Genetic Liability for Anorexia Nervosa: Exploratory Analysis of Behavioral and Emotional Indicators

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BACKGROUND & INTRODUCTION

- Anorexia nervosa (AN) is a multifactorial neuropsychiatric condition characterized by an overvaluation of an idealized body shape and pathological fear of becoming fat (APA, 2013).
- AN is related to a predisposition to temperament styles including striving for perfectionism, need for order, and sensitivity to praise and reward (Morris & Twaddle, 2007; Wade et al. 2008). Familial aggregation indicate that risk factors likely stems from some level of shared genetic liability (Wade et al. 2008).
- Understanding of the complex relationship between the genetic and environmental determinants of AN remains inadequate. Mortality rates amongst AN patients are high relative to other psychiatric disorders (Smink et al. 2012; Khalsa et al. 2017).
- Recent genome-wide associations studies (GWAS) identified genetic variants in samples of adults associated with the phenotype. Polygenic risk scores (PRS), a calculated sum of genome-wide genotypes weighted by corresponding genotype effect sizes from existing summary statistic GWAS data, may be useful in identifying individuals at risk.
- We conducted exploratory analyses to examine the relationship between AN genetic liability and behavioral and emotional problems. We calculated PRS for participants in the Child Development Project (CDP). We then tested the relationship between participants' genetic liability and averaged scores reported by mothers, teachers and youth from the Child Behavioral Checklist (CBCL).
- Results revealed a pattern between AN and scores reported by mothers, teachers and youth. Though these results should be interpreted with caution due to sample size and the number of tests run.

PARTICIPANTS & PROCEDURES

- The Child Development Project includes 585 participants. Families were recruited during kindergarten pre-registration from a community sample in 1987 and 1988. Average age at initial assessment was 5 years.
- Annual data collected from children, parents, teachers, peers, observers, and school records. Samples for DNA were collected via Oragene saliva testing kits in 2006 and 2007. Average age was 19 years when DNA was collected.
- All nonwhite participants were excluded to match summary statistics from the Eating Disorders Working Group of the Psych Genomics Consortium Anorexia Nervosa GWAS (see Watson et al. 2019). The remaining sample with genetic data included 348 youth (male = 172, female = 176).

MEASURES

Polygenic Risk Score

PRS served as a single value estimate of participants' propensity to developing AN. PRS is a calculated sum of genome-wide genotypes weighted by corresponding genotype effect sizes from existing summary statistic. Summary statistics were retrieved from the Eating Disorders Working Group of the Psych Genomics Consortium Anorexia Nervosa GWAS (see Watson et al. 2019).

Behavioral and Emotional Problems

The CBCL was used to measure problems with behaviors and emotions. Reports from mothers, teachers, and children were averaged as composite variables using longitudinal data measuring:

- Internalizing Problems
- Externalizing Problems
- Withdraw
- Somatic Complaints
- Anxiety / Depression
- Thought Problems
- Attention Problems
- Delinquent Behavior
- Aggressive Behavior
- Social Problems

Mother scores included ages 5 to 18 years

Teacher scores included ages 10 to 14 years

Youth scores included ages 13, 15 to 18, and 20 to 25 years

ANALYSIS PLAN

- PRSice was used to compute PRS based on the single-nucleotide polymorphism (SNP) estimates from the Eating Disorders Working Group of the Psych Genomics Consortium Anorexia Nervosa GWAS. Individual risk scores were computed using a linear function of the number of risk alleles, weighted by the magnitude of the effect report in the GWAS (see Watson et al. 2019).
- Composite variables were calculated for each measure of the CBCL using IBM SPSS for Mac OS Version 27. Mother, teacher, and youth reports were aggregated separately reports from each collection interval. Participant scores were excluded from the final composite variable if more than half of responses were missing. Final analytic sample ranged between 298 to 309 depending on the outcome variable.
- IBM SPSS for Mac OS Version 27 was also used to compute Pearson's R in order to evaluate the relationship between PRS and the composite variables for the CBCL.

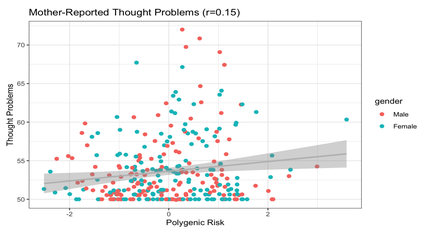
RESULTS

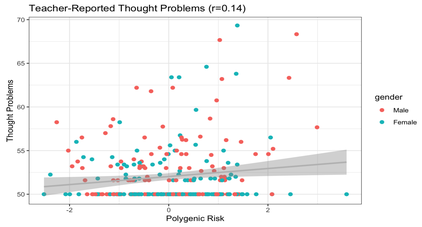
Correlations using CBCL reports and polygenic risk z-scores

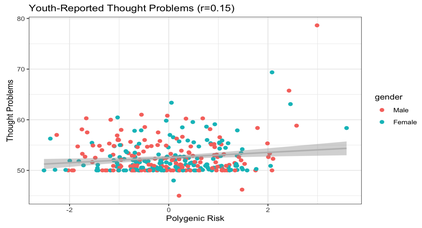
Variable	Person Correlation	Significance (2-Tailed)	N
Mother Report CBCL			
Internalizing	0.08	0.19	309
Externalizing	0.08	1.17	298
Withdrawn	0.06	0.28	309
Somatic Complaints	0.07	0.25	309
Anxiety / Depression	0.10	0.08	309
Thought Problems	0.15**	0.01	309
Attention Problems	0.12*	0.03	309
Delinquent Behavior	0.04	0.51	309
Aggressive Behavior	0.09	0.12	309
Social Problems	0.06	0.29	309
Teacher Report CBCL			
Internalizing	0.14*	0.02	298
Externalizing	0.06	0.31	298
Withdrawn	0.08	0.18	298
Somatic Complaints	0.12*	0.04	298
Anxiety / Depression	0.15**	0.009	298
Thought Problems	0.14*	0.02	298
Attention Problems	0.09	0.12	298
Delinquent Behavior	0.07	0.21	298
Aggressive Behavior	0.06	0.27	298
Social Problems	0.14*	0.02	298
Youth Report CBCL			
Internalizing	0.06	0.29	325
Externalizing	0.03	0.64	325
Withdrawn	0.11	0.06	325
Somatic Complaints	0.05	0.40	325
Anxiety / Depression	0.08	0.16	325
Thought Problems	0.15**	0.01	325
Attention Problems	0.09	0.12	325
Delinquent Behavior	-0.02	0.69	325
Aggressive Behavior	0.10	0.07	325
Social Problems	0.06	0.28	289

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).







CONCLUSIONS

•In summary our exploratory analyses revealed a pattern of associations between genetic risk of AN and mother, teacher, and youth reports.

•Although several scales were associated with genetic risk of AN, results must be interpreted with caution. E.g. Bonferroni correction results in correlations being significant when $p < .007$ level (2-tailed). No tests exceeded this threshold.

•Future research will investigate the validity and generalizability of these findings using a large sample in order to evaluate these relationships with appropriate statistical power. The present study will serve as the foundation for a Registered Report.

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