ScienceDirect

You have access to this article through ClinicalKey ↗

You have access to guidelines, clinical overviews, trials and more on ClinicalKey... Read more

Biological Psychiatry

Date: 15 September 2026

Show more

Research article Full text access Get rights and content ↗

Archival Report

Neurobiological Signatures of Trauma, Personality, and Depressivity: A Transdiagnostic Machine Learning Study in Adolescents and Young Adults

Clara Weyer [a b], Elif Sarisik [a c d], Santiago Tovar Perdomo [a], Clara Vetter [a c], Dominic B. Dwyer [a e], Linda A. Antonucci [f], Theresa Lichtenstein [g], Lana Kambeitz-Ilankovic [g h], Joseph Kambeitz [g], Stephan Ruhrmann [g], Katharine Chisholm [i], Frauke Schultze-Lutter [j k l], Peter Falkai [a c m], Kolja Schiltz [a], Giulio Pergola [f n o p], Giuseppe Blasi [f], Alessandro Bertolino [f], Georg Romer [q], Rebekka Lencer [s], Udo Dannlowski [s t u v]...Sara Piccin Show more

View full text Download full issue Cite Add to Mendeley Share 10.1016/j.biopsych.2026.03.994 ↗

Article Special issue articles Recommended articles Cited by (1) Metrics

Referred to by

When Trauma, Personality, and Depressivity Converge: From Brain Signatures to Precision Prevention?

Diego A. Pizzagalli

Biological Psychiatry, Volume 100, Issue 6, 15 September 2026, Pages 608-610

Abstract

Background

Adolescence and early adulthood are periods of increased vulnerability for psychiatric disorders, when trauma and personality development converge on shared and distinct, often unknown, brain signatures.

Methods

We used sparse partial least squares (SPLS) to identify multivariate signatures between voxelwise gray matter volume (GMV) and the following 3 domains: childhood trauma, personality, and depressivity. We performed structural equation modeling (SEM) among these domains, predicted functional outcome at 9-month follow-up via support vector machine classification, and correlated the SPLS signatures with resilience, coping, and visual dysfunctions. All models were cross-validated in the discovery sample [n = 633; 52.9% female, mean [SD] age = 25.41 [5.98] years] and validated in the replication sample (n = 343; 53.0% female, 24.69 [5.72] years) of the multisite prospective PRONIA (Personalised Prognostic Tools for Early Psychosis Management) cohort, comprising individuals with recent-onset depression or psychosis, psychosis risk syndromes, and healthy control individuals.

Results

We identified the following 3 signatures of interest: 1) depressivity, linked to reduced GMV [illegible]bic regions; 2) childhood trauma, associated with GMV in thalamic, frontotemporal, [illegible]arietal regions; and 3) a trauma-personality-depressivity signature, relating childhood [illegible]a, personality, and depressivity to GMV in thalamic, occipital, temporal, and limbic [illegible]ns. SEM revealed that childhood trauma was associated with depressivity directly and [illegible]ndirectly via a maladaptive personality structure. The trauma-personality-depressivity signature was the strongest predictor of poor functional outcome (balanced accuracy

Reading Assistant

Outline

Abstract

Keywords

Methods and Materials

Results

Discussion

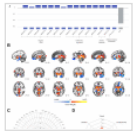
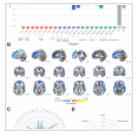
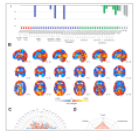
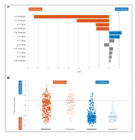
Acknowledgments and Disclosures

Supplementary Material

References

Show full outline

Figures (4)

Tables (2)

Table 1. Demographic and Clinical Charac...

Table 2. Atlas Readouts From LV2, LV3, an...

Extras (2)

Download all

Supplemental Methods, Results, Discussio...

[BAC]$_{Discovery}$ = 75.8%, BAC$_{Replication}$ = 83.2%). The depressivity and trauma-personality-depressivity signatures were linked to deficient resilience and coping styles as well as visual dysfunctions.

Conclusions

Childhood trauma, personality, and depressivity are associated with shared and distinct brain signatures spanning the affective-psychotic spectrum. If these factors converge, current and future mental health may be compromised.

Keywords

Childhood trauma; Depressivity; MRI; Partial least squares; Personality; Transdiagnostic

Key Resources Table

Previous article in this issue

Next article in this issue

SEE COMMENTARY ON PAGE 608

Adolescence and young adulthood are periods of heightened vulnerability to severe mental disorders, including depression and psychosis (1, 2, 3, 4). Despite prioritization of early recognition and intervention, recent meta-analytic evidence raises questions about the effectiveness of currently used strategies, suggesting that the heterogeneity within clinical populations may undermine outcomes (5, 6, 7). Prodromal and early disease stages are often characterized by a combination of subtle, nonspecific, and distributed symptoms, such as dysregulated affect, altered motivation, and aberrant salience, which cut across established diagnostic boundaries (8). Consequently, efforts to elucidate the mechanisms underlying these syndromes have increasingly focused on transdiagnostic risk factors, with childhood trauma among the most robust (4,9). Childhood trauma exposure increases the risk of developing depression or psychosis, is linked to earlier disease onset and more severe disease trajectories, and confers distinct clinical and neurobiological profiles compared with nonexposed individuals with the same primary psychiatric disorder (9, 10, 11, 12, 13, 14). However, not all trauma-exposed individuals develop a mental disorder, indicating additional modulating factors (12,15, 16, 17, 18). Personality represents one such factor, considered both a risk factor and protective factor for future psychopathology (18,19). Personality is not only influenced by childhood trauma (18,20, 21, 22, 23, 24, 25) but also mediates trauma's impact on functional outcomes (26) and depressivity (i.e., depressive symptom burden), one of the strongest transdiagnostic predictors of poor quality of life (20,27, 28, 29, 30, 31, 32). Depressive symptoms are common not only in depressive disorders but also in high-risk or early stages of psychotic disorders (33,34) and are generally highly prevalent in adolescents and young adults (35).

This interplay of childhood trauma, personality, and depressivity highlights the importance of a deeper neurobiological understanding of early disease stages, where diagnostic boundaries are less clear, and outcomes remain more amenable to intervention (36). Structural magnetic resonance imaging (MRI) studies have reported overlapping gray matter volume (GMV) alterations associated with childhood trauma, personality, and depressivity, particularly in the anterior cingulate cortex and prefrontal regions (37, 38, 39, 40, 41, 42), suggesting possible shared neural substrates. However, prior work has largely examined these factors in isolation or solely at the clinical level, leaving their joint interaction with brain morphology insufficiently understood (12,20,27, 28, 29, 30, 31,40, 41, 42, 43). Childhood trauma, personality, and depressivity reflect cumulative developmental and stress-related processes that are expected to manifest as distributed and interlinked ural brain variation, providing a conceptual basis for linking these dimensions to variate GMV patterns. A transdiagnostic approach across the affective-psychotic um may best capture the intersection of childhood trauma, personality, and ssivity across the earliest disease stages, enabling identification of shared and gent mechanisms for intervention (9,44).

Reading Assistant

Here, we investigated covariation between childhood trauma, personality, depressivity, and brain structure in adolescents and young adults from the multicenter PRONIA (Personalised Prognostic Tools for Early Psychosis Management) cohort, which comprises individuals with recent-onset depression (ROD) or recent-onset psychosis (ROP), clinical high-risk states for psychosis (CHR-P), and healthy control (HC) individuals. We combined unsupervised and supervised machine learning methods to integrate multidimensional data and deal with large-scale and complex effect patterns (45). Specifically, we used the multivariate sparse partial least squares (SPLS) algorithm (46,47) to identify associations between voxelwise whole-brain GMV and childhood trauma, personality, and depressivity. To explore dependencies within the identified patterns and individual susceptibility with implications for intervention-relevant processes, we conducted post hoc structural equation modeling (SEM)-based mediation analyses. Moreover, we evaluated the prognostic value of the SPLS-derived patterns for predicting functional outcome at 9-month follow-up using support vector machines (SVMs). Finally, we examined associations with coping, resilience, and visual dysfunctions, given their relevance to functional outcome and remission (16,48, 49, 50, 51).

Methods and Materials

The study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines (Table S1) (49).

Study Participants

Participants were recruited as part of the multicenter, prospective PRONIA study (German Clinical Trials Register: DRKS00005042) and followed for up to 36 months. The SPLS model was generated and prospectively validated in subsets from the original PRONIA discovery (n = 633) and replication (n = 343) samples, respectively, recruited across 7 European sites (Munich, Milan, Basel, Cologne, Birmingham, Turku, Udine) (Figure S1; Table 1; and Tables S2–S11). Due to attrition, SVM models were trained and validated in smaller subsamples from the discovery (n = 504) and replication (n = 312) samples, respectively. The study was approved by local ethics committees in accordance with the Declaration of Helsinki. Written informed consent or assent with guardian consent was obtained for all participants.

Table 1. Demographic and Clinical Characteristics of the Discovery Sample Used for Sparse Partial Least Squares Model Generation

Characteristics	All, n = 633	CHR-P, n = 122	HC, n = 260	ROD, n = 127	ROP, n =
Age, Years	25.41 (5.98)	23.97 (4.93)	25.42 (6.36)	26.32 (6.18)	25.89 (5
Sex					
Female	335 (53%)	60 (49%)	162 (62%)	67 (53%)	46 (37%
Male	298 (47%)	62 (51%)	98 (38%)	60 (47%)	78 (63%
Education, Years	14.86 (3.22)	13.83 (2.97)	15.71 (3.17)	14.87 (3.15)	14.07 (3
GAF:D/I					
Highest past month	65.78 (20.12)	55.95 (13.98)	85.19 (5.90)	56.56 (14.68)	44.29 (1
Highest past year	75.00 (14.46)	68.93 (12.29)	85.65 (5.60)	71.46 (13.59)	62.31 (1
Highest lifetime	82.63 (7.97)	79.64 (8.10)	86.68 (5.15)	81.72 (7.27)	78.00 (9
9-month follow-up, past month	75.33 (14.85)	68.91 (13.51)	85.11 (7.55)	70.56 (13.93)	62.85 (1
PANSS					
Total score	56.97 (18.4)	51.92 (13.18)	NA	47.98 (11.03)	70.82 (2
ive symptoms	13.21 (6.14)	11.73 (3.35)	NA	8.50 (1.86)	19.37 (5
ive symptoms	13.72 (6.30)	12.53 (5.8)	NA	12.47 (4.91)	16.13 (7.
al symptoms	30.01 (9.29)	27.62 (6.88)	NA	27.01 (6.56)	35.32 (1
Total	36.14 (11.29)	40.96 (12.73)	30.81 (5.82)	39.26 (14.01)	40.05 (1

Reading Assistant

Characteristics	All, *n* = 633	CHR-P, *n* = 122	HC, *n* = 260	ROD, *n* = 127	ROP, *n* =
Emotional abuse	8.30 (3.94)	10.08 (4.36)	6.55 (2.37)	9.11 (4.44)	9.45 (4.2
Physical abuse	5.97 (2.35)	6.42 (3.01)	5.38 (0.97)	6.48 (3.24)	6.27 (2.3
Sexual abuse	5.69 (2.38)	5.99 (2.79)	5.17 (0.95)	5.94 (2.87)	6.29 (3.2
Emotional neglect	9.96 (4.36)	11.78 (4.51)	7.95 (3.01)	11.10 (4.90)	11.27 (4
Physical neglect	6.71 (2.38)	7.24 (2.57)	5.82 (1.39)	7.06 (2.85)	7.73 (2.7
NEO-FFI					
Neuroticism	23.15 (10.63)	30.45 (8.61)	15.07 (7.11)	30.23 (8.22)	25.84 (9
Extraversion	26.26 (7.86)	21.48 (7.69)	31.10 (6.21)	22.93 (6.62)	24.03 (6
Openness	28.52 (6.12)	28.53 (6.70)	29.45 (6.09)	26.73 (5.63)	28.40 (5
Agreeableness	31.57 (6.64)	28.59 (6.26)	34.04 (6.09)	31.24 (6.44)	29.57 (6
Conscientiousness	30.17 (8.28)	25.62 (8.32)	34.4 (6.63)	27.77 (7.67)	28.39 (8
BDI-II					
Total	15.69 (14.58)	25.7 (12.25)	3.64 (5.11)	26.17 (13.83)	20.92 (1
Negative attention toward self	7.25 (7.52)	12.29 (6.73)	1.34 (2.38)	12.59 (7.43)	9.41 (6.7
Performance impairment	4.76 (4.70)	7.88 (4.17)	0.97 (1.65)	8.04 (4.38)	6.39 (4.1
Somatic symptoms	3.79 (3.58)	5.69 (3.27)	1.33 (1.90)	5.62 (3.83)	5.23 (3.2
SPI-A					
Impaired tolerance to unusual, unexpected, or specific novel demands, A1.1	1.09 (1.86)	1.86 (2.11)	0.03 (0.20)	1.64 (1.94)	2.06 (2.1
Impaired tolerance to certain social everyday situations, A1.2	1.16 (1.94)	2.10 (2.19)	0.03 (0.25)	1.85 (2.04)	1.93 (2.3
Impaired tolerance to working under pressure of time/rapidly changing different demands, A1.3	1.09 (1.96)	1.87 (2.29)	0.02 (0.17)	1.56 (2.08)	2.15 (2.4
Change in mood, A2.1	2.01 (2.45)	3.17 (2.36)	0.12 (0.62)	3.71 (2.28)	3.10 (2.4
Change in emotional responsiveness, A2.2	1.07 (1.95)	1.81 (2.29)	0.02 (0.17)	1.94 (2.25)	1.72 (2.2
Decrease in positive emotional responsiveness toward others, A3	1.07 (1.95)	1.79 (2.33)	0.06 (0.44)	1.90 (2.26)	1.70 (2.2
Visual dysfunctions	1.71 (4.74)	3.69 (5.46)	0.07 (0.34)	0.72 (2.22)	4.26 (8.0
Additional					
IQR	1.93 (0.14)	1.93 (0.16)	1.89 (0.10)	1.92 (0.13)	1.94 (0.1
Site					

Values represent the mean (SD) or *n* (%). Group-level differences were assessed between the subgroups (excluding HC group) using the Kruskal-Wallis test for continuous variables and the χ^2-test for categorical variables. Effect sizes were estimated using η^2 for continuous and Cramér's V for categorical variables. Based on a previous meta-analysis of factor analyses, the 21 BDI-II items were categorized into 3 factors: negative attitude toward self, performance impairment, and somatic symptoms (52). The visual dysfunctions score was computed as the sum of 14 SPI-A items (F1, F2, F3, O4.1–O4.10, O7) (51). *p* values were adjusted for multiple testing using the Benjamini-Hochberg FDR correction, the entire table representing a family of tests.

Reading Assistant

gnificant *p* values.

I-II, Beck Depression Inventory-II; CHR-P, clinical high-risk for psychosis; CTQ, Childhood Trauma estionnaire; FDR, false discovery rate; GAF:D/I, Global Assessment of Functioning: Disability and impairment; HC, healthy control participant; IQR, image quality rating; NA, not applicable; NEO-FFI,

NEO Five-Factor Inventory; PANSS, Positive and Negative Syndrome Scale; ROD, recent-onset depression; ROP, recent-onset psychosis; SPI-A, Schizophrenia Proneness Instrument, Adult version.

SPLS Analysis

We used the SPLS toolbox by Popovic *et al.* (47) (https://github.com/dpopovic30/spls_toolbox_compiled ↗) to analyze multivariate associations between 1) a phenotypic matrix (123 features) containing each item of the Beck Depression Inventory-II (BDI-II) (53,54), NEO Five-Factor-Inventory (NEO-FFI) (55), Childhood Trauma Questionnaire (CTQ) (56), and affective-dynamic disturbances section of the Schizophrenia Proneness Instrument, Adult version (SPI-A) (57), along with age, sex, study group, and image quality rating (IQR) (Table S12); and 2) a brain matrix (60 381 features) containing voxelwise whole-brain GMV. SPLS uses singular value decomposition to compute latent variables (LVs), each containing two weight vectors, one for each data domain, placing weights (−1 to 1) on every feature in the respective data matrix that indicate the strength and direction of covariance between features. Moreover, we computed participant-specific latent scores by projecting their phenotypic and brain data onto the corresponding weight vector, yielding individual loadings of each participant onto the LV. The correlation coefficient between these phenotypic and brain scores indicates the strength of covariance captured by the LV and served as the optimization criterion for SPLS model training. The SPLS algorithm was embedded within a nested cross-validation (CV) framework (58) with group stratification, correcting the GMV data for scanner effects via partial correlations (59). Model sparsity was optimized via 2 regularization hyperparameters imposing constraints on the weight vectors. Hyperparameter optimization was conducted within the CV framework using a standardized grid search. Significance was assessed through permutation testing, feature weight stability via bootstrap ratios (60). Following an iterative process, each significant LV was removed from the data matrices before the next LV was computed (46) (see Supplement).

Exploratory Mediation Analyses

SEM-based mediation analyses were conducted via maximum-likelihood estimation with 100 nonparametric bootstrap resamples in the discovery and replication samples, using the phenotypic features of the fifth identified LV (LV5) (61), which captured the coalescence of childhood trauma, personality, and depressivity, to clarify directional relationships within the phenotypic domain of the multivariate SPLS pattern; directional paths were informed by the temporal characteristics of the assessment instruments and prior literature. For each domain, raw item scores were multiplied by their corresponding SPLS weights and summed to generate composite scores that were entered into the SEM model (see Supplement).

Prediction of Functional Outcome

We used the Global Assessment of Functioning: Disability and Impairment (GAF:D/I) scale (62) and the participants' phenotypic and brain scores of all significant LVs to predict "good" (GAF:D/I ≥ 81) versus "poor" (GAF:D/I < 81) functional outcome at the 9-month follow-up, distinguishing individuals with good to superior functioning from those with impaired functioning, consistent with prior work using similar dichotomization strategies (63,64) (Tables S13–S15). We used a linear-kernel SVM classifier embedded in a repeated nested CV framework using the machine learning software NeuroMiner (version 1.1, http://proniapredictors.eu/neurominer/index.html ↗). Balanced accuracy (BAC) served as the model optimization criterion (58). In addition, we conducted a complementary support vector regression (SVR) using the same feature set and CV framework to predict GAF:D/I scores. The size and stability of predictive pattern elements was evaluated using CV ratio (|CVR| ≥ 1.96) and sign-based consistency (SBC) mapping (p_{SBC} < .05) (65,66) (see Supplement).

Relations With Coping, Resilience, and Visual Dysfunctions

We performed Spearman rank correlations between phenotypic and brain scores of the post hoc defined SPLS signatures of interest (i.e., LV2, LV3, LV5) and 1) the Coping Inventory for Stressful Situations subdomains (i.e., task-, emotion-oriented coping, avoidance, distraction, social diversion) (67), 2) the Resilience Scale for Adults (RSA) subdomains (i.e., perception of

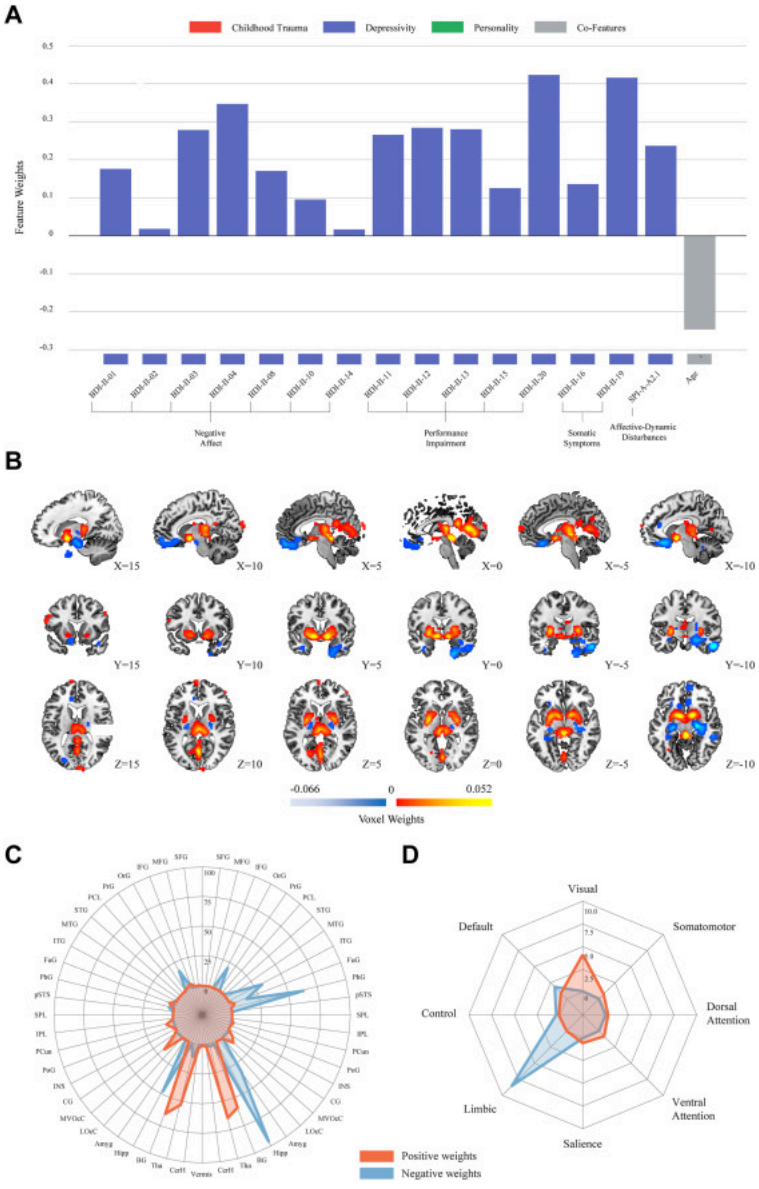
Reading Assistant

self, planned future, social competence, structured style, family cohesion, social resources) (68), and 3) visual dysfunctions, operationalized as the sum of 14 SPI-A items (51). Additional correlations with body mass index and prior medication intake, as well as complementary Pearson correlations to assess linear associations, are reported in the Supplement.

Results

SPLS Results

Six significant LVs were identified in the discovery sample and validated in the replication sample (Figure 1, Figure 2, Figure 3; Figures S2–S4; Table 2; and Tables S16–S21).



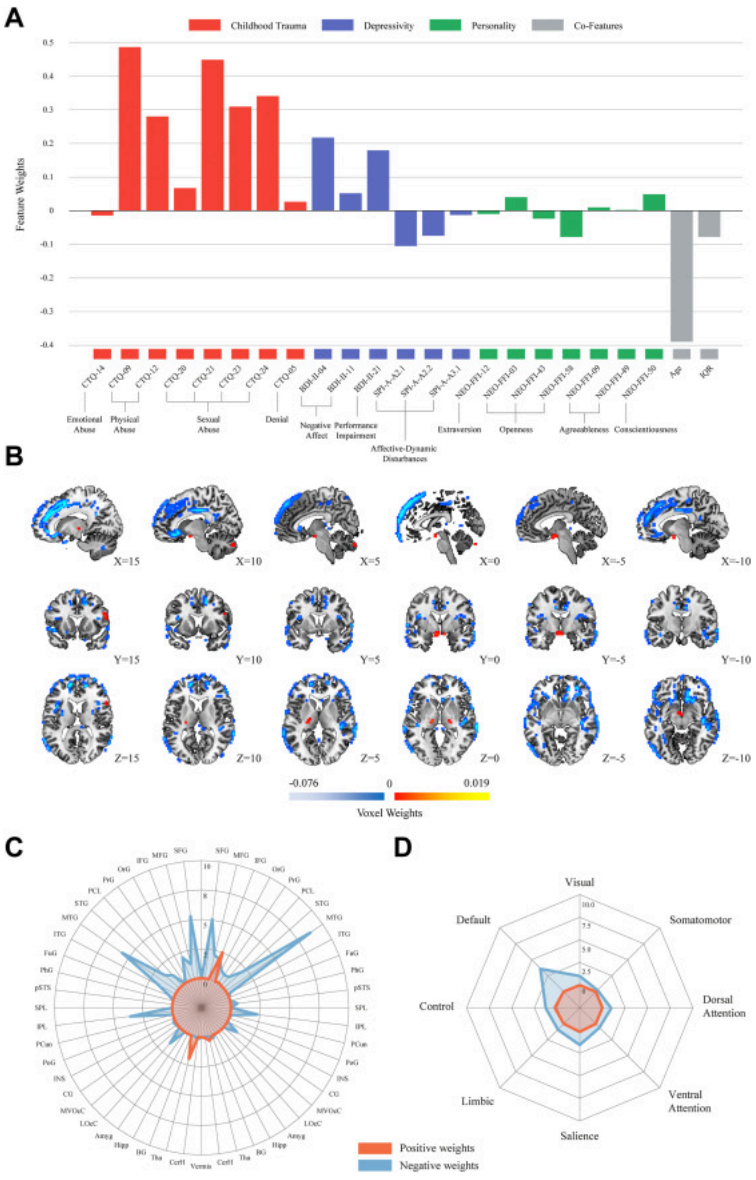
Download: Download high-res image (1MB)

Download: Download full-size image

Figure 1. Phenotypic and brain pattern of the depressivity signature (LV2). **(A)** The bar plot shows both the direction and the magnitude of the feature weights of the phenotypic pattern of LV2. Positive weights were assigned to 14 Beck Depression Inventory-II (BDI-II) items and 1 Schizophrenia Proneness Instrument, Adult version (SPI-A) item. Age was negatively weighted. Based on a previous meta-analysis of factor analyses, the 21 BDI-II items were categorized into the following 3 factors: negative attitude toward self, performance impairment, and somatic symptoms (54). Bar plots are labeled accordingly. **(B)** Surface rendering of positively and negatively weighted voxels making up the brain pattern component of the latent variable (LV). The brain pattern of LV2 was mapped onto the Montreal Neurological Institute 152 standard space via the open-source 3-dimensional rendering software Connectome Workbench

Reading Assistant

(https://humanconnectome.org/software/connectome-workbench ↗). The spider plots highlight the **(C)** top neuroanatomic brain regions [derived from the Brainnetome (120) and Diedrichsen (121) atlases] and **(D)** corresponding functional networks [derived from an adapted network solution of the Yeo and Buckner atlases (118,119)] according to the percentage of positively and negatively weighted voxels in these regions. **(B–D)** Positively weighted voxels are displayed in warm colors, negatively weighted voxels in blue-scale colors. Amyg, amygdala; BG, basal ganglia; CerH, cerebellar hemisphere; CG, cingulate gyrus; FuG, fusiform gyrus; Hipp, hippocampus; IFG, inferior frontal gyrus; INS, insular gyrus; IPL, inferior parietal lobule; ITG, inferior temporal gyrus; LOcC, lateral occipital cortex; MFG, middle frontal gyrus; MTG, middle temporal gyrus; MVOcC, medioventral occipital cortex; OrG, orbital gyrus; PCL, paracentral lobule; PCun, precuneus; PhG, parahippocampal gyrus; PoG, postcentral gyrus; PrG, precentral gyrus; pSTS, posterior superior temporal sulcus; SFG, superior frontal gyrus; SPL, superior parietal lobule; STG, superior temporal gyrus; Tha, thalamus.



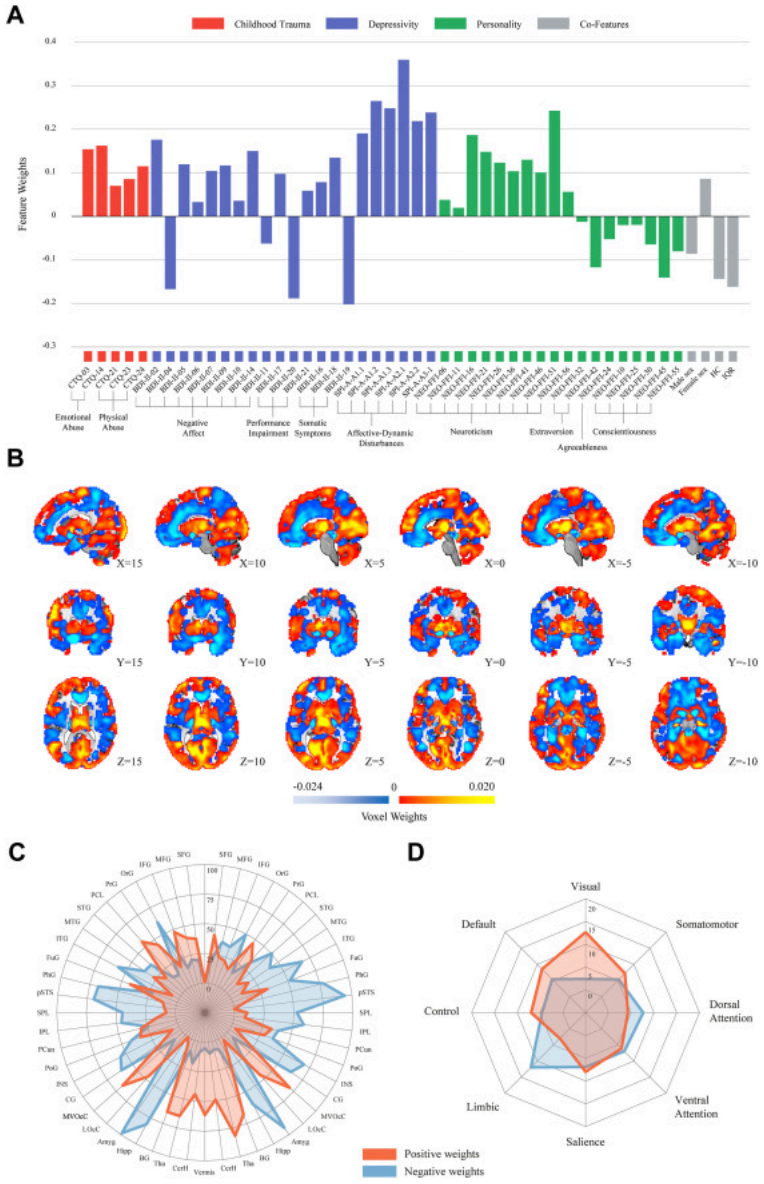
Download: Download high-res image (1MB)

Download: Download full-size image

Figure 2. Phenotypic and brain pattern of the childhood trauma signature (LV3). **(A)** The barplot shows both the direction and the magnitude of the feature weights of the phenotypic pattern of LV3. Positive weights were assigned to 7 Childhood Trauma Questionnaire (CTQ), 3 Beck Depression Inventory-II (BDI-II), and 4 NEO Five Factor Inventory (NEO-FFI) items. Three Schizophrenia Proneness Instrument, Adult version (SPI-A) items, NEO-FFI items, age, and image quality rating (IQR) were negatively weighted. Based on a previous meta-analysis of factor analyses, the 21 BDI-II items were categorized into the following 3 factors: negative attitude toward self, performance impairment, and somatic

Reading Assistant

symptoms (54). Bar plots are labeled accordingly. **(B–D)** See the legend for Figure 1B–D. Amyg, amygdala; BG, basal ganglia; CerH, cerebellar hemisphere; CG, cingulate gyrus; FuG, fusiform gyrus; Hipp, hippocampus; IFG, inferior frontal gyrus; INS, insular gyrus; IPL, inferior parietal lobule; ITG, inferior temporal gyrus; LOcC, lateral occipital cortex; LV, latent variable; MFG, middle frontal gyrus; MTG, middle temporal gyrus; MVOcC, medioventral occipital cortex; OrG, orbital gyrus; PCL, paracentral lobule; PCun, precuneus; PhG, parahippocampal gyrus; PoG, postcentral gyrus; PrG, precentral gyrus; pSTS, posterior superior temporal sulcus; SFG, superior frontal gyrus; SPL, superior parietal lobule; STG, superior temporal gyrus; Tha, thalamus.



Download: Download high-res image (1MB)

Download: Download full-size image

Figure 3. Phenotypic and brain pattern of the trauma-personality-depressivity signature (LV5). **(A)** The bar plot shows both the direction and the magnitude of the feature weights of the phenotypic pattern of LV5. Positive weights were assigned to 5 Childhood Trauma Questionnaire (CTQ) items, 6 Schizophrenia Proneness Instrument, Adult version (SPI-A) items, 11 Beck Depression Inventory-II (BDI-II) items, 10 NEO Five Factor Inventory (NEO-FFI) items, and female sex. Four BDI-II items and 8 NEO-FFI items as well as male sex, healthy control (HC) group membership, and image quality rating (IQR) were negatively weighted. Based on a previous meta-analysis of factor analyses, the 21 BDI-II items were organized into 3 factors: negative attitude toward self, performance impairment, and somatic symptoms (54). Bar plots are labeled accordingly. **(B–D)** See the caption for Figure 1B–D. Amyg, amygdala; BG, basal ganglia; CerH, cerebellar hemisphere; CG, cingulate gyrus; FuG, fusiform gyrus; Hipp, hippocampus; IFG, inferior frontal gyrus; INS, insular gyrus; IPL, inferior parietal lobule; ITG, inferior temporal gyrus; LOcC, lateral occipital cortex; LV, latent

Reading Assistant

variable; MFG, middle frontal gyrus; MTG, middle temporal gyrus; MVOcC, medioventral occipital cortex; OrG, orbital gyrus; PCL, paracentral lobule; PCun, precuneus; PhG, parahippocampal gyrus; PoG, postcentral gyrus; PrG, precentral gyrus; pSTS, posterior superior temporal sulcus; SFG, superior frontal gyrus; SPL, superior parietal lobule; STG, superior temporal gyrus; Tha, thalamus.

Table 2. Atlas Readouts From LV2, LV3, and LV5 for Large-Scale Brain Networks

Network	Total Voxels	LV2		LV3		LV5	
		Negative (−)	Positive (+)	Negative (−)	Positive (+)	Negative (−)	Pos
Visual	1990	−0.10	4.12	−1.06	0.00	−12.01	63.3
Somatomotor	2993	−0.00	0.74	−0.30	0.00	−26.46	36.(
Dorsal Attention	2567	−0.00	0.27	−0.97	0.00	−38.25	21.4
Ventral Attention	2339	−0.00	0.81	−0.56	0.00	−34.97	30.5
Salience	1871	−0.05	0.59	−1.55	0.16	−34.58	39.8
Limbic	2620	−8.51	0.00	−0.88	0.00	−59.81	14.9
Control	5048	−0.42	0.14	−1.25	0.26	−22.80	34.7
Default	6488	−1.85	0.88	−3.65	0.02	−26.94	42.5

Depicted are the percentages of positively and negatively weighted voxels (weighted voxels ratio) in 8 large-scale brain networks, derived from an adapted network solution of the Yeo and the Buckner atlases (118,119), for LV2, LV3, and LV5. Additionally, for each functional network, the total number of voxels is provided.

LV, latent variable.

LV1: Age ($\rho_{Discovery}$ = 0.56, $p_{Discovery}$ < .001; $\rho_{Replication}$ = 0.48, $p_{Replication}$ < .001)

Age, alongside smaller contributions from the IQR, SPI-A, BDI-II, CTQ, and NEO-FFI (Figure S2A), was linked to reduced GMV across all networks (Figure S2B–D), most prominently in the salience network, followed by the default mode and control networks.

LV2: Depressivity ($\rho_{Discovery}$ = 0.22, $p_{Discovery}$ = .002; $\rho_{Replication}$ = 0.44, $p_{Replication}$ < .001)

Positive weights on 14 BDI-II items and one SPI-A item as well as younger age (Figure 1A) were predominantly linked to higher GMV weights on the basal ganglia, thalamus, and medial ventral occipital cortex and lower GMV weights on the hippocampus, the amygdala, and the orbital, inferior temporal, and parahippocampal gyri. At the network level, this corresponded to higher GMV weights on the visual network and lower GMV weights on the limbic system (Figure 1B–D).

LV3: Childhood Trauma ($\rho_{Discovery}$ = 0.40, $p_{Discovery}$ < .001; $\rho_{Replication}$ = 0.45, $p_{Replication}$ < .001)

Positive weights on 6 CTQ items (i.e., physical and sexual abuse) and younger age, and smaller contributions from the BDI-II and SPI-A and only minimal contributions from the NEO-FFI and IQR (Figure 2A), were linked to lower GMV weights on the superior and middle temporal and the superior, middle, and inferior frontal gyri as well as the inferior parietal lobules, mapping most closely onto the default mode, salience, control, and visual networks (Figure 2B–D).

Sex ($\rho_{Discovery}$ = 0.33, $p_{Discovery}$ < .001; $\rho_{Replication}$ = 0.29, $p_{Replication}$ <

ve weights on female sex, and small weights on the NEO-FFI, CTQ, and HC participant study group status (Figure S3A), were linked to GMV alterations in brain regions mapping

Reading Assistant

most closely onto the dorsal attention, visual, and default mode networks (Figure S3B–D).

LV5: Trauma-Personality-Depressivity ($\rho_{Discovery}$ = 0.24, $p_{Discovery}$ < .001; $\rho_{Replication}$ = 0.45, $p_{Replication}$ < .001)

Positive weights on 6 SPI-A, 11 BDI-II, 10 NEO-FFI (i.e., neuroticism), and 5 CTQ items (i.e., emotional and physical abuse) as well as female sex and negative weights on 4 BDI-II and 8 NEO-FFI (i.e., extraversion, agreeableness, conscientiousness) items, HC participant status, and IQR (Figure 3A) were linked predominantly to higher GMV weights on the thalamus, basal ganglia, and medial ventral occipital cortex and lower GMV weights on the amygdala, parahippocampal gyri, insula, posterior superior temporal sulci, and hippocampus. At the network level, this pattern mapped most closely onto higher GMV weights on the visual network, followed by the default mode, salience, somatomotor, and control networks, and lower GMV weights on the limbic system and the dorsal and ventral attention networks as well as the salience network (Figure 3B–D).

LV6: Age and Sex ($\rho_{Discovery}$ = 0.23, $p_{Discovery}$ = .027; $\rho_{Replication}$ = 0.22, $p_{Replication}$ < .001)

Positively weighted male sex, together with negatively weighted female sex, age, and smaller contributions from BDI-II, SPI-A, and NEO-FFI scores (Figure S4A), were linked to GMV alterations in brain regions corresponding most closely to the limbic system, followed by the dorsal attention, control, and salience networks (Figure S4B–D).

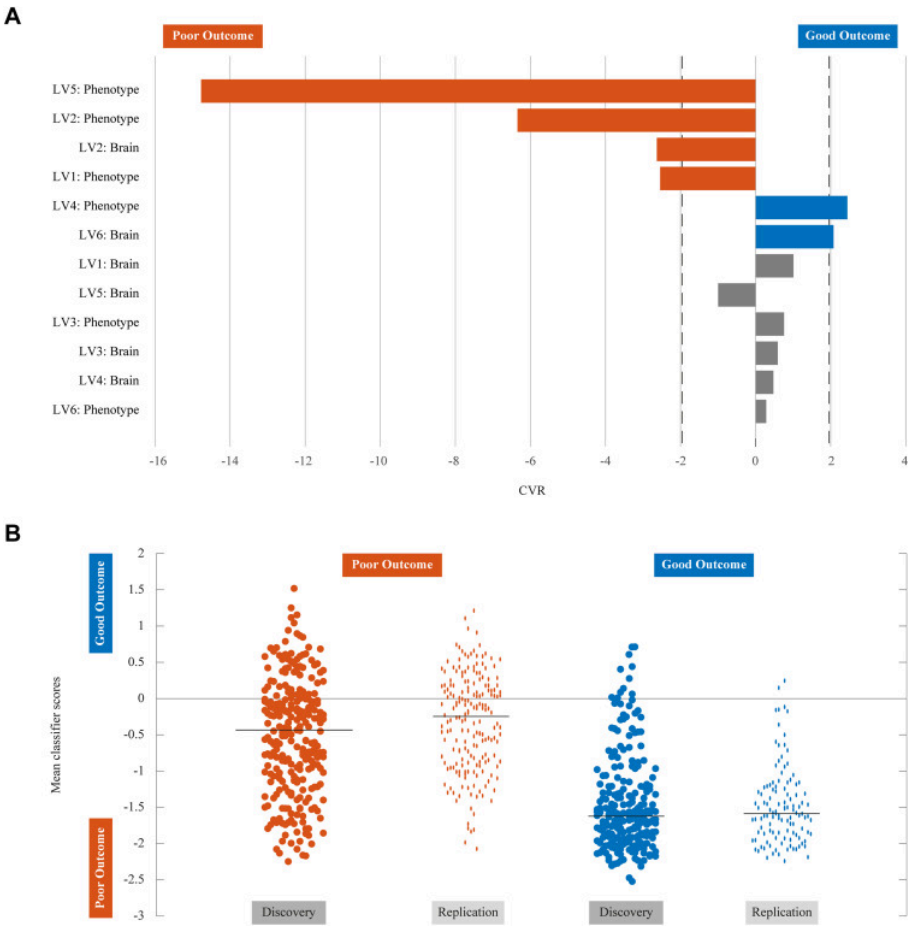
Exploratory Mediation Analyses

In-depth analysis of the trauma-personality-depressivity signature (LV5) via SEM-based mediation analyses (Figure S5; Tables S22–S23) using composite phenotypic scores revealed a significant indirect effect of childhood trauma on depressivity via personality in both the discovery and replication samples (all *p*s < .01; standardized β = 0.19–0.24). Direct effects of childhood trauma on personality (β = 0.36–0.40) and depressivity (β = 0.14–0.17) and of personality on depressivity (β = 0.52–0.58) were also significant (all *p*s < .01). Personality mediated 62% and 53% of the total effect of childhood trauma on depressivity in the discovery and replication samples, respectively.

Prediction of Functional Outcome

The brain and phenotypic scores from all 6 LVs predicted functional outcome with a BAC of 75.79% (area under the curve [AUC] = 0.82; sensitivity = 72.08%; specificity = 79.50%; p < .002) in the discovery sample and a BAC of 83.2% (AUC = 0.91; sensitivity = 81.1%; specificity = 85.3%) in the replication sample (Figure 4 and Tables S24, S25). The phenotypic scores of the sex signature (LV4) and the brain scores of the combined age and sex signature (LV6) were the most reliable predictors of good functional outcome (|CVR|: 2.08–2.44; p_{SBC}: $10^{-4.57}$), while the phenotypic scores of the trauma-personality-depressivity (LV5) signature, followed by the phenotypic and brain scores of the depressivity (LV2) signature and the brain scores of the age signature (LV1), were most closely linked to poor functional outcome (|CVR|: 2.54–14.77; p_{SBC}: $10^{-4.08}$–$10^{-4.57}$). The complementary SVR yielded a significant, robust prediction model in both the discovery (R^2 = 25.24%, mean absolute error [MAE] = 9.11) and replication (R^2 = 39.68%, MAE = 11.10) samples (Figure S6; Table S26).

Reading Assistant



Download: Download high-res image (646KB)

Download: Download full-size image

Figure 4. Prediction of functional outcome. The phenotypic and brain scores of all 6 significant latent variables (LVs) identified by the sparse partial least squares algorithm were used as features to predict good (GAF:D/I ≥ 81) and poor (GAF:D/I < 81) functional outcome at 9-month follow-up via support vector machine (SVM) classification. The SVM model was trained in the discovery sample and validated in the replication sample within a nested cross-validation framework. **(A)** In a 2-step feature inspection, the reliability of predictive pattern elements was evaluated using cross-validation ratio (CVR) mapping (|CVR| ≥ 1.96), and the significance of predictive features was assessed by means of sign-based consistency (SBC) mapping ($-\log_{10}(p) > 1.30$). The features are sorted in ascending order of their CVR. Highlighted in red and blue are those features that passed the combined significance threshold of CVR and SBC. Blue colored features were predictive of good functional outcome, while red color indicates that the feature was predictive of poor functional outcome. Nonsignificant features are marked in gray. **(B)** Mean classifier scores of the SVM model for poor (red) and good (blue) outcome of the discovery and replication samples. Horizontal lines represent the mean values of classifier scores. The values in **(A)** and **(B)** were inverted (multiplied by −1) to enhance interpretability. "Phenotype" and "Brain" denote latent phenotypic and brain scores, respectively. GAF:D/I, Global Assessment of Functioning: Disability and Impairment.

Associations With Coping, Resilience, and Visual Dysfunctions

Correlational analyses (Figures S7–S9; Tables S27–S29) indicated that in both the discovery and replication samples, higher brain scores of the depressivity (LV2) and trauma-personality-depressivity (LV5) signatures were associated with greater emotion-oriented coping, reduced RSA-rated perception of self, and greater visual dysfunctions (false discovery rate–adjusted $p < .05$). Higher brain scores of the trauma-personality-depressivity signature were further associated with reduced RSA-rated family cohesion, social competence, social resources, and structured style. Higher phenotypic scores of the depressivity (LV2) and trauma-personality-depressivity (LV5) signatures were associated with less task-oriented coping, social diversion, and avoidance; greater emotion-oriented

Reading Assistant

coping; reduced resilience across all domains; and greater visual dysfunctions. No associations with prior medication intake were consistently significant across the discovery and replication samples (Tables S30–S44).

Discussion

We used an integrated, data-driven approach to examine shared and distinct brain signatures of childhood trauma, personality traits, and depressivity in early-stage psychosis and depression. Of 6 SPLS-derived signatures, 3 reflected age or sex effects, while the others captured signatures of interest, which were linked to depressivity, childhood trauma, or their combined interplay and were associated with distinct clinical patterns and functional outcomes.

Depressivity Signature

The depressivity signature (LV2) captured core depressivity symptoms in younger individuals across the BDI-II domains of negative self-attitude, performance impairment, and somatic complaints (54). This depressivity pattern was associated with reduced GMV in the limbic system and, to a lesser extent, increased GMV in visual network regions. The limbic system, including the amygdala and hippocampus, is central to emotional processing, sexual behavior, vegetative functions, and memory and has been consistently implicated in depression (6,69, 70, 71, 72). Volumetric reductions in this system may reflect stress-related hypothalamic-pituitary-adrenal axis dysfunction (73), with heightened vulnerability in adolescence (74). Smaller GMV increases in the visual network may be consistent with its role in emotion regulation (75). Moreover, we observed volumetric increases of the thalamus and basal ganglia, both extensively connected to limbic circuits (76,77). While such increases may appear unexpected, structural findings in depressive disorders have generally been inconsistent (78). Importantly, all GMV associations observed here emerged within multivariate patterns rather than as isolated region-specific or univariate group-level effects. Large-scale meta-analytic work suggests that subcortical volume reductions are more prominent in recurrent depression, whereas first-episode cases often show no consistent subcortical alterations (78). Consistent with this, recent work on first-episode, unmedicated major depressive disorder reported increased basal ganglia volume, potentially reflecting early-phase or compensatory neurobiological mechanisms in early-stage illness (79).

Childhood Trauma Signature

The childhood trauma signature (LV3) linked self-reported sexual and physical abuse in younger individuals to GMV reductions within the default mode network, consistent with prior work on early-life adversity and altered default mode network development (12,80). The default mode network, central to autobiographical memory and social information integration (81), undergoes a second wave of synaptogenesis and pruning during adolescence (82), rendering it particularly vulnerable to environmental disruption during this period (42,83,84). Greater trauma exposure was also associated with reduced GMV in the middle temporal gyrus, inferior parietal lobule, and superior frontal gyrus, regions supporting attention, inhibitory control, emotion regulation, memory, and social cognition, suggesting that early adversity may impact networks essential for adaptive emotional and cognitive functioning in social contexts (85, 86, 87, 88). Moreover, smaller GMV increases in the thalamus and inferior frontal gyrus may reflect heightened cognitive and emotional demands from trauma (89, 90, 91). Sexual and physical abuse exposure was also related to BDI-II-reported loss of pleasure and sexual interest, consistent with links between such abuse and later anhedonia and sexual difficulties (92, 93, 94). Notably, the association with younger age in the absence of sex differences suggests a linear, sex-independent relationship between age and the neural correlates of childhood trauma. Finally, we also found that experiences of sexual and physical abuse were linked to less SPI-A-reported depressivity, suggesting potentially “silent” neurobiological marks, i.e., individuals with trauma exposure to childhood trauma presenting with brain changes but no clinically significant psychopathology, which may be shaped by genetic variation or compensatory functional connectivity (12,16).

Reading Assistant

Trauma-Personality-Depressivity Signature

The trauma-personality-depressivity signature (LV5) linked the convergence of childhood trauma (emotional and physical abuse), a maladaptive personality profile, and depressivity to a dense GMV pattern spanning all functional networks and was more pronounced in females and patient groups (CHR-P, ROP, ROD). The pervasive brain pattern subsumes limbic and default mode network alterations of the depressivity signature (LV2) and childhood trauma signature (LV3), respectively, while engaging additional large-scale networks, suggesting synergistic effects beyond a single factor's footprint. At the personality level, this signature was primarily characterized by elevated neuroticism (i.e., negative emotionality, emotional instability, stress sensitivity) and lower conscientiousness (i.e., self-discipline, organization, competence, goal-directed behavior) (19,95, 96, 97), with a selective contribution of extraversion via reduced positive affect and minimal item-level involvement of agreeableness. This pattern is consistent with extensive prior work linking both childhood trauma and depressive symptomatology to higher neuroticism and lower conscientiousness and extraversion (21, 22, 23,28,98,99), reflecting an overall maladaptive personality configuration that may confer increased vulnerability to unfavorable illness trajectories and outcomes. Given that conscientiousness, despite being a trait, shows developmental change over time (100,101), it may also be particularly sensitive to childhood trauma. The prominence of neuroticism and conscientiousness may help explain the pervasive GMV pattern, given their close links to emotion regulation, stress responsivity, and self-control processes supported by distributed large-scale brain networks. Consistent with accumulating evidence that these traits mediate pathways through which childhood trauma contributes to the development of depressive symptomatology and related psychiatric outcomes (27,28,31,98), our SEM supported a dual-pathway model in which childhood trauma contributes to emotional depressivity both directly and indirectly via maladaptive personality traits. Neuroticism, widely regarded as a central transdiagnostic dispositional vulnerability (95) and as being more prevalent in women (102,103), may drive depressivity by triggering episodes or amplifying other risks through negative attention bias, stress generation, heightened reactivity, and maladaptive coping (40,104,105), such that depressive symptomatology may in part reflect an expression of elevated neuroticism (95). Notably, the association with female sex is consistent with prior evidence for sex differences in the prevalence of affective symptomatology and trauma-related neurobiology (106, 107, 108), suggesting that this pattern reflects a sexual dimorphic vulnerability profile, which is, in contrast to the childhood trauma signature (LV3), independent of age and emerges in the context of affective dysregulation and maladaptive personality traits. Unlike the depressivity signature (LV2), which primarily captured self-reported depressive symptoms (53), the trauma-personality-depressivity signature (LV5) also encompassed observer-rated SPI-A disturbances in mood, stress tolerance, and emotional responsiveness (57), indicating a broader, more nuanced depressivity profile integrating both self- and observer-rated symptomatology. This signature distinguished patients from HC individuals, reflecting the highest overall psychopathological burden among all retrieved signatures.

Post Hoc Exploration of SPLS Signatures

The trauma-personality-depressivity signature (LV5) emerged as the strongest predictor of poor functional outcome, followed by the depressivity (LV2) and age (LV1) signatures. While a core depressivity profile (LV2) was linked to poor outcomes, the mixed profile with overlapping trauma, personality, and depressivity features (LV5) appeared to present the greatest challenge for functional recovery across diagnoses. Moreover, the depressivity (LV2) and trauma-personality-depressivity (LV5) signatures were linked to reduced resilience, maladaptive coping, and visual dysfunctions. Both signatures were most strongly linked to perception of self, capturing confidence in one's own abilities and judgments, self-efficacy and realistic expectations (50), and emotion-oriented coping, a maladaptive coping strategy associated with self-blame, anxiety, and negative emotionality (109). This corroborates prior evidence linking depressivity and a maladaptive personality structure to deficient resilience (16,68,110) and dysfunctional coping (109,111). Prior work indicates that resilience ...rates the mediating role of neuroticism in linking childhood trauma to depression, ...ting it as an intervention target for trauma-exposed individuals (112). Coping may be ...ctly affected by personality through its influence on stress exposure, reactivity, and ...ived coping resources or may also reflect a personal tendency toward less ...nctional coping strategies (111). Notably, the brain pattern of the trauma-personality-depressivity (LV5) signature was also correlated with additional RSA domains, including

Reading Assistant

family cohesion, social competence, social resources, and structured style, mirroring its extensive neuroanatomical footprint. Additionally, the phenotypic and brain patterns of both signatures were associated with greater visual dysfunctions, consistent with prior work linking impairments in visual processing to less functional remission in ROP and CHR-P individuals and greater depressivity and lower quality of life in CHR-P individuals (51). As visual dysfunctions are often underrecognized in clinical practice despite their clinical relevance and prevalence, this neurobiological and clinical linkage highlights the need for comprehensive multimodal assessment in early-stage mental disorders (53). The absence of significant links between the childhood trauma signature (LV3) and resilience, coping, and personality suggests that on both a clinical and a neurobiological level, it is not trauma exposure per se that determines outcome; rather, it is the reciprocal and complex interplay between childhood trauma, resilience, coping, and personality that shapes vulnerability and the emergence of psychiatric symptoms during adolescence and young adulthood.

Together, these findings underscore the heterogeneity of early psychosis and depression, showing that vulnerability is expressed through multiple, separable brain-phenotype patterns with distinct functional and adaptive correlates, rather than a single uniform profile. Notably, the signature capturing the coalescence of childhood trauma, personality, and depressivity showed the strongest association with functional outcome, representing a particularly promising starting point for future investigation. Therefore, risk is best captured through an integrated phenotypic and neurobiological assessment, motivating a multimodal framework for both research and clinical practice to identify risk profiles shaping illness trajectories. Future longitudinal and interventional observational studies can test whether these profiles differ in developmental course and sensitivity from targeted, multimodal interventions, thereby extending the current findings from outcome prediction toward trajectory-based models of illness progression.

Limitations

This study is limited by the associative nature of the SPLS signatures, precluding causal inferences, and the missing longitudinal assessment of the temporal stability of these signatures. In addition, we only assessed current or recent depressive symptomatology; persistent or trait-like depressive patterns, which may be particularly relevant in the context of personality pathology (113), were not directly captured, limiting conclusions regarding long-term depressivity. Furthermore, as the PRONIA cohort primarily comprises individuals at CHR-P and early stages of psychotic and depressive disorders, generalizability beyond the affective-psychotic spectrum may be limited. In addition, the childhood trauma (LV3) and trauma-personality-depressivity (LV5) signatures were associated with MRI data quality, although with comparably small weights for the quality measure. This association is most plausibly attributable to the naturalistic design of the PRONIA study, specifically the psychopathology and young age of the PRONIA cohort (114), rather than reflecting a substantive confound and driver of the identified signatures. Moreover, medication exposure was not included as a feature in the SPLS model; although the cohort was minimally medicated by design and post hoc analyses did not reveal consistent associations with medication exposure, residual medication effects cannot be fully excluded and should be addressed in future studies of entirely drug-naïve samples. Finally, the extensive use of self-report measures introduces potential biases, such as social desirability or mood state (115, 116, 117). Future research should extend this investigation to genetic predispositions and more detailed environmental factors (21).

Conclusions

We identified and replicated 3 neuroanatomical signatures spanning the affective-psychotic spectrum linked to depressivity, childhood trauma, and their interplay with personality traits. Signatures related to depressivity and trauma, personality, and depressivity combined were associated with reduced resilience, maladaptive coping, and poorer functional mes, whereas the pure trauma signature represented a distinct neural imprint without psychopathological correlates. These findings support stratification of risk profiles to n precision interventions that address trauma processing, alleviate symptoms, and gthen resilience at the earliest point of care.

Reading Assistant

Acknowledgments and Disclosures

All contributing authors were supported by PRONIA, which is a collaborative project funded by the European Union under the 7th Framework Programme (Grant No. 602152). This work has been partially supported by the European Research Area Network NEURON "Translational Biomarkers in Brain Disorders" (Project NicAb, Grant No. 01EW2012). TL is supported by the Advanced Cologne Clinician Scientist Program (adCCSP) / Faculty of Medicine / University of Cologne. DP and STP were supported by the Else Kröner-Fresenius-Stiftung" through the Clinician Scientist Program "EKFS-Translational Psychiatry." UD was funded by the German Research Foundation (Grant Nos. FOR2107 DA1151/5-1, DA1151/5-2, DA1151/9-1, DA1151/10-1, DA1151/11-1; SFB/TRR 393, and project Grant No. 521379614) and the Interdisciplinary Center for Clinical Research of the medical faculty of Münster (Grant No. Dan3/022/22). RU is funded/supported by the NIHR Oxford Health Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. NK is supported through grants from National Institutes of Health (Grant No. U01MH124639-01; ProNET), the German Innovation Fund (CARE project), the German Federal Ministry of Education and Research (COMMITMENT and BEST projects), as well as ERA PerMed (IMPLEMENT project). PF has received and is currently receiving grants from several national and international foundations and institutions, e.g., from the German Science Foundation, the German Ministry of Science, and the German Ministry of Health. RU is supported by the National Institute for Health and Care Research Oxford Health Biomedical Research Centre. The funding organizations were not involved in the design or conduct of the study; the collection, management, analysis, or interpretation of the data; the preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

CW, ES, STP, NK, and DP had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. CW, ES, STP, NK, and DP contributed to concept and design. CW, ES, STP, CV, DBD, LK-I, JK, SR, FS-L, GP, GB, AB, RL, UD, RU, CP, EM, SJW, PB, SB, NK, and DP contributed to acquisition, analysis, or interpretation of data. CW, STP, NK, and DP contributed to drafting of the manuscript. CW, ES, STP, CV, DBD, LAA, TL, LK-I, JK, SR, KC, FS-L, PF, KS, GP, GB, AB, GR, RL, UD, RU, RS, CP, EM, SW, PB, SB, NK, and DP contributed to critical revision of the manuscript for important intellectual content. CW, ES, ST, NK, and DP contributed to statistical analysis. STP, LK-I, SR, RKRS, CP, SJW, PB, SB, NK, and DP obtained funding. NK, KC, TL, RU, EM, AB, PB, and SB contributed administrative, technical, or material support. SR, FS-L, PF, GB, AB, GR, RL, UD, RU, RKRS, CP, EM, SJW, PB, SB, NK, and DP contributed to supervision.

The PRONIA Consortium: The following authors participated in the screening, recruitment, rating, examination, and follow-up of the study participants used in the current analyses. The authors are listed in alphabetical order according to the institution of affiliation. Department of Psychiatry and Psychotherapy, Ludwig-Maximilian-University, Munich, Germany: Shalaila Haas, Alkomiet Hasan, Claudius Hoff, Ifrah Khanyaree, Camilla Krämer, Eva Meisenzahl, Aylin Melo, Susanna Muckenhuber-Sternbauer, Yanis Köhler, Oemer Faruk Oeztuerk, Nora Penzel, David Popovic, Adrian Rangnick, Sebastian von Saldern, Rachele Sanfelici, Moritz Spangemacher, Ana Tupac, Maria Fernanda Urquijo, Johanna Weiske, Antonia Wosgien. Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany: Karsten Blume, Dennis Hedderich, Dominika Julkowski, Nathalie Kaiser, Thorsten Lichtenstein, Ruth Milz, Alexandra Nikolaides, Tanja Pilgram, Mauro Seves, Martina Wassen. Department of Psychiatry (Psychiatric University Hospital, UPK), University of Basel, Switzerland: Christina Andreou, Laura Egloff, Fabienne Harrisberger, Ulrike Heitz, Claudia Lenz, Letizia Leanza, Amatya Mackintosh, Renata Smieskova, Erich Studerus, Anna Walter, Sonja Widmayer. Institute of Mental Health & School of Psychology, University of Birmingham, United Kingdom: Chris Day, Sian Lowri Griffiths, Mariam Iqbal, Mirabel Pelton, Pavan Mallikarjun, Alexandra Stainton, Ashleigh Lin. Department of Psychiatry, University of [illegible], Finland: Alexander Denissoff, Anu Ellilä, Tiina From, Markus Heinimaa, Tuula Ilonen, [illegible]leikki Laurikainen, Antti Luutonen, Akseli Mäkela, Janina Paju, Henri Pesonen, [illegible]Lima Säilä, Anna Toivonen, Otto Turtonen. Department of Psychiatry (Psychiatric [illegible]rsity Hospital LVR/HHU Düsseldorf), University of Düsseldorf, Germany: Sonja [illegible]rweck, Norman Kluthausen, Gerald Antoch, Julian Caspers, Hans-Jörg Wittsack. Department of Basic Medical Science, Neuroscience and Sense Organs - University of Bari

Reading Assistant

Aldo Moro: Giuseppe Blasi, Giulio Pergola, Grazia Caforio, Leonardo Fazio, Tiziana Quarto, Barbara Gelao, Raffaella Romano, Ileana Andriola, Andrea Falsetti, Marina Barone, Roberta Passiatore, Marina Sangiuliano. Department of Psychiatry and Psychotherapy of the University of Münster, Germany: Marian Surmann, Olga Bienek, Alexandra Korda (associate from University of Lübeck), Andreas Sprenger (associate from University of Lübeck), Udo Dannlowski, Rebekka Lencer. General Electric Global Research Inc., USA. Ana Beatriz Solana, Manuela Abraham, Timo Schirmer. Workgroup of Paolo Brambilla, University of Milan, Italy: Department of Neuroscience and Mental Health, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy: Carlo Altamura, Marika Belleri, Francesca Bottinelli, Adele Ferro, Marta Re Programma2000, Niguarda Hospital, Milan: Emiliano Monzani, Maurizio Sberna San Paolo Hospital, Milan: Armando D'Agostino, Lorenzo Del Fabro. Villa San Benedetto Menni, Albese con Cassano (CO): Giampaolo Perna, Maria Nobile, Alessandra Alciati. Workgroup of Paolo Brambilla at the University of Udine, Italy. Department of Medical Area, University of Udine, Udine, Italy: Matteo Balestrieri, Carolina Bonivento, Giuseppe Cabras, Franco Fabbro. IRCCS Scientific Institute "E. Medea," Polo FVG, Udine: Marco Garzitto, Sara Piccin.

NK and EM own issued patent US20160192889A1 ("Adaptive pattern recognition for psychosis risk modeling"). As a member of Spring Health's Scientific Advisory Board, NK has advised that company on the development of tools to predict treatment outcomes for depression and psychosis. He holds no equity and has received no financial compensation from this company. PF received research support/honoraria for lectures or advisory activities from BMS, Boehringer-Ingelheim, JNJ, Lundbeck, Otsuka, Richter, and Rovi. These affiliations did not influence the writing of this manuscript. In the last 5 years PB received educational grants, participated in scientific boards, and/or had contacts unrelated to the current presentation with the following pharmaceutical companies: Angelini, Viatris, Lundbeck, Jansen, Otsuka, Compass, Neuraxpharm, Novartis, Brystol Myers. AB received consulting fees from Biogen and lecture fees from Otsuka, Janssen, and Lundbeck. GB, GP, and LAA received lecture fees from Lundbeck. All other authors report no biomedical financial interests or potential conflicts of interest.

Supplementary Material

Download all supplementary files included with this article What's this? ↗

Download: Download Acrobat PDF file (3MB)

Supplemental Methods, Results, Discussion, Figures S1–S9, Tables S1–S45.

Download: Download spreadsheet (13KB)

Key Resources Table.

References

1 F. Núñez-Regueiro, S. Núñez-Regueiro
Identifying salient stressors of adolescence: A systematic review and content analysis
J Youth Adolesc, 50 (2021), pp. 2533-2556
Crossref ↗ View in Scopus ↗ Google Scholar ↗

2 M.K. Holder, J.D. Blaustein
Puberty and adolescence as a time of vulnerability to stressors that alter neurobehavioral processes
Front Neuroendocrinol, 35 (2014), pp. 89-110
View PDF View article View in Scopus ↗ Google Scholar ↗

A. Oshri, F.A. Rogosch, D. Cicchetti
Child maltreatment and mediating influences of childhood personality types on the development of adolescent psychopathology
J Clin Child Adolesc Psychol, 42 (2013), pp. 287-301
Crossref ↗ View in Scopus ↗ Google Scholar ↗

4 B.L. Hankin

Reading Assistant

Depression from childhood through adolescence: Risk mechanisms across multiple systems and levels of analysis
Curr Opin Psychol, 4 (2015), pp. 13-20
View PDF View article View in Scopus ↗ Google Scholar ↗

5 M. Solmi, J. Radua, M. Olivola, E. Croce, L. Soardo, G. Salazar de Pablo, *et al.*
Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies
Mol Psychiatry, 27 (2022), pp. 281-295
Crossref ↗ View in Scopus ↗ Google Scholar ↗

6 G.S. Malhi, J.J. Mann
Depression
Lancet, 392 (2018), pp. 2299-2312
View PDF View article View in Scopus ↗ Google Scholar ↗

7 A. Minichino, C. Davies, O. Karpenko, N. Christodoulou, R. Ramalho, S. Nandha, *et al.*
Preventing psychosis in people at clinical high risk: An updated meta-analysis by the World Psychiatric Association Preventive Psychiatry section
Mol Psychiatry, 30 (2025), pp. 2773-2782
Crossref ↗ View in Scopus ↗ Google Scholar ↗

8 J. van Os
The dynamics of subthreshold psychopathology: Implications for diagnosis and treatment
Am J Psychiatry, 170 (2013), pp. 695-698
Crossref ↗ View in Scopus ↗ Google Scholar ↗

9 B. Hogg, I. Gardoki-Souto, A. Valiente-Gómez, A.R. Rosa, L. Fortea, J. Radua, *et al.*
Psychological trauma as a transdiagnostic risk factor for mental disorder: An umbrella meta-analysis
Eur Arch Psychiatry Clin Neurosci, 273 (2023), pp. 397-410
Crossref ↗ View in Scopus ↗ Google Scholar ↗

10 J.G.F.M. Hovens, E.J. Giltay, J.E. Wiersma, P. Spinhoven, B.W.J.H. Penninx, F.G. Zitman
Impact of childhood life events and trauma on the course of depressive and anxiety disorders
Acta Psychiatr Scand, 126 (2012), pp. 198-207
Crossref ↗ View in Scopus ↗ Google Scholar ↗

11 P. Fusar-Poli, M. Tantardini, S. De Simone, V. Ramella-Cravaro, D. Oliver, J. Kingdon, *et al.*
Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk
Eur Psychiatry, 40 (2017), pp. 65-75
View PDF View article Crossref ↗ View in Scopus ↗ Google Scholar ↗

12 M.H. Teicher, J.A. Samson, C.M. Anderson, K. Ohashi
The effects of childhood maltreatment on brain structure, function and connectivity
Nat Rev Neurosci, 17 (2016), pp. 652-666
Crossref ↗ View in Scopus ↗ Google Scholar ↗

13 R.K. Lipsky, C.C. McDonald, M.C. Souders, C.C. Carpio, A.M. Teitelman
Adverse childhood experiences, the serotonergic system, and depressive and anxiety disorders in adulthood: A systematic literature review
Neurosci Biobehav Rev, 134 (2022), Article 104495
View PDF View article View in Scopus ↗ Google Scholar ↗

K.L. Humphreys, J. LeMoult, J.G. Wear, H.A. Piersiak, A. Lee, I.H. Gotlib
Child maltreatment and depression: A meta-analysis of studies using the Childhood Trauma Questionnaire
Child Abuse Negl, 102 (2020), Article 104361
View PDF View article View in Scopus ↗ Google Scholar ↗

Reading Assistant

15 J.G. Green, K.A. McLaughlin, P.A. Berglund, M.J. Gruber, N.A. Sampson, A.M. Zaslavsky, R.C. Kessler
Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: Associations with first onset of DSM-IV disorders
Arch Gen Psychiatry, 67 (2010), pp. 113-123
Crossref ↗ View in Scopus ↗ Google Scholar ↗

16 S. Collishaw, A. Pickles, J. Messer, M. Rutter, C. Shearer, B. Maughan
Resilience to adult psychopathology following childhood maltreatment: Evidence from a community sample
Child Abuse Negl, 31 (2007), pp. 211-229
View PDF View article View in Scopus ↗ Google Scholar ↗

17 E.E. Werner
Vulnerable but invincible: High-risk children from birth to adulthood
Acta Paediatr Suppl, 422 (1997), pp. 103-105
Crossref ↗ View in Scopus ↗ Google Scholar ↗

18 L.A. Antonucci, A. Raio, G.C. Kikidis, A. Bertolino, A. Rampino, T. Banaschewski, *et al.*
Personality changes during adolescence predict young adult psychosis proneness and mediate gene-environment interplays of schizophrenia risk
Psychol Med, 54 (2024), pp. 3838-3848
Crossref ↗ View in Scopus ↗ Google Scholar ↗

19 T. A Widiger
Personality and psychopathology
World Psychiatry, 10 (2011), pp. 103-106
Google Scholar ↗

20 M.-A. Lee, R. Song
Childhood abuse, personality traits, and depressive symptoms in adulthood
Child Abuse Negl, 65 (2017), pp. 194-203
View PDF View article View in Scopus ↗ Google Scholar ↗

21 G. Schneider, C. Köhnke, H. Teismann, K. Berger
Childhood trauma and personality explain more variance in depression scores than sociodemographic and lifestyle factors—Results from the BiDirect Study
J Psychosom Res, 147 (2021), Article 110513
View PDF View article View in Scopus ↗ Google Scholar ↗

22 C. Adanty, J. Qian, Y. Wang, G. Remington, A. Shakeri, C. Borlido, *et al.*
Childhood trauma exposure and personality traits in schizophrenia patients
Schizophr Res, 241 (2022), pp. 221-227
View PDF View article View in Scopus ↗ Google Scholar ↗

23 M.P. Hengartner, L.J. Cohen, S. Rodgers, M. Müller, W. Rössler, V. Ajdacic-Gross
Association between childhood maltreatment and normal adult personality traits: Exploration of an understudied field
J Pers Disord, 29 (2015), pp. 1-14
Crossref ↗ View in Scopus ↗ Google Scholar ↗

24 Y.-J. Wen, Q.-J. Bo, W.-P. Hou, Z. Mao, F. Li, F. He, *et al.*
The effects of childhood trauma on personality in unaffected first-degree relatives of patients with major depressive disorder
BMC Psychiatry, 22 (2022), p. 312
View in Scopus ↗ Google Scholar ↗

H.W. de Carvalho, R. Pereira, J. Frozi, L.W. Bisol, G.L. Ottoni, D.R. Lara
Childhood trauma is associated with maladaptive personality traits
Child Abuse Negl, 44 (2015), pp. 18-25
View PDF View article Google Scholar ↗

Reading Assistant

26 L.K. Brents, G.A. James, J.M. Cisler, C.D. Kilts
Personality variables modify the relationship between childhood maltreatment history and poor functional outcomes
Psychiatry Res, 268 (2018), pp. 229-237
View PDF View article View in Scopus ↗ Google Scholar ↗

27 K. Ono, Y. Takaesu, Y. Nakai, A. Shimura, Y. Ono, A. Murakoshi, *et al.*
Associations among depressive symptoms, childhood abuse, neuroticism, and adult stressful life events in the general adult population
Neuropsychiatr Dis Treat, 13 (2017), pp. 477-482
Crossref ↗ View in Scopus ↗ Google Scholar ↗

28 M. Zhang, J. Han, J. Shi, H. Ding, K. Wang, C. Kang, J. Gong
Personality traits as possible mediators in the relationship between childhood trauma and depressive symptoms in Chinese adolescents
J Psychiatr Res, 103 (2018), pp. 150-155
View PDF View article View in Scopus ↗ Google Scholar ↗

29 Y. Hayashi, Y. Okamoto, K. Takagaki, G. Okada, S. Toki, T. Inoue, *et al.*
Direct and indirect influences of childhood abuse on depression symptoms in patients with major depressive disorder
BMC Psychiatry, 15 (2015), p. 244
View in Scopus ↗ Google Scholar ↗

30 S.A. Gamble, N.L. Talbot, P.R. Duberstein, K.R. Conner, N. Franus, A.M. Beckman, Y. Conwell
Childhood sexual abuse and depressive symptom severity: The role of neuroticism
J Nerv Ment Dis, 194 (2006), pp. 382-385
Crossref ↗ View in Scopus ↗ Google Scholar ↗

31 M. Koschig, I. Conrad, K. Berger, B.T. Baune, H.J. Grabe, D. Gerstorf, *et al.*
The mediating role of personality traits in the association between childhood trauma and depressive symptoms in young adulthood
J Affect Disord, 338 (2023), pp. 373-379
View PDF View article View in Scopus ↗ Google Scholar ↗

32 A.L. Tang, S.J. Thomas
Relationships between depressive symptoms, other psychological symptoms, and quality of life
Psychiatry Res, 289 (2020), Article 113049
View PDF View article View in Scopus ↗ Google Scholar ↗

33 H. Häfner, K. Maurer, G. Trendler, W. An Der Heiden, M. Schmidt, R. Könnecke
Schizophrenia and depression: Challenging the paradigm of two separate diseases—A controlled study of schizophrenia, depression and healthy controls
Schizophr Res, 77 (2005), pp. 11-24
View PDF View article View in Scopus ↗ Google Scholar ↗

34 P. Fusar-Poli, S. Borgwardt, A. Bechdolf, J. Addington, A. Riecher-Rössler, F. Schultze-Lutter, *et al.*
The psychosis high-risk state: A comprehensive state-of-the-art review
JAMA Psychiatry, 70 (2013), pp. 107-120
Crossref ↗ View in Scopus ↗ Google Scholar ↗

35 K.O. Schubert, S.R. Clark, L.K. Van, J.L. Collinson, B.T. Baune
Depressive symptom trajectories in late adolescence and early adulthood: A systematic review
Aust N Z J Psychiatry, 51 (2017), pp. 477-499
Crossref ↗ View in Scopus ↗ Google Scholar ↗

P.D. McGorry, R. Purcell, I.B. Hickie, A.R. Yung, C. Pantelis, H.J. Jackson
Clinical staging: A heuristic model for psychiatry and youth mental health

Reading Assistant

Med J Aust, 187 (2007), pp. S40-S42
View in Scopus ↗ Google Scholar ↗

37 K. Yucel, M.C. McKinnon, R. Chahal, V.H. Taylor, K. Macdonald, R. Joffe, G.M. MacQueen
Anterior cingulate volumes in never-treated patients with major depressive disorder
Neuropsychopharmacology, 33 (2008), pp. 3157-3163
Crossref ↗ View in Scopus ↗ Google Scholar ↗

38 D.A. Pizzagalli, A.C. Roberts
Prefrontal cortex and depression
Neuropsychopharmacology, 47 (2022), pp. 225-246
Crossref ↗ View in Scopus ↗ Google Scholar ↗

39 R.A. Cohen, S. Grieve, K.F. Hoth, R.H. Paul, L. Sweet, D. Tate, *et al.*
Early life stress and morphometry of the adult anterior cingulate cortex and caudate nuclei
Biol Psychiatry, 59 (2006), pp. 975-982
View PDF View article View in Scopus ↗ Google Scholar ↗

40 X. Liu, H. Lai, J. Li, B. Becker, Y. Zhao, B. Cheng, S. Wang
Gray matter structures associated with neuroticism: A meta-analysis of whole-brain voxel-based morphometry studies
Hum Brain Mapp, 42 (2021), pp. 2706-2721
Crossref ↗ View in Scopus ↗ Google Scholar ↗

41 H. Lai, S. Wang, Y. Zhao, L. Zhang, C. Yang, Q. Gong
Brain gray matter correlates of extraversion: A systematic review and meta-analysis of voxel-based morphometry studies
Hum Brain Mapp, 40 (2019), pp. 4038-4057
Crossref ↗ View in Scopus ↗ Google Scholar ↗

42 C. Paquola, M.R. Bennett, J. Lagopoulos
Understanding heterogeneity in grey matter research of adults with childhood maltreatment-A meta-analysis and review
Neurosci Biobehav Rev, 69 (2016), pp. 299-312
View PDF View article View in Scopus ↗ Google Scholar ↗

43 M. Amidfar, J. Quevedo, G. Z Réus, Y.K. Kim
Grey matter volume abnormalities in the first depressive episode of medication-naïve adult individuals: A systematic review of voxel based morphometric studies
Int J Psychiatry Clin Pract, 25 (2021), pp. 407-420
Crossref ↗ View in Scopus ↗ Google Scholar ↗

44 K.A. McLaughlin, N.L. Colich, A.M. Rodman, D.G. Weissman
Mechanisms linking childhood trauma exposure and psychopathology: A transdiagnostic model of risk and resilience
BMC Med, 18 (2020), p. 96
View in Scopus ↗ Google Scholar ↗

45 S. Bray, C. Chang, F. Hoeft
Applications of multivariate pattern classification analyses in developmental neuroimaging of healthy and clinical populations
Front Hum Neurosci, 3 (2009), p. 32
Google Scholar ↗

J.M. Monteiro, A. Rao, J. Shawe-Taylor, J. Mourão-Miranda, Alzheimer's Disease Initiative
A multiple hold-out framework for sparse partial least squares
J Neurosci Methods, 271 (2016), pp. 182-194
View PDF View article View in Scopus ↗ Google Scholar ↗

D. Popovic, A. Ruef, D.B. Dwyer, L.A. Antonucci, J. Eder, R. Sanfelici, *et al.*

Reading Assistant

Traces of trauma: A multivariate pattern analysis of childhood trauma, brain structure, and clinical phenotypes
Biol Psychiatry, 88 (2020), pp. 829-842
View PDF View article View in Scopus ↗ Google Scholar ↗

48 A. Feder, E.J. Nestler, D.S. Charney
Psychobiology and molecular genetics of resilience
Nat Rev Neurosci, 10 (2009), pp. 446-457
Crossref ↗ View in Scopus ↗ Google Scholar ↗

49 S.E. Taylor, A.L. Stanton
Coping resources, coping processes, and mental health
Annu Rev Clin Psychol, 3 (2007), pp. 377-401
Crossref ↗ View in Scopus ↗ Google Scholar ↗

50 O. Hjemdal, O. Friborg, S. Braun, C. Kempenaers, P. Linkowski, P. Fossion
The resilience scale for adults: Construct validity and measurement in a Belgian sample
Int J Test, 11 (2011), pp. 53-70
Crossref ↗ View in Scopus ↗ Google Scholar ↗

51 J.M. Schwarzer, I. Meyhoefer, L.A. Antonucci, L. Kambeitz-Ilankovic, M. Surmann, O. Bienek, *et al.*
The impact of visual dysfunctions in recent-onset psychosis and clinical high-risk state for psychosis
Neuropsychopharmacology, 47 (2022), pp. 2051-2060
Crossref ↗ View in Scopus ↗ Google Scholar ↗

52 E. von Elm, D.G. Altman, M. Egger, S.J. Pocock, P.C. Gøtzsche, J.P. Vandenbroucke, STROBE Initiative
The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies
Lancet, 370 (2007), pp. 1453-1457
View PDF View article View in Scopus ↗ Google Scholar ↗

53 A.T. Beck, R.A. Steer, G.K. Brown
Manual for the Beck Depression Inventory-II, Psychological Corporation, San Antonio, TX (1996)
Google Scholar ↗

54 A.B. Shafer
Meta-analysis of the factor structures of four depression questionnaires: Beck, CES-D, Hamilton, and Zung
J Clin Psychol, 62 (2006), pp. 123-146
Crossref ↗ View in Scopus ↗ Google Scholar ↗

55 L.A. Fink, D. Bernstein, L. Handelsman, J. Foote, M. Lovejoy
Initial reliability and validity of the childhood trauma interview: A new multidimensional measure of childhood interpersonal trauma
Am J Psychiatry, 152 (1995), pp. 1329-1335
View in Scopus ↗ Google Scholar ↗

56 D.P. Bernstein, L. Fink, L. Handelsman, J. Foote, M. Lovejoy, K. Wenzel, *et al.*
Initial reliability and validity of a new retrospective measure of child abuse and neglect
Am J Psychiatry, 151 (1994), pp. 1132-1136
View in Scopus ↗ Google Scholar ↗

F. Schultze-Lutter, J. Addington, S. Rurhmann
Schizophrenia Proneness Instrument, Adult Version (SPI-A)
Giovanni Fioriti Editore, Rome, Italy (2007)
Google Scholar ↗

58 D.B. Dwyer, P. Falkai, N. Koutsouleris

Reading Assistant

Machine learning approaches for clinical psychology and psychiatry
Annu Rev Clin Psychol, 14 (2018), pp. 91-118
Crossref ↗ View in Scopus ↗ Google Scholar ↗

59 J. Dukart, M.L. Schroeter, K. Mueller, Alzheimer's Disease Neuroimaging Initiative
Age correction in dementia—Matching to a healthy brain
PLoS One, 6 (2011), Article e22193
Crossref ↗ View in Scopus ↗ Google Scholar ↗

60 A. Krishnan, L.J. Williams, A.R. McIntosh, H. Abdi
Partial Least Squares (PLS) methods for neuroimaging: A tutorial and review
Neuroimage, 56 (2011), pp. 455-475
View PDF View article View in Scopus ↗ Google Scholar ↗

61 Y. Rosseel
lavaan: An R Package for Structural Equation Modeling
J Stat Soft, 48 (2012), pp. 1-36
Google Scholar ↗

62 G. Pedersen, K.A. Hagtvet, S. Karterud
Generalizability studies of the Global Assessment of Functioning-Split version
Compr Psychiatry, 48 (2007), pp. 88-94
View PDF View article View in Scopus ↗ Google Scholar ↗

63 L. San, A. Ciudad, E. Alvarez, J. Bobes, I. Gilaberte
Symptomatic remission and social/vocational functioning in outpatients with schizophrenia: Prevalence and associations in a cross-sectional study
Eur Psychiatry, 22 (2007), pp. 490-498
View PDF View article Crossref ↗ View in Scopus ↗ Google Scholar ↗

64 N. Koutsouleris, L. Kambeitz-Ilankovic, S. Ruhrmann, M. Rosen, A. Ruef, D.B. Dwyer, *et al.*
Prediction models of functional outcomes for individuals in the clinical high-risk state for psychosis or with recent-onset depression: A multimodal, multisite machine learning analysis
JAMA Psychiatry, 75 (2018), pp. 1156-1172
Crossref ↗ View in Scopus ↗ Google Scholar ↗

65 N. Koutsouleris, D.B. Dwyer, F. Degenhardt, C. Maj, M.F. Urquijo-Castro, R. Sanfelici, *et al.*
Multimodal machine learning workflows for prediction of psychosis in patients with clinical high-risk syndromes and recent-onset depression
JAMA Psychiatry, 78 (2021), pp. 195-209
Crossref ↗ View in Scopus ↗ Google Scholar ↗

66 V. Gómez-Verdejo, E. Parrado-Hernández, J. Tohka, Alzheimer's Disease Neuroimaging Initiative
Sign-consistency based variable importance for machine learning in brain imaging
Neuroinformatics, 17 (2019), pp. 593-609
Crossref ↗ View in Scopus ↗ Google Scholar ↗

67 N.S. Endler, J.D. Parker
Multidimensional assessment of coping: A critical evaluation
J Pers Soc Psychol, 58 (1990), pp. 844-854
View in Scopus ↗ Google Scholar ↗

68 O. Hjemdal, O. Friborg, T.C. Stiles, J.H. Rosenvinge, M. Martinussen
Resilience predicting psychiatric symptoms: A prospective study of protective factors and their role in adjustment to stressful life events
Clin Psychol Psychother, 13 (2006), pp. 194-201
Crossref ↗ View in Scopus ↗ Google Scholar ↗

D. Roddy, J.R. Kelly, C. Farrell, K. Doolin, E. Roman, A. Nasa, *et al.*
Amygdala substructure volumes in Major Depressive Disorder

Reading Assistant

NeuroImage Clin, 31 (2021), Article 102781

View PDF View article View in Scopus ↗ Google Scholar ↗

70 J. Graham, G. Salimi-Khorshidi, C. Hagan, N. Walsh, I. Goodyer, B. Lennox, J. Suckling
Meta-analytic evidence for neuroimaging models of depression: State or trait?
J Affect Disord, 151 (2013), pp. 423-431
View PDF View article View in Scopus ↗ Google Scholar ↗

71 W. Grodd, V.J. Kumar, A. Schüz, T. Lindig, K. Scheffler
The anterior and medial thalamic nuclei and the human limbic system: Tracing the structural connectivity using diffusion-weighted imaging
Sci Rep, 10 (2020), Article 10957
View in Scopus ↗ Google Scholar ↗

72 L. Cui, S. Li, S. Wang, X. Wu, Y. Liu, W. Yu, *et al.*
Major depressive disorder: Hypothesis, mechanism, prevention and treatment
Signal Transduct Target Ther, 9 (2024), p. 30
Google Scholar ↗

73 P. Videbech, B. Ravnkilde
Hippocampal volume and depression: A meta-analysis of MRI studies
Am J Psychiatry, 161 (2004), pp. 1957-1966
View in Scopus ↗ Google Scholar ↗

74 I. Dumontheil
Adolescent brain development
Curr Opin Behav Sci, 10 (2016), pp. 39-44
View PDF View article View in Scopus ↗ Google Scholar ↗

75 S. Xu, Z. Zhang, L. Li, Y. Zhou, D. Lin, M. Zhang, *et al.*
Functional connectivity profiles of the default mode and visual networks reflect temporal accumulative effects of sustained naturalistic emotional experience
Neuroimage, 269 (2023), Article 119941
View PDF View article View in Scopus ↗ Google Scholar ↗

76 H.H. Yin, B.J. Knowlton
The role of the basal ganglia in habit formation
Nat Rev Neurosci, 7 (2006), pp. 464-476
Crossref ↗ View in Scopus ↗ Google Scholar ↗

77 J.L. Price, W.C. Drevets
Neural circuits underlying the pathophysiology of mood disorders
Trends Cogn Sci, 16 (2012), pp. 61-71
View PDF View article View in Scopus ↗ Google Scholar ↗

78 L. Schmaal, D.J. Veltman, T.G.M. van Erp, P.G. Sämann, T. Frodl, N. Jahanshad, *et al.*
Subcortical brain alterations in major depressive disorder: Findings from the ENIGMA Major Depressive Disorder working group
Mol Psychiatry, 21 (2016), pp. 806-812
Crossref ↗ View in Scopus ↗ Google Scholar ↗

79 N. Xiao, R. Zheng, S. Han, Y. Chen, Y. Zhang
Abnormal gray matter volume and structural covariance network of basal ganglia-limbic system in patients with major depression disorder
Front Neurol, 16 (2025), Article 1712229
View in Scopus ↗ Google Scholar ↗

L. Tozzi, L. Garczarek, D. Janowitz, D.J. Stein, K. Wittfeld, H. Dobrowolny, *et al.*
Interactive impact of childhood maltreatment, depression, and age on cortical brain structure: Mega-analytic findings from a large multi-site cohort

Reading Assistant

Psychol Med, 50 (2020), pp. 1020-1031
Crossref ↗ View in Scopus ↗ Google Scholar ↗

81 R.L. Buckner, J.R. Andrews-Hanna, D.L. Schacter
The brain's default network: Anatomy, function, and relevance to disease
Ann N Y Acad Sci, 1124 (2008), pp. 1-38
Crossref ↗ View in Scopus ↗ Google Scholar ↗

82 T.C. Ho, L.S. King
Mechanisms of neuroplasticity linking early adversity to depression: Developmental considerations
Transl Psychiatry, 11 (2021), p. 517
View in Scopus ↗ Google Scholar ↗

83 K. Rebello, L.M. Moura, W.H.L. Pinaya, L.A. Rohde, J.R. Sato
Default mode network maturation and environmental adversities during childhood
Chronic Stress (Thousand Oaks), 2 (2018), Article 2470547018808295
Google Scholar ↗

84 J.N. Giedd, J.L. Rapoport
Structural MRI of pediatric brain development: What have we learned and where are we going?
Neuron, 67 (2010), pp. 728-734
View PDF View article View in Scopus ↗ Google Scholar ↗

85 S. Caspers, A. Schleicher, M. Bacha-Trams, N. Palomero-Gallagher, K. Amunts, K. Zilles
Organization of the human inferior parietal lobule based on receptor architectonics
Cereb Cortex, 23 (2013), pp. 615-628
Crossref ↗ View in Scopus ↗ Google Scholar ↗

86 R.G. Briggs, A.B. Khan, A.R. Chakraborty, C.J. Abraham, C.D. Anderson, P.J. Karas, *et al.*
Anatomy and white matter connections of the superior frontal gyrus
Clin Anat, 33 (2020), pp. 823-832
Crossref ↗ View in Scopus ↗ Google Scholar ↗

87 J. Xu, H. Lyu, T. Li, Z. Xu, X. Fu, F. Jia, *et al.*
Delineating functional segregations of the human middle temporal gyrus with resting-state functional connectivity and coactivation patterns
Hum Brain Mapp, 40 (2019), pp. 5159-5171
Crossref ↗ View in Scopus ↗ Google Scholar ↗

88 M. Liuzzi, F. Harb, T. deRoon-Cassini, C. Larson
424. Experiences of childhood threat and deprivation on superior frontal gyrus connectivity in an adult trauma sample
Biol Psychiatry, 97 (2025), Article S272
View PDF View article Google Scholar ↗

89 J.L. Luby, D. Barch, D. Whalen, R. Tillman, A. Belden
Association between early life adversity and risk for poor emotional and physical health in adolescence: A putative mechanistic neurodevelopmental pathway
JAMA Pediatr, 171 (2017), pp. 1168-1175
Crossref ↗ View in Scopus ↗ Google Scholar ↗

90 D.S. Roy, Y. Zhang, M.M. Halassa, G. Feng
Thalamic subnetworks as units of function
Nat Neurosci, 25 (2022), pp. 140-153
Crossref ↗ View in Scopus ↗ Google Scholar ↗

A.E. Guyer, J.S. Silk, E.E. Nelson
The neurobiology of the emotional adolescent: From the inside out
Neurosci Biobehav Rev, 70 (2016), pp. 74-85

Reading Assistant

View PDF View article View in Scopus ↗ Google Scholar ↗

92 C.M. Meston, J.R. Heiman, P.D. Trapnell
The relation between early abuse and adult sexuality
J Sex Res, 36 (1999), pp. 385-395
Crossref ↗ View in Scopus ↗ Google Scholar ↗

93 J. Fan, W. Liu, J. Xia, F. Gao, C. Meng, Y. Han, *et al.*
Childhood trauma is associated with social anhedonia and brain gray matter volume differences in healthy subjects
Brain Imaging Behav, 16 (2022), pp. 1964-1972
Crossref ↗ View in Scopus ↗ Google Scholar ↗

94 P.E. Mullen, J.L. Martin, J.C. Anderson, S.E. Romans, G.P. Herbison
The long-term impact of the physical, emotional, and sexual abuse of children: A community study
Child Abuse Negl, 20 (1996), pp. 7-21
View PDF View article View in Scopus ↗ Google Scholar ↗

95 T.A. Widiger, J.R. Oltmanns
Neuroticism is a fundamental domain of personality with enormous public health implications
World Psychiatry, 16 (2017), pp. 144-145
Crossref ↗ View in Scopus ↗ Google Scholar ↗

96 R.R. McCrae, P.T. Costa Jr.
Validation of the five-factor model of personality across instruments and observers
J Pers Soc Psychol, 52 (1987), pp. 81-90
View in Scopus ↗ Google Scholar ↗

97 P.T. Costa Jr., R.R. McCrae, D.A. Dye
Facet scales for agreeableness and conscientiousness: A revision of the NEO Personality Inventory
Pers Individ Dif, 12 (1991), pp. 887-898
View PDF View article View in Scopus ↗ Google Scholar ↗

98 J.S. Alnassar, M.F. Juruena, C. Macare, A.M. Perkins, A.H. Young
Effect of childhood emotional abuse on depression and anxiety in adulthood is partially mediated by neuroticism: Evidence from a large online sample
J Affect Disord, 359 (2024), pp. 158-163
View PDF View article View in Scopus ↗ Google Scholar ↗

99 K.S. Kendler, J. Kuhn, C.A. Prescott
The interrelationship of neuroticism, sex, and stressful life events in the prediction of episodes of major depression
Am J Psychiatry, 161 (2004), pp. 631-636
View in Scopus ↗ Google Scholar ↗

100 R.W. Robins, R.C. Fraley, B.W. Roberts, K.H. Trzesniewski
A longitudinal study of personality change in young adulthood
J Pers, 69 (2001), pp. 617-640
Crossref ↗ View in Scopus ↗ Google Scholar ↗

101 B.W. Roberts, K.E. Walton, T. Bogg
Conscientiousness and health across the life course
Rev Gen Psychol, 9 (2005), pp. 156-168
Crossref ↗ View in Scopus ↗ Google Scholar ↗

P.T. Costa, A. Terracciano, R.R. McCrae
Gender differences in personality traits across cultures: Robust and surprising findings
J Pers Soc Psychol, 81 (2001), pp. 322-331
View in Scopus ↗ Google Scholar ↗

Reading Assistant

103 Y.J. Weisberg, C.G. Deyoung, J.B. Hirsh
Gender differences in personality across the ten aspects of the Big Five
Front Psychol, 2 (2011), p. 178
Google Scholar ↗

104 C. Hakulinen, M. Elovainio, L. Pulkki-Råback, M. Virtanen, M. Kivimäki, M. Jokela
Personality and depressive symptoms: Individual participant meta-analysis of 10 cohort studies
Depress Anxiety, 32 (2015), pp. 461-470
Crossref ↗ View in Scopus ↗ Google Scholar ↗

105 J. Ormel, B.F. Jeronimus, R. Kotov, H. Riese, E.H. Bos, B. Hankin, *et al.*
Neuroticism and common mental disorders: Meaning and utility of a complex relationship
Clin Psychol Rev, 33 (2013), pp. 686-697
View PDF View article View in Scopus ↗ Google Scholar ↗

106 E.L. Weiss, J.G. Longhurst, C.M. Mazure
Childhood sexual abuse as a risk factor for depression in women: Psychosocial and neurobiological correlates
Am J Psychiatry, 156 (1999), pp. 816-828
Crossref ↗ View in Scopus ↗ Google Scholar ↗

107 K.A. McLaughlin, D. Weissman, D. Bitrán
Childhood adversity and neural development: A systematic review
Annu Rev Dev Psychol, 1 (2019), pp. 277-312
Crossref ↗ Google Scholar ↗

108 C. Heim, D.J. Newport, T. Mletzko, A.H. Miller, C.B. Nemeroff
The link between childhood trauma and depression: Insights from HPA axis studies in humans
Psychoneuroendocrinology, 33 (2008), pp. 693-710
View PDF View article View in Scopus ↗ Google Scholar ↗

109 L.A. McWilliams, B.J. Cox, M.W. Enns
Use of the Coping Inventory for Stressful Situations in a clinically depressed sample: Factor structure, personality correlates, and prediction of distress1
J Clin Psychol, 59 (2003), pp. 1371-1385
Google Scholar ↗

110 A. Oshio, K. Taku, M. Hirano, G. Saeed
Resilience and Big Five personality traits: A meta-analysis
Pers Individ Dif, 127 (2018), pp. 54-60
View PDF View article View in Scopus ↗ Google Scholar ↗

111 J.K. Connor-Smith, C. Flachsbart
Relations between personality and coping: A meta-analysis
J Pers Soc Psychol, 93 (2007), pp. 1080-1107
Crossref ↗ View in Scopus ↗ Google Scholar ↗

112 Y. Hu, J. Fei, J. Yue, R. Gao, Q. Song, X. Zhao, S. Mei
Emotional abuse and neglect, depression: A moderated mediation model of neuroticism and psychological resilience
Psychiatry Investig, 22 (2025), pp. 389-396
Crossref ↗ View in Scopus ↗ Google Scholar ↗

113 W.C. Sanderson, S. Wetzler, A.T. Beck, F. Betz
Prevalence of personality disorders in patients with major depression and dysthymia
Psychiatry Res, 42 (1992), pp. 93-99
View PDF View article View in Scopus ↗ Google Scholar ↗

M. Reuter, M.D. Tisdall, A. Qureshi, R.L. Buckner, A.J.W. van der Kouwe, B. Fischl

Reading Assistant

Head motion during MRI acquisition reduces gray matter volume and thickness estimates
Neuroimage, 107 (2015), pp. 107-115
View PDF View article View in Scopus ↗ Google Scholar ↗

115 D.P. Bernstein, T. Ahluvalia, D. Pogge, L. Handelsman
Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population
J Am Acad Child Adolesc Psychiatry, 36 (1997), pp. 340-348
View PDF View article View in Scopus ↗ Google Scholar ↗

116 M. Hunt, J. Auriemma, A.C.A. Cashaw
Self-report bias and underreporting of depression on the BDI-II
J Pers Assess, 80 (2003), pp. 26-30
Crossref ↗ View in Scopus ↗ Google Scholar ↗

117 J. Ormel, A.J. Oldehinkel, W. Vollebergh
Vulnerability before, during, and after a major depressive episode: A 3-wave population-based study
Arch Gen Psychiatry, 61 (2004), pp. 990-996
View in Scopus ↗ Google Scholar ↗

118 B.T.T. Yeo, F.M. Krienen, J. Sepulcre, M.R. Sabuncu, D. Lashkari, M. Hollinshead, *et al.*
The organization of the human cerebral cortex estimated by intrinsic functional connectivity
J Neurophysiol, 106 (2011), pp. 1125-1165
Google Scholar ↗

119 R.L. Buckner, F.M. Krienen, A. Castellanos, J.C. Diaz, B.T.T. Yeo
The organization of the human cerebellum estimated by intrinsic functional connectivity
J Neurophysiol, 106 (2011), pp. 2322-2345
Crossref ↗ View in Scopus ↗ Google Scholar ↗

120 L. Fan, H. Li, J. Zhuo, Y. Zhang, J. Wang, L. Chen, *et al.*
The human Brainnetome atlas: A new brain atlas based on connectional architecture
Cereb Cortex, 26 (2016), pp. 3508-3526
Crossref ↗ View in Scopus ↗ Google Scholar ↗

121 J. Diedrichsen, J.H. Balsters, J. Flavell, E. Cussans, N. Ramnani
A probabilistic MR atlas of the human cerebellum
Neuroimage, 46 (2009), pp. 39-46
View PDF View article View in Scopus ↗ Google Scholar ↗

† NK and DP contributed equally to this work.

View Abstract

Special issue articles

Articles part of:

Posttraumatic Stress Disorder, Stress, and Fear

View special issue Download full issue

Discussion

iming of Plasticity: Beyond Synapses in Psychedelic Therapeutics
J. Christoffel, Jessica J. Walsh
tember 2026

ion

When Trauma, Personality, and Depressivity Converge: From Brain Signatures to Precision Prevention?

Reading Assistant

Diego A. Pizzagalli

15 September 2026

Discussion

Genetics of Psychological Resilience: Is It More Than the Flip Side of Risk?

Karmel W. Choi, Karestan C. Koenen

15 September 2026

Recommended articles

Based on reading popularity

Research article

Increased amplitude of hippocampal low frequency fluctuations in early psychosis: A two-year follow-up study

Maureen McHugo, ..., Stephan Heckers

Schizophrenia Research • Volume 241 • 2022 • Pages 260-266

Research article

Episodic memory functions in first episode psychosis and clinical high risk individuals

Sarah E. Greenland-White, ..., Cameron S. Carter

Schizophrenia Research • Volume 188 • 2017 • Pages 151-157

Research article

Trans-developmental stability of self-criticism as a core target in adolescent anxiety-depression comorbidity: Insights from stage-specific network analysis and in silico interventions

Yichen Li, ..., Yanhe Deng

Journal of Affective Disorders • Volume 405 • 2026 • Article 121537

Research article Open access

Failure to integrate: Connector hub dysfunction in major depressive disorder

Norika Hayashi, Epifanio Bagarinao

NeuroImage: Clinical • Volume 50 • 2026 • Article 104010

View PDF

Discussion

US FDA premarket approval of tDCS depression treatment is not yet scientifically justified

Jana Klaus, ..., Dennis J L G Schutter

The Lancet Psychiatry • Volume 13, Issue 9 • 2026 • Pages 726-728

Research article Open access

Hippocampal Total, Subregion, and Subfield Volume Alterations in Late-Life Depression

Brianca Renfro, ..., Warren D. Taylor

Biological Psychiatry: Cognitive Neuroscience and Neuroimaging • 2026

View PDF

Cited by (1)

Discussion

When Trauma, Personality, and Depressivity Converge: From Brain Signatures to Precision Prevention?

Pizzagalli D.A.

Biological Psychiatry • Volume 100 • 2026

Metrics

Reading Assistant

n Indexes 1

res

Mendeley Readers 7

PLUMX View details ↗

© 2026 Published by Elsevier Inc on behalf of Society of Biological Psychiatry.

ELSEVIER

All content on this site: Copyright © 2026 Elsevier B.V., its licensors, and contributors. All rights are reserved, including those for text and data mining, AI training, and similar technologies. For all open access content, the relevant licensing terms apply.

RELX™

Reading Assistant