Disentangling Brain-Psychopathology Associations: A Systematic Evaluation of Transdiagnostic Bifactor Models

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Abstract

Understanding the neurobiological basis of mental health disorders remains a central goal in psychiatry. However, identifying robust brain-psychopathology associations with neuroimaging has proven difficult, in part due to substantial heterogeneity within and comorbidity between diagnostic categories. Transdiagnostic bifactor models aim to characterise this structure by separating shared from unique symptom variance, yielding more reliable and potentially more accurate latent dimensions of psychopathology. However, the extent to which these behavioural models improve brain-psychopathology associations remains largely uncharacterised. Using two large developmental cohorts, we compared 11 previously published bifactor models applied to the Child Behaviour Checklist (CBCL) to traditional CBCL summary scores. For both symptom-scoring approaches, we systematically evaluated their reliability and multivariate associations with whole-brain structure (MRI) and function (resting-state fMRI). We found no consistent evidence that bifactor-derived factor scores strengthened reliability or brain-psychopathology associations, relative to summary scores. Whole-brain predictive models revealed broadly distributed neural signatures that were highly similar between corresponding factor and summary score constructs, with general factors and total problems approaching numerical equivalence. Nevertheless, factor scores displayed more distinct neural signatures between general, internalising, and externalising dimensions than did summary scores. Together, these findings suggest that existing CBCL bifactor models of psychopathology do not systematically strengthen the predictive utility of psychiatric neuroimaging, possibly reflecting fundamental limits on the proportion of CBCL symptom variance captured by brain features. While bifactor models may aid in separating neural correlates across constructs, improving phenotypic assessment depth, rather than alternative phenotypic modelling, may provide more tangible improvements to association strength moving forward.

Introduction

Widespread symptom comorbidity and diagnostic heterogeneity have long been recognised as major limitations of traditional, categorical psychiatric diagnoses (L. A. Clark et al., 1995; Newman et al., 1998). Comorbidity and heterogeneity also pose challenges for psychiatric neuroimaging studies that seek to link brain and psychopathology (Feczko & Fair, 2020). These challenges have motivated proposals to better capture psychopathology as latent dimensions with a hierarchical structure (Krueger, 1999; Neale & Kendler, 1995). Building on this work, comprehensive dimensional models like the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017) formalise psychopathology as a hierarchy of empirically derived spectra and include a higher-order general "P" factor representing the general manifestation of psychopathology alongside more specific symptom liabilities. Bifactor models offer one implementation of this structure, partitioning variance into a general factor and orthogonal specific factors that can disentangle transdiagnostic and domain-specific processes (Caspi et al., 2014; Lahey et al., 2012). While not without criticism (Watts et al., 2020, 2024), bifactor models have been widely used to examine how common and unique features across symptoms relate to external outcomes like academic performance or cognition (Caspi & Moffitt, 2018; Smith et al., 2020). Importantly, recent perspectives (Zald & Lahey, 2017; Tiego et al., 2023) have proposed bifactor and other factor analytic models as potential solutions to widespread challenges in identifying robust and reproducible brain-behaviour relationships in mental health.

Factor analytic models, particularly bifactor and hierarchical approaches, offer potential advantages for studies linking brain and mental health phenotypes by improving the internal consistency, precision, and interpretability of measured constructs. These models extract latent dimensions that represent the shared variance across symptoms, while accounting for unique variance and measurement error; together, these properties may lead to larger brain-behaviour associations and enhance statistical power (Tiego et al., 2023). In contrast, typical, simple summary scores may inadvertently combine general, domain-level, and symptom-specific variance, producing heterogeneous phenotypes that obscure or dilute associations (Reise, 2012). This is critical because measurement imprecision and poor reliability attenuate brain-behaviour effect sizes and reduce the likelihood of detecting meaningful associations (Karvelis et al., 2023; Gell et al., 2024). Conversely, increasing reliability, while holding other factors constant, may lead to increased signal-to-noise ratios, in turn improving brain-behaviour associations (Milham et al., 2021; Nikolaidis et al., 2022). Finally, compared to alternative correlated factor models (Kotov et al., 2017; Sunderland et al., 2021), bifactor approaches partition variance explicitly into uncorrelated general and specific factors (which may otherwise result in correlated factors). Such orthogonal factors can potentially reduce confounding of brain-behaviour associations and help clarify whether brain correlates reflect general psychopathology or domain-specific liabilities (Zald & Lahey, 2017; Lahey et al., 2021). Nevertheless, the extent to which such psychometric advantages of bifactor models translate to stronger or more specific brain-psychopathology associations remains unexplored.

Prior studies have reported associations between bifactor-derived psychopathology dimensions and neuroimaging measures (Elliott et al., 2018; Kaczkurkin et al., 2018, 2019). However, because none have directly compared bifactor scores to alternative scoring

approaches (e.g., summary scores), it remains unclear whether the identified brain correlates reflect novel insights into the spatial organisation of brain-psychopathology associations. Furthermore, due to the large sample sizes required to detect robust and reproducible brain-behaviour associations (Marek et al., 2022), comprehensive evaluations of the relative utility of factor scores for brain-behaviour modelling were, until recently, not possible. Moreover, bifactor models themselves require substantial sample sizes to fit, often resulting in factor scores being computed on the same data used to test for associations with brain imaging, introducing the risk of embedded circularity ("double dipping"), train-to-test leakage, and overfitting.

Although bifactor models have shown psychometric advantages in behavioural research, it remains unknown whether these advantages confer stronger or more distinct brain-psychopathology associations than typical summary scores. Here, we systematically evaluate the reliability and whole-brain multivariate predictive accuracy of factor scores from cortical thickness (obtained from structural MRI) and functional connectivity (obtained from resting-state fMRI). To evaluate the potential measurement benefits afforded by factor analysis, we benchmark prediction accuracy and multivariate feature weights of factor scores against standard summary scores that do not require factor analysis (i.e., equally weighted sums of items). To ensure generalizability across bifactor model solutions, we utilised 11 previously published bifactor models to obtain factor scores from items of the Child Behavior Checklist (CBCL) in two large, diverse developmental samples: the Adolescent Brain Cognitive Development study (ABCD) (Volkow et al., 2018) and the Brazilian High-Risk Cohort (BHRC) (Salum et al., 2015).

Methods

Adolescent Brain Cognitive Development dataset

Participants

To investigate psychometric properties of bifactor models and their association with brain imaging, we used baseline and follow-up 1 data from the Adolescent Brain Cognitive Development study, a large longitudinal neuroimaging cohort study of 21 sites in the United States (Volkow et al., 2018). Only English-speaking participants without severe sensory, intellectual, medical, or neurological issues who completed all items of the CBCL at both time points (mean interval = 12.1 months) were selected. This resulted in a total of 10,897 participants (5698 female, ages = 9-11 at baseline) with complete CBCL data for both visits that were used to fit all bifactor models. A subset of ABCD participants who completed the baseline imaging session, finished all rs-fMRI sessions, and passed the ABCD quality control for their T1 and rs-fMRI were used for brain-behaviour analyses. This subset comprised 6,572 participants (3,277 female, ages = 9-11).

Neuroimaging data, preprocessing and analyses

The ABCD MRI acquisition protocol (Casey et al., 2018) was harmonised across 21 sites on Siemens Prisma, Phillips, and GE 750 3T scanners. It included high-resolution T1w MRI images with a 32-channel head coil using a 3D MPRAGE sequence (TR = 2500 ms, 1.0 mm isotropic voxels). The rs-fMRI images were acquired using gradient-echo echo planar imaging (TR = 800 ms, 2.4 mm isotropic voxels) and included four 5-minute runs totalling 20 minutes.

Structural and functional data were pre-processed using the ABCD-BIDS pipeline, available through the ABCD-BIDS Community Collection (ABCC; Collection 3165) as detailed in (Feczko et al., 2021). The preprocessing steps included distortion correction and alignment using Advanced Normalisation Tools (ANTS), FreeSurfer segmentation, and both surface and volumetric registration using FSL FLIRT rigid-body transformation. Resting-state fMRI data were further processed using the DCAN BOLD Processing (DBP) pipeline, which involved detrending, demeaning, and denoising via a general linear model incorporating tissue class and motion regressors. Following this, data were bandpass filtered between 0.008 and 0.09 Hz using a second-order Butterworth filter. Additional processing included respiratory motion filtering (targeting breathing rates between 18.58 and 25.73 breaths per minute) and censoring of frames exceeding a framewise displacement (FD) threshold of 0.2 mm or identified as statistical outliers (±3 standard deviations). The denoised time courses were parcellated using the HCP multimodal atlas with 360 cortical regions of interest (Glasser et al., 2016), together with 19 subcortical regions (Desikan et al., 2006). The signal time courses were averaged across all voxels of each parcel, and functional connectivity between them was calculated as Pearson correlation and Fisher Z-transformed. Region-wise cortical thickness was averaged across all vertices within each parcel of the HCP multimodal atlas.

Brazilian High-Risk Cohort study dataset

To replicate our reliability analyses of factor and standard CBCL summary scores in a dataset with different characteristics, we used CBCL scores from 771 participants (334 female, ages = 6 - 14) from the Brazilian high-risk cohort study (Salum et al., 2015). All participants had completed all items of the Portuguese version of the CBCL at baseline and the first follow-up session (mean interval = 17 months). The BHRC is a school-based community cohort from the cities of São Paulo and Porto Alegre that is enriched with children with current symptoms and/or family history of psychiatric disorders (for details, see Salum et al., 2015).

Common and Specific Variance of Psychopathology

Child Behavioural Checklist and summary score

The Child Behavioural Checklist (CBCL) (Achenbach, 1983) was used as the basis for calculating summary and bifactor scores reflecting various dimensions of psychopathology. The CBCL is a parent-reported assessment of 120 items/symptoms for subjects aged 6 to 18 using a 3-point scale (0 = not true; 1 = somewhat/sometimes true; 2 = very true/often). The CBCL organises scores into eight syndromic summary scores: anxious-depressed,

withdrawn-depressed, somatic complaints, rule-breaking behaviour, aggressive behaviour, social problems, thought problems, and attention problems. Additionally, the scores can be combined into broader indices by summing up item-scores, such as internalising problems (comprising anxious-depressed, withdrawn-depressed, and somatic complaints) and externalising problems (comprising rule-breaking behaviour and aggressive behaviour) that have been informed by factor analysis. Finally, a total problems score comprises the linear, equally weighted sum of all items. Here, we utilised the T-score values for all aforementioned CBCL summary scores that are typically used in the literature and available with many datasets, including the ABCD.

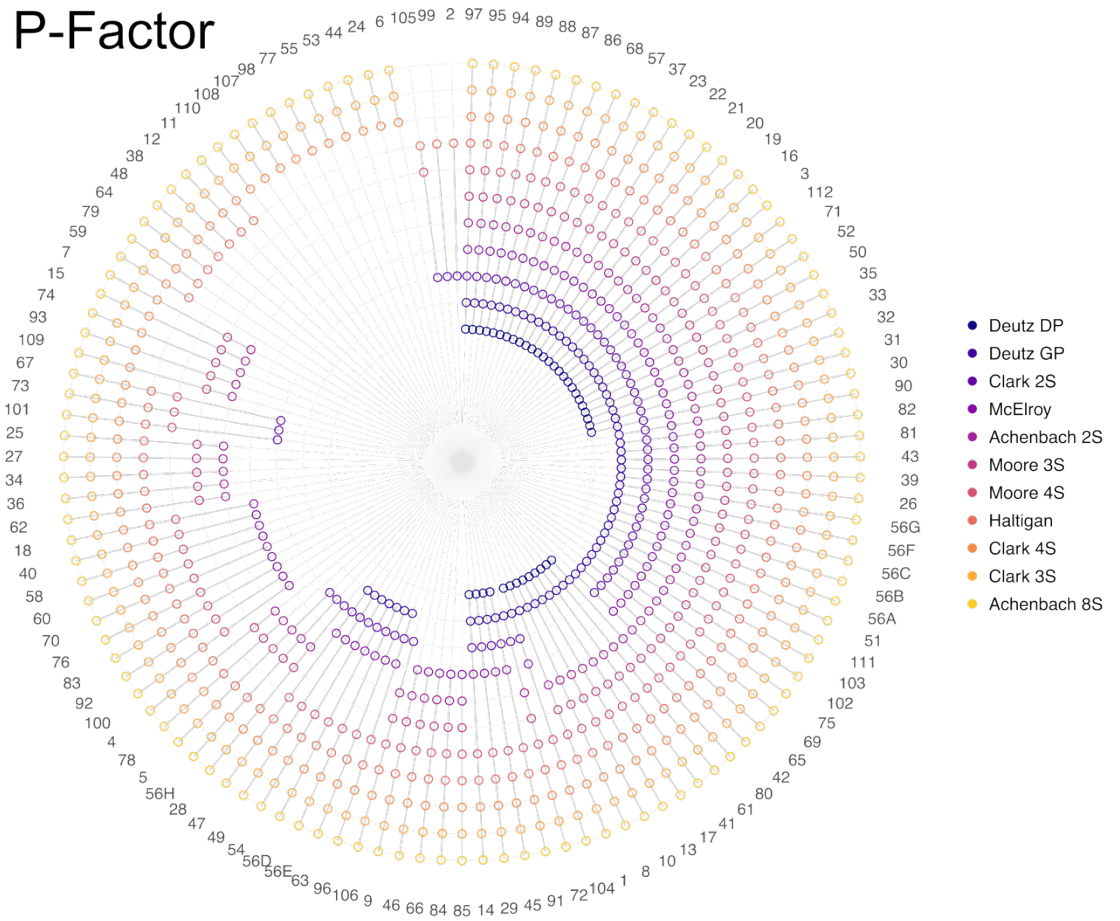
Bi-factor models

Recent work has identified 11 different bifactor model solutions for the CBCL (Constantinou & Fonagy, 2019; Hoffmann et al., 2022). Therefore, to comprehensively estimate the test-retest reliability of factor scores, we have investigated all 11 reported models (Achenbach, 1983; Haltigan et al., 2018; McElroy et al., 2018; Deutz et al., 2020; Moore et al., 2022; D. A. Clark et al., 2021). Following previous work (Hoffmann et al., 2022), we first rescored items to only indicate the presence or absence of symptoms (i.e., somewhat/sometimes true and very true/often were re-coded to both be 1), as the response frequency of “very often” was below 5% for 114 of 119 items. Within each bifactor model, all CBCL items present in the model definition (**Fig. 1**) were configured to load on a general “P-factor”. Additionally, a subset of items was set to residually load on “specific factors” that depended on the given model (see Supplementary Table 1). Following typical bifactor approaches (Hoffmann et al., 2022), specific factors were not allowed to correlate with each other, nor with the general factor. Confirmatory factor analyses (CFA) were carried out in using Mplus (Muthen & Muthen, 1998; Hallquist & Wiley, 2018) using delta parameterisation and weighted least squares with a diagonal weight matrix with standard errors and mean- and variance-adjusted chi-square test statistics (WLSMV) estimators. For fit indices, see Supplementary Tables 2 and 3. Factor scores were generated using a regression method, resulting in 11 P-factor scores and 38 specific factor scores per subject.

Reliability

We evaluated the test-retest reliability of bi-factor scores across all models, as well as summed scores between the baseline and the first follow-up session for both the ABCD and BHRC samples. To this end, we calculated linear bivariate correlation, corrected for participant age, time point, and their interaction. Correlation may be more robust to systematic age-related changes in development, as it is not penalised by differences in means between baseline and follow-up data and different development rates across participants (Anokhin et al., 2022). Additionally, we calculated ICC using a two-way mixed-effects model for consistency, previously described as [3,1] (Shrout & Fleiss, 1979). In the ABCD, reliability was calculated on a subset of individuals who had a maximum of 12 months retest interval (n = 7250; 3774 female; retest interval mean = 11.3 months). To estimate reliability at shorter intervals, only subjects with a maximum of 6 months retest interval were selected from the BHRC sample, resulting in 234 subjects (100 female, retest interval mean = 3.7 months). To assess the internal consistency of factor scores, we

P-Factor



Specific Factors

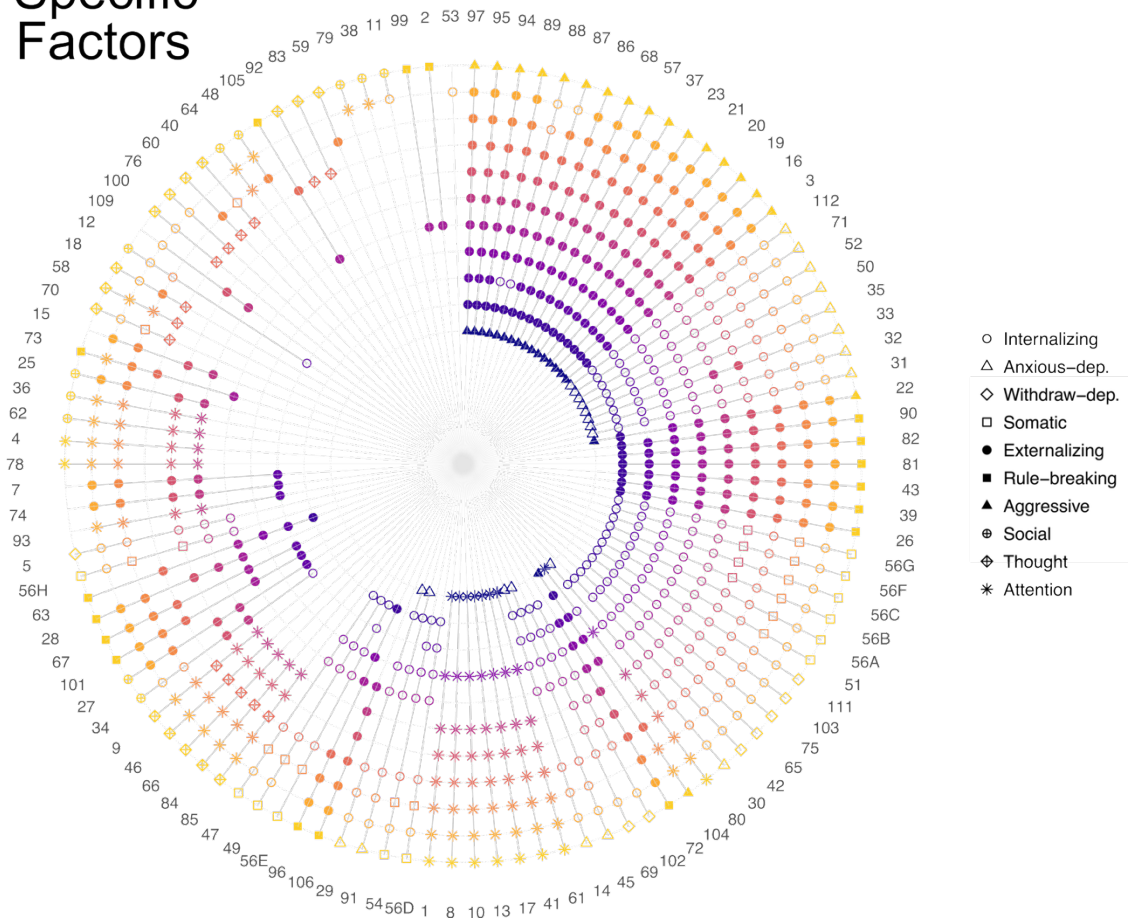


Figure 1. CBCL Items included in each model. Items included in the P-factor are depicted in the top panel, while specific factors are depicted in the bottom panel. GP = general psychopathology model; DP = dysregulation profile model; CBCL = Child and Behaviour Checklist.

calculated omega (ω), Hierarchical omega, and factor determinacy. For a detailed overview of each measure, see Supplementary Methods and Supplementary Table 4.

Brain-behaviour analyses

To systematically compare bifactor-derived scores to CBCL summary T-scores with respect to their neurobiological substrates, we used functional connectivity and cortical thickness features in the ABCD sample to predict both types of scores. Predictions we performed using linear ridge regression implemented in the scikit-learn library (version 0.24.2), wrapped in custom code [https://github.com/MartinGell/Prediction_Psychopathology]. To avoid test-to-train leakage and improve generalizability, we utilised two matched samples (N = 3242 and 3330) created by Feczko et al. (2021) (so-called “discovery” and “replication” samples). These were matched on acquisition site, age, sex, ethnicity, grade, highest level of parental education, handedness, combined family income, and prior exposure to anaesthesia. All 11 bifactor model solutions were fit separately within each sample to ensure factor score estimation remained independent across training and testing folds. Model evaluation was performed using a nested 2-fold cross-validation with 2 repeats, where each sample served once as training and once as testing data. Within each outer fold, the α regularisation parameter was optimised via efficient leave-one-out cross-validation (Rifkin & Lippert, 2007) on the training set, and performance was evaluated on the test fold. Sensitivity analyses using CBCL summary scores that did not require fitting separately on train and test sets showed that our 2-fold cross-validation yielded near-identical results to a more standard 5 times repeated 10-fold cross-validation (see Supplemental Methods for details).

Within each fold, neuroimaging features were z-scored across subjects (i.e. standard scaler) using training data, and the same transformation was applied to the test set using learned parameters from training data. To control for the effect of sex, given its common association with psychiatric phenotypes (Eaton et al., 2012), we performed feature-wise confound removal using linear regression (More et al., 2021). This was performed within each training fold, and the confound models were subsequently applied to test data to prevent data leakage. No other covariates were included due to the matched design. Prediction accuracy was quantified using Pearson correlation and the coefficient of determination (R^2), which reflects explained variance and is not equivalent to the squared correlation coefficient (Poldrack et al., 2020). Significance of predictions was assessed using 1000 permutations of target labels. Feature weights (indicating which edges contributed more to predictions) were Haufe transformed (Haufe et al., 2014; J. Chen et al., 2023) to improve interpretability (see Supplementary Methods for details). To assess model sensitivity, we repeated all predictions using a gradient-boosted decision tree model (XGBoost) (T. Chen & Guestrin, 2016), which accommodates non-linearities and zero-inflated outcomes (see Supplemental Methods).

To examine the similarity between regression feature weights (i.e. neural correlates) between as well as within factor and summary scores, we correlated the upper triangles of the Haufe-transformed feature weight matrices. The significance of these similarities was evaluated using a cortex-only spin test (Alexander-Bloch et al., 2018; Markello & Misic, 2021), as the inclusion of subcortical parcels removes the possibility of surface projection. For each comparison, we computed the Spearman correlation (ρ) between the vectorised upper triangles of the two 360×360 matrices. Parcel centroids were projected to the spherical surface (fs_LR), and rigid-body rotations ("spins") were applied while preserving left–right correspondence (Váša et al., 2018). For each spin, the resulting node permutation was applied to both rows and columns of one matrix, and ρ was recomputed. We repeated this procedure 10,000 times, each time recomputing ρ on the vectorised upper triangle to obtain the null distribution. To investigate the spatial embedding of the correlated connectomes, we used multidimensional scaling (see Supplementary Methods).

Results

Summary and bifactor-derived scores show comparable test–retest reliability

Reliability and longitudinal stability were assessed using test-retest correlations corrected for participant age, time point, and their interaction. We compared the reliability of standard CBCL summary T-scores, which do not require factor analysis, to bifactor-derived factor scores from CBCL item-level responses according to 11 model published studies (see Methods). Reliability in the summary scores was higher in ABCD (mean across all scales: r_{mean} = 0.68, range: r = 0.56 - 0.76) than in the BHRC (r_{mean} = 0.53, r = 0.39 - 0.67), with total problems, externalising, and attention showing the greatest stability across both datasets. To compare corresponding constructs between summary and factor scores, we focus on the total summary score, P-factor, externalising, internalising and attention in the following sections (**Table 1,** for reliabilities of all scores see Supplementary Fig. 2 and 3, Supplementary Table 4)**.**

Table 1

Test-retest correlation of corresponding constructs in summary and factor scores

Construct	ABCD		BHRC	
	Summary score	Factor score mean (range)	Summary score	Factor score mean (range)
Total score / P-factors	0.76	0.74 (0.70 - 0.76)	0.60	0.58 (0.55 - 0.62)
Externalising	0.74	0.58 (0.54 - 0.62)	0.61	0.48 (0.40 - 0.54)
Internalising	0.68	0.57 (0.52 - 0.59)	0.53	0.37 (0.30 - 0.46)
Attention	0.74	0.56 (0.52 - 0.57)	0.67	0.45 (0.24 - 0.53)

All 11 bifactor model solutions had a generally good fit to the data in both datasets when considering multiple fit indices (Supplementary Table 2-3). In the ABCD dataset (n = 7250; retest interval mean = 11.3 months), P-factors were the most reliable (r_{mean} = 0.74; 0.70 - 0.76), exceeding specific psychopathology factors (e.g., internalising, externalising, attention, thought disorders) across all solutions (r_{mean} = 0.55; 0.42 - 0.62). In the BHRC dataset (n = 234; retest interval mean = 3.7 months and max = 6 months), absolute reliability was lower overall, despite a shorter retest interval. As in the ABCD, P-factors (r_{mean} = 0.58, r = 0.55 - 0.62) displayed higher reliability than specific factors (r_{mean} = 0.40, r = 0.15 - 0.54); however, several specific factors approached P in the BHRC, suggesting specific factors may be more stable at shorter time intervals (see supplementary Fig. 3). Internal consistency reliability indices (ω, ωH, FD) were high for P and lower-to-acceptable for specific factors in both datasets (Supplementary Table 4). ICCs closely tracked test-retest correlations in both datasets (ABCD: r = 0.99, p < 0.001; BHRC: r = 0.99, p < 0.001).

