Reviewer's report

Title: Genomewide Association Study for Onset Age in Parkinson Disease

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Reviewer: jeff M vance

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For Authors:

This is a manuscript examining age at onset in Parkinson Disease from GWAS data. This study examined age at onset in their GWAS data, then used publically available data for a second GWAS. They then did a meta-analysis of the two studies and took the top findings to a replication dataset. That said, many of the same associations for PD have been reported as either age at onset or risk, usually depending on the type of dataset (multiplex or case-control). The authors did not discuss this point, nor did they discuss how their age at onset results matched their risk results.

Comments:

1) Age at onset analysis has been previously done with linkage analysis and follow-up of those results, but not directly reported from GWAS. There is essentially no discussion of previous studies and how their findings relate to other studies. Certainly, given the weak findings from this study, that would have added interest, rather than the standard paragraphs on possible candidate genes suggested by the study.

2) interestingly the authors focused on SNPs and not genes. While this allows for comparison across datasets, if a gene has biological relevance, there may be other SNPs in the gene that are more informative in one dataset than another, as it is highly unlikely that the SNPs measured are driving the actual association if real.

3) Was there stratification studies done? It is very clear from the literature that stratification can affect not only association but the allele associated with risk or later onset.

4) The different cutoffs for age in the samples could be a problem.

5) One complication of this approach is that two different genotyping platforms were used. One can assume this is one of the reasons for meta-analysis, but the authors need to rationalize that approach.

6) Discussion is needed about multiple testing. The authors did a large amount of imputed SNPs and tested three genetic models.

7) How many SNPs survived QC protocols after imputation? Were the
associations seen at imputated or genotyped SNPs?

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

**Quality of written English:** Acceptable

**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 interestes.