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Confirming the recessive inheritance of *SCN1B* mutations in developmental epileptic encephalopathy

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Introduction: Dominant *SCN1B* mutations are known to cause several epilepsy syndromes in humans. Only two epilepsy patients to date have been reported to have recessive mutations in *SCN1B* as the likely cause of their phenotype. Here, we confirm the recessive inheritance of two novel *SCN1B* mutations in five children from three families with developmental epileptic encephalopathy. The negative clinical exome in one of these families highlight the need to consider recessive mutations in the interpretation of variants in typically dominant genes.

Materials & Methods: We conducted autozygosity mapping and a multi-gene panel in five children with epileptic encephalopathy from three unrelated consanguineous families with normal parents.

Mutation Analysis: In family one and three the same splicing variant was identified (NM_001037.4:c.449-2A>G). In family two a missense homozygous *SCN1B* variant (NM_001037.4:c.355T>G:p.Y119D) was identified with high pathogenicity scores using *in silico* prediction tools (PolyPhen (0.997), SIFT (0) and CADD (27)). These variants were completely absent in >7,000 Saudis screened for these genes using exome sequencing and gene panel testing. They were also absent in ExAC.

Conclusion: Although dominant mutations are the typical class of mutations in *SCN1B* in the context of epilepsy, recessive mutations in this gene have also been reported, albeit very rarely (two patients to date). The negative clinical exome in one of these families highlight the need to consider recessive mutations in the interpretation of variants in typically dominant genes.

Biography

Wafaa Ramadan has completed her MBBS degree this June at the age of 24 years from AlFaisal University, Riyadh, KSA. She has a diploma in clinical research activities and a certificate for one year training in developmental genetic department. Dr. Wafaa graduated with first honor degree and has the award of being best intern of the year. She has three papers published, she is the first author in the one she's presenting. Her field of interest is neurology and neuroscience and her work is dedicated towards it.

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