Data-Driven Phenotypic Categorization for Neurobiological Analyses: Beyond DSM-5 Labels

Supplementary Information

Supplemental Methods

Clustering Analysis

Notably, HHC does not require arbitrary thresholding to model general relationships in the data (in contrast to some graph theory approaches that require *a priori* threshold selection – e.g., $r \geq 0.25$). Additionally, HHC balances the benefits of agglomerative hierarchical clustering and divisive hierarchical clustering.

Dimension Reduction. Selecting the appropriate number of factors to retain in exploratory factor analysis is a difficult enterprise. Based on simulations, numerous researchers recommend parallel analysis (1-4) to overcome limitations associated with other, more commonly employed methods (e.g., Scree test plots, Kaiser criterion). Although, one of the most robust methods for ascertaining factor number, parallel analysis exhibits limitations when using randomly generated data (3) and near the point where the raw data eigenvalues are just at or above the mean and/or 95th percentile value for the simulation/permutation data (1). To overcome the first limitation, we used permutation of the raw data rather than randomly generated data (3). To overcome the second limitation, we computed confidence intervals of factor loadings, based on 10,000 bootstrap-based re-samplings of the raw data. Factor loadings whose 95% confidence intervals overlapped 0 were deemed to be unstable and total factor number was adjusted (downward) when a given factor exhibited numerous unstable factor loadings.

Supplemental Results

Data Screening

Phenotypic Data Screening. All self-report data were checked for univariate and multivariate outliers. We also tested the assumption of missingness at random (MAR (5)). Missing data were imputed using an expectation-maximization algorithm (6). In total, 52 data points were missing (0.16%); no more than 3 data points per individual (< 5%) and there was not evidence that the MAR assumption was violated. Univariate outliers (i.e., $|Z| > 3.29$) were truncated (i.e., set to $|Z| = 3.29$) to retain their extremeness without violating assumptions of normality. Truncation was implemented on 62 data points across 37 individuals. Seven individuals (2.0% of total sample) were excluded as multivariate outliers.

Magnetic Resonance Imaging Data Screening. Sufficient imaging data (i.e., > 95% of volumes from resting state functional magnetic resonance imaging [R-fMRI]) were available for 86.7% of subjects. Of the 299 subjects, 6 were excluded due to excessive head motion (7), 2 due to failed registration, 10 due to insufficient functional coverage of the whole brain, and 4 due to technical errors in preprocessing, yielding a final R-fMRI analysis sample of n = 280. There were no significant differences in demographics or diagnostic characteristics between the imaging sub-sample (n = 280) and those who were excluded (n = 67) (see **Table S3**).

Factor Interpretations

Factor 1: Measures with high loadings were mostly comprised of TSC-40 subscales, which reflect a broad array of psychological and somatic symptoms. Given the additional contribution from the BDI-II subscales, we interpreted this factor as representing *General Distress and Impairment*, as is broadly observed across psychopathology (8).

Factor 2: Conscientiousness (NEO-FFI), perseverance (UPPS), and activation control (ATQ) exhibited the highest loadings for this factor. As these characteristics are largely consistent with the personality trait of *Conscientiousness* (9), we interpreted this factor accordingly.

Factor 3: The sensation seeking subscale (UPPS), which represents the domain of impulsivity related to a proclivity to engage in arousing events, was the highest loading scale. DOSPERT subscales, representing risky behaviors, also loaded strongly on this factor. Thus, we interpreted this factor as *Sensation and Risk Seeking.*

Factor 4: Negative and positive urgency (UPPS), followed by frustration (ATQ), exhibited the strongest loadings. Positive and negative urgency reflect rash decision-making in contexts of high emotionality (10). The additional association of frustration (ATQ), the opposite of inhibitory control (ATQ), and impulsivity and emotional lability (CAARS) suggested a tendency towards hastened self-gratification (11). We interpreted this factor as *Frustration Intolerance.*

Factor 5: The strongest loading subscales on this factor were openness (NEO-FFI), empathic concern (IRI), and affective perceptual sensitivity (ATQ). Other aspects of socioemotional function (e.g., fantasy [IRI], perspective taking [IRI], inverse of uncaring [ICU], inverse of unemotional [ICU], inverse of callousness [ICU]) were also present alongside agreeableness (NEO-FFI). The strong loadings of scales related to sensitivity (particularly emotional) to external changes led us to name this factor *Contextual Sensitivity,* a concept reflecting heightened somatosensory and emotional reaction to external experiences (12, 13).

Factor 6: Anxiety (STAI), introversion (negative loading of extraversion on the NEO-FFI), as well as self-concept problems (CAARS), lack of positive affect (ATQ), and neuroticism

(NEO-FFI) all exhibited high loadings on this factor. Accordingly, we labeled this factor *Neuroticism and Negative Affect.*

Phenotypic Differences in Adaptive Subclusters

Level 2. C1 generally exhibited higher adaptive functionality, though C1a was significantly higher on externalizing problems in relation to elevated sensation seeking while C1b exhibited high negative loadings on sensation seeking and frustration intolerance, along with relatively low levels of externalizing problems. About 25% of those in C1 had *T*-Scores ≥ 60 on the Substance Use Problems scale of the ASR (see **Figure S2**), and had a lifetime DSM-IV diagnosis of Substance Use Disorder (SUD). C1a seemed to be the driving force behind elevated substance use levels in C1, with significantly higher levels of Sensation & Risk Seeking (see **Figure S2, S3**), substance use problems, and Lifetime DSM-IV SUD. In contrast to C1a (functionally adaptive, but sensation-seeking), C1b exhibited a significantly lower negative mean level of Neuroticism (i.e., C1b was more extraverted and emotionally stable).

Level 3. C1a (functionally adaptive but sensation-seeking) was divided into C1a1 (relatively balanced) and C1a2 (conscientious and sensation-seeking). C1b (extraverted and emotionally stable) was divided into C1b1 (emotionally stable, but behaviorally inhibited) and C1b2 (calm, patient, conscientious, and behaviorally inhibited).

Differences in Thresholded and Raw ASR Scores

Recognizing the value in fully dimensional assessments, we also examined adjacent cluster group differences in ASR domains using raw scores (see **Figure S4**). The observed patterns between groups in ASR raw scores were largely consistent with the thresholded *T*-Score percentages. To compare thresholded *T*-Score differences to raw score differences, effect sizes were computed for thresholded *T*-Score differences. Since thresholded *T*-Scores were compared

between groups as a function of percentage of group members with $T \geq 60$, Φ was estimated. As Φ is known to closely approximate values for *r,* Φ values were converted to approximate Cohen's *d* values using the formula: $d \approx (2\Phi/(\sqrt{(1-\Phi)^2}))$. The raw score values exhibited more significant group differences that were larger with regard to their effect size, though the overall relative patterns were the same (see **Figure S4**).

Connectomic Differences between Subgroups at Lower Level Comparisons

While no significant findings were present between adjacent groups at the lower levels of the hierarchy with permutation-based cluster correction, additional neurobiological distinctions among subgroups defined by the 4- and 8-group solutions were indicated with less stringent corrections – voxelwise $p < .05$, GRF-corrected clusterwise $p < .05$ (See **Figures S5, S6, Tables S6-S9**). Readers should carefully consider recent findings regarding possible type I error inflation in cluster-extent thresholding (14) when viewing these results.

Group Differences Within the Functionally Maladaptive Subgroup. MDMR revealed differences in connectivity patterns for four regions, when comparing the two functionally maladaptive subgroups from the 4-cluster solution (C2a = internalizing problems: n = 55; C2b = externalizing problems: n = 60) (see **Figure S5**). These regions included the left dorsolateral prefrontal cortex, left superior temporal gyrus (extending to the amygdala), and the cerebellum, regions associated with risky decision-making (15), fear processing (16), and emotion regulation in anxiety (17), respectively (see **Figure S5**). Connectome alterations were also noted in the right frontal opercular cortex, near the inferior frontal gyrus and anterior insula, associated with indirect social fear learning (18).

When further subdividing the internalizing sub-group into C2a1 and C2a2 (C2a1 = distressed and frustration intolerant, but mildly careful/focused: n = 37; C2a2 = highly distressed,

frustration intolerant, and careless/distracted: n = 18), MDMR identified significant differences in four neuroanatomical regions (see **Figure S5**). These included the bilateral precuneus, bilateral anterior temporal and orbitofrontal cortex, and right lateral occipital cortex, which have been associated with self-other recognition in the context of empathy (19), the default mode network and higher order cognitive-emotional functions (20), and visual motion processing (21), respectively.

Within the *externalizing subgroup,* further division into the C2b1 and C2b2 subgroups (C2b1 = highly sensation-seeking and frustration intolerant: n = 33; C2b2 = careless, introverted, and somewhat impatient: n = 27), identified significant connectome differences in three neuroanatomical regions (see **Figure S5**). Locations included bilateral parietal regions, bilateral cerebellum, and regions near the left superior temporal gyrus and orbitofrontal cortex. These neuroanatomical regions have been identified as cingulate motor regions (22), and are associated with deficits in self-awareness (23), and cognitive reappraisal of emotion (24), respectively.

Group Differences within the Functionally Adaptive Subgroup. Further division into C1a and C1b (C1a = sensation and risk-seeking: n = 83; C1b = extraverted and emotionally stable: n = 82), at level 2 identified significant connectome differences in a single neuroanatomical region. The neuroanatomical cluster was located in the right posterior temporal lobe (see **Figure S6**), including the middle and inferior temporal gyri, angular gyrus, and fusiform face area, areas associated with social processing and the reorienting of attention (25).

Both C1a and C1b were further divided into two groups each, at the 8-group level. C1a, the more sensation and risk seeking of the functionally adaptive group, was further divided into C1a1 and C1a2 (C1a1 = relatively balanced: n = 52; C1a2 = conscientious and sensation seeking: n = 31). MDMR identified group differences in the left lingual gyrus, an area associated with

visual navigation (26) (see **Figure S6**). C1b, the more extroverted and emotionally stable of the functionally adaptive groups was further divided into C1b1 and C1b2 (C1b1 = emotionally stable and behaviorally inhibited: n = 50; C1b2 = calm, patient, conscientious, and behaviorally inhibited: n = 32). In comparing these two groups, MDMR identified connectome differences in four distinct neuroanatomical regions (see **Figure S6**). Differences were noted in the frontal pole, extending into the right anterior insula, the left and right superior parietal lobules, and the left cerebellum. These regions are associated with rapid processing of emotionally salient information (27), visuospatial processing and attention, as well as working memory (28), and visuomotor control, respectively.

Differences in MDMR results by thresholding method

Given recently raised concerns about inflated type I error rates in conditions of parametric statistics combined with GRF (cf. (14)), we conducted permutation-based cluster correction in addition to GRF cluster correction. Not surprisingly, the highest level cluster comparison (C1 vs. C2), which had the most statistical power, was relatively unchanged. Findings for lower levels, however, which passed GRF correction, did not survive the permutation-based cluster thresholding approach (the permutation approach notably yields substantially larger cluster estimates (cf. (14)). This outcome is not necessarily surprising given the substantially smaller sample sizes at the 2nd and 3rd levels relative to the 1st level. Given that the results of the study raising concerns about GRF (14) did not address situations where the initial statistic is nonparametric, it is hard to conclude much other than that our results beyond the first level were not sufficiently robust to survive the more stringent permutation-based cluster thresholding.

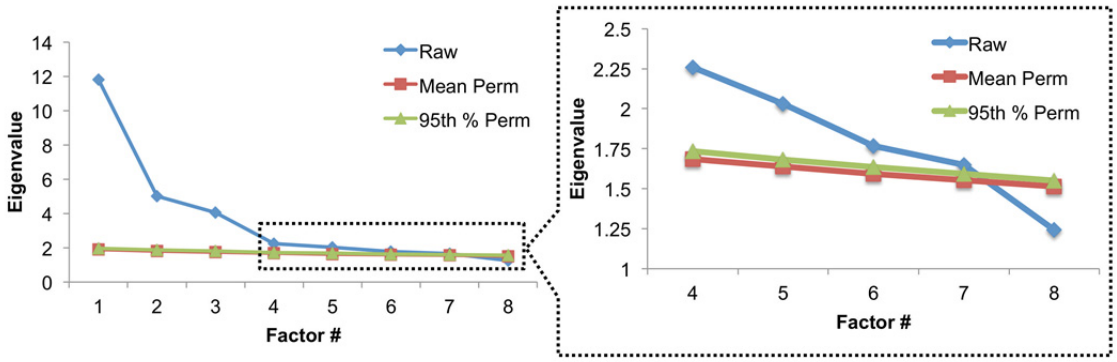

Figure S1. Results of parallel analysis using 10,000 permutations of the raw data. Parallel analysis compares the raw data eigenvalues at a given factor number (displayed in blue with diamond markers) with the mean eigenvalue (displayed in red with square markers) and the 95th percentile (displayed in green with triangle markers) for each factor from 10,000 permutations of the raw data. On the left is the comparison for factor numbers 1 through 7, while a zoomed figure displaying factors 4 through 8 is displayed on the right. As can be seen on the right, the raw data eigenvalue remains above the mean and 95th percentile values for the permutation data until 7 factors. These findings would suggest an optimal factor solution of n = 7, however, bootstrap-based confidence intervals for factor loadings suggested unreliable estimates for the 7th factor, and thus the final solution was n = 6 factors.

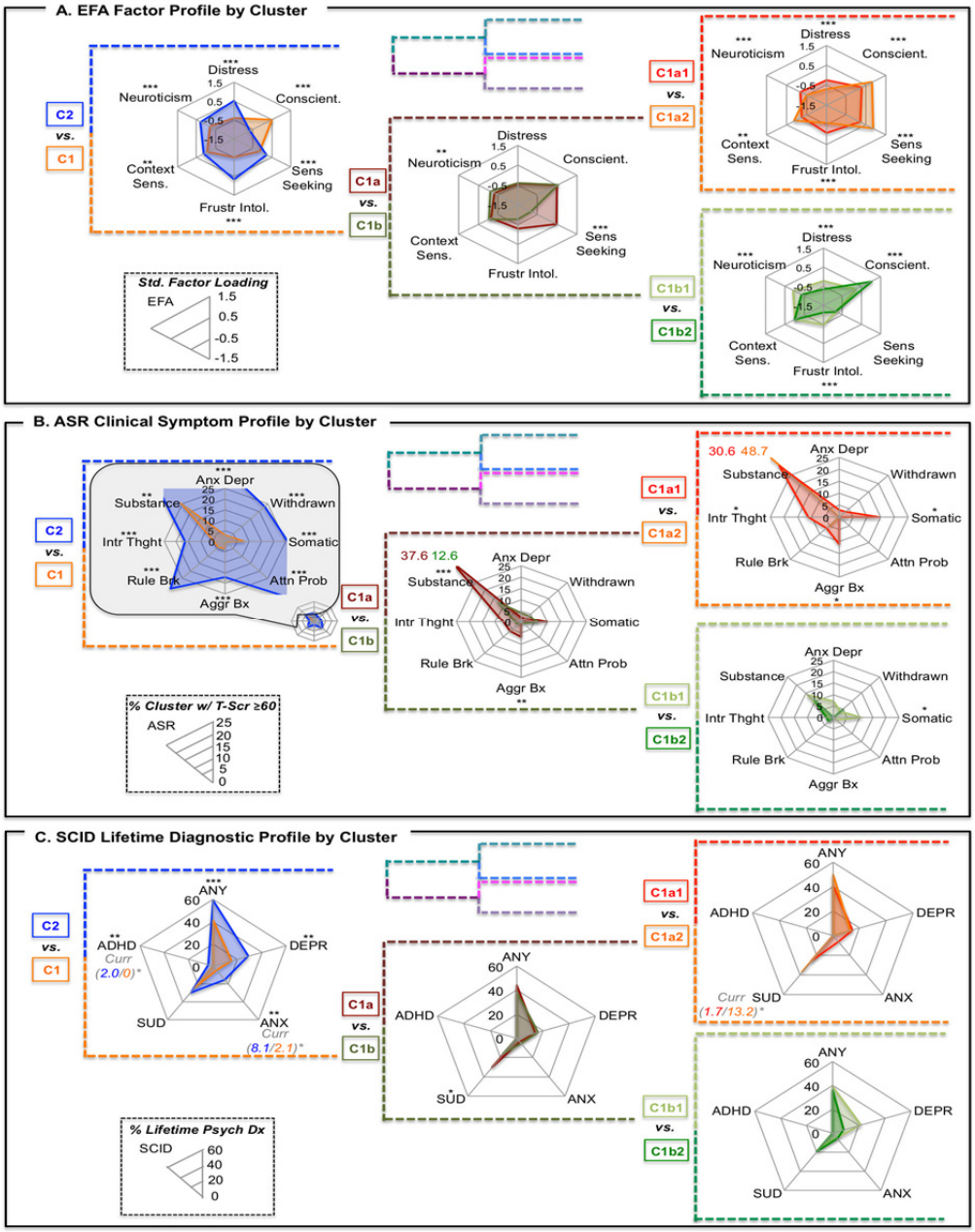

Figure S2. Factor, clinical symptom, and lifetime psychiatric profiles visualized as radar plots by cluster/group at three levels of hierarchical clustering, showing expansion within C1. All panels in this figure represent different measures pertaining to the same clusters (i.e., C1 is the same group of individuals, showing variation in factor profiles – Panel A; ASR clinical symptom profiles – Panel B; and lifetime psychiatric diagnosis – Panel C). **Panel A** represents mean values by cluster for each of the 6 factors from the exploratory factor analysis. Plots represent a standard loading of -1.5 at the origin and 1.5 at the maximum for each of the 6 factors. **Panel B** represents percent of individuals within a cluster exhibiting *T*-scores ≥ 60 (1 standard deviation above the mean; approaching clinical importance) for 8 domains from the

Achenbach Adult Self-Report. Plots represent 0 at the center and 25% at the periphery (unless otherwise denoted) for each of the 8 domains. **Panel C** represents percent of individuals within a cluster exhibiting a lifetime (i.e., past or current) psychiatric diagnosis (ANY = any diagnosis; DEPR = depressive disorder; ANX = anxiety disorder, excluding OCD and PTSD; SUD = substance use disorder; ADHD = attention-deficit/hyperactivity disorder). Where significant differences in current psychiatric diagnosis were observed, group percentages and significance is represented next to the diagnosis in italics. Plots represent 0 at the center and 60% at the periphery (unless otherwise denoted) for each of the 5 diagnostic categories. Note that diagnoses are not mutually exclusive. Significant group differences are represented by asterisks; * $p < .05$, ** $p < .01$, ***$p < .001$.

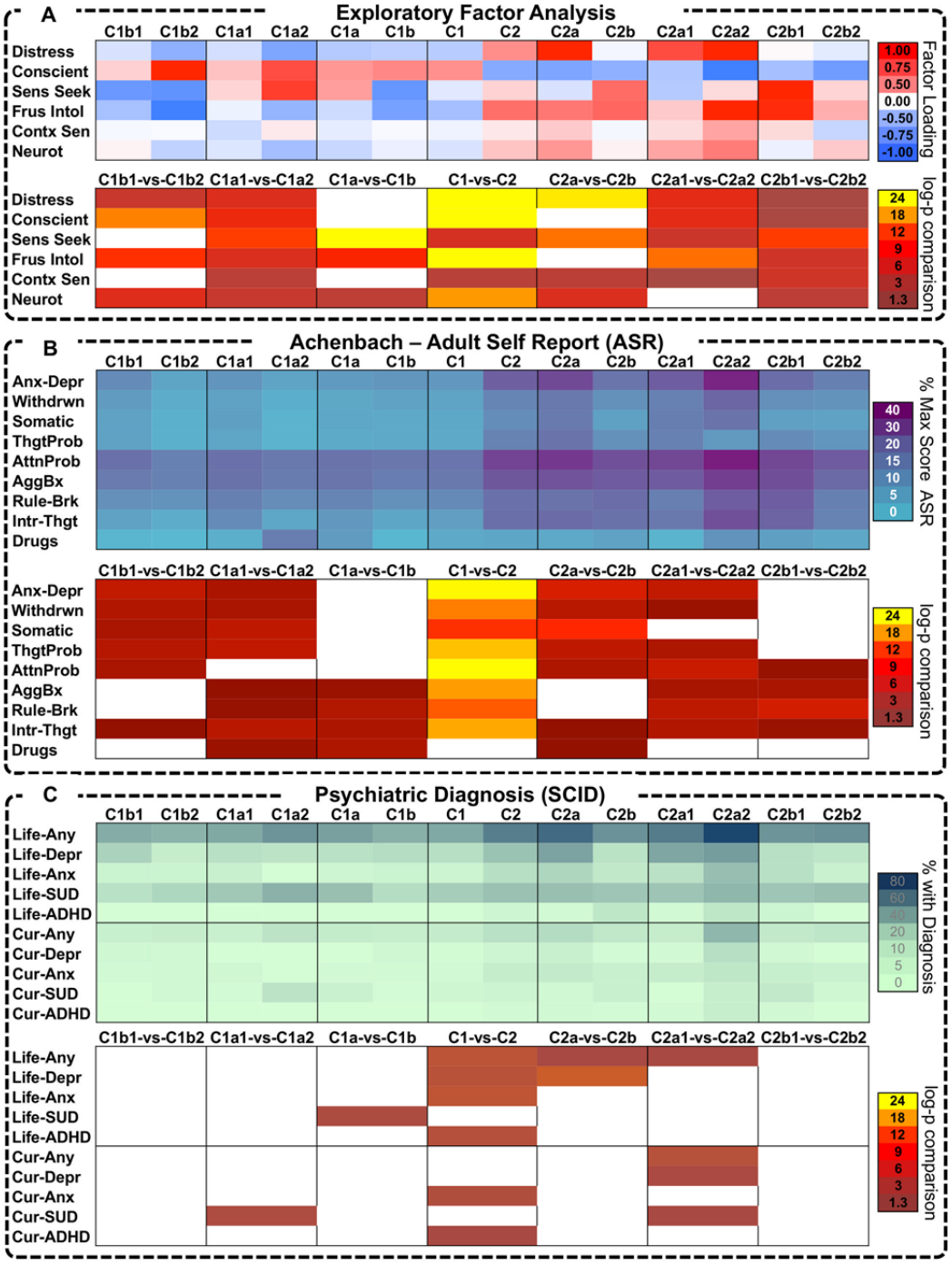

Figure S3. Factor, clinical symptom, and psychiatric profiles visualized as heatmaps by cluster/group at three levels of hierarchical clustering, along with indication of significant differences between adjacent clusters. All panels in this figure represent different measures pertaining to the same clusters (i.e., C2 is the same group of individuals, showing variation in factor profiles – Panel A; ASR clinical symptom profiles – Panel B; and psychiatric diagnosis – Panel C). Significance is indicated as the absolute value of the $\log_{10}$ of the p value, wherein a value of 1.3 is equivalent to p =.05. While log-p values range to approximately 50, the max was

set to 24 to facilitate visualization. **Panel A** represents mean values by cluster for each of the 6 factors from the exploratory factor analysis. Plots represent a standard loading of -1.5 - 1.5 (thresholded at -1, 1) at the maximum for each of the 6 factors. **Panel B** represents group mean reflected as a percentage of the maximum possible score for 8 domains from the Achenbach Adult Self-Report. **Panel C** represents percent of individuals within a cluster exhibiting a lifetime (i.e., past or current; Life) or current (Cur) psychiatric diagnosis (ANY = any diagnosis; DEPR = depressive disorder; ANX = anxiety disorder, excluding OCD and PTSD; SUD = substance use disorder; ADHD = attention-deficit/hyperactivity disorder). Note that while panels A (EFA) and B (continuous ASR) exhibit similar significant differences between groups, Panel C (SCID) does not.

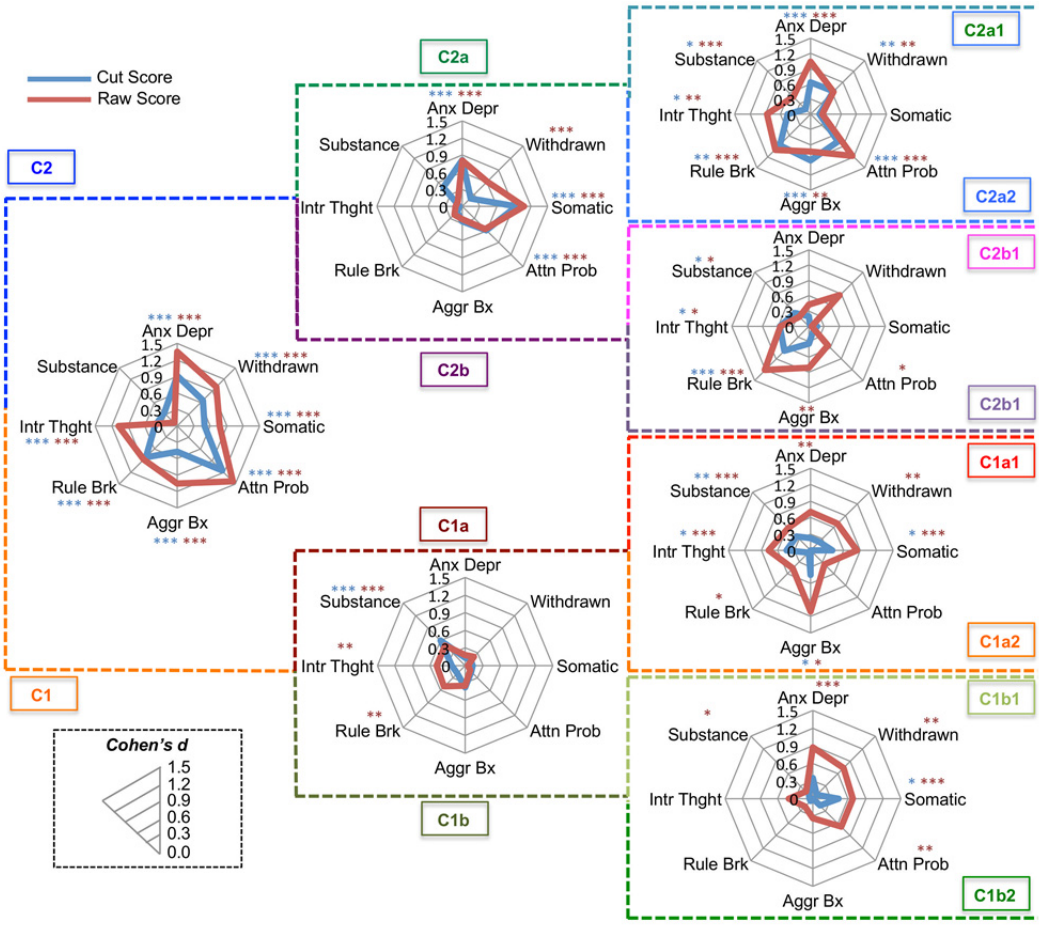

Figure S4. ASR symptom domain differences in effect size measures visualized as radar plots by cluster/group at three levels of hierarchical clustering. Each radar plot represents the single comparison of the two adjacent groups at a given cluster level using the effect size estimate Cohen's *d*. Red lines indicate raw score differences while Black lines indicate thresholded *T*-Score differences (i.e., between-group differences in percent of individuals with $T \geq 60$). The center of each plot represents a Cohen's $d = 0$ and the absolute periphery represents a Cohen's $d = 1.5$. Asterisks indicate significance (*** $p < .001$, **$p < .01$, *$p < .05$) for comparisons of raw scores (in red) and thresholded *T*-scores (in blue).

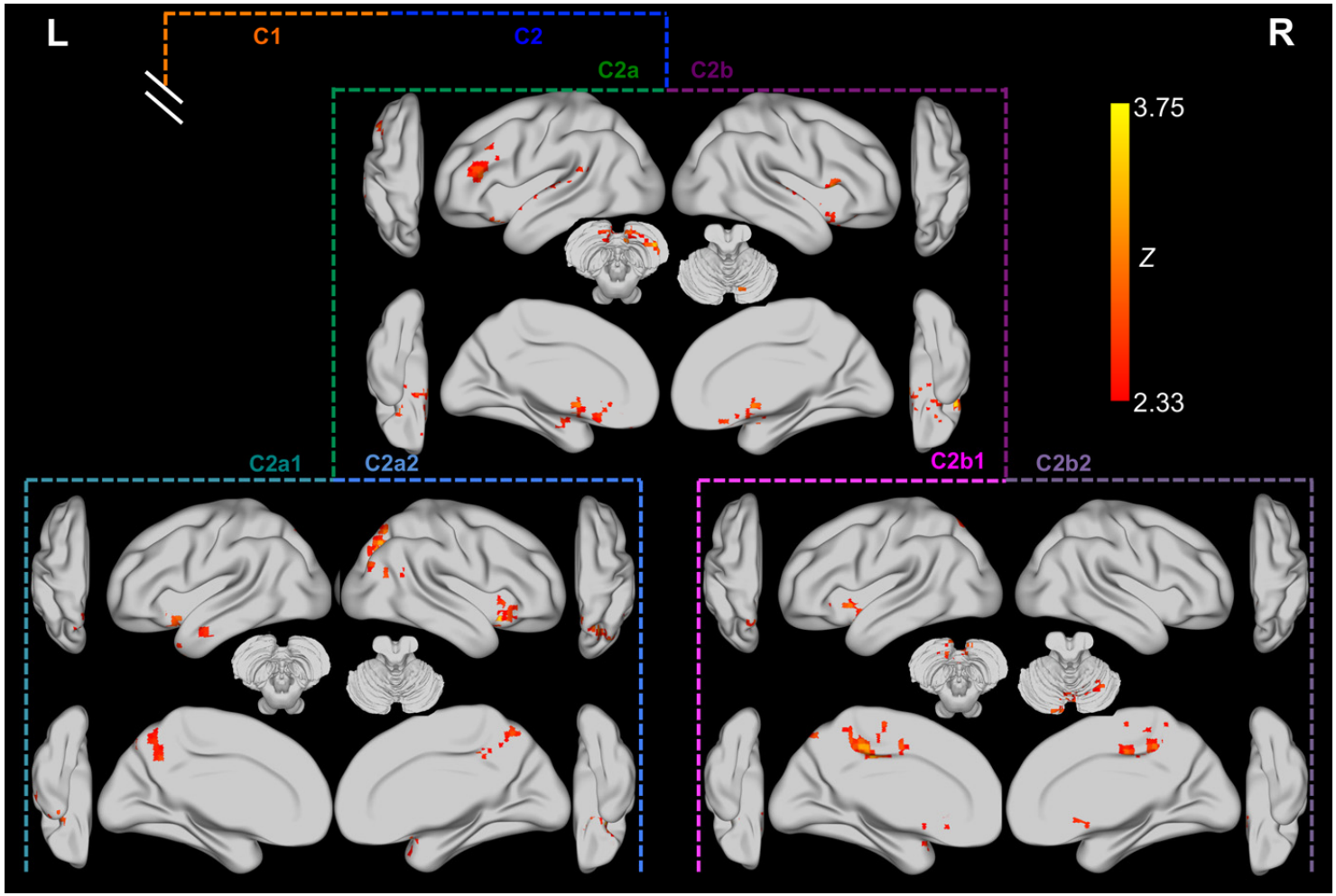

Figure S5. Results from multivariate distance matrix analysis of the functional connectome within the C2 arm. Adjacent groups at the middle and bottom levels (level 2: n_{C2a}= 55, n_{C2b}= 60; and level 3: n_{C2a1}= 37, n_{C2a2}= 18, n_{C2b1}= 33, n_{C2b2}= 27) of hierarchical clustering are displayed. Rendered cortical and cerebellar surfaces reflect multivariate distance matrix regression comparing intrinsic connectivity between groups; findings represent conversion of pseudo-*F* test results to Z values via permutation testing (10,000 resamplings of data) and Random Field Theory correction with cluster formation set at $p < .05$ and extent threshold set at $p < .05$. Surfaces have been visualized using nearest neighbor interpolation.

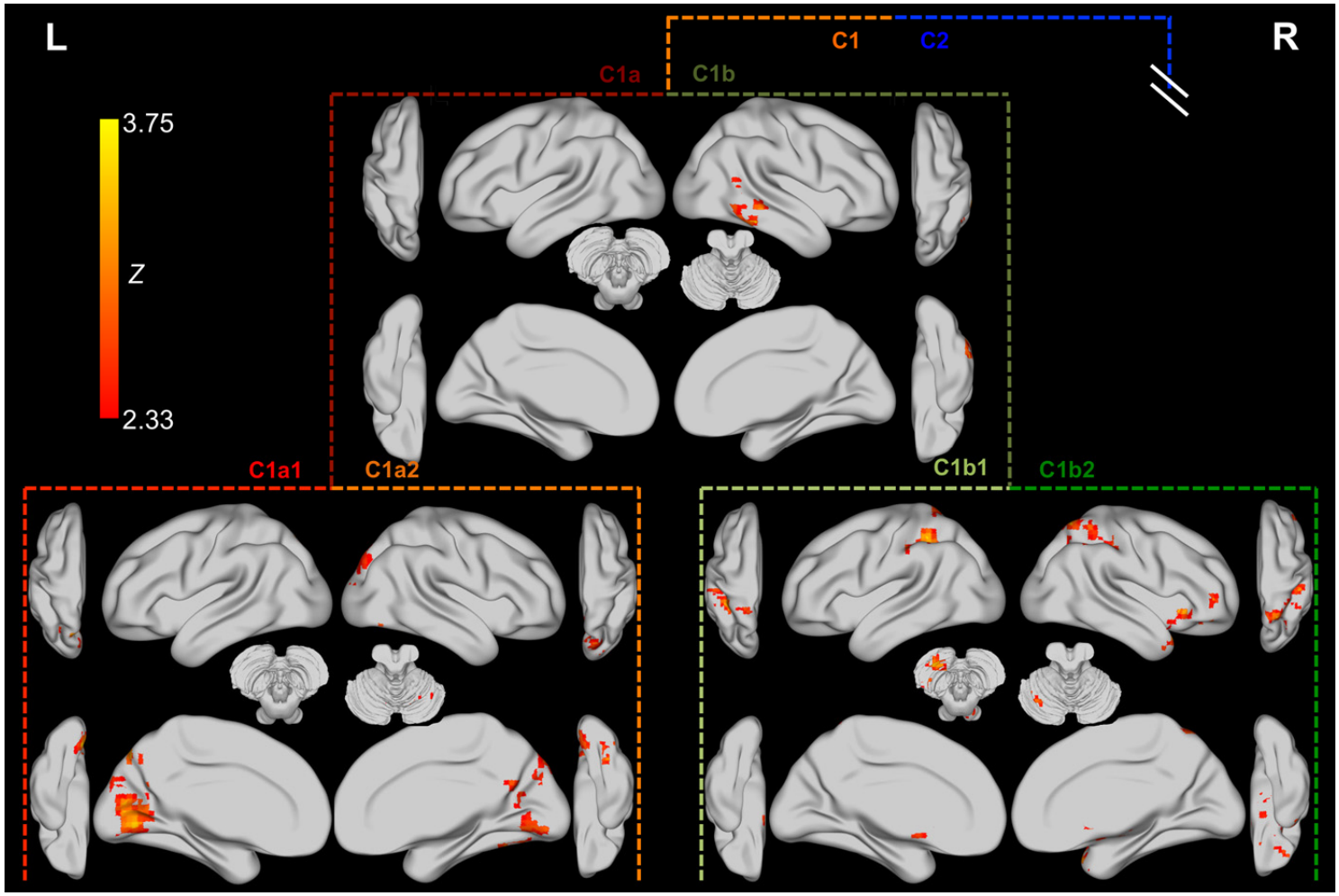

Figure S6. Results from multivariate distance matrix analysis of the functional connectome within the C1 arm. Adjacent groups at the middle and bottom levels (level 2: n_{C1a}= 83, n_{C1b}= 82; and level 3: n_{C1a1}= 52, n_{C1a2}= 31, n_{C1b1}= 50, n_{C1b2}= 32) of hierarchical clustering are displayed. Rendered cortical and cerebellar surfaces reflect multivariate distance matrix regression comparing intrinsic connectivity between groups; findings represent conversion of pseudo-*F* test results to Z values via permutation testing (10,000 resamplings of data) and Random Field Theory correction with cluster formation set at $p < .05$ and extent threshold set at $p < .05$. Surfaces have been visualized using nearest neighbor interpolation.

Table S1. Behavioral Measures and Subscales

Scale	Subscales
Adult Temperament Questionnaire (29)	Negative Affect: Fear, Sadness, Discomfort, Frustration Extraversion/Surgency: Sociability, Positive Affect, High Intensity Pleasure Effortful Control: Attentional Control, Orienting Sensitivity: Neutral Perceptual Sensitivity, Affective Perceptual Sensitivity, Associative Sensitivity
Beck Depression Inventory-II (30, 31)	Cognitive-Affective Somatic
Conners' Adult ADHD Rating Scales (32)	Inattention and Memory Problems Impulsivity and Emotional Lability Hyperactivity and Restlessness Self-Concept Problems
Domain-Specific Risk-Taking Scale (33)	Recreation Health and Safety Financial Social Ethical
Inventory of Callous and Unemotional Traits (34)	Uncaring Unemotional Callousness
Interpersonal Reactivity Index (35)	Empathic Concern Fantasy Perspective Taking Personal Distress
NEO Five Factor Inventory (36)	Openness Conscientiousness Extraversion Agreeableness Neuroticism
State Trait Anxiety Inventory (37, 38)	Anxiety Depression
Trauma Symptom Checklist 40-item (39)	Dissociation Anxiety Depression Sexual Abuse Trauma Index Sleep Disturbance Sexual Problems
UPPS (10, 40)	Positive Urgency Negative Urgency (lack of) Premeditation (lack of) Perseverance Sensation Seeking

Table S2. Full sample, imaging sub-sample, and non-imaging sub-sample demographics

	A: Full Sample (n = 347)	B: Imaging Sample (n = 280)	C: Non-Imaging (n = 67)	B *vs.* C *p*
Mean Age (SD)	37.5 (13.6)	37.1 (13.8)	38.7 (12.8)	0.40
% Female (n)	66.0 (229)	66.8 (187)	62.7 (42)	0.53
Ethnicity				0.63
% Hispanic/Latino (n)	13.8 (47)	11.9 (39)	14.2 (8)	
Racial Background				0.07
% White/Caucasian (n)	67.6 (230)	66.1 (185)	67.1 (45)	
% Black/African Am (n)	20.3 (69)	22.1 (62)	10.4 (7)	
% Asian (n)	7.6 (26)	6.1 (17)	13.4 (9)	
% Nat Am/Pac Island (n)	1.2 (4)	1.1 (3)	1.5 (1)	
% "Other" (n)	3.2 (11)	2.5 (7)	6.0 (4)	
Lifetime Psych History [a]				
% Any Disorder (n)	49.1 (167)	49.1 (136)	49.2 (31)	0.99
% Depression (n)	21.2 (72)	20.2 (56)	25.4 (16)	0.36
% Anxiety [b] (n)	9.4 (32)	9.0 (25)	11.1 (7)	0.61
% Substance Use (n)	26.2 (89)	26.4 (73)	25.4 (16)	0.88
% ADHD (n)	1.8 (6)	1.6 (5)	1.8 (1)	0.91
Current Psych History [a]				
% Any Disorder (n)	10.9 (37)	10.5 (29)	12.7 (8)	0.61
% Depression (n)	2.6 (9)	2.2 (6)	4.8 (3)	0.25
% Anxiety [b] (n)	4.7 (16)	4.3 (12)	6.3 (4)	0.50
% Substance Use (n)	4.1 (14)	3.2 (9)	7.9 (5)	0.09
% ADHD (n)	0.9 (3)	0.7 (2)	1.6 (1)	0.51
# *Lifetime Psych Dx*				0.85
% 0 (n)	52.3 (178)	52.3 (145)	52.4 (33)	
% 1 (n)	25.3 (86)	26.0 (72)	22.2 (14)	
% 2 (n)	12.4 (42)	12.3 (34)	12.7 (8)	
% 3 or more (n)	10.0 (34)	9.4 (26)	12.7 (8)	

[a] Total N = 340; diagnostic information missing for n = 7

[b] Excluding OCD and PTSD

Table S3. Factor loadings from confirmatory implementation of exploratory factor analysis

