Reviewer’s report

Title: Lack of association between serotonin transporter gene polymorphism 5-HTTLPR and smoking among Polish population: a case-control study.

Version: 1 Date: 20 June 2008

Reviewer: Ming Li

Reviewer’s report:

This manuscript reports an association study of 5-HTTLPR with smoking in a Polish sample. Their results reveal no association of the 5-HTTPLP L/S alleles with smoking dependence in their sample. Generally speaking, the ms is well-written and easy to follow. However, there are following concerns that should be addressed prior to be accepted for publication.

1) One of the major concerns is sample size used in the study. It is very clear the sample size is relatively small. Given such a sample size, it has limited power to detect association even it was there. So, it is strongly suggested that the authors discussed this point.

2) The second concern is about the criteria used for the categorization of cases and controls. By using “ever-smokers” as cases may open up several issues. 1) It gives the impression that the authors were trying to study the genetics for ever smoking (a cigarette) rather than genetics of nicotine dependence. There is no mentioning in the paper whether they excluded subjects who did not meet criteria for nicotine dependency, in association analyses for allele frequencies and quantitative measures. From Tables 2, we can see the FTND scores for the 2 groups analyzed for quantitative measures were above 5. Thus, the authors should state clearly in the methods section, whether all cases (smokers) in their analyses had met criteria for nicotine dependence. If indeed the authors were trying to study 5-HTTLPR associations with ever smoking (a cigarette), then they should explain the basis for this hypothesis in detail in the introduction.

3) In the Introduction section, while the authors discussed the progress of genetic study on nicotine dependence, it is suggested that the authors use more updated references, instead of those ones published prior to 2000. This is because significant progress has been made during the past years. The authors should update their literature.

4) Also, in the Introduction section, it is suggested that the authors point out sample size in those early study on this polymorphism with smoking. This is important for readers to know those results might have power issue as well.

5) Describe all the quantitative measures for smoking tested in the study, in a separate paragraph in the methods section.

6) Listed medications for other psychiatric disorders can alter smoking patterns. It is not stated whether these 17 smokers were excluded from smoking quantity association analyses. If they were not, that may have been a factor for not seeing
an association with quantitative measures.

7) Finally, more attention should be paid to the writing style of the paper in general. For example, in the discussion section, it states “In the surveyed population from the North of Poland, we found 36% of carriers of the 5-HTTLPR short variant allele, which has been hypothesized to exert a protective effect against smoking [13, 15].” ; this sentence does not clearly indicate whether the 36% of S-carriers were in the whole cohort or in the smoking sample.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.