GENERAL SCIENTIFIC SUMMARY

There are individual differences in how depression symptoms progress over time, but little is known about the risk factors that underlie these developmental patterns. This study identifies distinct correlates and risk factors that underlie the various developmental pathways of depression. We found that transdiagnostic polygenic risks for psychopathology are predictive of worsening patterns of adolescent to adult depression and indirectly associated with the less severe patterns of depression via negative emotionality.

INTRODUCTION

- Adolescence is a period of heightened vulnerability to depression
- There is also substantial heterogeneity in how depression develops (Costello et al., 2008; Olino et al., 2010).
- Little is known about the risk factors that associate with individual differences in depressive development.
- The Research Domains Criteria (RDoC) aims for an integrative understanding of the mechanisms underlying psychopathology.
- RDoC investigations of depression have focused on measures within the negative valence (e.g., negative emotionality; Gore & Widiger, 2018; Woody & Gibb, 2015), positive valence (e.g., novelty seeking; Ortin et al., 2012), and cognitive systems (e.g., verbal reasoning and knowledge) (Goodall et al., 2018).
- This study integrates genetic methods with the RDoC framework to understand the mechanisms by which transdiagnostic risks eventuate into specific developmental trajectories of depression.

METHODS

Participants

- National Longitudinal Study of Adolescent to Adult Health (Add Health) (N=7,088)

Measures

- Depression: CES-D Depression Symptoms, Waves 1-4
- RDoC Language: Add Health Picture Vocabulary Test (AHPVT), Wave 1
- RDoC Negative Valence: 6 items from neuroticism on the NEO Personality Inventory, Wave 1
- RDoC Reward Responsivity: 7 items related to novelty seeking at Wave 3

Polygenic Scores (PGS)

- A "p-factor" PGS via GenomicSEM (Grotzinger et al., 2019)
  - GWAS summary statistics for MDD, schizophrenia, bipolar disorder, PTSD, and anxiety disorders
  - *p*-value threshold: $p = 1.0$

Phenotypic Analysis

- Latent class growth (LCG) analysis of depression symptoms
- Multiple mediation models, testing direct and indirect effects by which the p-factor PGS associates with each trajectory of depression via RDoC constructs
- Covariates: 10 genetic PCs, age, sex, and parent education

SCAN ME

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RDoC Mechanisms of Transdiagnostic Polygenic Risk for Trajectories of Depression: From Early Adolescence to Adulthood

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Negative emotionality may be a primary mechanistic pathway through which transdiagnostic genetic risk leads to the development of early forms of depression

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RESULTS

Fig. 1. Latent class growth trajectories of depression

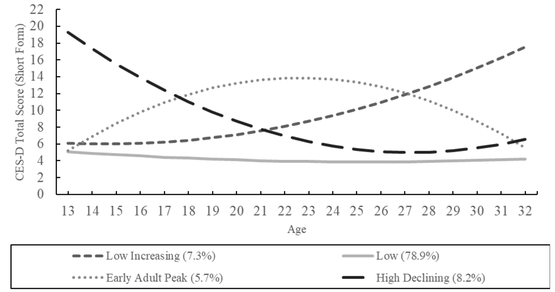
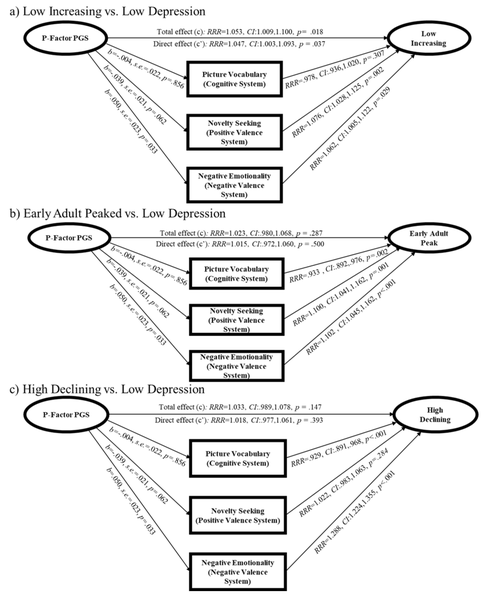


Fig. 2. Direct and indirect effects of the p-factor PGS on trajectories of depression via RDoC



DISCUSSION

- Developmental pathways of depression may have unique genetic and mechanistic origins.
- The p-factor PGS was associated with the more severe low increasing depression trajectory relative to the low depression trajectory,
- The p-factor PGS was associated with early adult peaked and high declining depression through the effects of negative emotionality, but not picture vocabulary or novelty seeking.
  - Supports prior evidence that negative emotionality may be a primary mechanistic pathway through which early risk factors can lead to the development of depression (Barrocas & Hankin, 2011); current results suggest that this mechanism may be specific to the patterns of depression that attenuate by or during the adult years.
- Findings reinforce the importance of accounting for development in RDoC models, as there may be distinct correlates and risk factors that underlie the various developmental pathways of depression

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