Reviewer's report

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

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Reviewer: Marcus Munafo

Reviewer's report:

This manuscript reports data which fail to show an association between the 5-HTTLPR variant and smoking status. In principle I am supportive of the publication of null results, to avoid publication bias. However, I have several recommendations regarding revisions that might be necessary before this were to happen.

Major Compulsory Revisions:

My main confusion lies with the phenotype definition - in most places this is described as ever vs never smoking, whereas in the detailed description it appears to be ever vs ex smoking. This itself is not an appropriate comparison, since ever smokers will include current and ex smokers. The comparison of ever vs never smoking (i.e., smoking initiation) is appropriate but, given the social context, I would be surprised if the authors genuinely mean "never" smoking. Indeed, the authors themselves allude to this, describing smoking as a "national habit" within Poland. Far more clarity is required regarding the phenotypes under investigation. Moreover, the lack of biochemical verification of smoking status is problematic.

In addition, the sample size is plainly insufficient to detect small genetic effects, which are likely for single loci and complex behavioral phenotypes. Although studies of similar size have been published in the past, there is growing consensus that sample sizes in the 100s are insufficient, and those in the 1000s will be necessary to provide sufficient statistical power. A much shorter brief report, detailing the lack of observed association for the smoking phenotypes only, might be valuable to avoid publication bias in the literature, but the current report is not justified as it lacks the power to meaningfully exclude a plausible (but small) effect of the 5-HTTLPR.

Minor Essential Revisions:

Relatedly, the discussion of psychiatric co-morbidity, and the familial aggregation of smoking behavior etc., is unnecessary. These effects are already well-established, and do not bear on the central question of whether variation at the 5-HTTLPR influences smoking behavior.

A SNP within the 5-HTTLPR has recently been reported, which appears to modify the effect of the L allele. It appears that the authors did not genotype this
variant, in which case they should discuss this as a limitation of this study, in particular as the result is likely to be a reduction in statistical power.

Discretionary Revisions:

In some places the language is somewhat difficult to follow - the manuscript might benefit from some minor editing for style.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests.