Reviewer's report

Title: Two-stage case-control association study of dopamine-related genes and migraine

Version: 1 Date: 9 June 2009

Reviewer: Lyn Griffiths

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Review for BMC Medical Genetics on Corominas et al 2009 paper on 2-stage case-control association study of dopamine-related genes.

This is a well written paper that outlines the results of a SNP investigation of dopamine-related genes in migraine. The authors have used a good design with well powered study populations and have used appropriate technology and statistical analysis of their results. There are only a few minor criticisms that require addressing in the manuscript.

• The authors have undertaken a number of SNP association analyses and after applying a false discovery rate of 10% found only 2 SNPs in the DRD2 and TH genes that showed association. Haplotype analyses of the tested SNPs in these genes were then undertaken, as was sub-group analyses for the DRD2 risk haplotype. It would be of interest to see if the original SNP associations in these two genes relate more to MA or MO sub-types. Results of analysis of these sub-types for the associated SNPs should be presented, as well as for the risk haplotypes for both markers.

• The authors have discussed other published results for dopamine-related genes in the Discussion section of the paper. In relation to the DBH results, they note that polymorphisms in the DBH promoter have shown association in some studies but “other DBH polymorphisms were not associated with migraine [9, 26, 32, 35]”. This is a confusing statement and does not clarify or accurately present the results from other studies – in particular in Todt et al's recently published study on dopamine-related genes in migraine with aura, the most positively associated marker for their study was a DBH non-promoter polymorphism. It is clear that the authors understand this and even discuss these results in more detail later in their discussion, but this initial inaccurate statement needs correction.

• Finally there are a few minor grammatical corrections needed in the paper including:

  - “It is to mention, however, that a …” correct to “It is worth mentioning however,…”

  - “Conversely, many evidences point to …” correct to “Conversely, much evidence points to…”
**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.