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Recurrent ATP1A2 mutations in Portuguese families with familial hemiplegic migraine

Castro MJ, Stam AH, Lemos C, Barros J, Gouveia RG, Martins IP, Koenderink JB, Vanmolkot KR, Mendes AP, Frants RR, Ferrari MD, Sequeiros J, Pereira-Monteiro JM, van den Maagdenberg AM.

Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal.

Abstract

Familial hemiplegic migraine is a rare autosomal dominant subtype of migraine with aura. Three genes have been identified, all involved in ion transport. There is considerable clinical variation associated with FHM mutations. Genotype-phenotype correlation studies are needed, but are challenging mainly because the number of carriers of individual mutations is low. One exception is the recurrent T666M mutation in the FHM1 CACNA1A gene that was identified in almost one-third of FHM families and showed variable associated clinical features and severity, both within and among FHM families. Similar studies in the FHM2 ATP1A2 gene have not been performed because of the low number of carriers with individual mutations. Here we report on the recurrence of ATP1A2 mutations M731T and T376M that affect sodium-potassium pump functioning in two Portuguese FHM families. Considerably increasing the number of mutation carriers with these mutations indicated a clear genotype-phenotype correlation: both mutations are associated with pure FHM. In addition, we show that recurrent mutations for ATP1A2 are more frequent than previously thought, which has implications for genotype-phenotype correlations and genetic testing.

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