Reviewer's report

Title: Insights into the genetics of blood pressure in black South African individuals: The Birth to Twenty cohort

Version: 1 Date: 15 Oct 2017

Reviewer: Tamar Sofer

Reviewer's report:

I commend the authors for performing an association study in a relatively under-studied population of south African individuals. The study population is very small in GWAS terms, limiting the power to discover genetic associations.

The major limitation of this manuscript is the lack of replication. Given that some association results are freely available online, the authors should at least perform a look-up of the top results in their GWAS, in such studies. For example, in the website https://grasp.nhlbi.nih.gov/FullResults.aspx there are results from Liu et al. (Nat Gen 2016), which include a GWAS of BP traits in African Americans. It will be also useful to perform generalization analysis, in which previously reported genetic associations are investigated in the current study, to examine the genetic overlap between populations. This is increasingly done in GWAS of relatively small populations.

Other comments:
1. Please describe the methods more thoroughly. For example:
   a. How was the subset of individuals from the Birth to Twenty cohort selected for genotyping? at random?
   b. How did you compute and center the relatedness matrix?
   c. How many PCs did you adjust for? how did you determine how many PCs to use? (you referred to QQ plots?).
   d. How did you compute the number of unlinked markers?
   e. Did some of the study individuals use anti-hypertensive medications? if so, how did you account for it?

2. It is great that you provided in Table 1 allele frequencies of Bt20, YRI, and CEU. A discussion about it would be useful. (E.g. is it surprising that some detected variants are common in CEU but are unknown to be associated with BP in populations of European ancestry?).

3. In table 1, please provide results for both traits, in all rows.

4. Figure 1: what do you mean by “with correction for covariates and PCs where necessary”? did you not use a single approach for all traits and SNPs?
5. I recommend re-writing the last paragraph of the discussion, so that the first sentence states what it is about. Currently it seems like it is about the PAGE study, but in fact it is about the Metabochip, and the implications of using it.

6. Hypertension analysis: the KCNQ1 gene is association with Diabetes, including an African-American specific allele reported in Qi et. al. (Diabetes, 2017).

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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