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EDITORIAL COMMENTARY

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Commentary to 'Comorbidity in Finnish migraine families'

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The discovery that the rare subtype of migraine *familial hemiplegic migraine* is a channelopathy was a major breakthrough in migraine research [1]. Since then two other ion-channel genes have been identified as causing familial hemiplegic migraine [2, 3]. However, some families do not carry a mutation in one of the three genes identified so far. Thus, at least four genes can cause familial hemiplegic migraine, i.e., genetic heterogeneity. In order to make it even more complex, the phenotype of familial hemiplegic migraine is mimicked by sporadic hemiplegic migraine [4]. As few sporadic hemiplegic migraine cases are caused by mutations in the known genes, the majority of cases may have another cause. Comorbidity of familial hemiplegic migraine and cerebellar ataxia has been described in several families [5]. All these families carry a mutation in the CACNA1A gene, causing familial hemiplegic migraine type 1. Comorbidity of familial hemiplegic migraine and epilepsy has been described in some of the ATA2 Na^+/K^+-ATPase mutations causing familial hemiplegic migraine type 2.

The common types of migraine, i.e., migraine without aura and migraine with aura, are most likely also channelopathies, due to the paroxystic nature of the syndromes. However, the genetics of migraine without aura and migraine with aura are even more complex than familial hemiplegic migraine, as inheritance in both types is multifactorial [6–8]. Thus, the aetiology of the common types of migraine constitutes a major challenge. The paper 'Comorbidity in Finnish migraine families' by Artto et al. [9] is an important contribution on the road to clarifying what causes migraine without aura and migraine with aura. Studies of comorbidity should preferably be conducted in the general population with diagnoses ascertained by physicians in order to render the results generalisable. Artto et al. included 251 consecutive identified migraine families with at least three affected first-degree relatives ascertained by a questionnaire. This family setting is likely to increase the chance of detecting comorbid factors, assuming that migraine without aura and migraine with aura are more uniform in the familial than the sporadic form, like familial and sporadic hemiplegic migraine. Migraine without aura and migraine with aura are two distinct syndromes [10]. Thus, for scientific reasons it is important to analyse the two common types of migraine separately. Artto et al.'s main findings are the statistically significantly increased OR of hypotension, allergy and psychiatric

in migraineurs compared to non-migraineurs, and the statistically significantly increased OR of stroke and epilepsy in men with migraine with aura compared to men without migraine with aura. Some of the findings are new, while others confirm earlier reports on comorbidity. For details see reference 9. The reported comorbid disorders of migraine are all complex genetic disorders. Thus, future genetic studies face a major challenge if they are to benefit from studies of comorbidity.

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