Reviewer's report

Title: Association of 5HTR2A gene with suicidal behavior: Case-control study and updated meta-analysis.

Version: 3 Date: 28 November 2012

Reviewer: Marcus Sokolowski

Reviewer's report:

This is an small scale association study of one SNP in the HTR2A gene on suicidal behavior, which is then put into a broader context by meta-analysis. After Major Compulsory Revision of the points raised below, it might be of interest for the journal and its readers, given its the first such study in the Mexican population.

1. Background:
"Recently, several lines of evidence have suggested that altered serotonergic neural transmission is involved in the pathogenesis of suicidal behavior [3, 4]."

This suggestion is not "recent", studies have suggested a role for serotonin since at least the 1980s.

2. Background:
"more than 200 SNP along the gene have been identified [10, 12]. However, only a small number of SNPs have so far been investigated as candidates for suicidal behavior."

A recent publication "Ben-Efraim YJ, Wasserman D, Wasserman J, Sokolowski M. 2012. Mol Psych." investigated all SNPs HTR2A in relation to suicide attempts, which should be of interest to reference here.

3. Methods, Clinical evaluation:
"Following the reports in the literature, we defined suicide attempt as a self-harm behavior with at least some intent to end one's life."

Can this definition of the suicide attempt be described more specifically, or is this whole definition that was used?

4. Discussion:
Add to the discussion other aspects raised in "Ben-Efraim YJ, Wasserman D, Wasserman J, Sokolowski M. 2012. Mol Psych.", as to why no association is found in meta-analysis, e.g. possible roles of different genetic inheritance models, epigenetics and/or GxEs.

5. For limitations, another one should be that the e.g. cases used in the current study seem not very well defined, neither for their "suicidal behavior" per se or
other suicide-related psychopathologies or covariates, e.g. "DSM-IV Axis-I and II diagnoses" mentioned in the Methods section are not described. Also, the drawbacks of case-control designs may be of interest to mention.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests’