Pairnomix

The value of genetic testing in epilepsy

Genetic testing presents the opportunity for physicians to potentially identify a causal mutation in their patients.

In the past, genetic testing was able to pinpoint a mutation as contributing to epileptic encephalopathies in only a handful of cases.[1,2] However, today this frequency has risen to an estimated 15-20%[3] and is expected to increase further as new genes are discovered in the field.

One question remaining in the field is this: **When is it most valuable to order genetic testing for people with epilepsy?**

The International League Against Epilepsy (ILAE) — an association of healthcare professionals dedicated to improving epilepsy education and research — has provided some perspective on this topic. This group advises that physicians consider prescribing genetic testing when there is:

- ***Clinical validity*** (the physician has made an informed opinion that their patient has epilepsy or a seizure disorder with a genetic basis), and
- ***Clinical utility*** (the results of the test are likely to positively impact the patient's health or well-being).[4]

It's important to know that if clinical utility and clinical validity can be established for genetic testing, insurers may cover the cost of testing.

While the ultimate decision of whether to order genetic testing — particularly in regard to clinical validity — rests with the treating physician, there are a number of instances where the clinical utility of genetic testing has been demonstrated. Examples are shown in the table below.

This identification of *specific genetic mutations* may have implications for clinical management by enabling an earlier diagnosis, informing therapy choice, or preventing unnecessary invasive procedures.

Gene	Clinical utility of testing for mutation
ALDH7A1	Dietary lysine restriction along with pyridoxine treatment may reduce seizures and allow for developmental gains.[5]
DEPDC5	Surgery has been shown to reduce seizures in some patients with mutations in this gene.[6]
EMP2A or EMP2B	Sodium channel blockers and GABAergic drugs may exacerbate seizures.[7,8]
FOLR	Patients with mutations in *FOLR* may respond well to treatment with folinic acid.[9] Treatment with folic acid may worsen symptoms.[7,10]
GRIN2A	Memantine has been shown to reduce seizures in those with specific *GRIN2A* mutations.[11]
KCNT1	Treatment with quinidine may reduce seizures in patients with specific *KCNT1* mutations.[12,13,14]
PNPO	Pyridoxal-5-phosphate treatment can reduce seizure recurrence and may improve cognitive function.[15]
POLG	Treatment with valproic acid may induce liver failure in patients with *POLG* deficiency.[16]
PRRT2	Seizures induced by *PRRT2* mutations may respond well to carbamazepine, phenobarbital, valproate, or zonisamide.[7,17,18]
SCN1A	Carbamazepine and phenytoin may exacerbate seizures.[2,7,19]
SCN8A	Carbamazepine and phenytoin may help reduce seizures in patients with specific *SCN8A* mutations.[20,21,22]
SLC2A1	A ketogenic diet can reduce seizures in these patients.[2] Steroids and carbonic anhydrase inhibitors may improve seizure control.[7]
TSC1 or TSC2	Monitoring of certain organs in these patients may be essential.[23] Treatment with everolimus may reduce seizures.[24]

Pairnomix empowers people living with rare disease by performing personalized genetic research that enables physicians to make better-informed healthcare decisions. We're here to answer your questions about genetic research.

Contact us to learn more.

Pairnomix helps people with epilepsy who have already received genetic sequencing and have successfully identified the gene mutation that is known or believed to cause their condition. We do not perform genetic sequencing tests, but we encourage you to speak with your physician about your options.

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