Reviewer's report

Title: Epigenetic and association study of FOXP2 gene in schizophrenia

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Reviewer: Martin Poot

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Review of a manuscript entitled "Epigenetic and association study of FOXP2 gene in schizophrenia" by Amparo Tolosa, Julio Sanjuán, Adam M Dagnal, Maria D Moltó, Neus Herrero and Rosa de Frutos for BMC Medical Genetics.

This manuscript describes both a SNP-based study of putative FOXP2 haplotype association with schizophrenia and a study of DNA methylation and expression of FOXP2 in the brain. While both studies have been carried out carefully their description in this manuscript needs thorough revision.

Major Compulsory Revisions:

1. The authors treat an essentially disappointing SNP-haplotype association study on equal footing with interesting investigations of FOXP2 methylation and expression in the human brain. I would propose that the authors significantly shorten the association study part of their results section and place Table 1, which is a comprehensive listing of essentially non-significant data, in the supplement. In this way, this data will still be available, without distracting the reader from the core message of the manuscript.

2. The background section seems to direct the reader towards a study of Darwinian selection, while the data relate to an entirely different subject. The authors should re-write this section to point the readers to the pertinent literature relating FOXP2 gene function to neurodevelopmental disorders involving, among other features, impaired language development. A recent review by D.F. Newbury and co-workers (Genome Med. (2010) 2, 6), in particular the papers mentioned in their Table 1, may help to define the scope of this manuscript. The latter may also include Autism Spectrum Disorder and Gilles de la Tourette Syndrome as manifestations of perturbed language development in humans. As a consequence the list of references should be drastically reduced.

3. Likewise the abstract is not intelligible and does not really summarize the findings reported. Therefore the abstract needs to be re-written entirely.

Minor essential revisions:

1. Figures 2 and 3 seem to be switched (relative to the text of the results section and the Legends).

2. On page 11, line 9 from bottom, the authors indicate that the have tested "structural variations of the FOXP2 gene …". From what follows I guess they...
mean gene mutations (repeat expansion) or SNP haplotypes. The authors should clarify this and enter the appropriate description.

3. At multiple instances the language of this manuscript differs from common English usage. Improvements are clearly in need.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests to declare.