Supplementary information for a systematic review of associations between common SNCA variants and clinical heterogeneity in Parkinson's disease

Supplementary excel files

Supplementary Table 1. Risk of bias assessment for the articles included in the review

Supplementary Table 2. Summary of the polymorphisms identified in the review

Supplementary Table 3. Summary of the outcomes and polymorphisms reported in each article included in the review

Supplementary Table 4. Exclusion criteria used to screen studies from the database search.

Exclusion criteria

Not primary literature

Not Parkinson's disease

Only LRKK2-associated Parkinson's disease

Clear diagnostic criteria not reported

Genetic polymorphisms not in SNCA gene region

Genetic variants other than individual polymorphisms considered, e.g. haplotypes, mutations or copy number variations

Only the association with risk of developing Parkinson's disease reported

Only the association with neuroimaging markers reported

Subgroups of patients with Parkinson's disease only compared to healthy controls

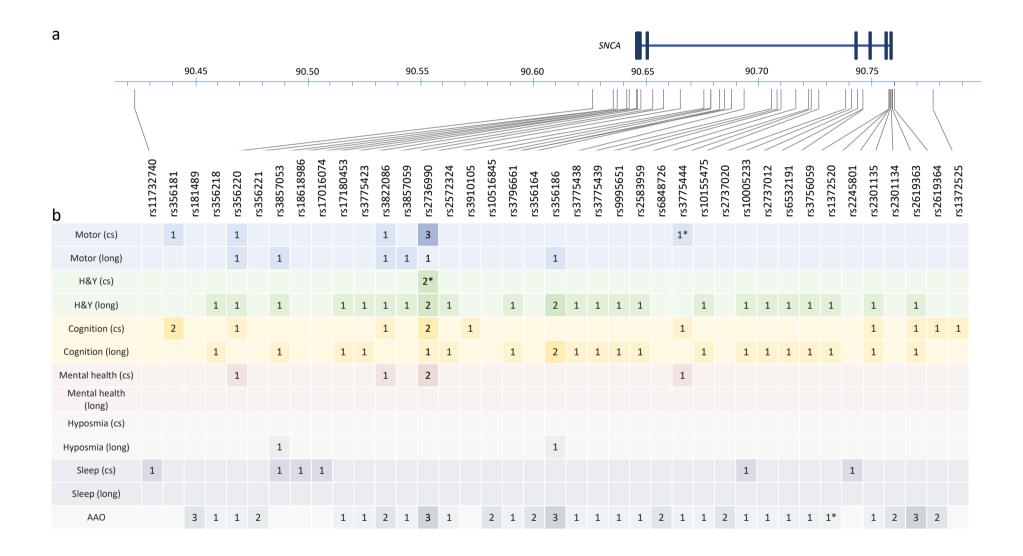
The study was only descriptive

In a language other than English

Supplementary Table 5. Search terms used to identify studies related to the objective of the systematic review.

	PubMed	Web of science
Search terms	(parkinson*) AND (SNCA) AND (variant* OR polymorphism* OR SNP* OR GWAS OR genome-wide) English filter on	ALL FIELDS: ((parkinson*) AND (SNCA) AND (variant* OR polymorphism* OR SNP* OR GWAS OR genome-wide)) LANGUAGE: (English)
		DOCUMENT TYPES: (ARTICLE OR REVIEW)
		Timespan: All years.
		Indexes: SCI-EXPANDED, SSCI, A&HCI, ESCI.
Yield	472 results	451 results

Supplementary Figure 1.



Supplementary Figure 1. Summary of *SNCA* polymorphisms identified in this review that were reported not to be associated with clinical outcome measures or age of onset.

- (a) Schematic of SNCA showing the location of each polymorphism. Exons indicated by boxes. Chromosome 4 positions according to GRCh 37. Adapted from the output generated by LDLink.¹ (b) The number of studies reporting no significant association between a clinical outcome with the polymorphism indicated. The analysis of clinical outcomes is separated according a cross-sectional or longitudinal study design, and accordingly, a study can be recorded more than once if both designs were included in the manuscript. For full details of the studies are given in Supplementary file 3 and 4.
- * The p value for the unadjusted association test was <0.05 but the authors reported it not to remain significant after adjustment for multiple testing or covariates.

References

Machiela, M. J. & Chanock, S. J. LDlink: a web-based application for exploring population-specific haplotype structure and linking correlated alleles of possible functional variants. *Bioinformatics* **31**, 3555-3557, doi:10.1093/bioinformatics/btv402 (2015).

Supplementary Figure 2.

SCREENING OF THE PRIMARY SEARCH RESULT: TITLE AND ABSTRACT **Exclusion examples:** NO Reason: START: Original article? Review, opinion, book chapter, off topic comment, editorial, reply **Exclusion examples:** NO Study reports results Reason: Other patient groups, animal models, from PD patients fundamental research (cell models off topic etc.) NO **Exclusion examples:** ... and common genetic Reason: Rare mutations or other variants in SNCA region Off topic genes/genomic regions studied ... and outcomes were any NO Exclusion examples: Reason: clinical feature attributed to Gene-environment studies, Off topic PD or age at onset neuropathology outcomes etc. ADD TO FULL TEXT LIST **EXCLUDE**

Supplementary Figure 2. Flow diagram for the first round of screening of the articles identified by the database searches. In the first round of filtering, articles were excluded for clearly not meeting the inclusion and exclusion based on the contents of the title and abstract. If the relevance was unclear from the title/abstract alone, the article proceeded to the next step of the screening process.