# New two findings in idiopathic generalized epilepsy-15 (EIG-15); happy demeanor and gait disturbance: two cases report

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## INTRODUCTION

Susceptibility to idiopathic generalized epilepsy-15 (EIG-15) related RORB (retinoid-related orphan receptor b) gene is an autosomal dominant inherited disease characterized by variable seizures. RORB gene expressed in the cortex, spinal cord,and pituitary is hypothesized to have a role in neuronal cell differentiation. Therefore, pathogenic variants obtained by mutations can alter the function of the gene appearing in different clinical phenotypes of epilepsy. We described the case of two adolescent patients from the same family affected by focal, generalized, and predominantly absence seizures, intellectual disability, attention deficit hyperactivity disorder (ADHD), gait disturbance, and happy facial appearance with a heterozygous mutation of the RORB gene on chromosome 9q22. Also, their father had same clinical symptoms. Here we show a happy facial appearance, a previously unidentified phenotypic trait, and it is the first time that gait abnormality described in humans associated with the RORB gene before in rabbits.

## CASE REPORT

7 and 13-year-old two sisters from a consanguineous family, diagnosed with epilepsy. They developed febrile seizures at the age of 1 year that progressed to febrile and non-febrile generalized tonic-clonic seizures. At age of 2, the seizure type changed to absence seizures. They had also focal seizures and head drop attacks. Neuropsychological assessment showed mild to moderate intellectual disability and attention deficit hyperactivity disorder. In addition, two patients had gait disturbance with a posture of semi-flexed lower limbs. Frequent smiling was present in both of them. The electroencephalography (EEG) pattern seen in these two cases, generalized polyspikes followed by typical 3-Hz spike-and-wave mostly triggered with intermittent photic stimulation (IPS). Because of consanguineous parents and similar clinical symptoms in their father, we performed exome sequencing that resulted in a new variant mutation of the RORB gene. They were treated with combination of sodium valproate and clobazam, and one of patients recieved additional phenobarbital with good efficacy.

## DISCUSSION

We reported two sisters from a consanguineous family with idiopathic generalized epilepsy. Both of them had an intellectual disability and gait disturbance. Idiopathic generalized epilepsy (EIG), also known as generalized genetic epilepsy is the most common form of epilepsy and is thought to have predominant genetic etiology (1). EIG is clinically characterized by absence, myoclonic, or generalized tonic-clonic seizures with the electroencephalographic pattern of bilateral, synchronous, and symmetrical spike-and-wave discharges (2). Despite their strong heritability, the genetic basis of generalized epilepsies remains largely elusive. In these two cases, we performed whole-exome sequencing and we found a variant mutation in the RORB gene. The RORB gene expressed in cortex, spinal cord, and pituitary is hypothesized to have a role in neuronal cell differentiation. we support the role of RORB gene variants in neurodevelopmental disorders including epilepsy, and especially in generalized epilepsies with predominant absence seizures. RORB is also expressed in the retina and necessary for the proliferation and differentiation of retinal cells (3). Although our patients did not show any visual abnormalities, they had clinical and/or electrical photosensitivity. Although gait disturbance has been shown in RORB gene mutations in previous animal studies, especially in rabbits, there is no data on this issue in humans (4). We wanted to present this case, thinking that we can contribute to the literature both for this reason and because happy facial appearance is a previously unidentified phenotypic trait.

## REFERENCES

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