Title

Eating Disorders and Parkinson's Disease—2: Genetic Epidemiology and Shared Genomics

Journal

European Eating Disorders Review

ISSN

1072-4133

Authors

Bergen, Andrew W

Makowski, Carolina

Garvin, Michael

et al.

Publication Date

2026-09-09

DOI

10.1002/erv.70158

European Eating Disorders Review

WILEY

BRIEF REPORT

Eating Disorders and Parkinson's Disease—2: Genetic Epidemiology and Shared Genomics

Andrew W. Bergen[1] | Carolina Makowski[2] | Michael Garvin[1] | Gulcan Cil[1] | Angeline Krueger[2] | Karlee McGlone[2] | Irene Litvan[2] | Heather Hower[2] | Walter H. Kaye[2]

[1]Oregon Research Institute (ORI), Springfield, Oregon, USA | [2]University of California San Diego (UCSD), La Jolla, California, USA

Correspondence: Andrew W. Bergen (abergen@ori.org)

Received: 21 November 2025 | **Revised:** 12 July 2026 | **Accepted:** 20 July 2026

Handling Editor: Nadia Micali

Keywords: anorexia nervosa | epidemiology | genetic pleiotropy | genomics | Parkinson's disease

ABSTRACT

Objective: Individuals with anorexia nervosa (AN) share premorbid traits with Parkinson's Disease (PD) (e.g., anxiety) and exhibit a two-fold relative risk of a reported family history of PD. Published estimates of intra- and inter-disorder genetic architecture were extracted and compared prior to conducting novel analyses to provide evidence for cross-disorder genetic risk.

Methods: National register or meta-analytic familial, twin, and common variant genome-wide studies were searched; estimates and findings were extracted and compared. Novel cross-disorder conditional and conjunctional false discovery rate analyses were performed.

Results: Sibling relative risks and additive genetic estimates of the two disorders were similar. AN had greater common variant heritability than PD whether measured via infinitesimal model (linkage disequilibrium score regression, LDSC) or causal mixture model (MiXeR). AN had greater polygenicity than PD (mean (SD) 2.50E-03 (1.64E-04) versus 2.72E-4 (1.47E-05), $p < 0.001$), but lower discoverability than PD (4.20E-05 (2.69E-06) versus 1.40E-04 (6.95E-06), $p < 0.001$). Global genetic correlation was significant (e.g., bivariate LDSC $r_g = 0.10$, $p = 0.0033$). Novel analyses identified cross-disorder enrichment, and cross-disorder risk at chr3p21.31.

Conclusions: Cross-disorder AN and PD research identified shared risk variants at chr3p21.31, genes and mechanisms (e.g., conditioning, fear, and reward) linked to a shared endophenotype.

1 | Introduction

Anorexia nervosa (AN) is a complex neuropsychiatric-metabolic eating disorder (ED) with a strong genetic component, common early onset, and substantial morbidity and mortality (Bulik et al. 2022; Kaye and Bulik 2021; Watson et al. 2019). Parkinson's Disease (PD) is a neurological disorder with significant interactions between genetic and environmental factors, common late onset, and progressive movement impairment (Ben-Shlomo et al. 2024; Noyce et al. 2019).

While AN may appear unrelated to PD given differences in age of onset and course, the disorders share traits in multiple domains, suggesting a common genetic vulnerability (Krueger et al. 2026). Shared characteristics include dopaminergic alternations (Jiménez-Jiménez et al. 2014; Kaye et al. 2020), premorbid anxiety (Marzola et al. 2019; Overton and Coizet 2020), harm avoidance (Atiye et al. 2015; Santangelo et al. 2018), and weight loss and reduced adiposity (Hebebrand et al. 2025; Pak et al. 2018; Noyce et al. 2019; Duncan et al. 2017).

Highlights

- Anorexia nervosa (AN) and Parkinson's Disease (PD) have similar intra-disorder relative risk, and robust additive genetic and non-shared environmental risks.
- AN has more estimated causal variants accounting for a larger portion of genetic risk than PD, but their average effect size is smaller, requiring larger sample sizes for discovery.
- AN and PD are globally genetically correlated and share risk variants at chr3p21.31, the second densest region of cross-disorder findings in psychiatry.

Indeed, comprehensive analysis of genome-wide association scan (GWAS) analyses of psychiatric and neurological disorders found significant shared genetic risk architecture between AN and PD (Smeland et al. 2025). Common variant genetic correlations between AN and PD were identified via multiple methods, including common variant polygenic correlation, specification of heritability, and causal mixture modelling (Bulik-Sullivan et al. 2015; Speed and Balding 2019; Holland et al. 2020). Review of AN and PD comorbidities and neurobiology suggested shared aetiologies, and a clinical study of family history demonstrated a significant two-fold relative risk of a reported family history of Parkinson's Disease in individuals with AN (Krueger et al. 2026).

The present study aimed to build upon these neurobiological, genetic, and clinical findings by reviewing intra- and inter-disorder measures of genetic architecture and conducting a search for shared variants. We had three research questions: (1) What are the intra-disorder genetic architectures of AN and PD?; (2) What is the common variant global genetic correlation between AN and PD?; and, (3) What common variants are identified in novel cross-disorder analysis of AN and PD? For questions 1 and 2, we extracted, compared and discussed existing estimates to provide context for cross-disorder research. For question 3, we hypothesised there would be genome-wide significant (GWS) shared variants, and that such variants might inform our understanding of risk factors shared between AN and PD.

2 | Methodology

2.1 | Study Design

We compared extracted genetic and genomic epidemiologic measures from the literature and we present the results of novel secondary data analysis of GWAS summary statistics.

2.2 | Literature Search

The genetic and genomic epidemiologic literature was searched to find generalisable studies by sample base or number of component studies, that is, national registry analyses, or clinically-based meta-analyses. See Supporting Information S1.

2.3 | Extracted Measures

We extracted measures of sibling relative risk, twin model parameters, common variant heritability, polygenicity and discoverability, and global genetic correlation. We report mean estimates, 95% Confidence Intervals (95CI), standard deviation of the sample, or standard error of the mean as provided by data sources. We used a test of interaction to compare sibling familial risk estimates (Altman and Bland 2003), and either a Z-score test or t-test to compare mean estimates; tests were two-sided and $\alpha < 0.05$.

2.4 | Novel Analyses

2.4.1 | *AN and PD Locus Overlap*

We extracted GWS single nucleotide polymorphisms (SNPs), genes and linkage disequilibrium (LD) regions from published AN GWAS (Duncan et al. 2017; Watson et al. 2019). We searched the National Human Genome Research Institute-European Bioinformatics Institute (NHGRI-EBI) GWAS catalogue (Cerezo et al. 2025) for associations at these SNPs, genes and linkage disequilibrium (LD) regions with PD, and PubMed for mechanistic associations with PD. We calculated LD statistics (Gabriel et al. 2002) from 1000 Genomes Project HapMap data (Fairley et al. 2020) using LDpair (Machiela and Chanock 2015).

