Reviewer's report

Title: Effects of MTHFR gene polymorphism on the clinical electrophysiological characteristics of migraine

Version: 1 Date: 27 February 2013

Reviewer: Gretchen E Tietjen

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Major compulsory revisions:
Title: Is it correct as is, or should it be “Effects...on the clinical and electrophysiological characteristics of migraine”

Background. This section is overly long going over both the epidemiology and the potential mechanisms by which the MTHFR 677TT genotype influences clinical and electrophysiological features.

The question posed needs better definition. There is mention of evaluating the effects of T allele on the clinical progression of migraine, yet this is a cross sectional study.

Methods. These need to be better described. Are the participants consecutive patients meeting enrollment criteria? The inclusion and exclusion criteria are unclear. Is it MA and MO patients who are refractory to prophylactic medications and therefore not taking them? Or is it MA and MO patients, who are 1) not taking prophylactic medications for any number of reasons, including too infrequent, or 2) severe, but refractory? Were patients allowed to discontinue prophylactic medications to participate in the study. Where did the control group come from?

The rationale for why only MO patients were evaluated electrophysiologically by RR-VEP is not stated, and how was this subset within the MO cohort chosen?

The text mentions that MO participants were free from migraine attacks, but not how long after the last attack.

Results. This is a small sample but is the distribution of genotypes across the migraine group significantly different than across the control group?

In table 1, please note if there are significant differences in each parameter across the 3 genotypes.

For the whole migraine group TT genotype shows more photophobia than CC, but not a greater number of attacks. For the whole migraine group, does the TT genotype have more resistance to therapy than the CC genotype, or is this only true in the MO cohort? How was resistance defined?

How were clinical features measured? Were there questions regarding other migraine or associated features that are not reported? How was it determined
how sensitive a person was to a particular trigger? Does “more sensitive to migraine attack triggers” mean that the persons in the group endorsed a larger number of triggers, or was sensitivity quantitatively measured?

What is the p-value for the trend that T-allele carriers had decreased N75/P100 amplitudes and a positive habituation index c/t CC patients (figures 2 and 3)?

Discussion. This section mostly recaps what is written in the Results section; there are only 2 new references. The authors mention higher rates of accompanying symptoms in TT, but this only true with regards to photophobia. There is more “resistance” in those with TT, but only for those with MO.

Minor Essential revisions: References. Citation 13 out of place in the text (mentioned before references 11, 12)

Discretionary revisions: Overall there is need for editing the language which is often stylistically awkward. Replace the phrase “statistically significant” significant.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests’