Reviewer's report

Title: Angiotensin-converting enzyme gene insertion/deletion polymorphism in migraine patients

Version: 1 Date: 6 November 2007

Reviewer: Pasquale Montagna

Reviewer's report:

General
Review of paper “Angiotensin-converting enzyme gene insertion/deletion polymorphism in migraine patients” by Tronvik et al.

This paper reports the findings of a genetic association study performed on 347 patients with migraine (either with or without aura) versus 403 controls in regard of the insertion and deletion polymorphisms of the ACE gene, previously found associated with migraine. Furthermore, it reports the findings of a pharmaco-genomic study in which genotype at the ACE gene was compared to clinical response to ACE or ARB drugs.

The results of the study were uniformly negative, thus disproving a genetic association between ACE and migraine, and also between drugs investigated and ACE genotypic status.

The text is well written, extremely clear and concise. In particular, the authors should be complimented for having performed a genetic association study on relevant numbers of patients and controls, practically approaching the limits already suggested for association studies of complex traits; these numbers are not usual in the field of migraine and this is probably at the root of the discordant results obtained in previous studies. Therefore, I regard the results obtained in this study as sound, and the conclusion thereof both appropriate and to the point.

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

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

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Discretionary Revisions (which the author can choose to ignore)

There are some points of interest (at least to this reviewer) on which the authors could comment if they wish (and can):

The unsatisfactory points that I note with this study are 2: one is that controls
were not analysed by direct interview as in the case of the migraine patients, and this could have led to the inclusion of falsely negatives in the control material; this difficulty is acknowledged in the paper. Second point, we know that some migraine without aura patients also experience migraine with aura and viceversa: how was the status of these “intermediate” patients (if any) defined in this study? Moreover: was there any difference in blood pressure status according to ACE genotype in this (patient and control) population? It is conceivable that the drugs adopted did lower blood pressure: was the amount of lowering in migraineurs related to ACE genotype?

**What next?:** Accept after discretionary 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