2.4.2 | *Novel Analyses for Shared SNPs*

We performed novel cross-trait enrichment between AN and PD using conditional and conjunctional false discovery rate (condFDR and conjFDR) analyses (https://github.com/precimed/pleiofdr) (Smeland et al. 2020; Andreassen et al. 2013). Briefly, condFDR was first applied, which conditions the GWAS summary statistics for each pair of traits onto each other in both directions. We then applied conjFDR to extract the maximum of the two mutual condFDR for a specific SNP. Openly available summary statistics were prioritised, where AN data were obtained from the Eating Disorders Working Group of the Psychiatric Genomics Consortium and PD data were obtained from http://research-pub.gene.com/chang_et_al_2017. Given the exploratory nature of these analyses, we first utilised a stringent 0.05 FDR whole-genome significance threshold, and explored results at a more liberal 0.10 FDR threshold.

SNPs with conjFDR $p > 0.05$ and $p < 0.10$ and those in LD ($r^2 > 0.6$) were mapped to genes using positional, gene expression (eQTL), and chromatin interaction information in the SNP2GENE modules of Functional Mapping and Annotation (FUMA) (Watanabe et al. 2017); FUMA extracts and integrates data using multiple databases summarising SNP location and effects relative to gene structure, gene and protein sequence, coding and conservation; effects on gene expression; and long-range chromatin interactions.

When the text introduces a SNP, the reference SNP cluster ID (rsID), chromosome coordinate (hg19 genome assembly) and physical location with respect to gene structure are given (https://www.ncbi.nlm.nih.gov/snp/).

3 | Results

3.1 | Genetic Epidemiology Measures

See Table 1 for extracted measures and Supporting Information S1 for details on the literature search, short descriptions of the measures, studies chosen to extract and compare measures, and GWASs selected by Anttila et al. (2018), Smeland et al. (2025), and this study for cross-disorder analyses (Smeland et al. 2025; Anttila et al. 2018).

3.1.1 | *Familial Risk Estimates*

We compared sibling risk estimates from: a population-based cohort study of AN risk leveraging 1969-2004 data from the Danish Psychiatric Central Research Register (Steinhausen et al. 2015), a meta-analysis of PD family history studies published between 1967 and 2006 (Thacker and Alberto 2008), and a population-based cohort study of PD risk using 1999–2015 data from the Taiwanese National Health Insurance Research Database (Liu et al. 2018). The population-based cohorts adjusted for demographics; Liu et al. (2018) used population prevalence instead of control families to calculate sibling risk. Sibling relative risk estimates for AN and for PD were between two and four; there were no significant differences between the estimates (p-values > 0.113).

3.1.2 | *Additive Genetic and Shared and Non-Shared Environment (ACE) Model Parameters*

Studies using data from the Swedish Twin Registry were chosen to compare ACE model parameters. The AN study reported parameters with 95CIs in female twins born between 1935 and 1958 in two AN models by source of diagnostic information, narrow (structured clinical interview) and broad (multiple sources) (Bulik et al. 2006); the PD study reported parameters without 95CIs in 18 models including two sets of twins born before 1953 with longitudinal or cross-sectional ascertainment, and two diagnostic models, narrow (PD diagnoses) and broad (PD and parkinsonism) (Wirdefeldt et al. 2011). We chose to report the results from the narrow models. For AN, modelling indicated all three variance components may be contributing to liability using 95CI as an indicator, where a^2 and e^2 95 CIs excluded zero. For PD, modelling of the longitudinal sample indicated A and E are important variance components in both women and men, with a non-zero C parameter estimated in the unconstrained female model. There were no significant differences between AN and PD parameter estimates (p-values > 0.472).

3.1.3 | *Common Variant Heritability (h^2_g)*

We extracted h^2_g estimates calculated using the univariate LDSC model in each of two recent comprehensive analyses of brain disorders (Smeland et al. 2025; Anttila et al. 2018) and h^2_g estimates calculated using the univariate MiXeR model (Smeland et al. 2025; Anttila et al. 2018). In all comparisons, AN h^2_g exceeded PD h^2_g (p-values < 0.015).

3.1.4 | *Mixture Model Polygenicity and Discoverability*

Polygenicity (proportion and number of causal variants) of AN was an order of magnitude greater than that of PD (Smeland et al. 2025). Discoverability (effect size variance of causal variants) of AN was an order of magnitude smaller than that of PD (Smeland et al. 2025). AN and PD estimates were significantly different (p-values < 0.001).

3.1.5 | *Common Variant Genetic Correlation*

Genetic correlation estimated in the Anttila et al. (2018) analysis was non-significant ($p = 0.77$). Estimated r_gs with effective AN and PD sample sizes five and 10 times larger were significant and similar in magnitude by inspection: bivariate LDSC $r_g = 0.10$, $p = 0.0033$; bivariate MiXeR $r_g = 0.09$, SD = 0.01 (Smeland et al. 2025).

3.2 | AN and PD GWAS Locus Overlap

AN and PD GWAS locus overlap from the GWAS catalogue are summarised in Table 2. The chr3p21.31 SNP rs9821797 (chr3:48,718,253; *NCKIPSD* IVS5) was the lead AN SNP in a region of SNPs with $p <$ 1E-5 and $r^2 > 0.1$ spanning 3.79 Mbp with 95 protein-coding genes, assigned to *NCKIPSD* by proximity (Watson et al. 2019). This region includes the SNP rs12497850 (chr3:48,748,989; *IP6K2* IVS1), associated with PD and assigned to *IP6K2* by eQTL analysis (Chang et al. 2017; Nalls et al. 2019). The AN SNP and the PD SNP (30 kilobasepairs distal) are in LD ($D' = 0.92$ and $r^2 = 0.23$, $\chi^2 = 235.1$, $p < 0.0001$).

3.3 | AN and PD Shared Risk SNPs

Motivated by a significant r_g of 0.10 ($p = 0.0033$) found in Smeland et al. (2025) obtained through LDSC, cross-disorder analyses with conjFDR were explored to identify SNPs shared between AN and PD. It is important to note that the total number of matching SNPs between the AN and PD datasets was limited to 7411 given the reduced number of SNPs in the openly available summary statistics, reducing power for cross-disorder analyses. Nevertheless, cross-disorder enrichment is visible in the combined conditional quantile-quantile plot where PD nominal p-values conditional on AN p-values show substantial enrichment; AN nominal p-values are truncated due to the much lower number of significant p-values, however, a slight enrichment is observed at a empirical $-\log_{10}(q)$ of 3 (Figure 1).

Although no SNPs were found at the stringent FDR < 0.05 threshold, exploratory analysis at a more liberal threshold of FDR < 0.1 revealed one putatively shared risk SNP (rs12497850, chr3:48,748,989; *IP6K2* IVS1) between AN and PD (Tables 3 and 4; Figure 2). This SNP was the same SNP identified as GWS for PD in the AN chr3p21.31 region (Chang et al. 2017; Nalls et al. 2019). We mapped this SNP to 42 genes using FUMA, where four genes were mapped by all methods (*NCKIPSD*, *P4HTM*, *WDR6*, and *DALRD3*) and one by all methods excluding chromatin interaction (*IP6K2*); most genes were mapped using gene expression and chromatin interaction methods (Supporting Information S1: Table S3).

4 | Discussion

We hypothesised existing findings and novel analyses might provide evidence to support AN and PD cross-disorder research. Common neurobiological, psychological, and metabolic characteristics, a family history study, and estimates of global genetic correlation indicated common genetic factors, however, a search

TABLE 1 | Familial, twin and common variant measures of anorexia nervosa (AN) and Parkinson's disease (PD) and sources.

Measure	Measure detail	AN estimate(s) (95 CI)	Sources of data and estimates	Measure detail	PD estimate(s) (95 CI)	Sources of data and estimates
Sibling relative risk (RR)[a] Case/Control sample size	Conditional logistic OR (95% CI)[b]	3.45 (1.93–6.17) 5224 case probands & siblings/16,327 control probands & siblings	Steinhausen et al. (2015) Table 4	Meta-analytic random-effects RR and adjusted RR[c]	4.4 (3.1–6.1) and 2.20 (1.41–3.45)	(Thacker and Alberto 2008, Table 3) and (Liu et al. 2018, Table 3)
Diagnostic model Twin ACE model estimates Twin pair sex & sample size	Narrow AN diagnosis Parameter estimates for additive genetics (a^2), shared environment (c^2) and non-shared environment and measurement error (e^2)	Narrow AN diagnosis a^2 = 0.56 (0.00–0.87), c^2 = 0.05 (0.00–0.64), e^2 = 0.38 (0.13–0.84) 49 female pairs	Bulik et al. (2006) Abstract and Table 5	Narrow PD diagnosis Longitudinal design Parameter estimates (a^2, c^2, and e^2)	a^2 = 0.19, c^2 = 0.12, e^2 = 0.69 267 female pairs a^2 = 0.34, c^2 = 0.00, e^2 = 0.66 259 male pairs	(Wirdefeldt et al. 2011, Table 4) (95 CIs not reported)
LDSC heritability (h^2_g), liability scale Case (Ca)/Control (Co) N[d] Effective sample size, ESS[e] Population prevalence, PP Assumed lifetime risk, ALR	LDSC h^2_g (SE) Ca/Co N ESS PP and LDSC h^2_g (SE) Ca/Co N ESS ALR	0.172 (0.023) 3495/10,382 10,633 0.006 and 0.1345 (0.0090)[f] 16,992/55,525 52,042 0.009	(Duncan et al. 2017; Anttila et al. 2018, Table S1) and (Watson et al. 2019; Smeland et al. 2025, Table S1)	LDSC h^2_g (SE) Ca/Co N ESS PP and LDSC h^2_g (SE) Ca/Co N ESS ALR	0.105 (0.017) 5333/12,019 14,776 0.002 and 0.0817 (0.0092) 20,184/397,324 76,833 ALR = 0.016	(International Parkinson's Disease Genomics Consortium (IPDGC), and Wellcome Trust Case Control Consortium 2 (WTCCC2) 2011; Anttila et al. 2018, Tables S1 & S2) and (Smeland et al. 2025; Nalls et al. 2014, 2019; Chang et al. 2017, Table S1)
MiXeR heritability (h^2_g), liability scale Ca/Co N, ESS, ALR	MiXeR h^2_g (SE) Ca/Co N ESS ALR	0.1170 (0.0026) 16,992/55,525 52,042 0.009	(Watson et al. 2019; Smeland et al. 2025, Table S1)[g]	MiXeR h^2_g (SE) Ca/Co N ESS ALR	0.0683 (0.0026) 20,184/397,324 76,833 0.016	(Smeland et al. 2025; Nalls et al. 2014, 2019; Chang et al. 2017, Table S1)[g]
MiXeR heritability (h^2_g), observed scale Ca/Co N, ESS, ALR	MiXeR h^2_g (SE) Ca/Co N ESS ALR	0.2173 (0.0035) 16,992/55,525 52,042 0.009	(Watson et al. 2019; Smeland et al. 2025, Table S2)[h]	MiXeR h^2_g (SE) Ca/Co N ESS ALR	0.0789 (0.0014) 53,858/846,380 202,543 0.016	(Smeland et al. 2025; Nalls et al. 2014, 2019; Chang et al. 2017, Table S2)[h]

(Continues)

TABLE 1 | (Continued)

Measure	Measure detail	AN estimate(s) (95 CI)	Sources of data and estimates	Measure detail	PD estimate(s) (95 CI)	Sources of data and estimates
Polygenicity (π_1), proportion of causal variants, and *N* causal variants (*N*c) to explain 90% variance	π_1 (SD) and Nc (SD)	2.50E-03 (1.64E-04) and 7983 (523)	(Watson et al. 2019; Smeland et al. 2025, Table S2) Sample size as above	π_1 (SD) and Nc (SD)	2.72E-4 (1.47E-05) and 867 (47)	(Smeland et al. 2025; Nalls et al. 2014, 2019; Chang et al. 2017, Table S2) Sample size as above
Discoverability (σ^2_β), Effect size variance per causal variant	Effect size variance of causal variants (σ^2_β)	4.20E-05 (2.69E-06)	(Watson et al. 2019; Smeland et al. 2025, Table S2) Sample size as above	Effect size variance of causal variants (σ^2_β)	1.40E-04 (6.95E-06)	(Smeland et al. 2025; Nalls et al. 2014, 2019; Chang et al. 2017, Table S2) Sample size as above

Abbreviations: OR = Odds Ratio; SD = standard deviation; SE = standard error.
[a]Risk of disorder in proband and sibling with disorder versus no disorder in proband and sibling with disorder or versus population prevalence rate.
[b]Adjusted for age, sex, year of birth, month of birth and region.
[c]Prevalence ratios between individuals with affected relative and general population; adjusted for age, sex, residence, income, occupation, and family size.
[d]For ascertainment of cases (Ca) and controls (Co), see Supporting Information.
[e]ESS = the calculated effective sample size corresponding to a 1:1 case:control ratio (4 × total sample size x proportion of cases x proportion of controls), used in calculating LDSC and MiXeR model heritability and genetic correlation.
[f]Watson et al. used a range of lifetime prevalence (0.9%–4%) and estimated LDSC h^2_g (SE) which ranged from 0.11–0.17 (0.01).
[g]MiXeR heritability estimates were transformed from the observed scale for case:control disorder into the liability scale and (to match LDSC heritability calculation) removed cohorts containing proxy cases from PD heritability estimates.
[h]MiXeR heritability estimates were calculated and reported on the observed scale and included cohorts with proxy cases.

TABLE 2 | Genome-wide significant (GWS) AN loci, genes, LD region, protein names and GWS loci for PD.

SNPs, gene(s), and/or LD region reported by GWAS	Recommended protein name (UniProt Consortium 2025)	Search NHGRI-EBI GWAS catalogue for: SNP, gene(s), or LD region, & "Parkinson"
rs4622308, chr12:56075401; Genes (all gene-wise significant): chr12q13.2-13.3: *PMEL*, *CDK2*, *RAB5B*, *SUOX*, *IKZF4*, *RPS26*, *ERBB3*, *ENSG00000257411*, *PA2G4*, *RPL41*, *ZC3H10*, *ESYT1*, and, *chr12q14.1*: *TAFA2/FAM19A2* (Duncan et al. 2017)	Melanocyte protein PMEL, Cyclin-dependent kinase 2, Ras-related protein Rab-5B, Sulphite oxidase, mitochondrial, Zinc finger protein Eos, Small ribosomal subunit protein eS26, Erb-b2 receptor tyrosine kinase 3, Proliferation-associated protein 2G4, Small ribosomal subunit protein eS32, Zinc finger CCCH domain-containing protein 10, Extended synaptotagmin-1, TAFA chemokine like family member 2 (formerly, family with sequence similarity 19, member A2)	No PD association with SNP reported. No PD associations with 13 genes reported. No LD region reported.
rs9821797*, chr3:48718253, *NCKIPSD* IVS5 *(nearest gene, 110 other genes identified, 95 protein-coding genes)*; 2nd locus rs73088112*, chr3:49413352, *RHOA* IVS1, LD region chr3:47588253-51368253	NCK-interacting protein with SH3 domain	Within chr3p21.31 LD region, rs12497850, chr3:48748989, *IP6K2* IVS1, GWS with PD: 9E-9 (Chang et al. 2017), 1E-10 (Nalls et al. 2019), and 3E-9 (Kim et al. 2024). *IP6K2* selected by functional analysis (Nalls et al. 2019; Chang et al. 2017).
rs6589488*, chr11:114997256-115424956, *CADM1 IVS5 (nearest)*	Cell adhesion molecule 1	No NHGRI-EBI GWAS catalogue association w/PD
rs2287348*, chr2:53881813-54362813, *ERLEC1* IVS10 *(nearest, 12 other genes)*	Endoplasmic reticulum lectin 1	No NHGRI-EBI GWAS catalogue association w/PD
rs2008387*, chr10:131269764-131463964, *MGMT* IVS2 *(nearest, 1 other)*	Methylated-DNA—Protein-cysteine methyltransferase	No NHGRI-EBI GWAS catalogue association w/PD
rs9874207*, chr3:70670750-71074150, *FOXP1* IVS19 *(nearest, 1 other)*	Forkhead box protein P1	No NHGRI-EBI GWAS catalogue association w/PD
rs10747478*, chr1:96699455-97284455, intergenic, *LINC01787 & PTBP2 (nearest protein coding)* are flanking	Polypyrimidine tract-binding protein 2	No NHGRI-EBI GWAS catalogue association w/PD
rs370838138*, chr5:24945845-25372845, intergenic, *CHD10 (nearest protein-coding)*	Cadherin-10	No NHGRI-EBI GWAS catalogue association w/PD
rs13100344*, chr3:93968107-95059107, intergenic, *MIR6730* & *LINC00879* are flanking, *NSUN3 (nearest protein coding)*	tRNA (cytosine (34)-C (5))-methyltransferase, mitochondrial	No NHGRI-EBI GWAS catalogue association w/PD

Note: *These GWAS loci were reported by (Watson et al. 2019), who defined: "Nearest gene is the nearest gene within the region of LD "friends" of the lead variant (LD-$r^2 > 0.6$ +/− 500 Kb)"; GWAS locus region as "SNPs with $p <$ 1e-05 and linkage-disequilibrium (LD) $r^2 > 0.1$ with the most associated "lead" SNP, the location of which is given in BP (basepair);" "nearest gene" as "the nearest gene within the region of LD with lead variant "($r^2 > 0.6$ +/−500 Kb)"; and, number of genes was determined by genomic location, adult brain eQTL, regulatory chromatin interactions, and MAGMA gene-wise analysis (see Methods)."
Abbreviations: AN = anorexia nervosa; eQTL = Expression Quantitative Trait Locus; GWAS = genome-wide association study; GWS = genome-wide significant; LD = linkage disequilibrium; MAGMA = Multi-marker Analysis of GenoMic Annotation; NHGRI-EBI = National Human Genome Research Institute-European Bioinformatics Institute; PD = Parkinson's disease; SNP = single nucleotide polymorphisms.

for shared SNPs had not yet been reported. Given the known influence of environmental and Mendelian risk factors in PD, we hypothesised the genetic architectures for the disorders might differ, but there were no comparisons covering genetic or genomic epidemiologic measures focusing exclusively on AN and PD.

Our literature search, selection and comparison of studies and measures discovered three main findings: (1) no differences in sibling relative risk or additive genetic architecture; (2) greater heritability and polygenicity in AN but reduced discoverability compared with PD; and, (3) modest global genetic correlation exists between the disorders. By GWAS catalogue queries guided

by AN GWAS, we identified locus overlap between AN and PD; a SNP associated with PD at GWS was 30 kilobasepairs distal and in LD with the lead AN SNP at chr3p21.31. By condFDR and conjFDR analysis, we identified a cross-disorder association at the exploratory FDR < 0.1 level at the same SNP (rs12497850). To the best of our knowledge, this shared risk SNP is the first shared SNP to be described from hundreds of SNPs expected to be jointly associated with AN and PD (Smeland et al. 2025). These results should be interpreted as preliminary efforts that require replication with emerging efforts across both AN and PD GWAS initiatives (Termorshuizen et al. 2026; The Global Parkinson's Genetics Program and Leonard 2025).

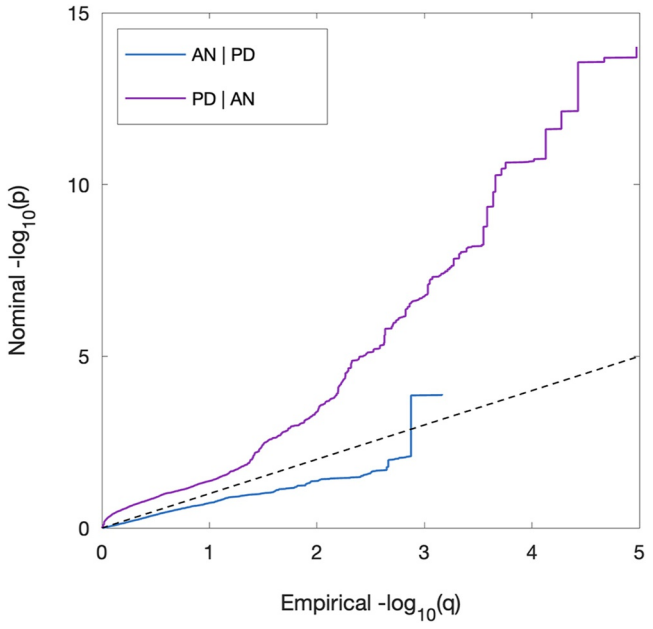

FIGURE 1 | Conditional quantile-quantile plot demonstrates cross-disorder enrichment between AN and PD. A combined quantile-quantile plot of nominal *p* values (*y*-axis) versus the corresponding value of the empirical cumulative distribution function of *p*-values (denoted by q) of one disorder stratified by the *p*-values of the second disorder (*x*-axis). The purple line represents the nominal PD *p*-values versus the empirical quantiles stratified (conditioned) on AN *p*-values. The blue line represents the nominal AN *p*-value versus the empirical quantiles stratified (conditioned) on PD *p*-values. The black dotted line indicates the expected plot under the null hypothesis (no enrichment of variants). Initially, the nominal data aligns with the empirical cumulative distribution functions. The progressive leftward deflection from the null line of the PD *p*-values (purple line) shows significant cross-trait enrichment between AN and PD (more shared variants as the stratification increases). The AN *p*-values conditioned on PD *q*-values (blue line) show enrichment at an empirical -log(q) ~3; the abrupt stop of the blue line is due to the limited number of significant AN *p*-values in the matched variant set of 7411 variants. The jagged appearance of both lines is due to limited numbers of variants in the matched variant set. AN = anorexia nervosa; PD = Parkinson's disease.

The chr3p21.31 AN:PD shared locus is associated with multiple cognitive and neurobiological phenotypes of interest to both psychiatry and neurology and is located within the second largest hotspot in the genome for psychiatric disorder local genetic correlation (Grotzinger et al. 2025). The top AN and other chr3p21.31 SNPs were found to be jointly associated with AN and Educational Attainment using methods distinct from condFDR and conjFDR (Chen et al. 2023). The top AN SNP, multiple functionally-linked genes, the chr3p21.31 region and AN associated SNPs across the genome exhibit evidence of recent positive selection in the human lineage, and genetic overlap with body mass index and menarche (Breton and Kaufmann 2025). The cross-disorder SNP with conjFDR < 0.1 and top-ranked for PD at chr3p21.31 (rs12497850) is in LD with rs9877501 (chr3:48,718,390; $D' = 0.92$ and $r^2 = 0.23$, $\chi^2 = 235.1$, $p < 0.0001$; 31 kilobasepairs distal), top-ranked in a trans-diagnostic analysis of AN and obsessive-compulsive disorder (Yilmaz et al. 2023), and with rs7626445 (chr3:49,114,544; $D' = 0.96$ and $r^2 = 0.91$, $\chi^2 = 914.9$, $p < 0.0001$; 366 kbp distal), ranked fifth out of 30 GWS loci found in the largest GWAS of obsessive-compulsive disorder (Strom et al. 2025).

Several genes mapped to our cross-disorder SNP within chr3p21.31 hold particular relevance for neuropsychiatric conditions, and may help elucidate biological mechanisms in future AN-PD cross-disorder research. One of our top mapped genes, *NCKIPSD*, is enriched for brain gene expression functional imaging maps of anxiety mechanisms of conditioning, fear, and reward (Murray et al. 2023). *IP6K2* variants are associated with cognitive impairment at motor symptom onset, and further cognitive decline in PD (Cao et al. 2024; Chevalier et al. 2023); IP6K2 protein mediates apoptosis through heat-shock protein 90 and is dependent upon PINK1, a PD protein (Nagpal et al. 2022), and the polyol/inositol phosphate biosynthetic pathway was identified as associated with PD via both common and rare variant methods (Yu et al. 2024). There are multiple genes at the chr3p21.31 joint locus involved in regulation of homoeostasis, metabolism, anxiety and cognition for future study.

Limitations of this study included selection of population-based or meta-analytic studies for reporting and analysis, rather than a systematic literature review. The common variant models cited and used for analysis also do not include rare or structural variants and their genetic effects. We did not report on AN (Watson et al. 2022) or PD (Blauwendraat et al. 2019) age-of-onset genetic risk. The sample of SNPs from publicly available summary statistics was underpowered for cross-disorder analyses and requires larger samples to observe shared SNPs at a stringent genome-

TABLE 3 | Variant rs12497850 location and association with AN and PD.

Variant	Chromosome	Position (hg19)	OR_AN	se_AN	pval_AN	OR_PD	se_PD	pval_PD
rs12497850	3	48748989	1.078	0.014	9.70e-08	0.93	0.013	6.80e-08

Note: The OR, se and pval cells provide effect size and significance from AN GWAS (Watson et al. 2019) and PD GWAS (Chang et al. 2017).
Abbreviations: AN = anorexia nervosa; GWAS = genome-wide association study; hg19 = Human Genome Reference Assembly 19; OR, se and pval = odds ratio, standard error and *p* value of disorder association at variant; PD = Parkinson's Disease.

TABLE 4 | Conditional and conjunctional FDR of variant rs12497850.

pval_ANcondPD	pval_PDcondAN	FDR_AN	FDR_PD	conjFDR_AN_PD	conjFDR_PD_AN	min_conjFDR
1.32e-04	4.83e-02	7.60e-01	1.66e-01	8.66e-02	8.59e-02	8.59e-02

Note: Table 4 presents conditional and false discovery rate (FDR) statistics for rs12497850, the single variant reaching the AN-PD conjunctional FDR threshold < 0.1. The conditioned *p*-value and the conditional FDR are reported for both directions of one disorder conditioned on another. The baseline FDR value is also reported.
Abbreviations: AN = anorexia nervosa; cond = conditioned on; condFDR = conditional FDR; FDR = false discovery rate; min_conjFDR = minimum conjunctional FDR; PD = Parkinson's disease; pval = *p* value.

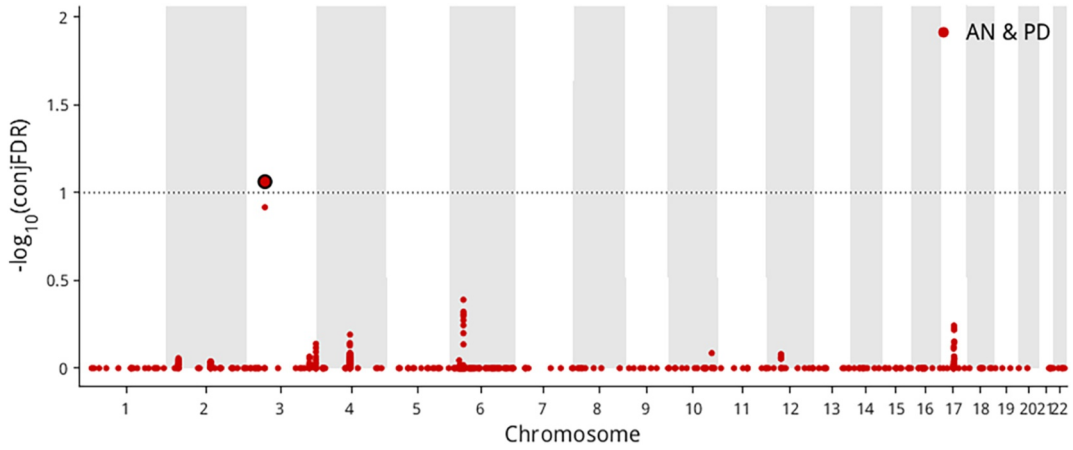

FIGURE 2 | Manhattan plot of the conjFDR values of variants jointly associated with AN and PD. The −log10 (conjFDR) values are shown on the *y* axis, and the chromosomes are ordered on the *x* axis. One genetic locus surpassed the FDR liberal threshold (−log10(FDR) > 1.0 = $q < 0.1$, indicated by the dashed line).

wide threshold. Except where noted, reported findings and analyses were from European ancestry genetic and genomic epidemiology literature and databases, and/or high socio-demographic index counties, with attendant limitations to generalisability.

5 | Conclusions

We compared AN and PD genetic architecture with selected genetic and genomic epidemiologic measures—the disorders are genetically correlated. We estimated AN and PD cross-disorder enrichment and association. As far as we are aware, this is the first in-depth description of genetic pleiotropy between AN and PD. This initial cross-disorder analysis supports shared genetic risk between the disorders, and identified chr3p21.31 genes point to mechanisms of a shared endophenotype, for example, *NCKIPSD* and anxiety (Murray et al. 2023). Existing estimates of polygenicity and discoverability of AN and PD suggest cross-disorder research will support further discovery and improved mechanistic understanding, essential for the translational research trajectory towards precision treatment.

Author Contributions

Andrew W. Bergen: conceptualization, investigation, formal analysis, funding acquisition, writing – original draft, writing – review and editing. **Carolina Makowski:** methodology, writing – review and editing. **Michael Garvin:** methodology, writing – review and editing. **Gulcan Cil:** methodology, writing – review and editing. **Angeline Krueger:** data curation, project administration, writing – review and editing. **Karlee McGlone:** methodology, writing – review and editing. **Irene Litvan:** methodology, writing – review and editing. **Heather Hower:** writing – review and editing. **Walter H. Kaye:** conceptualization, investigation, project administration, supervision, writing – original draft, writing – review and editing.

Acknowledgements

The authors also wish to thank the clinical, research, information technology, and biorepository teams in the cited population, epidemiology, and genomics research for their generation of research resources and findings, and for the data we used for novel analyses in this study. Our review, interrogation of databases and novel genomic research relied upon findings and data from: the Danish Three Generation Study (3GS); the Danish Psychiatric Central Research Register (DPCRR), the Swedish Twin Registry (STR), the NHGRI-EBI GWAS Catalog, the Cross-Disorders & Eating Disorders Working Groups of the Psychiatric Genomics Consortium (CDWG & EDWG PGC), the Brainstorm Consortium, and the International Parkinson Disease Genomics Consortium (IPDGC). Of note, the EDWG PGC incorporated data from the Anorexia Nervosa Genetics Initiative (ANGI), Klarman Family Foundation, National Institute of Mental Health (NIMH), Children's Hospital of Philadelphia (CHOP), Price Foundation Collaborative Group, Genetic Consortium for Anorexia Nervosa, Wellcome Trust Case-Control Consortium-3, and the UK Biobank. The IPDGC incorporated data from the Parkinson's Foundation's PDGene, the Web-Based Study of Parkinson's Disease (PDWBS), the 23 and Me (TTAM) Research Institute, Genentech, the Laboratory of Neurogenetics at the National Institute on Aging (NIA), Data Tecnica International, and E-Scape Bio. We also thank Luciana Price of the Price Foundation for her long-standing support of AN genetic research.

Funding

AWB thanks the Scientific Development Fund of Oregon Research Institute (ORI) for financial support. CM is supported by NIMH (R00MH132886) and the Brain Behaviour Research Foundation (31876). The views expressed in this publication are solely those of the authors.

Ethics Statement

This study conforms to the Declaration of Helsinki recognized standards for research with human participants. All analyses performed were with summary statistics; no individual patient data was used. Ethical approval was sought and granted by the University of California, San Diego (UCSD) Institutional Review Board (IRB).

Conflicts of Interest

Andrew W. Bergen declares employment at ORI and a consulting agreement with Rutgers University and declares no conflict of interest related to this study. Irene Litvan has received research funding from the National Institutes of Health (NIH: 101AG085029-01, U19AG063911, U01NS100610, 2P30AG062429, R01AG085029, U01NS112010, P30AG062429-06, and 1R61 NS141119-01); the Michael J Fox Foundation; Parkinson's Foundation; Lewy Body Association; CurePSP; Roche; AbbVie; EIP-Pharma; Novartis; and UCB. Her salary is paid by UCSD, and as the Chief Editor of Frontiers in Neurology. She serves on the Scientific Advisory Board for the Rossy PSP Program at the University of Toronto. She declares no conflict of interest related to this study. Walter H. Kaye declares ownership of Next Generation Therapies, and a consulting agreement with EDCare. All other authors declare no conflicts of interest related to this study.

Data Availability Statement

The data that support the findings of this study are summarized in the text, Tables, Figures, and Supporting Information. Data underlying the estimates, findings, and comparisons from the studies, registries, research institutes, consortiums, and published literature are available from the organizations listed above. Each cited or novel finding has its own source of data and access requirements. Data are available from the corresponding author under reasonable request.

References

Altman, D. G., and J. M. Bland. 2003. "Interaction Revisited: The Difference Between Two Estimates." *BMJ* 326, no. 7382: 219. https://doi.org/10.1136/bmj.326.7382.219.

Andreassen, O. A., S. Djurovic, W. K. Thompson, et al. 2013. "Improved Detection of Common Variants Associated With Schizophrenia by Leveraging Pleiotropy With Cardiovascular-Disease Risk Factors." *American Journal of Human Genetics* 92, no. 2: 197–209. https://doi.org/10.1016/j.ajhg.2013.01.001.

Anttila, V., B. Bulik-Sullivan, H. K. Finucane, et al. 2018. "Analysis of Shared Heritability in Common Disorders of the Brain." *Science (New York, N.Y.)* 360, no. 6395: eaap8757. https://doi.org/10.1126/science.aap8757.

Atiye, M., J. Miettunen, and A. Raevuori-Helkamaa. 2015. "A Meta-Analysis of Temperament in Eating Disorders: Temperament in Eating Disorders." *European Eating Disorders Review: The Journal of the Eating Disorders Association* 23, no. 2: 89–99. https://doi.org/10.1002/erv.2342.

Ben-Shlomo, Y., S. Darweesh, J. Llibre-Guerra, C. Marras, M. S. Luciano, and C. Tanner. 2024. "The Epidemiology of Parkinson's Disease." *Lancet* 403, no. 10423: 283–292. https://doi.org/10.1016/S0140-6736(23)01419-8.

Blauwendraat, C., K. Heilbron, C. L. Vallerga, et al. 2019. "Parkinson's Disease Age at Onset Genome-Wide Association Study: Defining Heritability, Genetic Loci, and α-Synuclein Mechanisms." *Movement Disorders: Official Journal of the Movement Disorder Society* 34, no. 6: 866–875. https://doi.org/10.1002/mds.27659.

Breton, É., and T. Kaufmann. 2025. "An Evolutionary Perspective on the Genetics of Anorexia Nervosa." *Translational Psychiatry* 15, no. 1: 59. https://doi.org/10.1038/s41398-025-03270-1.

Bulik, C. M., J. R. I. Coleman, J. A. Hardaway, et al. 2022. "Genetics and Neurobiology of Eating Disorders." *Nature Neuroscience* 25, no. 5: 543–554. https://doi.org/10.1038/s41593-022-01071-z.

Bulik, C. M., P. F. Sullivan, F. Tozzi, H. Furberg, P. Lichtenstein, and N. L. Pedersen. 2006. "Prevalence, Heritability, and Prospective Risk Factors for Anorexia Nervosa." *Archives of General Psychiatry* 63, no. 3: 305–312. https://doi.org/10.1001/archpsyc.63.3.305.

Bulik-Sullivan, B., H. K. Finucane, V. Anttila, et al. 2015. "An Atlas of Genetic Correlations Across Human Diseases and Traits." *Nature Genetics* 47, no. 11: 1236–1241. https://doi.org/10.1038/ng.3406.

Cao, L.-X., W. L. Kong, P. Chan, W. Zhang, M. J. Morris, and Y. Huang. 2024. "Assessment Tools for Cognitive Performance in Parkinson's Disease and Its Genetic Contributors." *Frontiers in Neurology* 15, no. June: 1413187. https://doi.org/10.3389/fneur.2024.1413187.

Cerezo, M., E. Sollis, Ji Yue, et al. 2025. "The NHGRI-EBI GWAS Catalog: Standards for Reusability, Sustainability and Diversity." *Nucleic Acids Research* 53, no. D1: D998–D1005. https://doi.org/10.1093/nar/gkae1070.

Chang, D., M. A. Nalls, I. B. Hallgrímsdóttir, et al. 2017. "A Meta-Analysis of Genome-Wide Association Studies Identifies 17 New Parkinson's Disease Risk Loci." *Nature Genetics* 49, no. 10: 1511–1516. https://doi.org/10.1038/ng.3955.

Chen, D., Yi Zhou, Y. Zhang, H. Zeng, L. Wu, and Y. Liu. 2023. "Unraveling Shared Susceptibility Loci and Mendelian Genetic Associations Linking Educational Attainment With Multiple Neuropsychiatric Disorders." *Frontiers in Psychiatry* 14: 1303430. https://doi.org/10.3389/fpsyt.2023.1303430.

Chevalier, G., L. Udovin, M. Otero-Losada, et al. 2023. "Genetics of Neurogenic Orthostatic Hypotension in Parkinson's Disease, Results From a Cross-Sectional in Silico Study." *Brain Sciences* 13, no. 3: 506. https://doi.org/10.3390/brainsci13030506.

Duncan, L., Z. Yilmaz, H. Gaspar, et al. 2017. "Significant Locus and Metabolic Genetic Correlations Revealed in Genome-Wide Association Study of Anorexia Nervosa." *American Journal of Psychiatry* 174, no. 9: 850–858. https://doi.org/10.1176/appi.ajp.2017.16121402.

Fairley, S., E. Lowy-Gallego, E. Perry, and F. Paul. 2020. "The International Genome Sample Resource (IGSR) Collection of Open Human Genomic Variation Resources." *Nucleic Acids Research* 48, no. D1: D941–D947. https://doi.org/10.1093/nar/gkz836.

Gabriel, S. B., S. F. Schaffner, H. Nguyen, et al. 2002. "The Structure of Haplotype Blocks in the Human Genome." *Science (New York, N.Y.)* 296, no. 5576: 2225–2229. https://doi.org/10.1126/science.1069424.

Grotzinger, A. D., J. Werme, W. J. Peyrot, et al. 2025. "Mapping the Genetic Landscape Across 14 Psychiatric Disorders." *Nature* 649, no. 8096: 406–415. https://doi.org/10.1038/s41586-025-09820-3.

Hebebrand, J., J. Seitz, and A. Matthews. 2025. "Considering Sufficient Weight Loss as a Prerequisite for Development of Anorexia Nervosa and Atypical Anorexia Nervosa." *International Journal of Eating Disorders* 58, no. 1: 162–167. https://doi.org/10.1002/eat.24313.

Holland, D., O. Frei, R. Desikan, et al. 2020. "Beyond SNP Heritability: Polygenicity and Discoverability of Phenotypes Estimated With a Univariate Gaussian Mixture Model." *PLoS Genetics* 16, no. 5: e1008612. https://doi.org/10.1371/journal.pgen.1008612.

International Parkinson's Disease Genomics Consortium (IPDGC), and Wellcome Trust Case Control Consortium 2 (WTCCC2). 2011. "A Two-Stage Meta-Analysis Identifies Several New Loci for Parkinson's Disease." *PLoS Genetics* 7, no. 6: e1002142. PMID: 21738488.

Jiménez-Jiménez, F. J., H. Alonso-Navarro, E. García-Martín, and J. A. G. Agúndez. 2014. "Cerebrospinal Fluid Biochemical Studies in Patients With Parkinson's Disease: Toward a Potential Search for Biomarkers for This Disease." *Frontiers in Cellular Neuroscience* 8, no. November: 369. https://doi.org/10.3389/fncel.2014.00369.

Kaye, W. H., and C. M. Bulik. 2021. "Treatment of Patients With Anorexia Nervosa in the US-A Crisis in Care." *JAMA Psychiatry* 78, no. 6: 591–592. https://doi.org/10.1001/jamapsychiatry.2020.4796.

Kaye, W. H., C. E. Wierenga, A. Bischoff-Grethe, et al. 2020. "Neural Insensitivity to the Effects of Hunger in Women Remitted From Anorexia Nervosa." *American Journal of Psychiatry* 177, no. 7: 601–610. https://doi.org/10.1176/appi.ajp.2019.19030261.

Kim, J. J., D. Vitale, D. V. Otani, et al. 2024. "Multi-Ancestry Genome-Wide Association Meta-Analysis of Parkinson's Disease." *Nature Genetics* 56, no. 1: 27–36. PMID: 38155330.

Krueger, A., A. W. Bergen, I. Litvan, et al. 2026. "Eating Disorders and Parkinson's Disease-1: Comorbidities, Neurobiology, and Family History." *European Eating Disorders Review: The Journal of the Eating Disorders Association*, no. May: erv.70121. https://doi.org/10.1002/erv.70121.

Liu, Fu-C., H.-T. Lin, C.-Fu Kuo, M.-Y. Hsieh, L.-C. See, and H.-P. Yu. 2018. "Familial Aggregation of Parkinson's Disease and Coaggregation With Neuropsychiatric Diseases: A Population-Based Cohort Study." *Clinical Epidemiology* 10, no. May: 631–641. https://doi.org/10.2147/clep.s164330.

Machiela, M. J., and S. J. Chanock. 2015. "LDlink: A Web-Based Application for Exploring Population-Specific Haplotype Structure and Linking Correlated Alleles of Possible Functional Variants." *Bioinformatics* 31, no. 21: 3555–3557. https://doi.org/10.1093/bioinformatics/btv402.

Marzola, E., S. Fassino, G. Migliaretti, G. Abbate-Daga, and W. H. Kaye. 2019. "Development and Validation of the Premorbid Childhood Traits Questionnaire (PCT-Q) in Eating Disorders." *Eating and Weight Disorders: EWD* 24, no. 5: 815–823. https://doi.org/10.1007/s40519-019-00748-y.

Murray, S. B., J. Rokicki, A. M. Sartorius, et al. 2023. "Brain-Based Gene Expression of Putative Risk Genes for Anorexia Nervosa." *Molecular Psychiatry* 28, no. 6: 2612–2619. https://doi.org/10.1038/s41380-023-02110-2.

Nagpal, L., M. D. Kornberg, and S. H. Snyder. 2022. "Inositol Hexakisphosphate Kinase-2 Non-Catalytically Regulates Mitophagy by Attenuating PINK1 Signaling." *Proceedings of the National Academy of Sciences of the United States of America* 119, no. 14: e2121946119. https://doi.org/10.1073/pnas.2121946119.

Nalls, M. A., C. Blauwendraat, C. L. Vallerga, et al. 2019. "Identification of Novel Risk Loci, Causal Insights, and Heritable Risk for Parkinson's Disease: A Meta-Analysis of Genome-Wide Association Studies." *Lancet Neurology* 18, no. 12: 1091–1102. https://doi.org/10.1016/S1474-4422(19)30320-5.

Nalls, M. A., N. Pankratz, C. M. Lill, et al. 2014. "Large-Scale Meta-Analysis of Genome-Wide Association Data Identifies Six New Risk Loci for Parkinson's Disease." *Nature Genetics* 46, no. 9: 989–993. https://doi.org/10.1038/ng.3043.

Noyce, A. J., S. Bandres-Ciga, J. Kim, et al. 2019. "The Parkinson's Disease Mendelian Randomization Research Portal." *Movement Disorders: Official Journal of the Movement Disorder Society* 34, no. 12: 1864–1872. https://doi.org/10.1002/mds.27873.

Overton, P. G., and V. Coizet. 2020. "The Neuropathological Basis of Anxiety in Parkinson's Disease." *Medical Hypotheses* 144, no. 110048: 110048. https://doi.org/10.1016/j.mehy.2020.110048.

Pak, K., H. K. Shin, E.-J. Kim, et al. 2018. "Weight Loss Is Associated With Rapid Striatal Dopaminergic Degeneration in Parkinson's Disease." *Parkinsonism & Related Disorders* 51, no. June: 67–72. https://doi.org/10.1016/j.parkreldis.2018.02.044.

Santangelo, G., F. Garramone, C. Baiano, et al. 2018. "Personality and Parkinson's Disease: A Meta-Analysis." *Parkinsonism & Related Disorders* 49, no. April: 67–74. https://doi.org/10.1016/j.parkreldis.2018.01.013.

Smeland, O. B., O. Frei, A. Shadrin, et al. 2020. "Discovery of Shared Genomic Loci Using the Conditional False Discovery Rate Approach." *Human Genetics* 139, no. 1: 85–94. https://doi.org/10.1007/s00439-019-02060-2.

Smeland, O. B., G. Kutrolli, S. Bahrami, et al. 2025. "A Genome-Wide Analysis of the Shared Genetic Risk Architecture of Complex Neurological and Psychiatric Disorders." *Nature Neuroscience* 28, no. 12: 2439–2450. https://doi.org/10.1038/s41593-025-02090-2.

Speed, D., and D. J. Balding. 2019. "SumHer Better Estimates the SNP Heritability of Complex Traits From Summary Statistics." *Nature Genetics* 51, no. 2: 277–284. https://doi.org/10.1038/s41588-018-0279-5.

Steinhausen, H.-C., H. Jakobsen, D. Helenius, P. Munk-Jørgensen, and M. Strober. 2015. "A Nation-Wide Study of the Family Aggregation and Risk Factors in Anorexia Nervosa Over Three Generations." *International Journal of Eating Disorders* 48, no. 1: 1–8. https://doi.org/10.1002/eat.22293.

Strom, N. I., Z. F. Gerring, M. Galimberti, et al. 2025. "Genome-Wide Analyses Identify 30 Loci Associated With Obsessive-Compulsive Disorder." *Nature Genetics* 57, no. 6: 1389–1401. https://doi.org/10.1038/s41588-025-02189-z.

Termorshuizen, Jet D., Helena L. Davies, Sang-Hyuck Lee, et al. 2026. "Genomic Meta-Analyses of Binge-Eating Behavior and Anorexia Nervosa Yield Insights into the Unique and Shared Biology of Eating Disorder Phenotypes." *Nature Mental Health*, ahead of print, August 19. http://dx.doi.org/10.1038/s44220-026-00698-2

Thacker, E. L., and A. Alberto. 2008. "Familial Aggregation of Parkinson's Disease: A Meta-Analysis." *Movement Disorders: Official Journal of the Movement Disorder Society* 23, no. 8: 1174–1183. https://doi.org/10.1002/mds.22067.

The Global Parkinson's Genetics Program. and Leonard, H. L. 2025. "Novel Parkinson's Disease Genetic Risk Factors Within and Across European Populations." *medRxiv*. https://doi.org/10.1101/2025.03.14.24319455.

UniProt Consortium. 2025. "UniProt: The Universal Protein Knowledgebase in 2025." *Nucleic Acids Research* 53, no. D1: D609–D617. https://doi.org/10.1093/nar/gkae1010.

Watanabe, K., E. Taskesen, A. van Bochoven, and D. Posthuma. 2017. "Functional Mapping and Annotation of Genetic Associations With FUMA." *Nature Communications* 8, no. 1: 1826. https://doi.org/10.1038/s41467-017-01261-5.

Watson, H. J., L. M. Thornton, Z. Yilmaz, et al. 2022. "Common Genetic Variation and Age of Onset of Anorexia Nervosa." *Biological Psychiatry Global Open Science* 2, no. 4: 368–378. https://doi.org/10.1016/j.bpsgos.2021.09.001.

Watson, H. J., Z. Yilmaz, L. M. Thornton, et al. 2019. "Genome-Wide Association Study Identifies Eight Risk Loci and Implicates Metabo-Psychiatric Origins for Anorexia Nervosa." *Nature Genetics* 51, no. 8: 1207–1214. https://doi.org/10.1038/s41588-019-0439-2.

Wirdefeldt, K., M. Gatz, C. A. Reynolds, C. A. Prescott, and N. L. Pedersen. 2011. "Heritability of Parkinson Disease in Swedish Twins: A Longitudinal Study." *Neurobiology of Aging* 32, no. 10: 1923.e1. https://doi.org/10.1016/j.neurobiolaging.2011.02.017.

Yilmaz, Z., K. Schaumberg, M. Halvorsen, et al. 2023. "Predicting Eating Disorder and Anxiety Symptoms Using Disorder-Specific and Transdiagnostic Polygenic Scores for Anorexia Nervosa and Obsessive-Compulsive Disorder." *Psychological Medicine* 53, no. 7: 3021–3035. https://doi.org/10.1017/S0033291721005079.

Yu, E., R. Larivière, R. A. Thomas, et al. 2024. "Machine Learning Nominates the Inositol Pathway and Novel Genes in Parkinson's Disease." *Brain: Journal of Neurology* 147, no. 3: 887–899. https://doi.org/10.1093/brain/awad345.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting Information S1: erv70158-sup-0001-suppl-data.docx.