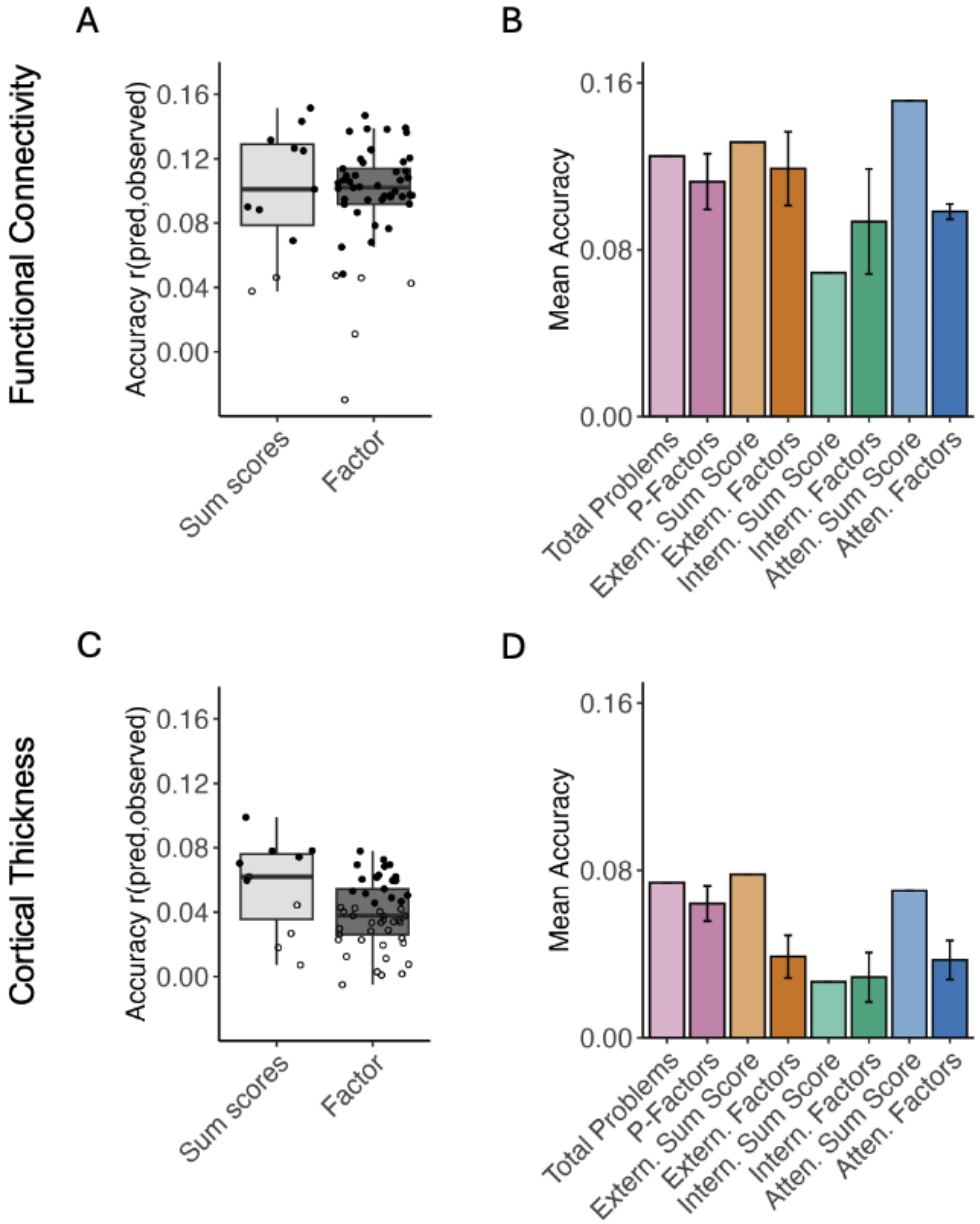


Figure 2. Prediction accuracy of CBCL summary scores and commonly represented factors. The upper panel displays functional connectivity, and the lower panel shows cortical thickness-based prediction accuracy. Panels (A) and (C) show boxplots of prediction accuracies for summary scores (left) and bifactor-derived factor scores (right). Panels (B) and (D) show the corresponding construct summary score and mean factor score prediction accuracy. Error bars indicate standard deviation in accuracy across individual bifactor model solutions. Filled points in panels (A) and (C) represent permutation-based significant predictions at $p < 0.001$.

Summary and bifactor-derived scores show comparable prediction accuracy

In the ABCD dataset, we used functional connectivity and cortical thickness features in a multivariate linear ridge regression to benchmark the prediction accuracy of bifactor-derived scores across all model solutions against standard CBCL summary T-scores. Overall, most constructs could be significantly predicted from functional connectivity (**Fig. 2A** - outline only points) and accuracies across all summary scores and factor scores were highly similar and generally low (summary scores: $r_{mean} = 0.1$; $r = 0.04 - 0.15$; $R^2_{mean} = 0.01$; $R^2 = 0.0 - 0.021$; factor scores: $r_{mean} = 0.1$; $r = -0.03 - 0.15$; $R^2_{mean} = 0.008$; $R^2 = -0.016 - 0.019$; for a complete table of results see supplementary Table 5). For corresponding constructs (e.g., externalising factors vs externalising summary score), prediction accuracy for summary scores was highly similar to the mean accuracy achieved for factor scores (**Fig. 2B**; for the coefficient of determination see Supplementary Fig. 4). One exception to this similarity was attention, where the summary score prediction outperformed the corresponding attention factor mean.

Prediction accuracy from cortical thickness was not significant for most factors and summary scores (**Fig. 2C** - outline only points) and produced near-chance results when evaluated using the coefficient of determination, rather than correlation, as a model performance metric (Supplementary Fig. 4). Most of the significant factor score predictions were of P-factors (Supplementary Fig. 5; Supplementary Table 5). Owing to the overall poor predictive performance of cortical thickness, subsequent analyses focused on functional connectivity.

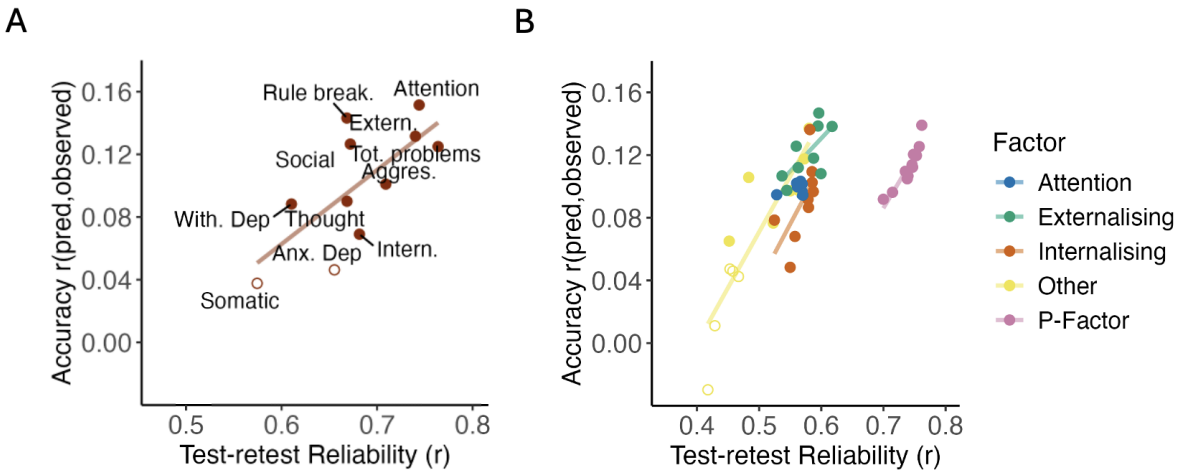


Figure 3. Impact of reliability on the prediction accuracy of factor scores by functional connectivity. The relationship between score reliability and prediction accuracy for summary scores (A) and factor scores (B). Results for whole-brain prediction of factor scores by linear ridge regression. Filled points represent permutation-based significant predictions at $p < 0.001$. Each point refers to one model solution. For the impact of internal consistency reliability on prediction accuracy, see (Supplementary Fig. 8).

General p and specific psychopathology factors can be predicted with comparable accuracy

Replicating prior work (Gell et al., 2024), summary scores with higher reliability had higher prediction accuracy (**Fig. 3A**). Similarly, within a given factor (i.e., P, externalising, internalising, attention), higher reliability also generally resulted in higher prediction accuracy across model solutions (**Fig. 3B**; each factor group illustrated by colour). However, when comparing between factors (e.g., P vs. externalising), higher reliability didn't translate to higher prediction accuracy. These results were consistent across predicted longitudinal timepoints in the ABCD and machine learning algorithms (Supplementary Fig. 6).

For bifactor models, despite having higher reliability and internal consistency than all other factors, P-factors could be predicted ($r_{mean} = 0.11$; $R^2_{mean} = 0.012$) using functional connectivity with comparable accuracy to most specific factors (**Fig. 3B**; for the coefficient of determination see Supplementary Fig. 7). Externalising ($r_{mean} = 0.12$; $R^2_{mean} = 0.013$) and attentional ($r_{mean} = 0.10$; $R^2_{mean} = 0.009$) factors showed the most similar prediction strength to P-factors. Internalising displayed a slightly lower, yet still overlapping prediction accuracy ($r_{mean} = 0.09$; $R^2_{mean} = 0.002$) to P-factors. Similarly to test-retest reliability, neither higher internal consistency reliability (ω, ωH, and factor determinacy) nor item variance explained by the corresponding factor could consistently index improvement to prediction accuracy for general compared to specific factors (Supplementary Fig. 8).

Collectively, these results underscore a distinction between and within constructs in neuroimaging-based prediction of bifactor models. One possibility is that there is a limited amount of overall predictable CBCL variance from brain imaging that places a theoretical ceiling on prediction accuracy. Importantly, this appears to be the case no matter how

different factor model solutions partition this variance into general or specific factors. Examination of all 11 bifactor model solutions demonstrates differing proportions of item-level variance attributed to general and specific factors (**Fig. 4A**). Nevertheless, the average or overall prediction accuracy from functional connectivity (**Fig. 4B** - grey line) across factors within each model solution was nearly identical (r = 0.10 - 0.12; R^2 = 0.008 - 0.013).

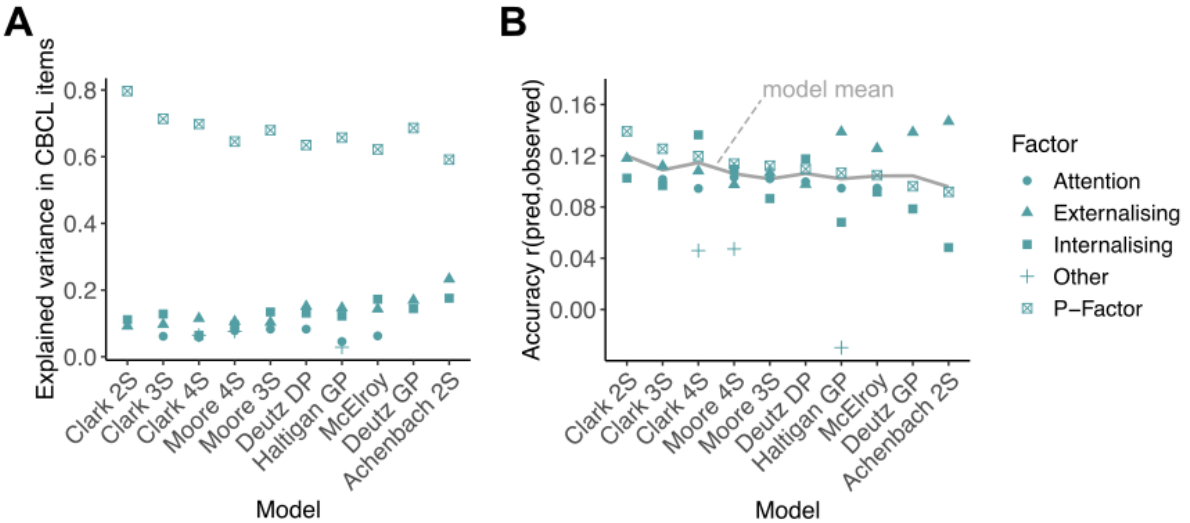


Figure 4. Explained item variance and prediction accuracy by functional connectivity. Results for whole-brain prediction of factor scores by linear ridge regression. Each point represents one factor. The Achenbach 8S model was removed as more than half of its specific factors could not be significantly predicted.

Diverging and converging neural correlates of psychopathology estimated from factor scores and summary scores

Having shown that factor scores from bifactor models did not enhance predictive performance relative to simple summary scores, we next tested whether these approaches might nevertheless reveal distinct biological information. To this end, we examined the Haufe transformed feature weights (see supplementary methods for details) from our ridge regression prediction models in the broader indices of total problems/P-factors, externalising and internalising (**Fig. 5** - left panel). Connectivity within the default mode (DMN) as well as between the DMN and the frontoparietal (FPN) and cingulo-opercular (CO) networks were the most informative for predicting the total problems score. The externalising summary score prediction was most informed by an overlapping network of DMN and FPN edges with additional sensorimotor and attention network components. The prediction of the summary score of internalising symptoms was most informed by connectivity between visual, attention and FPN networks (**Fig. 5A**).

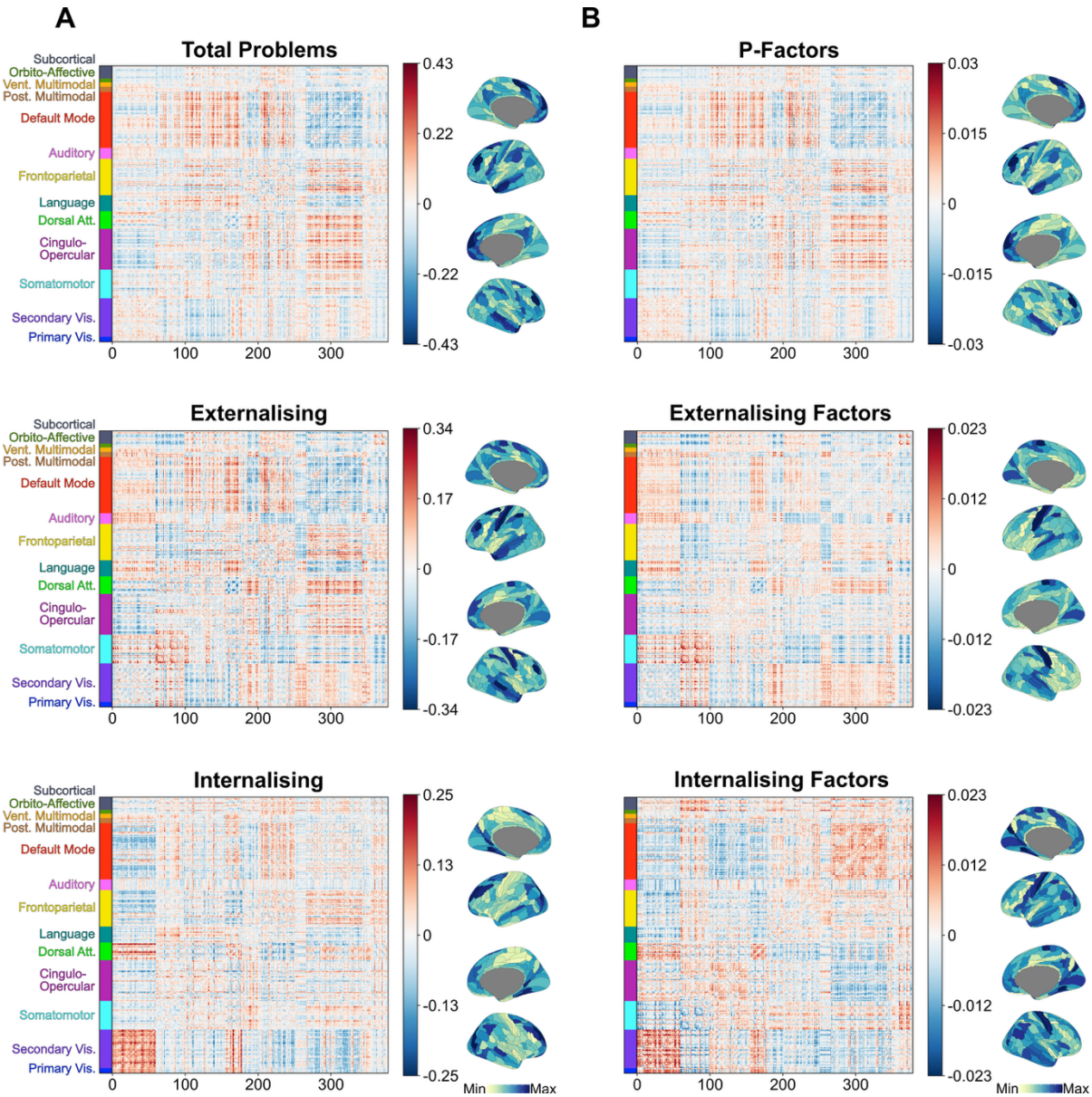


Figure 5. Haufe transformed feature importance weights of edges between all cortical parcels. Corresponding construct (A) summary score and (B) mean factor score Haufe-transformed feature weights. In this case, positive or negative feature weight for an edge indicates that higher connectivity for that edge was associated with predicting higher or lower behavioural value. On the left side of each panel is the full feature weight matrix, ordered using the functional network definition by Ji et al. (2019). The right side displays the mean absolute value weight for each cortical region.

Within factors (e.g. externalising), the consistency in feature weights across model solutions was generally very high (Supplementary Fig. 9): P-factors (ρ_{mean} = 0.94), externalising (ρ_{mean} = 0.91), internalising (ρ_{mean} = 0.94) and was therefore averaged across models, resulting in one matrix of weights per construct. First, we compared the most informative features for the prediction of corresponding constructs from the summary and factor score (**Fig. 6A** - highlighted diagonal values). This indicated a generally high similarity in feature weights between corresponding constructs (e.g., externalising factors vs externalising summary score). Functional connectivity features that predicted P-factors were almost perfectly

spatially aligned with the total problems score (ρ = 0.98, p_{spin} < 0.001), also indicating DMN, FPN and CO network connections (**Fig. 5**). Feature weights of externalising factors were likewise highly correlated with the externalising summary score (ρ = 0.85, p_{spin} < 0.001), mainly differing in the involvement of DMN connections in factor score predictions. Internalising factor and summary score feature weights showed the lowest, albeit still high similarity (ρ = 0.50, p_{spin} < 0.001), mostly differing in the increased importance of DMN and cingulo-opercular connectivity in factor score prediction.

The high similarity between corresponding factors was likely driven by the high associations between the factor and summary score phenotypes themselves (**Fig. 6A**; see Supplementary Fig. 10 for correlations between all individual factor scores and Supplementary Fig. 11 for average correlations between individual factors and all summary scores). The total problems score showed an almost perfect correlation with most P-factors (ρ_{mean} = 0.94, ρ = 0.88 - 0.97). Externalising and internalising factors showed lower, albeit still high, correlations with the externalising (ρ_{mean} = 0.62; ρ = 0.49 - 0.69) and internalising (ρ_{mean} = 0.71; ρ = 0.57 - 0.75) summary scores, respectively.

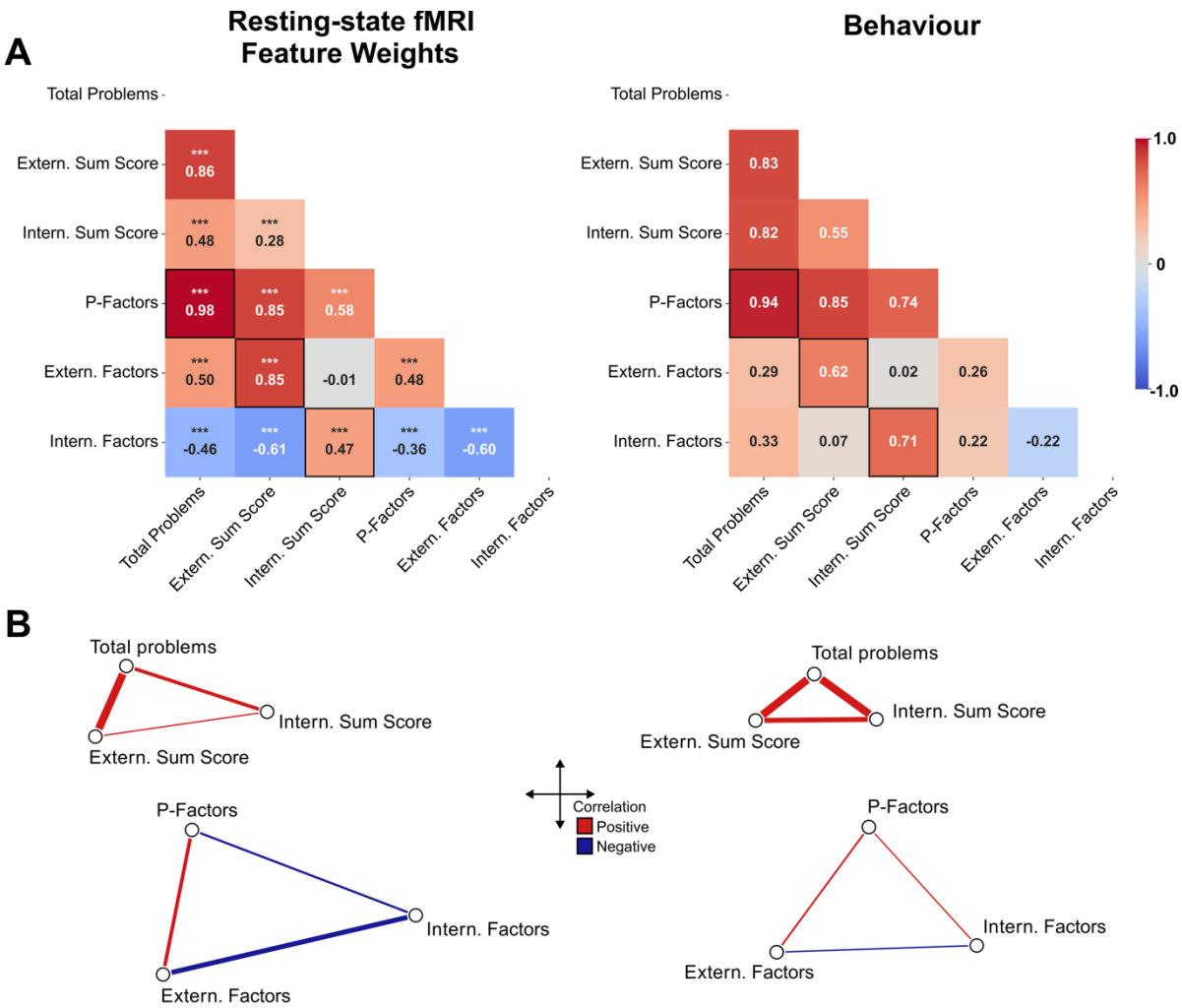


Figure 6. Correlation between informative features of the CBCL summary and factor scores. The left panel displays Spearman correlations between Haufe-transformed feature importance weights, while the right panel displays correlations between the actual phenotypic summary and factor

scores used for prediction. Panel (A) shows the full matrix of between and within correlations. For any correlation involving the factor scores, the median across all correlations is displayed. Highlighted sections refer to correlations along the “theoretical diagonal”, i.e., between corresponding constructs (e.g., total summary and mean of P-factor weights). Significance p-values obtained using spin permutations. Panel (B) visualises the pattern of similarity (also shown as correlations in A) between general, externalising, and internalising constructs for summary (top) and factor (bottom) scores using a 2-D embedding computed from a distance matrix of correlations. Line thickness refers to correlation strength. Abbreviations: Extern: externalising; Intern: internalising; Prob: problems

Finally, we investigate the similarity within factor score and within summary score predictions to directly assess the across construct overlap (**Fig. 6A**). Standard CBCL summary scores were highly intercorrelated on the phenotypic or behavioural level (ρ = 0.83 - 0.53) as well as on feature weight level, outside of internalising and externalising summary scores which showed a weak relationship (ρ = 0.28). In contrast, factor scores generally showed low correlations (ρ = -0.30 - 0.44), likely due to the orthogonalization of specific, externalising and internalising symptom factors. Conversely, the most predictive features of factor scores showed negative correlations between the maps of their predictive weights, indicating high dissimilarity. To examine the pattern of similarity among factor and summary scores, we calculated a two-dimensional embedding of their similarity (**Fig. 6B**). These plots recapitulate our results, indicating that summary score feature weights have higher similarity than factor score feature weights. Overall, these results suggest that orthogonalization of specific psychopathology dimensions may offer novel insights into neural correlates.

Discussion

In this study, we investigated whether latent variable approaches to modelling psychopathology, specifically bifactor-derived factor scores for CBCL, confer measurable advantages for brain-psychopathology association studies. Guided by the premise that bifactor models may strengthen or clarify brain-psychopathology associations by improving reliability and measurement precision, we compared bifactor-derived factor scores to simple CBCL summary scores. We found no consistent advantage of factor scores for the magnitude of brain-behaviour prediction. On average, both test-retest reliability and prediction accuracy were comparable between factor and summary scores from corresponding constructs (e.g., externalising factors vs. externalising summary score) and generally low. Feature weights from whole-brain predictive models of transdiagnostic psychopathology were broadly distributed across the connectome and consistent with prior theories emphasising higher-order networks (default mode, frontoparietal, and cingulo-opercular networks). However, these were likewise highly similar between factor scores and summary scores from corresponding constructs, with P-factors and total problems summary scores approaching numerical identity on both the feature and phenotypic level. One potential advantage of bifactor models over summary scores was that the pattern of neural correlates across constructs (e.g., p-factor vs. externalising vs. internalising) was more separable (i.e., less correlated), likely due to orthogonalization of general and specific factors. This suggests factor scores may provide novel insights (analogous to improved

discriminant validity) into neural correlates, without substantial loss to prediction, though further work is necessary to adjudicate whether these insights are valid.

The overarching results from this study challenge the assumption that factor analytic scores will inherently yield superior neurobiological insights, relative to simple summary scores. Prior work has proposed that hierarchical latent variable approaches like bifactor modelling can enhance reliability, interpretability and the robustness of brain-behaviour associations by reducing measurement error and emphasising shared variance across symptoms, respectively (Tiego et al., 2023; Zald & Lahey, 2017). While the theory behind this is clear and may show practical gains in other contexts, the empirical pattern observed here suggests that bifactor models do not lead to systematically stronger predictions relative to simple summary scores. Rather, the small proportion of behavioural variance that can be explained by neuroimaging-derived brain features shown here and in the literature (J. Chen et al., 2022; Marek et al., 2022; Ooi et al., 2022; Heckner et al., 2023) may impose a ceiling on predictive accuracy irrespective of the scoring approach. In other words, psychometric refinements alone may not be sufficient to overcome fundamental constraints of effect size in large-scale brain-behaviour studies. Instead, a richer assessment of symptoms, environmental exposures, and developmental context (analogous to improving construct validity) may be necessary before reparametrizing existing symptom inventories.

Our results indicate that greater reliability (test-retest, internal consistency and factor determinacy) for P-factors did not improve the strength of brain–behaviour associations compared to specific factors (e.g., externalising, internalising) with lower reliability. While these results suggest that general psychopathology symptoms are only weakly associated with brain structure and function, they also illustrate a fundamental distinction between reliability and construct validity: reliability is necessary but not sufficient for strong associations with external variables (Cronbach & Meehl, 1955). Psychopathology measures must index variance that is relevant to brain imaging (the external criterion), and increasing reliability does not necessarily increase this relevant variance. A similar principle can be illustrated for internal consistency reliability (for example, factor determinacy, FD), which quantifies how precisely latent factors are measured by their indicators relative to error (Grice, 2001). While general factors consistently demonstrated higher FD than specific factors, precision in estimating a latent construct did not guarantee better alignment with biologically meaningful variance. Nevertheless, reliability remains an important consideration for brain imaging of psychopathology – even if not sufficient, it is still necessary. For example, model solutions with higher reliability have better predictive performance than those with lower reliability for a given construct (e.g., across all P-factors), even if that does not generalise across constructs (i.e. P-factors vs. externalising factors).

The comparison of neural correlates of transdiagnostic psychopathology between summary and factor scores resulted in both overlapping and distinct network features underlying predictions. Most corresponding factor and summary scores shared largely overlapping neural correlates, which aligns with prior evidence for broad transdiagnostic connectivity patterns across youth psychopathology (Menon, 2011). Connectivity within and between the DMN, FPN and CO networks observed here has been consistently linked to mental health problems across samples (Lee et al., 2018; Xia et al., 2018; Sripada et al., 2021; Dhamala et al., 2023). Mirroring our findings, Qu et al. (2023) demonstrated that both internalising and externalising behaviours were predicted by DMN-FPN coupling, with externalising also

supported by sensorimotor and FPN connectivity. Interestingly, the DMN-FPN interaction was informative for the prediction of the externalising and internalising summary scores, but not the factor scores. This divergence from the summary score findings is not surprising given the orthogonalization of shared symptom variance from specific factors on the phenotypic level in the bifactor models. Indeed, the importance of the pattern of DMN-FPN connectivity for prediction survived in all three summary score predictions. However, across factor score predictions, it was only observed for P-factors that also showed nearly identical feature weights and phenotypic scores (see Fried et al., (2021) for analogous findings about score similarity) with the total problems summary score. Instead, internalising factors were more reliant on DMN-CO connectivity, echoing work showing the importance of the salience network and limbic regions in internalising symptoms (Menon, 2011; Cash et al., 2021; Pawlak et al., 2022). Furthermore, these results underlie the potential benefits resulting from higher separability in feature weights and behavioural data observed for factor scores compared to summary scores. However, it is also important to stress that while general and unique neural correlates may be informative, there is currently no ground truth to which they can be compared. Together, these findings suggest that while many constructs derived from the CBCL map onto a general, transdiagnostic network architecture, examining latent factors of specific symptom domains may reveal meaningful deviations in network topology.

Several limitations should be considered when interpreting these findings. First, all psychopathology measures were derived from parent-reported CBCL data, which may differentially capture externalising versus internalising behaviours. Externalising symptoms such as aggression or impulsivity are more readily observable, potentially inflating their predictive associations with neural features compared with less overt internalising symptoms (De Los Reyes & Kazdin, 2005; Rescorla et al., 2013). Second, our focus was on comparing factor and summary scores in their psychometric utility and association with brain imaging. Therefore, our findings of limited practical gains from bifactor models are specific to brain-behaviour associations. It remains possible that bifactor-derived factor scores could offer advantages over summary scores in other studies of criterion validity, such as predicting clinical outcomes or cognitive performance. Alternatively, the lack of differential effects observed here may be driven by characteristics of the adolescent sample with relatively low base rates and limited severity of psychiatric symptoms. Such restricted individual variability may attenuate the ability to detect differences in brain-psychopathology associations between scoring approaches (Pavlovich et al., 2025). By extension, it remains plausible that stronger associations and more distinct patterns in neural correlates could emerge in contexts where psychopathology is more severe or prevalent, such as later developmental periods or in symptom-enriched cohorts (Kang et al., 2024; Gell et al., 2025).

Together, these findings suggest that bifactor models of psychopathology offer limited added utility for explaining individual differences in brain structure and function beyond simple symptom summary scores. While latent modelling may improve psychometric precision and provide novel insights into neural correlates, its benefits for neuroimaging applications appear constrained by inherently small effect sizes and are unlikely, on their own, to substantially improve neuroimaging-based prediction of mental health. Improving phenotypic assessment depth, before exploring alternative phenotypic modelling, may provide more tangible improvements moving forward.

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