Reviewer's report

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

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Reviewer: Elisa Rubino

Reviewer's report:

The authors of this manuscript evaluated the potential relationship between different MTHFR genotypes and the clinical and electrophysiological characteristics of the disease in a group of 83 migraineurs. A significant association was found between the examined polymorphism and the accompanying symptoms of migraine, other than the electrophysiological characteristics.

The topic is of interest even if a large number of studies already suggested that the MTHFR gene variant C677T is involved in the etiopathogenesis of migraine, particularly of migraine with aura. However it adds some significant new findings about the modulation of the C677T polymorphism on the electrophysiological characteristics.

In order to improve the manuscript, I have some suggestions:

1. In the abstract, Methods section, clarification is needed with respect to the characteristics of patients (MO and MA).
2. Contrariwise to some previous studies suggesting a role for the MHTFR gene as genetic risk factor for migraine (mainly MA), your data seem not reach the same findings. In fact, in the Results section, there is a description of the genotypic distribution in patients and controls, but no statistical analysis has been shown. The authors of the manuscript must comment on these findings.
3. The definition of “resistant migraine” is lacking.
4. The Discussion, in the present form, is very weak. Neurobiological mechanisms supporting a role for the MTHFR gene in modifying the clinical characteristics must be discussed in details. Limitations of the study also need to be stated.
5. There are several typing and/or grammatical errors (pag.2 – Shurks instead of Schurks, pag.4 – ICH-2 instead of ICHD-II, etc.). In addition, a careful revision of the English language of the manuscript is necessary.

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