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Mechanism-based subtyping in binge eating: understanding neurobehavioral heterogeneity across negative emotionality, approach behavior, and executive function

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Binge eating (BE), a transdiagnostic feature that occurs across eating disorders and in the general population, carries significant health risks even in the absence of a full-syndrome diagnosis. The limited efficacy of current treatments for binge-type eating disorders highlights the need to better understand the mechanistic heterogeneity underlying BE to optimize treatment allocation, advance personalized medicine, and ultimately improve outcomes. We hypothesized considerable heterogeneity within three neurofunctional domains prevalent across compulsive behaviors and implicated in BE: approach-related behavior, executive function, and negative emotionality. We analyzed data from 612 participants (ages 18–59, 66% female) from the enhanced Nathan Kline Institute-Rockland Sample, including 461 controls and 151 individuals with BE behaviors. Using data-driven statistical modeling of comprehensive, multimodal measures across the three hypothesized domains, we identified subtypes of BE. Subtypes were validated using assessments of eating pathology, substance use, clinical diagnostics, and resting-state functional magnetic resonance imaging. Three distinct and stable subtypes emerged: a 'Negative Emotionality' subtype characterized by greater negative affect, emotion dysregulation and psychiatric comorbidity, an 'Approach' subtype with higher approach-related and impulsive behaviors, and a 'Restrained' subtype that was overcontrolled and harm avoidant. The Approach and Restrained subtypes further demonstrated unique neurobiological profiles, as determined by graph theory analysis of resting-state functional connectivity. All subtypes showed similar proportions of BE episodes meeting clinical-level threshold (≥4 objective binge episodes/month), and no differences in BMI, indicating functionally distinct expressions of BE, beyond clinical severity and diagnostic classification. This study is the first to explore the mechanistic heterogeneity of BE through a comprehensive multi-modal assessment across three neurofunctional domains in a single sample. Findings highlight the need for updated models of BE etiology that integrate approach/reward-related behaviors, impulsivity and overcontrolled behaviors, and negative emotionality, and suggest the potential of these functionally-derived subtypes to inform the development of personalized, targeted interventions.

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INTRODUCTION

Binge eating (BE) is a core transdiagnostic behavior prevalent across eating disorders (ED), including binge-eating disorder (BED), bulimia nervosa (BN), and anorexia nervosa-binge/purge type [1]. BE is characterized by consuming large amounts of food within a discrete period of time, while experiencing a sense of loss of control [1]. The prevalence of EDs marked by recurrent BE, herein binge-type eating disorders (BT-EDs), has increased [2]. BT-EDs are the most commonly diagnosed EDs with prominent global disease burden [3] and significant lifetime prevalence (0.6–2.8%) [2]. BE behaviors present substantial health risks, including psychiatric and physical comorbidity, escalated medication and healthcare utilization, and elevated risks of mortality and suicidality - irrespective of comorbid obesity [4–8]. Strikingly, 7–13% of community samples regularly engage in BE behaviors, indicating substantial prevalence in the general population [9]. This is crucial because BE behaviors are detrimental even in the absence of a full-syndrome ED diagnosis. That is, subclinical and low-frequency BE demonstrate similar consequences as full-syndrome BT-EDs [10–13] and are highly predictive of later diagnosed disorders [14, 15].

Standard treatments for BT-EDs demonstrate limited efficacy, with over 50% of individuals failing to achieve remission after treatment [16–18]. Longitudinal studies in BED patients showed that 3–48 months post-treatment, only about 50% abstained from BE [17], while 12 years post-treatment, 36% still retained the full-syndrome diagnosis [19]. Similarly, in a longitudinal study of BN inpatients, only 38 and 42% of patients achieved remission 11 and 21 years, respectively, post-treatment [20]. The inefficacy of these standard treatments is often attributed to the 'heterogeneity

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problem,' which suggests that distinct causal mechanisms underlie psychiatric disorders in different subsets of individuals [21]. Methods such as latent class or clustering approaches, when applied to psychiatric populations, aim to dissect this heterogeneity, stratifying individuals into homogenous subgroups, termed subtypes, maximizing similarity within each group and distinctiveness between them [22, 23]. Previous efforts within EDs have, largely, focused on delineating subtypes using ED symptomatology or a combination of eating and comorbid psychopathology [24–27]. While these methods show advantages over traditional diagnostic classification in terms of diagnostic stability [28] and improved prediction of treatment outcomes [26, 29], they remain inconclusive regarding the number and validity of subtypes [24, 25, 29]. Importantly, even though 'symptom-based' subtyping approaches can help refine current categorical diagnostics, relying solely on ED symptoms for subtyping may not be sufficient to inform clinical practice. To improve efficacy, shifting towards 'mechanism-based' subtyping, which identifies subtypes based on data reflecting the underlying functional processes of EDs, is essential. This approach has the potential to personalize clinical practice by identifying subtype-specific mechanisms that can be targeted differentially [23, 29–31].

Several theoretical models emphasize multifactorial mechanisms in BE [32], supported by a broad span of evidence [33–42]. This research supports three neurobehavioral or 'functional' domains underlying BE behaviors: a) approach behavior, b) executive functioning, and c) negative emotionality. These domains, present not only in BE but also across various disorders characterized by impulsive-compulsive behaviors [30, 31, 43–46], are functionally independent and associated with distinct brain networks [8, 34, 36–45]. The 'Approach Behavior' domain is characterized by sensation seeking, incentive motivation, and engagement in reward-related processes, with neural underpinnings in the brain's reward and salience networks [44, 47]. These networks involve regions critical for appraising rewarding value and directing attention toward salient stimuli [44, 47]. Impairments within this domain – such as heightened reward-driven motivations and impulsive behaviors - contribute significantly to the pathology of BE, leading to excessive approach behaviors toward food as a primary reinforcer [36, 37].

The 'Executive Function' domain encompasses behaviors ranging from cognitive control, set shifting, inhibition to attention shifting [47] and is supported by the brain's executive or frontoparietal network (FPN) which integrates distributed brain regions essential for cognitive and attentional control [48]. Both extremes within this domain, ranging from excessive restraint or overcontrol to disinhibition or undercontrol, contribute to the risk and maintenance mechanisms in BE [32, 34]. Undercontrol leads to difficulties inhibiting impulses to engage in rewarding but harmful behaviors, increasing the risk of losing control over eating and BE [32–34], while overcontrol, often involving dietary restraint, has been evidenced to increase the likelihood of subsequent binge episodes, reinforcing a harmful cycle of restriction and bingeing [15, 32, 34].

The 'Negative Emotionality' domain involves an increased sensitivity to negative emotions and punishments, often also manifesting as impulsive behavior during negative mood states [33, 47], with impairments observed in the reward, salience, FPN, and the default-mode network (DMN) [49]. Numerous studies suggest that negative affect often precedes BE, and individuals who engage in BE struggle to regulate negative emotions [35, 50]. This difficulty is a significant factor in the development and frequency of BE, serving to regulate or escape negative affective states [32, 35, 50]. Despite evidence for the significant role of approach behavior, executive function, and negative emotionality across BT-EDs, existing research and theoretical models have not fully integrated these neurobehavioral domains [51]. This hinders our understanding of how these domains interrelate and contribute to BE, impeding the development of comprehensive BE pathology models [51]. Examining these domains collectively could reveal distinct processes driving heterogeneity in BE, facilitating the development of precision medicine approaches. However, existing ED subtyping research often overlooks the full spectrum of underlying mechanisms, and none have explored the neurobiological correlates of the subtypes identified.

Numerous studies, frequently using samples of mixed ED diagnoses, have characterized subtypes based on various combinations of comorbid symptoms (e.g., anxiety, depression), diagnoses (e.g., mood, personality disorders), or personality traits, with most focusing on personality psychopathology (see review: 29). Despite differences in the number of identified subtypes (ranging from 2–6), a variation of three potential mechanistic clusters have emerged: a) 'undercontrolled', marked by impulsivity, novelty seeking, emotional dysregulation, and heightened negative emotions; b) 'overcontrolled', characterized by inhibition, avoidance, emotional dysregulation, internalizing behaviors and poor self-esteem; and c) 'low psychopathology', with minimal comorbidities [29]. Subtyping studies that use a comprehensive comorbid psychopathology approach within samples specifically with BT-EDs are rare [29, 52]. Research in BT-EDs has generally subtyped participants on the basis of a combination of negative affect (e.g., depressive symptoms) and ED-specific behaviors, such as dietary restraint [29]. This approach primarily identified two subtypes: 'dietary' subtypes, characterized by heightened dietary restraint, and 'dietary-negative affect' subtypes, marked by both dietary restraint and increased negative affect [29]. In summary, previous subtyping approaches in samples with mixed EDs or within BT-EDs each offer unique strengths and limitations. While mixed ED subtyping typically adopts a broader psychopathology approach, assessing heterogeneity across aspects of different functional domains (e.g., negative emotionality, executive functioning domain), BT-ED subtyping often focuses more narrowly on a single-domain – frequently assessing heterogeneity within the functional domain of negative emotionality [29]. Importantly, neither approach has considered non-food related approach behaviors (e.g., increased reward seeking independent of food) as a potentially relevant underlying mechanism. Additionally, both approaches share a common limitation: they generally rely on narrow assessments (e.g., a depression scale) to represent broad functional domains (e.g., negative emotionality) using a single measurement tool as a proxy [29]. As a result, these approaches oversimplify the complexities of the mechanisms underlying these disorders [29]. To comprehensively understand BE heterogeneity and inform effective treatments, a mechanism-based subtyping approach incorporating a broad, multi-modal assessment of neurobehavioral domains is necessary.

Our study aimed to address this gap by applying a data-driven, mechanism-based approach to identify latent subtypes of BE, using a comprehensive, multi-modal assessment that captures the three neurobehavioral domains - approach behavior, executive functioning, and negative emotionality - that are hypothesized to drive BE. Importantly, ED psychopathology and eating-related attitudes were excluded from the subtyping process. Instead, these measures were used to clinically validate and characterize the derived subtypes. Furthermore, we investigated the neurobiological underpinnings of these subtypes using whole-brain resting-state functional magnetic resonance imaging (rs-fMRI) graph theory analysis [53]. We hypothesized that BE behaviors would exhibit considerable variability, such that impairments in any one functional domain – approach behavior (e.g., elevated sensation seeking/risk-taking), executive functioning (e.g., poor cognitive control), or negative emotionality (e.g., increased negative affect/ internalizing and emotional dysregulation) – would be sufficient to drive BE [31]. We thus expected to identify three subtypes, each characterized by distinct functional domain impairments and corresponding rs-fMRI network alterations.

METHODS

Participants

We analyzed data from the enhanced Nathan Kline Institute-Rockland Sample study conducted at the Nathan Kline Institute in New York between 2012 and 2016 [54]. This study was approved by the Nathan Kline Institute Institutional Review Board in accordance with the Declaration of Helsinki. Written informed consent and permission to share de-identified data were obtained from all study participants. A protocol filed with the University of Minnesota Institutional Review Board met criteria for exemption. After removing measures with > 10% missing data, 612 participants aged 18–59 had complete phenotypic data. Among them, individuals with BE behaviors ($N = 151$, 66% female) and Controls ($N = 461$, 66% female) were identified based on the Eating Disorder Examination Questionnaire's (EDE-Q) [55] reported frequency of objective binge-episodes (OBE; BE > = 1 OBE; Controls: 0 OBE), including participants with a range of BE behaviors from low frequency to clinical (≥4 OBEs/month). We excluded outliers based on OBE frequency ($N = 1$). See Supplementary Table 1 for details on the full sample, and Table 1 for demographics by subtype.

Phenotypic measures

To encompass the entire phenotypic space, we refrained from selecting measures based on theoretical considerations and instead included all available assessments, spanning a diverse range across behavior, affect, clinical symptoms, and cognition. When summary scores encompassing the task construct of interest were absent, we used all item-level scores. Our primary behavioral analysis included 74 item-level and summary scores derived from 18 assessments (see Supplementary Table 2 for a comprehensive list). Notably, we excluded measures of ED psychopathology and eating behavior from this analysis and instead used these for internal validation of the behavioral results (see 'Internal clinical validation measures' below).

Factor analysis of phenotypic data

We conducted an exploratory factor analysis (EFA), involving all study participants ($N = 612$), to reduce our phenotypic dataset into underlying latent variables while maintaining a comprehensive representation of the entire phenotypic space. This analysis was very well powered ($N > 600$; participant/variable ratio = 8.0), based on sample size recommendations for EFA [56]. Monte Carlo permutation analysis (parallel analysis) was implemented to determine the number of factors to retain at a statistical significance of $p < 0.05$ [57], ensuring factor selection remains independent of distributional assumptions [58]. Subsequently, latent factors were extracted using maximum likelihood estimation with the expectation-maximization (EM) algorithm [59], which has been shown to be robust to distributional violations [58, 60–62]. To accommodate correlated factors, we utilized 'direct oblimin' rotation, essential for data reduction over a large variable space where factors are expected to be closely related but separable [59]. Both the parallel analysis and EFA were conducted in R using the 'psych' package [63]. To best operationally define our factors, factor loadings > 0.3 were retained [59]. Factor scores quantifying individual differences in underlying factors were obtained using the regression method. Functional domains describing the interrelationships of factors were empirically determined via factor score correlations and visualized using a spring-embedded graph [64]. This spring-embedded graph was computed in MATLAB (*'graph'* function) using minimal correlation weights, such that each factor was connected to at least one other factor.

Subtype identification

To identify whether distinct phenotypic subtypes exist within the BE group ($N = 149$), we implemented a latent profile analysis (LPA) using the EFA factor scores as input. LPA, a form of Gaussian-mixture modelling (GMM), is a commonly used model-based clustering approach which assumes the data is distributed according to a mixture of multivariate Gaussian distributions [65]. The LPA was performed in R (4.1.2) using the *'mclust'* package [65]. The model was fitted by the EM algorithm and initialized by model-based hierarchical clustering based on scaled singular value decomposition [65]. LPA models with one to nine profiles were fit to determine the optimal number of clusters/subtypes. Bayesian Information Criterion (BIC) [66] and Integrated Complete-Data Likelihood (ICL) [66] were used to assess model fit [66], with model selection determined by the lowest BIC and ICL [65]. Bootstrap Likelihood Ratio Tests (BLRTs) [66] were conducted to compare the fit between a k-profile and a k − 1-profile model. We additionally considered model parsimony and whether a solution included small profiles (<5% of the sample size) [67, 68]. According to simulations [69–71], this analysis had adequate statistical power (sample size: $N = 149$; 12 continuous input variables; $N = 24$ in the smallest profile; observed effect sizes for profile differentiation: partial-eta squared = 0.08–0.48). Briefly, the power was considered adequate due to subtype sample sizes being expected to be equal based on theoretical considerations [see [31]], the large number of (continuous) input variables included for profile differentiation, the smallest observed subtype sample size being $N > 20$, and robust group separation being demonstrated by the large effect sizes distinguishing the subtypes [69–71].

Model stability and validation

When utilizing a mixture model for subtyping, uncertainties arise regarding the optimal model choice (e.g., number of clusters/subtypes, certainty of profile assignments) and the estimation of model parameters. To address these concerns, we employed various diagnostic statistics and sensitivity analyses as summarized here and reported more fully in the Supplementary Methods. To validate the model, we employed: a) entropy, which assesses the model's certainty in assigning individuals to clusters [67, 68], b) Average Posterior Probability, which gauges the accuracy of individual profile membership predictions [67, 68], and c) mixture model discriminant analysis, assessing the ability of a classifier to predict the obtained clusters under 10-fold cross-validation [65, 72]. All uncertainty metrics were evaluated against standard goodness-of-fit thresholds specific to each measure. We additionally validated the stability of our GMM under random restarts of the EM algorithm to avoid local maxima [65], and we quantified uncertainty of the resulting model parameters via resampling with the percentile bootstrap approach [65, 73].

Subtype phenotypic characterization

Control group assignment. To reduce bias and avoid skewed results in statistical comparisons due to unbalanced sample sizes, we matched a control group to the largest subtype. This control group, selected from the existing sample of controls, was matched for age, gender, and body mass index (BMI), using the 'matchControls' function from the R 'e1071' library [74]. We verified the control group was consistently well-matched across all identified subtypes, ensuring no significant differences in age, gender, or BMI.

Phenotypic profiles. To delineate phenotypic profiles, we characterized the subtypes using the EFA-derived factors. In the primary analysis each subtype was compared to the matched control group, while the secondary analysis compared the subtypes to each other. We utilized multivariate analysis of covariance (MANCOVA), covarying for age, gender, and BMI. All comparisons were corrected for multiple testing (adjusting for number of EFA factors) using a false discovery rate (FDR) threshold of $p\text{-}FDR < 0.05$.

Internal clinical validation measures. We additionally used measures of demographics and clinical characteristics, not incorporated in the subtyping analysis (LPA), to internally validate the subtyping solution. These measures included: a) the EDE-Q [55], capturing ED symptoms and pathology, b) the Three-Factor Eating Questionnaire (TFEQ) [75], examining cognitive and behavioral aspects of eating behavior, c) the Adult Self-Report (ASR) [76], measuring substance use frequency, and 4) the Structured Clinical Interview for DSM-IV [77], assessing subject clinical diagnoses. Further measurement details are provided in the Supplementary Methods. MANCOVAs and chi-squared analyses were applied where appropriate (two-sided), with FDR adjustment for multiple comparisons (corrected for number of measures) in post-hoc analyses.

Subtype neurobiological characterization

Detailed information on the MRI acquisition, quality control, pre-processing, functional connectivity (FC) and graph theory analysis can be found in the Supplementary Methods. In short, after assessing data quality using the automated MRI Quality Control tool (MRIQC) [78], we preprocessed the anatomical and functional data (rs-fMRI) using fMRIPrep 20.2.1 [79] on the Minnesota Supercomputing Institute's High Performance Computing cluster (www.msi.umn.edu). Next, we conducted the FC analysis in MATLAB (version 2021a; The MathWorks, Inc.), using the brain connectivity toolbox (https://sites.google.com/site/bctnet/) to compute

Table 1. Subtype and control profiles: demographics and LPA input variables.

Characteristic	1. Negative Emotionality $N = 24$	2. Approach $N = 75$	3. Restrained $N = 50$	0. Controls $N = 75$	Post-Hoc Comparison ($pFDR < 0.05$)	Effect Size (η_p^2)
Age, mean (SD), years	44.10 (13.19)	39.55 (12.39)	44.38 (12.68)	39.22 (12.57)	N.S.	–
Gender, *n* (%)					N.S.	–
Male	9 (37%)	29 (39%)	11 (22%)	29 (39%)		
Female	15 (62%)	46 (61%)	39 (78%)	46 (61%)		
Race/Ethnicity, *n* (%)						
Asian	1 (0.04%)	3 (0.04%)	4 (0.08%)	6 (0.08%)	N.S.	–
Black/AA	4 (0.17%)	15 (0.20%)	8 (0.16%)	19 (0.25%)	N.S.	–
Caucasian	18 (0.75%)	55 (0.73%)	35 (0.70%)	48 (0.64%)	N.S.	–
NA	0 (0%)	1 (0.01%)	0 (0%)	1 (0.01%)	N.S.	–
NH	1 (0.04%)	0 (0%)	1 (0.02%)	0 (0%)	N.S.	–
Other	0 (0%)	1 (0.01%)	2 (0.04%)	0 (0%)	N.S.	–
Education, mean (SD), years	14.75 (1.85)	15.16 (2.24)	15.24 (2.13)	15.08 (2.17)	N.S.	–
SES, mean (SD)	40.33 (12.55)	44.68 (12.13)	46.48 (10.18)	42.94 (13.65)	N.S.	–
FD, mean (SD)	0.11 (0.06)	0.12 (0.06)	0.13 (0.04)	0.12 (0.04)	N.S.	–
BMI, mean (SD), kg/m^2	28.41 (6.14)	30.80 (6.10)	28.62(5.89)	27.27 (5.70)	**2 > 0***	0.06
Number of OBE, mean (SD)	10.33 (9.17)	5.19 (6.40)	3.12 (3.18)	0 (0)	**1 > 0,2,3*; 2 > 0,3*; 3 > 0***	0.29
Number of SBE, mean (SD)	8.83 (8.86)	5.97 (6.80)	3.90 (4.09)	0 (1.49)	**1 > 0,2,3*; 2 > 0*; 3 > 0***	0.15
Purging Behaviors, mean (SD)	0.33 (1.17)	0.68 (2.83)	0.12 (0.52)	0 (0)	**N.S.**	–
Purging, *n* (%), past 28 days	2 (8.33%)	6 (8.00%)	3 (6.00%)	0 (0%)	**N.S.**	–
BE, *n* (%)				–	**1 > 2,3***	
Clinical: OBE ≥ 4 (per month)	17 (70.83%)	28 (37.33%)	12 (24.00%)			
Sub: ≥1 OBE < 4 (per month)	7 (29.17%)	47 (62.67%)	38 (76.00%)			
Measures Used In Subtype Formation						
EFA Factors, mean (SD)	**1. Negative Emotionality $N = 24$**	**2. Approach $N = 75$**	**3. Restrained $N = 50$**	**0. Controls $N = 75$**	**Post-Hoc Comparison ($pFDR < 0.05$)**	**Effect Size (η_p^2)**
Internalizing	1.90 (0.90)	0.28 (0.68)	−0.42 (0.47)	−0.11 (0.95)	**1 > 0,2,3*; 2 > 0,3*; 0 > 3***	0.43
General Psychiatric	1.71 (1.00)	0.07 (0.55)	−0.41 (0.31)	−0.08 (0.65)	**1 > 0,2,3*; 2 > 3***	0.49
(Lack of) Effortful Control	1.19 (1.21)	0.34 (0.78)	−0.57 (0.58)	0.03 (0.89)	**1 > 0,2,3*; 2 > 0,3*; 0 > 3***	0.26
Negative Affect	0.95 (0.75)	0.23 (0.78)	0.11 (0.78)	−0.20 (0.84)	**1 > 0,2,3*; 2 > 0***	0.15
Openness/Sensitivity	0.30 (0.94)	0.02 (0.95)	−0.11 (0.83)	−0.05 (0.83)	N.S.	–
Risk Perception	0.39 (0.99)	−0.12 (0.86)	0.47 (0.66)	0.06 (0.87)	**1 > 2*; 3 > 0,2***	0.08
Unethical Behavior/Norm-Breaking	0.18 (0.94)	0.32 (0.82)	−0.65 (0.57)	−0.11 (0.91)	**1 > 3*; 2 > 0,3*; 0 > 3***	0.17
Social-Risk Taking	−0.14 (1.00)	0.13 (1.02)	−0.26 (0.82)	0.04 (0.87)	N.S.	–
Urgency	0.22 (1.26)	0.53 (0.68)	−0.37 (0.68)	−0.19 (0.89)	**1 > 3*; 2 > 0,3***	0.17
IQ/Executive Function	−0.29 (0.95)	−0.13 (0.97)	−0.28 (0.67)	−0.01 (1.02)	N.S.	–
Extraversion/Sociability	−0.84 (1.12)	0.01 (0.97)	0.39 (0.54)	−0.08 (0.72)	**2 > 1*; 3 > 0,1,2*; 0 > 1***	0.14
Sensation Seeking	−0.29 (1.05)	−0.03 (0.88)	−0.23 (0.84)	−0.02 (0.94)	N.S.	–

Groups compared with either MANCOVAs (for continuous variables) or chi-square tests (for categorical variables). All comparisons were corrected for multiple-comparisons (p-$FDR < 0.05$). Bold font with asterisk denotes statistically significant p-values.

AA african american, *Behav* behavior, *BE* binge eating, *BMI* body mass index, *EDE-Q* eating disorder examination questionnaire, *EFA* exploratory factor analysis, *FA* framewise displacement, *FD* framewise displacement, *NA* native american, *NH* native hawaiian, *N.S* not significant, *OBE* objective binge episode, *SBE* subjective binge episode, *SES* socioeconomic status, *SD* standard deviation, *Sub* subthreshold. 1 = Negative Emotionality Subtype, 2 = Approach Subtype, 3 = Restrained Subtype, 0 = Controls.

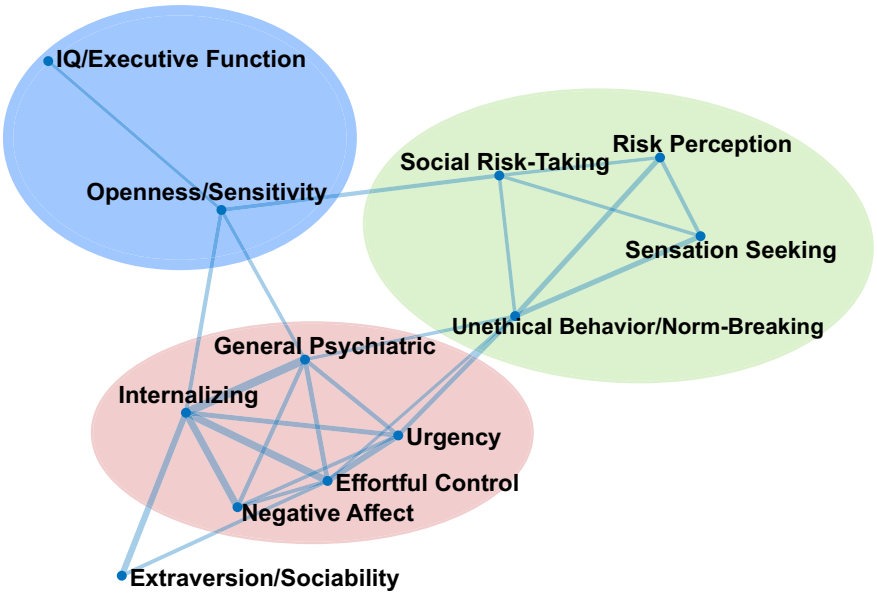

Fig. 1 Spring-embedded plot: extraction of functional domains. Visualization of how the latent factors, identified through exploratory factor analysis, empirically self-organized into the hypothesized three domains. Each node represents a latent factor, with spatial proximity reflecting the strength of correlations – strongly correlated nodes are plotted closer together. The emergent functional domains are color-coded in the spring-embedded network: Blue = Executive Functioning Domain, Red = Negative Emotionality Domain, Green = Approach Behavior Domain.

graph theory metrics. The graph analysis focused on four key metrics that were computed for each brain region (or 'node'): global functional integration (global efficiency), local functional integration/ global segregation (local efficiency), modularity (participation coefficient), and centrality (degree centrality). These metrics assess functional topology during resting-state. *Global efficiency* measures how efficiently brain regions are functionally coupled across the entire brain, reflecting a region's capacity to effectively communicate and integrate information across the brain, while *local efficiency* measures functional coupling with neighboring brain regions, reflecting its capacity for locally integrated (but globally segregated) processing [80, 81]. The *participation coefficient* quantifies a region's functional integration within its own (versus other) 'module', while *degree centrality* assesses a brain region's overall functional connectedness, reflecting its functional importance and influence on information processing [80, 81]. For further details, see the Supplementary Methods. We conducted generalized linear models (GLMs), comparing each subtype to the matched control group for each of the four graph metrics, adjusting for age and BMI, and correcting for multiple comparisons (correcting for number of parcellated brain regions [$N = 379$]) at $p\text{-}FDR < 0.05$.

RESULTS

Phenotypic results

Bartlett's test of Sphericity ($\chi^2 = 21{,}947.39$, $p < 0.001$) and Kaiser–Meyer–Olkin test (KMO = 0.86) confirmed data suitability for EFA. Across all participants ($N = 612$), parallel analysis and EFA identified 12 significant latent factors ($p < 0.05$), reducing the initial 74-variable phenotypic space to a 12-dimensional phenotypic latent space, explaining 45% of the common variance (see Supplementary Fig. 2 for the scree plot). Model fit indices indicated good separation (RMSEA = 0.046, Tucker-Lewis Index = 0.82), and each factor met the minimum requirement of three salient loadings (>|0.30|) [59]. See Supplementary Table 3 and Supplementary Table 4 for details on the 12 factors, labels, and loadings. Subjects with outliers on factor scores (>3 SD from the mean) were excluded from further analysis ($N = 1$). The spring-embedded plot, derived from the underlying factor correlations, revealed the self-organization of the twelve latent factors into the three hypothesized functional domains (Fig. 1; see Supplementary Table 5 for factor correlations).

Subtyping results

Among the nine profiles assessed, the three-profile model exhibited the lowest BIC and ICL indicating superior fit (see Supplementary Table 6 for model fit indices). The significant BLRT supported the three-profile model's goodness-of-fit relative to the two-profile model (Supplementary Table 6). Of note, BLRT p-values were significant for all models, except when comparing the seven-profile to the six-profile models, limiting the utility of this indicator in model selection (Supplementary Table 6). Given the convergence of BIC and ICL on the three-profile solution for optimal fit, and that this solution provided a sufficient sample size for each profile (>5% of sample), this model was selected for further validation.

Multiple model stability and validation analyses all strongly supported the robustness of the three-profile model (Supplementary Tables 7–10, Supplementary Fig. 3, and Supplementary Fig. 4). Overall, model entropy (0.82), average posterior probability (0.91–0.96), and cross-validated mixture model discriminant analysis (F1 score = 0.98) all indicated high quality classification and profile separation. Results held over repeated random initializations, identified a 3-profile solution with VEI variance-covariance parameterization as the optimal model. See Supplement for mixture model SEs and CIs, based on non-parametric bootstrap (Supplementary Table 10, Supplementary Fig. 4).

Subtype phenotypic & clinical characterization. Based on the 3-profile solution, we found a) a 'Negative Emotionality' type ($N = 24$) with significantly higher internalizing, general psychiatric symptoms, negative affect, (lack-of) effortful control, and lower extraversion/sociability; b) an 'Approach' type ($N = 75$) with significantly higher unethical behavior/norm-breaking, extraversion/sociability, urgency and lower risk perception; c) and a 'Restrained' type ($N = 50$) with significantly higher risk perception, effortful control, extraversion/sociability, and lower unethical behavior/norm-breaking, urgency, internalizing and general psychiatric symptoms (See Fig. 2, and Table 1). Secondary analysis confirmed that subtype profiles were consistent in both between-subtype comparisons and comparisons with controls (Table 1, Fig. 3, and Supplementary Table 11). Results of MANCOVAs and chi-squared tests for these comparisons are detailed in Table 1, Fig. 3, and

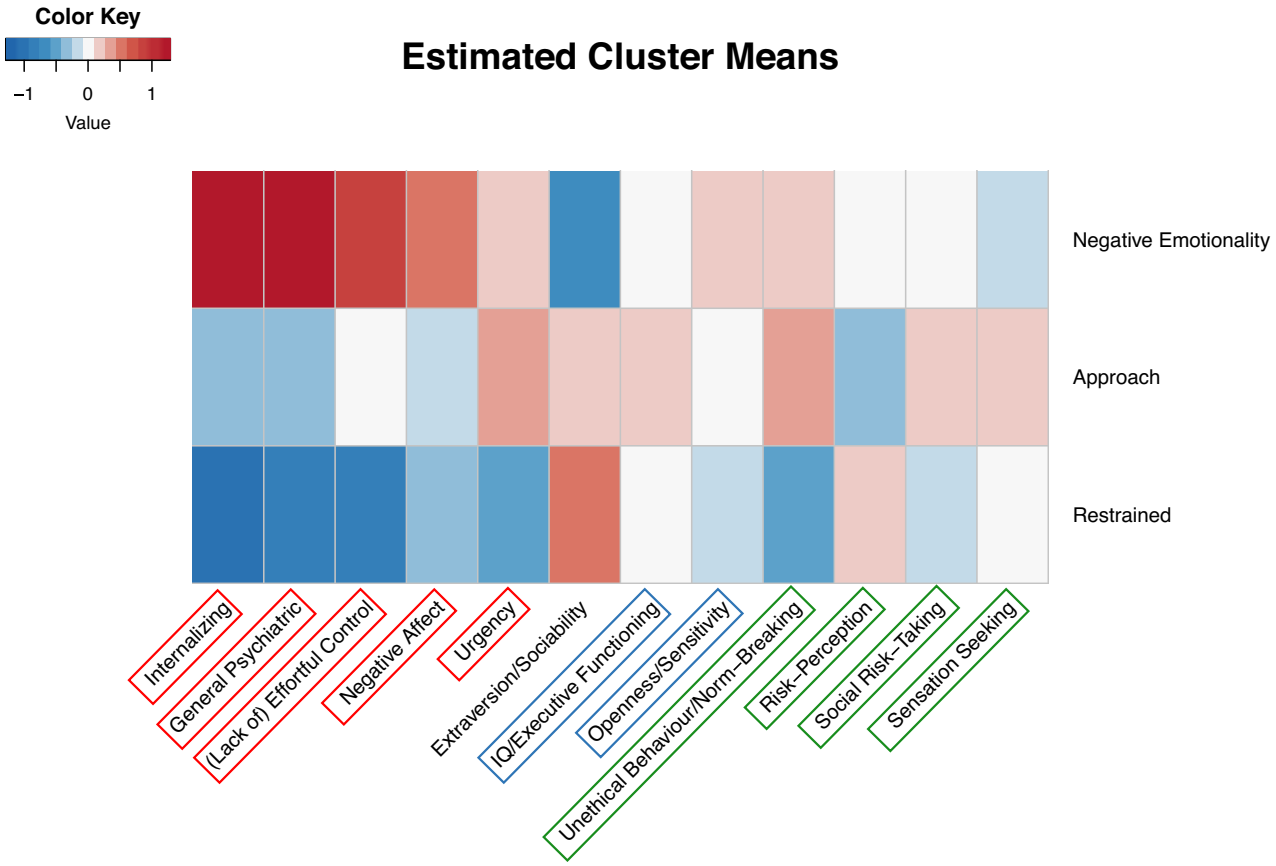

Fig. 2 Heatmap depicting the phenotypic profiles for each subtype. Heatmap illustrating the contribution of input variables to the three-profile subtyping solution. Each cell represents the relative impact or importance of a feature (x-axis) to defining the profile, with color indicating both the direction and strength of the contribution. Red indicates a strong, positive contribution (i.e., an increase in the feature significantly influences the profile); Blue indicates a strong, negative contribution (i.e., a decrease in the feature significantly influences the profile). Positive and negative contributions are weighted equally. Values are standardized to the [−1,1] range. Colored boxes around feature labels (x-axis) indicate relationship to phenotypic domain: Red = Negative Emotionality, Green = Approach Behaviors, Blue = Executive Function.

Supplementary Table 11. Each subtype also demonstrated distinct clinical profiles, generally consistent in comparisons both between subtypes and with controls. The 'Negative Emotionality' type exhibited significantly higher ED psychopathology (EDE-Q: Restraint, Eating, Shape and Weight Concern) (Fig. 3), and a greater prevalence of current internalizing disorders (SCID-IV) (Supplementary Table 11). The 'Approach' type reported significantly more frequent substance use (over past 6-months), particularly in days drunk (ASR), had the lowest dietary restraint levels (TFEQ), and a higher prevalence of past substance use disorders (Fig. 3, Supplementary Table 11). The 'Restrained' type exhibited significantly lower disinhibition (TFEQ) and higher levels of dietary restraint (TFEQ) (Fig. 3), with psychiatric disorder prevalence similar to matched controls (Supplementary Table 11). Among the identified subtypes, only the 'Negative Emotionality' type had a significantly higher proportion of OBEs meeting clinical-level threshold, while the 'Approach' and 'Restrained' types had similar proportions of both clinical and subclinical OBEs (Table 1). Additionally, no differences between subtypes were observed regarding purging behaviors (Table 1). Lastly, the 'Approach' type had a higher BMI compared to controls (Table 1), with no other demographic differences observed across subtypes or between subtypes and controls regarding age, gender, race, education or socioeconomic status (Table 1).

Subtype functional connectivity profiles

No significant differences in framewise displacement were observed between groups (Table 1). Unique neurobiological patterns linked to BE were identified in two subtypes as described below ($p\text{-}FDR < 0.05$; Fig. 4, see Supplementary Table 12 and Supplementary Table 13 for subtype- and metric-specific details). After multiple comparison correction ($p\text{-}FDR < 0.05$), the 'Negative Emotionality' subtype ($N = 24$) did not exhibit significant differences compared to matched controls across FC metrics.

Compared to matched controls, after multiple comparison correction ($p\text{-}FDR < 0.05$), the 'Approach' type ($N = 75$; Fig. 4, Supplementary Table 12) demonstrated increases in both local efficiency and degree centrality. Increased local efficiency was observed in regions of the DMN (ventral and dorsal posterior cingulate), Parietal Association (Premotor cortex), and Sensorimotor (Early somatosensory and motor cortex), while increased degree centrality was observed in regions of the Dorsal FPN (dorsolateral prefrontal [dlPFC], Superior parietal, Inferior parietal), Somatosensory (Posterior opercular), and Visual (Inferior parietal, Dorsal stream) networks. Additionally, a few regions demonstrated decreased global efficiency, including the dorsal ACC, dlPFC, and within the temporal-parietal-occipital junction, whereas increased global efficiency was observed in two regions of the visual cortex.

Compared to matched controls, after multiple comparison correction ($p\text{-}FDR < 0.05$), the 'Restrained' type ($N = 50$; Fig. 4, Supplementary Table 13) exhibited widespread changes, marked by reductions in global efficiency, local efficiency, and participation coefficient. Decreased global efficiency was observed in regions of the Salience (anterior cingulate cortex/medial prefrontal cortex), Ventral FPN (inferior frontal, inferior parietal), Dorsal FPN

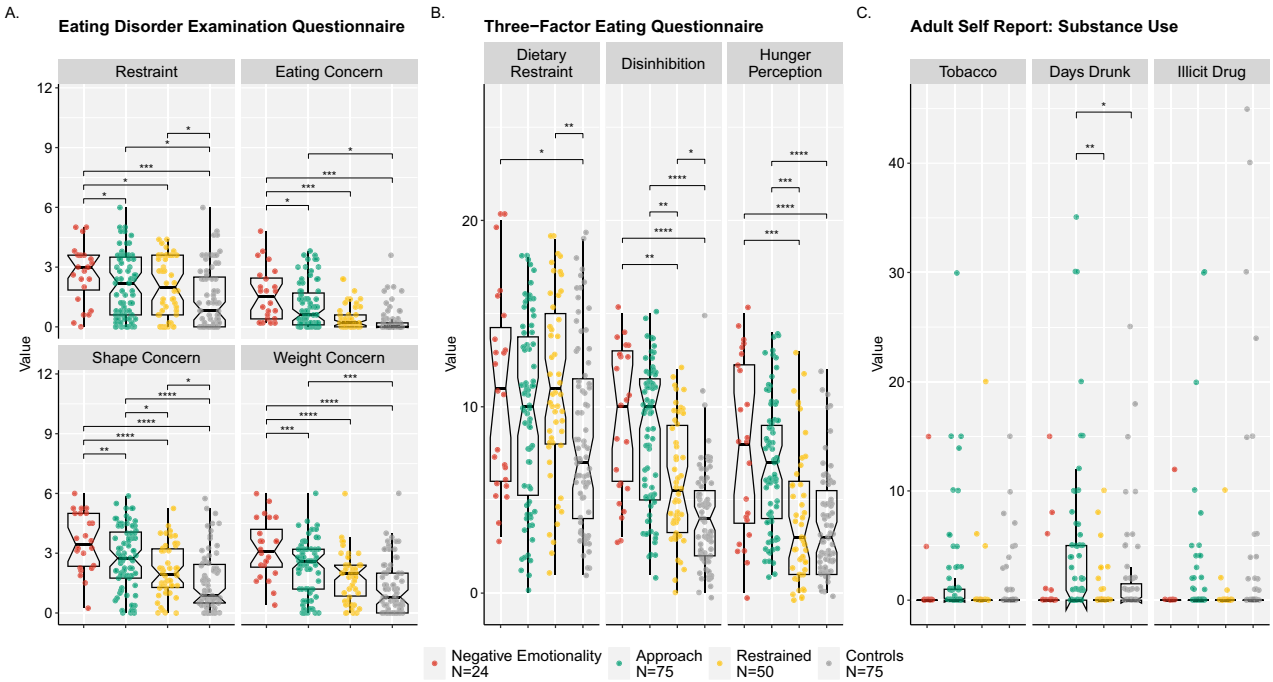

Fig. 3 Validation measures: clinical characteristics of each subtype. A–C: Subtype and control comparisons on internal clinical validation measures - assessments not included in subtype formation. All comparisons were corrected for multiple-comparisons (*p-FDR* < 0.05). Asterisk denotes statistical significance at **p-FDR* < 0.05, ***p-FDR* < 0.01, ****p-FDR* < 0.001, *****p-FDR* < 0.0001.

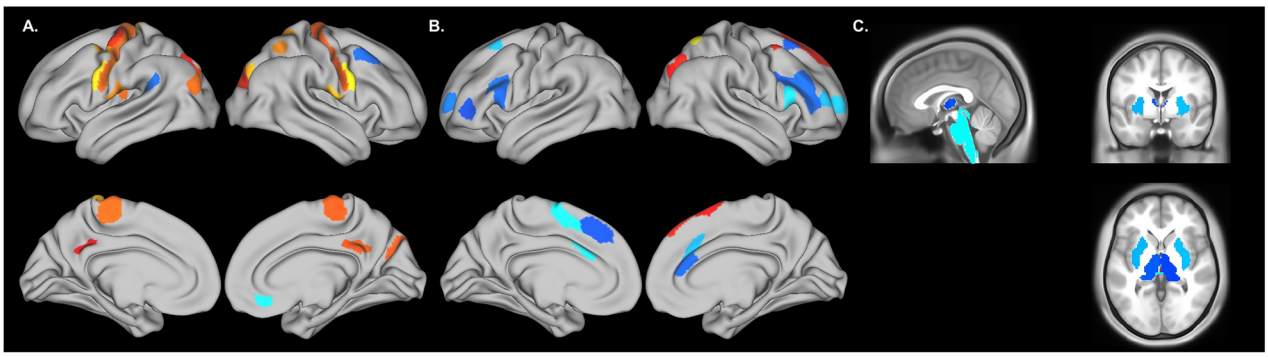

Fig. 4 Graph theory results per subtype. Subtype-specific neurobiological profiles, determined by graph theory analysis of resting-state functional connectivity (*p-FDR* < 0.05). **A** Approach Subtype: Cortical results. **B** Restrained Subtype: Cortical results. **C** Restrained Subtype: Subcortical results. Depicted results are collapsed across graph metrics. For subtype-specific results by graph metric, see Supplementary Table 12 and 13. Warm colors represent increased beta values, and cool colors represent decreased beta values.

(posterior dlPFC) and Reward (inferior frontal) networks. Decreased local efficiency was demonstrated in regions of the Salience (anterior cingulate cortex/medial prefrontal cortex), Ventral FPN (inferior frontal), Dorsal FPN (dlPFC), Reward (orbital-polar frontal) networks, and sub-cortically (bilateral thalamus). Decreased participation coefficient was observed in regions of the Salience (anterior cingulate cortex/medial prefrontal cortex), Dorsal FPN (dlPFC), Ventral FPN (inferior frontal), Reward (orbital-polar frontal, inferior frontal) networks, and in subcortical regions (bilateral putamen, bilateral thalamus, and brain-stem).

DISCUSSION

We applied a rigorous, data-driven, mechanism-based approach to characterize heterogeneity in the mechanisms underlying BE behavior using integrated multidimensional data across three hypothesized neurobehavioral domains: approach behavior, executive functioning, and negative emotionality. Three subtypes emerged, each demonstrating unique profiles across these domains, as well as distinct clinical characteristics and neurobiological functioning. Individuals in the 'Negative Emotionality' type exhibited greater negative affect, lack of effortful control (poorer emotion regulation) and increased psychiatric comorbidity (e.g., highest general psychiatric and internalizing behaviors). Individuals in the 'Approach' type exhibited higher approach-related and impulsive behaviors (e.g., highest unethical behavior/norm-breaking, urgency, and current substance use, lowest risk-perception) and increased brain connectivity in regions of the frontoparietal, somato-motor and visual networks. Individuals in the 'Restrained' type were characterized by overcontrolled, restrictive and harm-avoidant behaviors (e.g., highest effortful control and risk-perception, lowest unethical behavior/norm-breaking), along with decreased functional connectivity in regions of the salience, frontoparietal and reward networks and subcortical regions. Importantly, while previous research has emphasized the importance of approach behavior, executive functioning,

and negative emotionality in BT-EDs [36, 37, 42, 51], this study represents the first to investigate heterogeneity in BE across a comprehensive and multi-modal assessment of these domains in a single sample, revealing complexities of BE pathology beyond clinical severity and diagnostic classification.

Our factor analysis provided strong empirical support for a phenotypic space of functioning which empirically self-organized into the three hypothesized functional domains of interest: negative emotionality, executive function, and approach behavior. Additionally, consistent with previous research in an independent dataset [58], our analysis revealed that two typically 'cognitive' factors, specifically 'effortful control' and 'urgency', did not self-organize into the executive function domain but were robustly associated with factors in the negative emotionality domain. This link between these typically 'cognitive' factors and negative emotionality aligns with the well-established relationship between affective processes and emotion regulation [82, 83]. Further examination of the 'executive function' and 'negative emotionality' domains reveals critical distinctions in their construction which may also contribute to this finding. The 'executive function' domain primarily consisted of factors that loaded on task-based measures of cognition, while the 'effortful control' and 'urgency' factors—linked to the negative emotionality domain—were derived from questionnaires on impulsivity, temperament, and personality. This distinction between data modalities is important, as questionnaires and task-based measures capture different constructs that are minimally correlated [84, 85]. Task-based measures probing cognition evaluate cognitive performance under standardized conditions, whereas questionnaires assess self-reported executive difficulties influenced by mood and context [84].

The 'Negative Emotionality' subtype that we identified was characterized by heightened affective disturbance and emotion dysregulation. Emotion/affect regulation is a central and empirically supported concept across several BE theories, which propose that BE functions to manage, moderate, and avoid aversive emotions and states [32]. Accordingly, individuals within this subtype may uniquely struggle with self-regulating negative affect, potentially driving BE as a form of negative reinforcement to escape or relieve aversive states [35, 50]. This 'Negative Emotionality' type shared characteristics with both the commonly identified 'dietary-negative affect' and 'undercontrolled' subtypes from prior ED research [29]. Similar to the 'dietary-negative affect' subtypes, our 'Negative Emotionality' type was marked by heightened negative affect and internalizing behaviors. Clinical validation measures further supported these similarities, demonstrating that our 'Negative Emotionality' subtype similarly exhibits elevated ED psychopathology (EDE-Q), increased rates of clinical-level OBEs, and a higher prevalence of current internalizing disorders compared with the other identified subtypes and controls. The 'Negative Emotionality' type also resembled the 'undercontrolled' subtype identified in prior research, which is characterized by emotion dysregulation, heightened negative emotions, and a lack of effortful control. However, an important distinction was that previously-defined 'undercontrolled' subtypes have also demonstrated approach-related dysregulation and novelty seeking, while our identified subtype was distinctly driven by dysregulation related to negative affect, lacking any approach-related deficits. Interestingly, our 'Negative Emotionality' subtype also paralleled a similar subtype identified in individuals with Substance Use Disorders, known as the 'Relief' subtype. This 'Relief' type is also characterized by heightened negative affect and emotion dysregulation, where negative affect is believed to drive alcohol or substance use as a means of 'relief' or coping mechanism [30, 86]. This underscores the crucial role of negative emotionality as a transdiagnostic construct underlying compulsive consumption of food, alcohol, and other substances, revealing shared mechanisms across disorders and its potential to differentially drive BE.

The 'Approach' subtype was characterized by high levels of impulsive, risk-taking, and externalizing behaviors. Adaptations (e.g., sensitization or habituation) in reward sensitivity may drive impulsive actions and poor decision-making, leading to maladaptive reward-driven behaviors that uniquely reinforce compulsive BE despite negative outcomes within this subtype [36, 37, 45]. This subtype also shared similarities with the 'undercontrolled' subtypes identified in prior ED research [29, 52], particularly in behaviors related to dysregulation and impulsivity within the context of approach behavior – such as heightened positive urgency and novelty-seeking. However, these similarities in dysregulation were not additionally related to negative emotions as observed in prior ED subtypes [29]. Unlike previous research, our findings distinguish two subtypes based on different aspects of dysregulation: one characterized by heightened negative affect, internalizing symptoms and emotion dysregulation (the 'Negative Emotionality' type), and another marked by uninhibited approach-related behaviors (the 'Approach' type). This characterization was further supported by clinical validation measures, which indicated the highest frequency of current substance use among this group, the lowest levels of dietary restraint, and a higher proportion of past substance use disorders among its members. We further found that this 'Approach' subtype closely resembled the 'Reward' type observed in individuals with Substance Use Disorder, where alcohol/drug-seeking behaviors are driven by underlying impairments in approach-related, sensation-seeking tendencies [30, 86]. Overall, these findings reaffirm the transdiagnostic nature of compulsive consumption and emphasize the role of approach-related mechanisms in differentially contributing to BE behaviors.

The 'Restrained' subtype was characterized by low approach behaviors and low negative emotionality, demonstrating risk-aversion and overcontrolled behaviors. This profile shared similarities with several previously identified subtypes in the ED literature [29], exhibiting inhibited and avoidant traits akin to the 'overcontrolled' ED subtypes, while also demonstrating characteristics of the 'low psychopathology' and 'dietary' subtypes [29], albeit with distinct differences. Despite having the lowest ED pathology (EDE-Q) and comorbid psychopathology among subtypes, this group demonstrated dietary restraint levels (TFEQ) comparable to the 'Negative Emotionality' type and a similar proportion of clinical-level OBEs as the 'Approach' type. The characteristic overcontrolled, restrained and harm-avoidant behaviors underlying this 'Restrained' type, identified even without BMI variations between groups, suggests a pathway to BE that is distinct from typical internalizing or externalizing pathways to compulsive behavior. This observation challenges notions of severity based primarily on the presence of comorbid psychopathology or obesity, highlighting the complex role of restraint in BE. Historically, restraint was among the first cognitive factors linked to BE development and maintenance [32], theorized to function as either a cause or consequence of BE behaviors. While recognized as a risk factor for (and/or a consequence of) BE, only a small subset of highly restrained individuals develop BE [87], indicating that restraint may increase susceptibility to BE and BT-EDs, especially in individuals with a genetic predisposition [87]. This interpretation could offer an explanation into the distinct features contributing to the risk and development of BE in individuals within this subtype. Interestingly, the concept of restraint is not uncommon in compulsive disorders, particularly substance addiction [88]. Unsuccessful attempts to cut down or abstain, despite wanting to, are prevalent in addiction and included in DSM substance use criteria, reflecting the unsuccessful restraint observed in BE [88]. Importantly, while the 'Negative Emotionality' and 'Approach' types in this study appeared to replicate the 'Relief' and 'Reward' phenotypes from the broader addiction literature [30, 86], this 'Restrained' subtype, to our

knowledge, has not been similarly identified in addiction. This suggests that the 'Restrained' subtype represents a unique perspective and potential pathway for compulsive BE, where unsuccessful restraint and overcontrolled behaviors may serve as both a cause or consequence underlying compulsive behaviors [32, 88].

Our subtype-specific findings revealed distinct neurobiological features aligned with each subtype's phenotypic profile, demonstrating distinct brain functional topology and information processing patterns per subtype. The 'Approach' subtype exhibited increased local efficiency in regions of the DMN, Sensorimotor, and Parietal Association networks. Heightened local efficiency reflects enhanced local information processing but reduced cross-talk globally between brain networks [89]. Degree Centrality was both increased and decreased in different regions of the FPN, and increased in Visual and Somatosensory networks. Such dysregulated functional organization in frontoparietal brain networks has been associated with cognitive deficits, impulsivity, biased attention, and impaired motor planning [37, 38, 49, 90–95], and also distorted self- and body-image perceptions central to ED pathology [39, 40, 92, 93]. Notably, aberrant connectivity in the sensorimotor and visual networks also contributes to impaired attentional processing, motor control, and body perception, as observed in BT-EDs [92–94, 96, 97]. Increased connectivity within these networks has also been linked to psychopathological symptoms in BN patients [92, 93]. Furthermore, the DMN, crucial for self-referential processing and interoception [49, 98], shows both significant hyper- and hypo-connectivity connectivity across BT-EDs, suggesting a role in maladaptive self-focused processing, emotional memories, and persistent preoccupation with food and body image [38, 40, 94, 97]. Enhanced segregation of processing in these networks may also reflect enhanced sensory and self-referential processing [89]. Interestingly, crucial regions in the Salience and FPN, including the dorsal ACC and dlPFC, also showed decreased global efficiency. This finding points to decreased global processing efficiency in networks critical for attentional control, and re-orienting salient stimuli [34, 45, 49, 98], aligning with the impulsive and compulsive characteristics observed in this subtype. Connectivity disruptions within the ACC and PFC, have also been associated with maladaptive response inhibition and reward processing, potentially underlying the loss-of-control and impulsive behaviors observed in BT-EDs [34, 37, 38, 40, 45] and with other compulsive behaviors [43, 45, 49]. Taken together, these neurobiological findings support prior research linking disruptions in these networks to maladaptive impulsivity, compulsivity, and ED-related pathology in BT-EDs and other impulsive-compulsive populations [37, 38, 45]. In particular, this subtype-specific neurobiological pattern may reflect a maladaptive prioritization of sensory and self-referential processing, limiting the brain's ability to allocate attention, motor control, and goal-directed behaviors to other processes, ultimately reinforcing compulsive BE. This distinct pattern may serve as a unique marker for the characteristic externalizing, impulsive behaviors, and elevated ED pathology in this 'Approach' subtype, and potentially guide the development of targeted, brain-based interventions.

