Reviewer’s report

Title: Familial association of neurological soft signs in schizophrenia: a systematic review and meta-analysis

Version: 1  Date: 8 February 2011

Reviewer: Marie-Odile Krebs

Reviewer’s report:

The paper offers a meta-analysis of studies in patients with schizophrenia, first degree relatives and controls in order to further examine whether neurological soft signs are endophenotypes (familial transmission);

The authors examined studies that were published until 2009. The meta analysis confirms that NSS are more common in first degree relatives than in controls and more common in patients than in first degree relatives.

Although, the meta analysis is well conducted and the paper is overall clear and straightforward, the paper brings only little contribution to the addressed question of familial transmission.

First there is a similar paper now published by Chan et al (Neurosci Biobehav Rev. 2010 May;34(6):889-96. Epub 2009 Nov 27)

Second, meta analysis might not be the best way to address the question since it overlook a number of pitfalls : for instance, the heterogeneity of explored populations (siblings, offspring, parents) while there is indication of age effect and heterogeneity of the scoring (qualitative rating as present /absent or semi quantitative).

Third, it cannot be definitively concluded on familial transmission only by comparing first degree relative to patients and controls. Actually a true familial transmission can only be explored by exploring intra familial transmission while in the considered studies the first degree relatives are not always related to the patients.

These two latter points should be directly addressed and documented the discussion.

Fourth, 7 studies might not be enough to truly take advantage from meta analysis as this limited number hamper some detailed analysis. An intrinsic limitation that is correctly addressed in the discussion.

Overall, the discussion could be improved. The suggestions at the end of the discussion are out of the topic since the paper does not bring any information on NSS in prodromal subjects.

In addition the discussion of endophenotype vs biomarker (and the possibility that NSS are not only related to genetic transmission ) is some what contradictory. It could be further address by quoting the studies truly exploring
intra familial transmission. Actually, there is indication in the literature that some markers of developmental markers (MPA, dermatoglyphic) may be more related to environment or gene x environment while NSS appear related to genetic transmission. If resubmitted, this paragraph should be modified or deleted

Minor points: first the authors are advised to included 2010’s studies. It is unclear why the authors selected Gourion 2003 rather than Gourion 2004 which included the 3 groups with larger sample size.

**Level of interest:** An article of limited interest

**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