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OC.1- NOVEL CHD2 AND KIAA2022 MUTATIONS ASSOCIATED WITH EYELID MYOCLONIA WITH ABSENCES

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Purpose: Eyelid myoclonia with absences (EMA) is a generalized genetic epilepsy syndrome characterised by the hallmark of rapid blinking of the eyelids and an upward deviation of the eyeballs. Understanding the genetic architecture of EMA is a challenging task as eyelid myoclonia is also seen in other epilepsy syndromes.

Method: The present study is based on a cohort of individuals with either only EMA, showing eyelid myoclonia with eye closure EEG bursts and/or photosensitivity (EMA), or with EMA associated with clinically evaluated intellectual disability or psychiatric conditions (EMA+).Whole-exome sequencing (WES) was performed on probands and their parents, when available. WES data was analysed, trios were analysed for de novo and/or unique variants and the singletons for unique variants. Sanger sequencing was used to confirm variants.

Results: We sequenced 112 individuals, including 19 trios, 40 singletons and 2 multiplex families. We identified 2 novel de novo CHD2 mutations in 2 EMA+ trios: a missense variant [c.4598 T>G] and a splice donor variant [c.3455+2 T>G]. We also identified a de novo frameshift deletion affecting KIAA2022 [c.2171del] in another EMA+ trio. All these variants were unique, with CADD score>20. Two singletons showed a previously reported mutation in the CHD2 gene: a frameshift variant [c.3734dupA] and a splice region variant [c.2577+7T>C]. The former variant was identified in an EMA+ case, and the latter in an EMA case. Overall, 10.5% of trios showed a de novo CHD2 variant and 5% of singletons harboured mutation in this gene.

Conclusion: CHD2 gene plays a key role in cerebral cortical development. Mutations in this genehave been reported for a broad spectrum of neurodevelopmental disorders, including EMA. KIAA2022 encodes a neurite extension and migration factor. Mutations in this gene have never been associated with EMA. Our study adds growing evidence implicating novel CHD2 and KIAA2022 mutations in EMA.