

Genetic Basis of Monogenic Epilepsies **Isa Abdi Rad***

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Editorial

Epilepsy as a common neurologic disorder is defined as at least two unprovoked seizures more than 24 hours apart, which occur in 0.5-0.8 of population. Approximately, half of all epilepsies are idiopathic which may have a genetic basis with a monogenic or polygenic pattern of inheritance, so that, the risk of developing epilepsy is 2 to 5 times higher in the relatives of patients with epilepsy [1,2]. Determining the genetic basis of epilepsies would be very helpful in classification, unraveling mechanism and pathogenesis of epilepsies, and in genetic counseling. Monogenic pattern of inheritance has been recognized in only about 1-2% of the idiopathic epilepsies, so, genetic involvement and underlying mechanism still remain unclear in the majority of idiopathic epilepsies [3]. Most of monogenic epilepsies are voltage-gated ion channelopathies such as sodium, potassium, and chloride channelopathies, or defects in neurotransmitter receptors such as GABA_A receptor, and nicotinic acetylcholine receptor [4-9].

Most monogenic epilepsies with identified genes or loci have autosomal dominant pattern of inheritance, although, all other patterns of inheritance are also reported. Autosomal recessive inheritance is common in epilepsies with an early age of onset and with a progressive course, and sometimes may be associated with other movement disorders such as autosomal recessive rolandic epilepsy with paroxysmal exercise induced dystonia and writer's cramp which mapped to chromosome 16p12-11.2 [10].

Autosomal dominant epilepsies with identified genes can be classified according to the involved proteins such as channelopathies or receptors. Benign familial neonatal convulsions are a voltage-gated potassium channelopathy due to mutations in *KCNQ2* and *KCNQ3* genes. Voltage-gated sodium channelopathies include benign familial neonatal-infantile seizures (*SCN2A* gene), generalized epilepsy with febrile seizures plus (*SCN1A*, *SCN1B*, and *SCN2A* genes) and Dravet's syndrome or severe myoclonic epilepsy in infancy (*SCN1A* gene). Generalized epilepsy with febrile seizures plus can result from mutations in $\gamma 2$ subunit of the GABA_A receptor (*GABRG2* gene). Mutation in $\alpha 1$ subunit of the GABA_A (*GABRA1* gene) results in Juvenile myoclonic epilepsy.

Autosomal dominant nocturnal frontal lobe epilepsy resulted from mutations in $\alpha 4$ and $\beta 2$ subunits of nicotinic acetylcholine receptor (*CHRNA4* and *CHRN2* genes). Defect in Epitempin protein results in familial lateral temporal-lobe epilepsy with auditory symptoms (*LGI1* gene) which is an autosomal dominant

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disorder. Infantile convulsions and choreoathetosis is also autosomal dominant epilepsy resulted from mutations in *KST1* gene. Obviously, the list of epilepsies with Mendelian inheritance will be longer with determination of related genes in future.

In summary, the genetic factors play an important role in epilepsy. Determination of genetic basis of epilepsy would be essential and very helpful in genetic counseling and prevention of disease in the high risk families via prenatal diagnosis.

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