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The Role of Whole Exome Sequencing in the Diagnosis of Epileptic Encephalopathies

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Abstract

Objective: Epileptic encephalopathies are a devastating group of electroclinical syndromes with early onset of drug-resistant seizures in which the epileptiform abnormalities may contribute to progressive dysfunction or developmental stagnation and consequent cognitive and behavioral impairments.

A genetic etiology can be identified in a considerable proportion of patients with epileptic encephalopathy. Most have de-novo dominant mutations, but a growing proportion of patients has a polygenic inheritance in which the interaction of several genetic variants is responsible for the phenotype.

The increased efficiency and the reduced cost of next-generation sequencing tests promoted their implementation into the routine diagnostic process. Whole-exome sequencing (WES) is a technique for comprehensively sequencing all the protein-coding regions of the genome (~20,000 genes). It has proven successful in identifying undiagnosed genetic disorders in many patients with a broad phenotypic spectrum.

Methods: We report our experience in the use of WES as a first-tier molecular test in 40 patients with undiagnosed epileptic encephalopathies at Oasi Research Institute-IRCCS, Troina, Italy. The test was performed on probands and their unaffected parents (trio analysis). Each genetic variant found has been compared to known variables in main polymorphism and mutation databases and a deeply in silico analysis for predicting pathogenicity was performed. All variants found were confirmed by sanger sequencing.

Results: About a third of patients received a genetic diagnosis. And WES proved to have a good cost-effectiveness ratio. Our data highlight the clinical utility and feasibility of WES in individuals with undiagnosed forms of epileptic encephalopathies.

Biography:

Luigi Vetri is a physician and researcher at Department of Sciences for Health Promotion and Mother and Child Care "G. D'Alessandro," at University of Palermo. He has been collaborating for two years with Oasi Research Institute-IRCCS in Troina in the field of congenital and inborn causes of intellectual disabilities and neurodevelopmental disorders.

Speaker Publications:

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