In contrast, the 'Restrained' subtype demonstrated a pattern of disrupted information processing, evidenced by the decreased global efficiency, local efficiency, and participation coefficient in brain regions associated with the FPN, salience and reward networks, and notably the bilateral putamen and thalamus - regions consistently implicated in BT-EDs [34, 37, 39–41, 92, 99]. These findings suggest a disruption in information flow and network integration crucial for approach behaviors and effortful control, aligning with prior research indicating reduced participation coefficient in these networks and subcortical regions in BN [100] and reduced fronto-striatal functional connectivity in BED [101] and across BT-EDs [38, 101]. Furthermore, reflecting the overcontrolled and restrained characteristics of this subtype, its neurobiological profile aligns with and extends previous research on the neural correlates of restrained eating [102–107]. While similar patterns are observed among highly restrained, yet healthy, 'emotional eaters' [105], fMRI research investigating restraint in clinically-relevant populations are rare, including only (to our knowledge) two studies [106, 107]. Consistent with our findings, these studies revealed reduced activation in impulse-control regions inversely correlated with dietary restraint in BED [106] and hypoconnectivity within the dlPFC and between the dlPFC and regions related to attention and reward valuation in individuals with high BN symptoms and restrained eating tendencies [107]. This pattern of dysconnectivity may potentially serve as a biomarker for individuals with risk-averse, highly restrained tendencies and BE, providing potential for neurobiologically targeted subtype-specific interventions. While previous research has identified neurobiological differences in BE and in BT-EDs, particularly in networks related to reward-related processing, executive control, and self-referential processing [37–42], definitive biomarkers remain elusive [37–39, 41, 42], likely due to a reliance on categorical diagnoses and standard case-control comparisons that obscure or lack sensitivity in identifying neurobiological impairments [21, 30, 108]. Our findings provide additional support for the notion that BT-EDs are characterized by disrupted communication between distributed brain regions and networks [96] and provide the first evidence within BT-EDs that a mechanism-based subtyping approach can reveal distinct neurobiological patterns aligned with each subtype's unique phenotypic profile and BE behaviors. This highlights the potential for identifying subtype-specific biomarkers to inform the development of targeted interventions.

Our findings demonstrate the heterogeneous roles of negative emotionality, approach behaviors, and effortful control/urgency in BE within a single sample, underscoring the importance of assessing these domains in future research to inform more comprehensive models of BE etiology and treatments. They also demonstrate how different approach behaviors contribute to distinct pathways of BE (e.g., increases or decreases in unethical behaviors, risk-perception), supporting recent calls to integrate a range of reward-related processes alongside established factors like affect and cognition in BT-ED research [36, 37, 42, 51]. The involvement of these functional domains in BE supports the growing evidence that links BE to other conditions characterized by impulsive and compulsive behaviors, emphasizing their dimensional nature [30, 42–46, 51, 109]. Moreover, our inclusive sample encompassed a range of BE behaviors, from low frequency to clinical tendencies, recognizing the transdiagnostic nature of BE and the significance of subclinical and low-frequency presentations.

The potential of psychiatric subtyping ultimately lies in its ability to improve mechanistic understanding of pathophysiology and guide precision medicine. Tailoring interventions to address the most pertinent underlying mechanisms driving each subtype offers substantial clinical promise [29, 30, 110]. Our findings provide empirical evidence for significant variation in neurobehavioral impairments associated with BE highlighting opportunities for targeted, subtype-specific interventions. The 'Negative Emotionality' subtype, like previously identified ED subtypes with heightened affective disturbance, may benefit most from treatments focused on affect regulation and enhancing tolerance to negative emotions [29, 52], including psychotherapies and pharmacotherapies used in anxiety and depression [111–113]. Interventions addressing impulsivity, risk-perception, and addictive behaviors may be particularly effective for the 'Approach' subtype. Interventions focused on impulse control and urgency, especially those targeting approach behaviors and self-regulation, are likely to benefit this group [110, 112, 113]. For example, lisdexamfetamine, a medication also used for enhancing effortful

control in ADHD, demonstrates efficacy in reducing BE frequency, trait-impulsive features of BE, and improving regulation of eating and goal-directed behaviors [112, 114]. Given this subtype's neurobiological profile, brain-based interventions such as excitatory non-invasive brain stimulation (NIBS) targeting hypo-active salience network nodes have shown efficacy in reducing impulsivity, improving attention, and decreasing cue-induced cravings and BE behaviors [38, 110], potentially offering targeted benefits for this subtype. For the 'Restrained' subtype, interventions targeting cognitive flexibility and rigidity, rather than emotional targets, may provide an effective therapeutic approach [110, 112, 113]. Given this subtype's neurobiological profile, inhibitory NIBS targeting the dlPFC and FPN, rather than excitatory, may be most effective in addressing overcontrolled and rigid behaviors [110]. Overall, we argue that therapies targeting mechanism-based skills, may prove effective in addressing the characteristic impairments associated with the identified BE subtypes.

The current study is only an initial step into the comprehensive investigation of mechanism-based subtypes of BE and is not without limitations. While clustering methods have limitations [23, 108], we took several steps to validate and ensure subtype stability. Nonetheless, external validation remains the gold standard for confirming cluster generalizability and replicability, necessitating independently collected datasets [115]. Additionally, while the power for the current study was adequate, replication will provide a more robust characterization of the recovered subtypes. For example, the smaller sample size of the 'Negative Emotionality' subtype ($N = 24$) likely impeded the detection of widespread, robust, and meaningful neurobiological findings for this group [116]. Notably, the cross-sectional nature of this sample limits our ability to determine whether these subtypes predate the onset of BE or emerge as a consequence of BE. Future research should utilize larger sample sizes and longitudinal, follow-up or post-treatment data to enhance the identification of subtype-specific neurobiological markers, as well as evaluate developmental trajectories, treatment efficacy and changes over time [23].

CONCLUSIONS

This study is the first to investigate the mechanistic heterogeneity of BE through a comprehensive, multi-modal assessment of three neurofunctional domains linked to compulsive behaviors in a single sample. Using a purely data-driven mechanism-based approach, three distinct subtypes of BE were identified, characterized by unique behavioral and neurobiological profiles, capturing functionally distinct expressions of BE pathology beyond clinical severity and diagnostic classifications. These findings underscore the need for updated BE etiology and maintenance models that integrate approach/reward, effortful control/impulsivity, and negative emotionality and their underlying neural correlates. With further validation, these findings could inform nosology and bolster the development of personalized behavioral, pharmacological, and neurobiological interventions tailored to individual mechanistic differences in BE and BT-EDs.

DATA AVAILABILITY

Nathan Kline Institute-Rockland Sample data access and details are available on the study website (https://fcon_1000.projects.nitrc.org/indi/enhanced/access.html). Phenotypic data are protected by a Data Usage Agreement, which must be completed and approved by an institutional official before access is granted (https://fcon_1000.projects.nitrc.org/indi/enhanced/phenotypicdata.html). The neuroimaging data are available for download from an Amazon S3 Bucket: s3://fcp-indi/data/Projects/RocklandSample/RawDataBIDSLatest.

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Leyla Brucar: Conceptualization, Methodology, Validation, Formal Analysis, Data Curation, Writing – Original Draft, Visualization. Eric Rawls: Methodology, Validation, Writing – Review & Editing. Ann Haynos: Conceptualization, Writing – Review & Editing. Carol Peterson: Conceptualization, Writing – Review & Editing. Anna Zilverstand: Conceptualization, Methodology, Resources, Writing – Review & Editing, Visualization, Supervision, Project Administration, Funding Acquisition.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Nathan Kline Institute Institutional Review Board in accordance with the Declaration of Helsinki. Written informed consent and permission to share de-identified data were obtained from all study participants. For the present study, after data use permission was obtained, a protocol filed with the University of Minnesota Institutional Review Board met criteria for exemption (STUDY00007003, initial approval 06-27-2019).

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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