Reviewer's report

Title: Influences of polymorphic variants of DRD2 and SLC6A3 genes, and their combinations on smoking in Polish population

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Reviewer: Marcus Munafo

Reviewer's report:

This manuscript reports the results of a genetic association study of the DRD2 Taq1A and SLC6A3 VNTR polymorphisms and smoking status, and a range of smoking-related phenotypes such as age at initiation and heaviness of smoking. The manuscript is well-written and concise. However, the small sample size is a considerable concern.

The proliferation of under-powered genetic association studies has led to concerns that the literature may contain more false positives than true positives, and that this hampers our attempts to further our understanding of the neurobiology and genetic architecture of complex phenotypes such as tobacco dependence.

The authors are correct that simple categorical phenotypes such as smoking status may not do justice to the complexity of smoking behaviour, but this advantage (of testing multiple phenotypes) is offset in this study by very low statistical power and the use of uncorrected alpha levels for statistical significance.

These problems are further compounded by the investigation of multiple genetic variants (and their interactions). This, in conjunction with the multiple phenotypes tested, raises the multiple statistical testing burden considerably. It is also not clear whether any further testing of unreported genetic variants took place.

The study is technically sound (in terms of phenotype definition, genotyping, etc.), and I am sympathetic to the need to publish the results of all genetic association studies to minimise the risk of publication bias, but this needs to be weighed against the risks associated with further flooding the literature with false positives.

Major Essential Revisions

A brief report, clearly describing the number of genetic variants (and their interactions) and the number of phenotypes examined, using a corrected alpha level for the corresponding number of statistical tests, would be more helpful, even if this means that the reported results are described as non-significant.

Level of interest: An article of limited interest
Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests.