe), a significant

proportion of the stigma and disability associated with epilepsy is still caused not by the disorder, per se, but by social reactions to it (Gehlert et al., 2000; Jacoby et al., 2004; Morrell, 2002). People with epilepsy describe their fears of experiencing stigma and discrimination as a significant component of the burden of being diagnosed with epilepsy. This fear may be so strong as to constitute a "special view of the world in which fear of enacted stigma dominates," and everyday life is organized to conceal the presence of the disease (Scambler, 1994).

Although perceived stigma might be more prevalent than actual experiences of stigma (Scambler, 1994), survey research in both the United States and Britain suggests that people with epilepsy are often viewed as "violent, likely to go berserk, retarded, sluggish or slow, antisocial, and physically unattractive" (Jacoby, 2002). They are also much more likely to experience social rejection than are persons with cerebral palsy or mental illness, although a possible confounding factor in this research is that many Americans believe that epilepsy is a mental illness (Krauss et al., 2000; Jacoby, 2002). People with epilepsy already report difficulty obtaining health insurance, life insurance, and employment (Morrell, 2002). Epilepsy also is associated with reduced social interactions, lower rates of marriage, lower reproductive rates, low self-reported health-related quality of life, and increased rates of psychological distress (Morrell, 2002; Jacoby et al., 2004). Insofar as it amplifies or reifies stigma and discrimination, genetic information has the potential to increase these challenges. Research is needed to ascertain the ways in which genetic information may affect stigma, discrimination, social isolation, and other adverse outcomes associated with epilepsy.

Genetic information may also transform the experience of being the family member of a person with epilepsy. Insofar as epilepsy becomes popularly conceived as something that "runs in the family," relatives of persons with epilepsy may be affected by "courtesy stigma." This occurs when stigma becomes attached to a person "who is related through the social structure to a stigmatized individual—a relationship that leads the wider society to treat both individuals in some respects as one" (Goffman, 1963). In the context of inherited genetic conditions, family members of persons with an illness are at risk for courtesy stigma, discrimination, and social isolation. Associative stigma effects resulting from an assumed genetic etiology have been demonstrated for mental illness (Phelan, 2005), but these matters have not been investigated in the epilepsies.

In addition, identifying genetic etiologies of epilepsy may have consequences for familial relations (Schneider and Conrad, 1983; Mitchell et al., 1994; Morrell, 2002). Sociological researchers have observed that parental efforts to reconcile themselves to a child's epilepsy diagnosis may include attributions of likeness between the person with epilepsy and family members thought to manifest analogous "defects" or "genetic weaknesses" (West, 1979). For example, in families wherein epilepsy is referred to as "fits," parents may make associations between a child with epilepsy and family members who are prone to "fits of anger" or "alcoholic fits" (West, 1979). Research on other inherited neurologic conditions has highlighted the importance of studying perceptions of hereditary risk within the context of familial beliefs and communication patterns (Cox and McKellin, 1999). However, few studies have been done on the social relationships and family-communication dynamics of persons with epilepsy (Gehlert et al., 2000). Moreover, no systematic studies have investigated how families affected by epilepsy discuss heritability and risk, among themselves, with their clinicians, or in their broader social networks.

GENETIC TESTING IN THE EPILEPSIES: CURRENT STATUS

Current information about genetic testing for many disorders, including several forms of epilepsy, is available from the GeneTests website (www.genetests.com), a publicly funded medical genetics information resource developed by investigators at the University of

Washington. The GeneTests site identifies both clinical laboratories and research laboratories that provide testing. Clinical laboratories are defined as those that perform analyses and give results to providers and/or patients for the purpose of diagnosis, prevention, or treatment, usually for a fee. In the United States, the Clinical Laboratory Improvement Act (CLIA) requires that clinical laboratories be certified to meet certain federal quality and proficiency standards. Research laboratories perform analyses for research only; test results are not given to patients or providers, and CLIA certification is not required.

A search of the GeneTests site with the word “epilepsy” indicates that testing in a clinical laboratory is currently available for several progressive myoclonic epilepsies (myoclonic epilepsy with ragged red fibers, several neuronal ceroid lipofuscinoses, Lafora disease, and Unverricht–Lundborg disease) as well as for X-linked myoclonic epilepsy and mental retardation and SMEI. Testing in clinical laboratories also is available for two nonsymptomatic epilepsies: autosomal dominant nocturnal frontal lobe epilepsy and GEFS+. For GEFS+, this testing is available for only one of the four genes discovered so far, *SCN1A*.

Despite the availability of these tests, no guidelines are currently available to decide for which of these syndromes testing is warranted. The decision whether or not to offer testing resides solely with clinicians, who may not have sufficient information to evaluate the advantages and disadvantages for patients and their family members. Moreover, in the absence of guidelines for when and how to offer testing, no assurance exists that patients will be offered genetic counseling to help them understand the potential ramifications of testing, the results of tests, or that their rights to choose whether or not to be tested will be respected.

GENETIC TESTING IN THE EPILEPSIES: GUIDELINES AND PRINCIPLES

In general, molecular genetic testing can be carried out for three different purposes: (a) diagnostic testing in a symptomatic individual, to confirm or exclude a suspected genetic disorder, (b) predictive testing in an asymptomatic individual, at risk of disorder by virtue of his or her family history, and (c) preimplantation genetic diagnosis and prenatal genetic testing (special types of predictive testing) to determine whether an embryo or fetus is likely to become affected with the disorder. No National Institute of Health consensus statements, professional association guidelines, or policy statements specifically address genetic counseling, testing, or screening for epilepsy for any of these purposes.

The Epilepsy Foundation has developed a Statement on Genetic Testing that emphasizes preventing discrimination, noting that “inadequate safeguards are in place to protect individuals from discrimination based on their genes” and asserting that “the presence of a gene associated with epilepsy should not be used to deny employment, housing, health care, or any other goods or services to any individual” (http://www.epilepsyfoundation.org/advocacy/care/gene-disc.cfm; URL accessed 1 March, 2005). The potential of genetic testing to exacerbate stigma and discrimination against people with epilepsy is a critical ethical and legal concern. However, more comprehensive guidelines for genetic testing in the epilepsies are needed. These guidelines should be informed by the perspectives of people with epilepsy and their family members, in addition to those of clinicians, scientists, ethicists, and policymakers, to ensure that a diversity of expertise, insights, and concerns may be adequately considered.

Until data are available to inform guidelines and policy making, people with epilepsy, their family members, and clinicians may find it helpful to draw on more general policy statements and guidelines to inform their choices and practices regarding genetic counseling and testing for epilepsy. The National Human Genome Research Institute (NHGRI) website provides resources on ethical, legal, and social issues raised by genetic information in both research and clinical contexts (e.g., genetic discrimination, intellectual property, commercialization, and

patenting) (URL: http://www.genome.gov/PolicyEthics/, accessed January 31, 2006). The website of the Ethical, Legal, and Social Implications (ELSI) Program of the NHGRI also provides a searchable database of the extramural research projects and conferences that it has funded to address these issues (URL: http://www.genome.gov/17515632, accessed January 31, 2006). Additionally, several types of guidelines are available, specific to genetic testing.

First, general guidelines and position statements regarding genetic testing have been developed by societies representing medical genetics professionals. The American College of Medical Genetics/American Society of Human Genetics (ACMG/ASHG) offers general guidelines for genetic counseling, screening, testing, as well as disease-specific guidelines (http://www.acmg.net/resources/policy-list.asp; URL accessed 18 July, 2005). The National Society of Genetic Counselors (NSGC) has also formulated a number of concise position statements regarding ethical issues pertaining to genetic counseling and testing, reproductive freedom, access to care, confidentiality of test results, disclosure and informed consent, and pre-natal and childhood testing for adult-onset disorders (http://www.nsgc.org/about/position.asp; URL accessed 18 July, 2005). As these guidelines have been developed by societies for health care professionals, they are likely to be particularly helpful to clinicians in addressing ethical concerns that arise in medical settings.

Second, guidelines proposed for genetic testing for other neurologic conditions may also offer some assistance. For example, the Huntington's Disease Society of America (HSDA) has proposed 12 guidelines for genetic testing for Huntington disease. Although epilepsy and Huntington disease differ markedly (genetically, biologically, and socially), the HDSA guidelines are procedural, and many are broad enough to be relevant to genetic counseling and testing for epilepsy. The full text of the HDSA guidelines is available on the Columbia University HDSA Center for Excellence website (http://www.hdny.org/genetic_testing_guidelines.htm; URL accessed 18 July, 2005). A number of guidelines are available regarding genetic testing for Alzheimer's disease (American College of Medical Genetics/American Society of Human Genetics Working Group on ApoE and Alzheimer disease, 1995; Brodaty et al., 1995; National Institute on Aging/Alzheimer's Association Working Group, 1996; McConnell et al., 1998).

Third, the Centers for Disease Control Office of Genomics and Prevention has developed a model process for evaluating data on emerging genetic tests: ACCE, which takes its name from the four components of evaluation—analytic validity, clinical validity, clinical utility, and associated ethical, legal and social issues (Haddow and Palomaki, 2004, http://www.cdc.gov/genomics/gtesting/acce.htm; URL accessed September 22, 2006.). ACCE evaluation is carried out in the context of the specific disease and the setting of the test. ACCE has not been applied to the epilepsies but may provide a useful framework for these considerations in the near future. The evaluation considers, first, the analytic validity of the test (i.e., does the test accurately detect the presence or absence of a mutation?).

Next, the evaluation considers clinical validity (i.e., does the test accurately predict which patients have the disorder?). For forms of epilepsy in which mutations in multiple genes have been found, a negative test for one gene does not rule out the presence of the disorder. Also, if the gene has reduced penetrance or variable expressivity, a positive test will not accurately predict the presence of the disorder or its clinical features. This distinction is well illustrated in considering possible genetic testing for *SCN1A*, in which mutations have extremely variable expressivity, ranging from simple febrile seizures in families with GEFS+ to SMEI. Predictive testing in this case would have low clinical validity, because multiple outcomes would be possible if a mutation were found in an asymptomatic individual. Conversely, diagnostic testing of *SCN1A* in individuals suspected to have SMEI might have higher clinical validity, given the high prevalence of mutations in symptomatic individuals.

The third factor considered in the evaluation of a test is clinical utility (i.e., are the test results likely to have an important impact on patient care?). In some cases, the knowledge that a form of epilepsy is caused by a mutation in a specific gene might be irrelevant for treatment, whereas in others, the knowledge might predict treatment response or obviate the need for difficult diagnostic procedures.

The fourth factor considered is ethical, legal, and social implications (i.e., how does the test affect stigmatization; discrimination; privacy; personal, family, or social relationships; and legal issues?) (Haddow and Palomaki, 2004).

As evident in our review of social scientific research on epilepsy, the social consequences of genetic testing may be particularly acute for people with epilepsy, as they already experience significant stigma and discrimination. A framework developed by Burke and colleagues provides one means of further specifying the ethical, legal, and social implications of genetic testing (Burke et al., 2001). Drawing on criteria similar to those of the ACCE process, they use four evaluative categories to describe the primary concerns raised by genetic tests (Burke et al., 2001):

1. High clinical validity, no effective treatment. The primary concern is adequate nondirective counseling to ensure an informed, autonomous decision; other concerns are adverse labeling, psychological distress, and potential for discrimination;
2. High clinical validity, effective treatment. The primary concern is that eligible people have access to testing and treatment;
3. Low clinical validity, no effective treatment. Recommending against test use can be justified on the principle of avoiding harm; and
4. Low clinical validity, effective treatment. The issue is maximizing net benefit, by minimizing the potential for adverse effects from labeling, while maximizing the potential for improved health outcomes.

Given the heterogeneity of the epilepsies, both clinically and genetically, this typology might prove helpful to clinicians in conjunction with ACCE. However, as with the other guidelines described earlier, it offers less guidance for persons with epilepsy and their family members, as they consider the uses and meanings of genetic information in their lives.

CONCLUSIONS

As demonstrated by this review, emerging genetic information about epilepsy and the advent of genetic testing for some types of epilepsy both open new opportunities for diagnosis and treatment and raise important concerns for people with epilepsy and their family members. Such ethical, legal, and social issues are also highly relevant for clinicians who provide services to people with epilepsy, as it is likely that patients will increasingly ask them for assistance in making sense of emerging genetic information and making decisions regarding available tests.

Although guidelines and research on other neurologic disorders may provide an empirical basis for understanding and addressing some of these issues, the social scientific literature on the lived experience and consequences of having epilepsy suggests that research on the ethical, legal, and social dimensions of genetic testing specific to epilepsy is of critical importance.

The experience of being diagnosed with epilepsy, living with epilepsy, and being the family member of a person with epilepsy is imbued with social meanings. These meanings are constituted within and express dimensions of the specific social realities in which persons with epilepsy live, that is, “how the sick person and the members of the family or wider social network perceive, live with, and respond to symptoms and disability” (Kleinman, 1988).

Therefore empirical research that examines the perspectives of people with epilepsy, their family members, and members of their social networks (e.g., health care providers) is imperative to the understanding of the ethical, legal, and social dimensions of genetic information about epilepsy. As powerfully demonstrated by ethnographic research on the social consequences of amniocentesis in America, "consumers (or. . .nonconsumers) of a biomedical technology can be seen as experts capable of analyzing its burdens and benefits and casting a rather different light on the contests for meaning and rationality. . ." (Rapp, 1999). Importantly, if we understand public discourse about of the ethical, legal, and social implications of genetic testing as providing "a negotiation space to explore the socially acceptable limits of [a] technology" (Hedgecoe and Martin, 2003), it is critical that potential users of genetic testing be included in such discussions. Additionally, ensuring that the perspectives of people living with epilepsy and their family members are well represented in consideration of the ethical, legal, and social implications of genetic testing will contribute to our understanding of how people assess and make decisions about genetic testing in the context of their families, communities, religious institutions, and other social organizations; this will enable us to attend to "not only to the ethics of specific clinical practices, but also to the wider social practices and communal narratives that provide the context for our basic notions of the good life, including living well and dying well. . ." (Barns et al., 2000). As genetic information becomes increasingly salient to the experience of having epilepsy, such broad ethical, legal, and social considerations deserve careful and sustained attention.

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