Reviewer's report

Title: Association Analysis of Chromosome 1 Migraine Candidate Genes

Version: 2 Date: 28 February 2007

Reviewer: Pasquale Montagna

Reviewer's report:

General

This paper details the findings of a genetic association study done in a sample of migraine patients with and without aura (243 patients versus 243 controls matched for age, sex and ethnicity). Several genes were investigated, all located on chromosome 1 regions found associated with FHM type 2 and actually containing the gene ATP1A2 responsible for this disease.

The results of the association study were in the end negative for all markers, even though some significance was obtained for a marker in the KCN J10 gene at least for the overall migraine sample (p 0.02). The conclusion was reached that ATP1A2 does not contribute to the typical migraines and that indeed the genetic basis of migraine with aura is different from that of FHM, a maybe disappointing conclusion but one on which several other lines of evidence converge.

The paper is well written (except for the occasional typographical error), the rationale sound and well defined, methods are well described and appropriate.

---------------------------------------------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Arguably, the numbers may be few, some authors believing that at least 500 patients are required for an association study of this kind. I think that the authors should acknowledge this difficulty, since no power calculation was done.

Also this seems to be a Hospital population, and as such it may be not representative of the general population.

The authors should also mention that genotyping failures occurred, and what kind of quality control over the genotyping procedures was performed.

---------------------------------------------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

I take exception with the starting line in the abstract, that MA is a subtype of common migraine (“common” migraine was the old term for migraine without aura, typical is better); and with the opening sentence of the introduction (common again, and also there are no “normal” symptoms of migraine; maybe the authors mean usual or common symptoms). I am also puzzled by the description of ATP1A4 as a subunit of ATP1A2 (maybe of the Na/K ATPase? pages 3 and 10) and of CACNA1E as a subunit of CACNA1A (pages 5 and 10); Zayas et al (page 7) is not referenced properly; and the authors reported no association rather than they “did not report an association” (page 9, line 13); KCNJ9 and KCNJ10 are KCN 9 and 10 in table 3; reference 1 should be replaced by the original one; and is reference 7 the correct one?

---------------------------------------------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests