

Reviewer's report

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

Version: 3 **Date:** 21 July 2006

Reviewer: Sevilla Detera-Wadleigh

Reviewer's report:

General

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

Gawlik and colleagues report on an attempt to replicate previous findings on 3 FKBP5 SNPs that showed association with response to antidepressant treatment and number of depressive episodes (Binder et al. 2004). The sample consisted of German Caucasians identical to the ethnicity of those in the study by Binder et al. Weak evidence for association was detected in unipolar depression with the AA genotype of rs4713916 and the haplotype rs1360780 T " rs3800373 T.

Just like Binder et al (2004), the authors studied German Caucasians and used the same 3 SNPs that showed association in that previous study. Beyond these, several critical elements were different which the authors must address.

1. 77% of the samples in the present study were manic depressives. Not clearly indicated in the text is the fact that when the total sample was used for association that manic depression was the major phenotype that was being tested.
2. The titles in one of the tables and two figures indicate "affective psychosis" as the phenotype tested. This is confusing because in the description of the sample, there was no mention that the cases were psychotic. The authors must indicate the proportion of patients with psychosis in the unipolar and bipolar subsets.
3. Did the authors perform association tests solely on the manic depression subset? This would be an important analysis to include in the manuscript.
4. The diagnosis of the manic depressives needs to be mentioned, how many had bipolar I or bipolar II? Any schizoaffectives in the sample?
5. The duration of disease as defined in the text is unclear, as stated it is the "period of time between first hospitalization and age of recruitment". Do the authors mean that after the first hospitalization the symptoms did not recur?
6. Because of the issues indicated above, it makes one wonder whether the question in the title of the manuscript is appropriate.

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

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 of limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

'I declare that I have no competing interests'