

## Reviewer's report

**Title:** Is FKBP5 a genetic marker of depression? A case-control study and analysis of disease related traits

**Version:** 3 **Date:** 25 July 2006

**Reviewer:** Elisabeth Binder

### Reviewer's report:

General

In this study the authors investigate the association of 3 SNPs within the FKBP5 locus and affective disorders and other disease related variables.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The authors should provide more detail on how cases and controls have been matched, especially regarding gender and age. The authors should also provide information on how ethnicity was assessed. Through-out the manuscript, the authors closely compare their data to a previous publication by Binder et al., 2004. The authors need to elaborate more on the fact that the patient composition in the 2 studies is in fact very different with 77% of bipolar patients in this study, but only 7.5% of bipolar I patients in the Binder et al., sample. So this study does in fact report a novel aspect of the genetics of FKBP5, namely the impact of FKBP5 polymorphisms on susceptibility to bipolar disorder and to disease-related variables in this disease, more so than being a replication of the findings reported by Binder et al.,. The subsample of patients with a diagnosis of major depression only consists of 57 individuals, dramatically reducing the power to detect associations specific to this disorder.

This paper reports interesting data, but the focus should be changed to the association of polymorphisms in FKBP5 with bipolar disorder (which this paper has enough power to address) and not focus so much on the replication of findings by Binder et al., as the comparable subsample with major depression is too small in this study to draw any conclusions. Introduction, results and discussion should be revised accordingly.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Is the period of in-patient treatments the sum or the average duration of hospitalization?

Figure 1 is difficult to read because the grey scales for the three SNPs are not distinguishable. A different presentation or a table format may increase clarity of the figure.

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Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

- 1) no
- 2) no

3) yes: co-patent holder of "FKBP5: a novel target for antidepressant therapy. International publication number: WO 2005/054500"

4) no

5) no