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## Associations between psychiatric polygenic risk scores and general and specific psychopathology symptoms in childhood and adolescence: A co-twin control study

Running head: Psychiatric PRS and childhood psychopathology

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### ABSTRACT:

Although genetics and psychiatric conditions are correlated, the associations might be indirectly mediated via broad comorbidity, attributable to the correlations among genetics factors, or accounted for by familial factors (including population stratification, dynastic effects, and assortative mating). We estimated direct genetic effects by analyzing associations within dizygotic (DZ) twin pairs, who are perfectly matched for familial factors but vary in genetic similarity due to random allele assignment during meiosis. We regressed a bifactor model based on 98 parent-rated symptoms in childhood (N = 3,907 DZ twin pairs), and a subsample followed up in adolescence with both self- and parent-ratings on 20 symptoms (n = 2,393 DZ pairs), onto 10 polygenic risk scores (PRS) between individuals ( $\beta$ ) and within ( $\beta_w$ ) DZ twin pairs. In childhood, the PRS for ADHD predicted general psychopathology ( $\beta = 0.09$ , [0.06, 0.12];  $\beta_w = 0.07$  [0.01, 0.12]). Furthermore, the PRS for ADHD predicted specific inattention ( $\beta = 0.04$  [0.00, 0.08];  $\beta_w = 0.09$  [0.01, 0.17]) and hyperactivity ( $\beta = 0.07$  [0.04, 0.11];  $\beta_w = 0.09$  [0.01, 0.16]); the PRS for schizophrenia predicted specific learning ( $\beta = 0.08$  [0.03, 0.13];  $\beta_w = 0.19$  [0.08, 0.30]) and inattention problems ( $\beta = 0.05$  [0.01, 0.09];  $\beta_w = 0.10$  [0.02, 0.19]). In the aggregate, the PRS-general factor associations were similar between individuals and within twin pairs, whereas the PRS-specific factors associations amplified by 84% within pairs. Genetic factors appear primarily directly associated with psychopathology symptoms, but the pattern might vary for the general and specific factors.

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