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Contributions

T.J., G.S., T.W.R. and J.F. conceptualized the study. C.X. and T.J. designed the analytic approach. C.X. analyzed the data. C.X. and T.J. wrote the manuscript. S.X. preprocessed the neuroimaging data. Y.L. and S.X. helped with visualization. C.S., X.P., W.C. and S.H. helped in interpreting the results. J.K. calculated the PRS. T.W.R., G.S., B.J.S. and J.F. revised the first draft. T.B., G.J.B., A.L.W.B., C.B., S.D., H.F., A.G., H.G., P.G., A.H., B.I., J.-L.M., M.-L.P.M., F.N., L.P., J.H.F., M.N.S., H.W., R.W. and G.S. were the principal investigators of IMAGEN. S.D. was the principal investigator of ESTRA. G.S. was the principal investigator of STRATIFY. T.B., G.J.B., A.L.W.B., C.B., H.F., A.G., H.G., P.G., A.H., B.I., J.-L.M., M.-L.P.M., F.N., D.P.O., L.P., J.H.F., M.N.S., H.W., R.W., S.D. and G.S. acquired the IMAGEN data. M.B., M.J.B., B.M.v.N., Z.Z., L.R., N.V., J.W., Y.Z., S.K., H.L., U.S., J.S., A.S., S.D. and G.S. acquired the STRATIFY/ESTRA data. All authors critically revised the manuscript.

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Ethics declarations

Competing interests

T.B. served in an advisory or consultancy role for Lundbeck, Medice, Neurim Pharmaceuticals, Oberberg GmbH and Shire. He received conference support or speaker's fee from Lilly, Medice, Novartis and Shire. He has been involved in clinical trials conducted by Shire and Viforpharma. He received royalties from Hogrefe, Kohlhammer, CIP Medien and Oxford University Press. The present work is unrelated to the above grants and relationships.

G.J.B. received honoraria from General Electric Healthcare for teaching scanner programming courses. All other authors declare no competing interests.

Peer review

Peer review information

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Additional information

Extended data

Extended Data Fig. 1 The construction process of the NP factor.

a. For each participant, we first constructed the brain connectome for each task condition of the three tasks with a whole-brain 268 region atlas. Specifically, the EFT contained angry and neutral conditions; the SST contained go wrong, stop success, and stop failure conditions; the MID task contained positive feedback, reward anticipation, and negative feedback conditions. We also collected eight behavioural symptoms: four externalising symptoms (ASD, ADHD, ODD, and CD) and four internalising symptoms (GAD, ED, Dep. And SP). We then estimated the brain signature for each behavioural symptom with each task-based connectome by the machine-learning method of Connectome-based predictive modeling (CPM). b. With the identified brain signature for behavioural symptoms, we next constructed the Neuropsychopathological (NP) Factor in three steps. First, for each task condition, we counted the number of cross-disorder edges that the edge was predictive of both externalising and internalising symptoms. Then we used the permutation test to identify reliable conditions where the number of cross-disorder edges was significantly higher than random discovery. These reliable cross-disorder edges were then divided into four groups regarding their simultaneous predictive effects for externalising and internalising symptoms (that is positive-positive, positive-negative, negative-positive and negative-negative), and we conducted longitudinal analyses to identify which groups of cross-disorder edges could be used to form the NP factor that is still predictive to both externalising and internalising symptoms at age 19.

Extended Data Fig. 2 The group difference of the NP factor scores between comorbid-diagnoses, single-diagnosis and healthy control groups.

The upper and lower bars represent the Q3 + 1.5xIQR and Q1–1.5xIQR, respectively. Abbreviation: Q1: the 1st quartile; Q3: the 3rd quartile; IQR: the interquartile range; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; ns. not significant.

Extended Data Table 1 Characteristics of the IMAGEN cohort at age 14
Full size table

Extended Data Table. 2 Characteristics of the ABCD cohort at age 10
Full size table

Supplementary information

Supplementary Information

Supplementary Figs. 1–6.

Reporting Summary

Supplementary Tables

Supplementary Tables 1–11.

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