Factor	Subscale	F1	F2	F3	F4	F5	F6
F1	TSC40 - Depression	1.00					
	TSC40 - Anxiety	0.89					
	TSC40 - Dissociation	0.89					
	TSC40 - Sex Abuse	0.86					
	TSC40 - Sex Problems	0.80					
	TSC40 - Sleep Disturb	0.78					
	BDI - Somatic	0.72					
	BDI – Cognitive & Affective	0.61					0.36
	ATQ - Discomfort	0.44					
F2	NEO - Conscientiousness		1.00				
	UPPS - Perseverance		-0.97				
	ATQ - Activation Control		0.90				
	CAARS - Inattention & Memory	0.27	-0.80				
	UPPS - Premeditation		-0.57				
	ATQ - Attentional Control	-0.24	0.53		-0.22		
F3	UPPS - Sensation Seeking			1.00			
	DOSP – Recreation Risk			0.89			
	DOSP - Health & Safety Risk			0.71			
	ATQ - High Intensity Pleasure			0.64			
	DOSP – Financial Risk			0.50			
	DOSP – Social Risk			0.36			
	DOSP – Ethical Risk			0.36	0.39		
F4	UPPS - Negative Urgency				1.00		
	UPPS - Positive Urgency				0.81		
	ATQ - Frustration				0.55		
	ATQ - Inhibitory Control				-0.55		
	CAARS – Imp. & Emo. Lability	0.32			0.52		
	IRI - Personal Distress				0.50		
	ATQ - Fear	0.42		-0.39	0.43		
	CAARS – Hyperact/Restlessness	0.27		0.31	0.33		
F5	NEO - Openness			0.27		1.00	
	IRI - Empathic Concern			-0.34		0.97	
	ATQ - Affective Percep. Sens.					0.97	
	IRI - Fantasy					0.84	
	IRI - Perspective Taking				-0.41	0.75	
	NEO - Agreeableness			-0.37	-0.45	0.67	
	ATQ - Affective Sensitivity	0.32		0.38		0.65	
	ICUY - Uncaring		-0.64			-0.65	
	ATQ - Neutral Percep. Sens.					0.64	
	ICUY - Unemotional					-0.64	0.59
	ATQ - Sad	0.44				0.57	
	ICUY - Callousness			0.37		-0.41	
F6	STAI - Anxiety	0.26			0.38		1.00
	NEO - Extraversion						-0.99
	CAARS – Self-Concept Prob.	0.26			0.33	0.29	0.89
	ATQ - Positive Affect					0.53	-0.83
	NEO - Neuroticism	0.25			0.50		0.79
	ATQ - Sociability						-0.67
	STAI - Depression	0.29			0.43		0.61
% Total Variance		13.71	8.99	8.31	8.85	14.53	10.99

N.B. Factor loadings < |.25| are possible here because only those loadings < |.25| in the full exploratory model were constrained to 0. The above factor loadings represent the results of a different, constrained model.

Table S4. Correlations between latent and estimated factor scores for full sample (n = 347).

	F1	F2	F3	F4	F5	F6
F1	-	-.425	-.007	.466	.274	.352
F2	-.467	-	-.191	-.600	-.040	-.471
F3	-.004	-.151	-	.345	.033	-.105
F4	.515	-.654	.383	-	.042	.201
F5	.314	-.039	.031	.043	-	.033
F6	.418	-.529	-.118	.276	.038	-
Mean	0.00	0.00	0.00	0.00	0.00	0.00
SD	0.80	0.83	0.81	0.84	0.59	0.56
Rmult	.674	.749	.486	.770	.366	.602

Rmult = multiple regression of single factor on all other factors

Note: Upper right triangle = latent factor score correlations; Lower left triangle = estimated factor score correlations

Table S5. Local maxima (8mm minimum distance) associated with level 1 group contrast, using Gaussian Random Field Theory.

		MNI Coordinates					
Region	**L/R**	**x**	**y**	**z**	***Z***	***mm*^{3}**	**p_k**
Primary Somatosensory Cortex	R	52	-32	58	3.72	133,248	.0005
Primary Somatosensory Cortex	R	40	-16	46	3.72		
Premotor Cortex	L	-52	-4	42	3.72		
Premotor Cortex	L	-60	4	38	3.72		
Primary Motor Cortex	L	-44	-8	38	3.72		
Postcentral Gyrus	R	64	-16	38	3.72		
Supramarginal Gyrus	L	-36	-40	38	3.72		
Precentral Gyrus	R	64	8	22	3.72		
Precentral Gyrus	R	56	4	22	3.72		
Secondary Somatosensory Cortex	L	-44	-28	22	3.72		
Secondary Somatosensory Cortex	L	-56	-16	18	3.72		
Secondary Somatosensory Cortex	R	52	-18	18	3.72		
Secondary Somatosensory Cortex	R	64	-20	18	3.72		
Secondary Somatosensory Cortex	L	-48	-4	6	3.72		
Superior Temporal Gyrus	L	-64	-40	6	3.72		
Middle Temporal Gyrus	R	72	-36	-2	3.72		
Superior Temporal Gyrus	L	-60	-8	-6	3.72		
Temporal Pole	L	-48	8	-22	3.72		
Temporal Pole	L	-56	12	-26	3.72		
Temporal Pole	R	40	20	-30	3.72		
Premotor Cortex	R	12	-16	66	3.54		
Supplementary Motor Area	-	0	-4	62	3.54		
Premotor Cortex	R	24	-16	62	3.54		
Premotor Cortex	L	-32	-8	58	3.54		
Primary Somatosensory Cortex	R	40	-36	58	3.54		
Primary Motor Cortex	L	-40	-20	50	3.54		
Inferior Parietal Lobule	L	-52	-28	38	3.54		
Premotor Cortex	R	60	0	34	3.54		
Primary Somatosensory Cortex	R	48	-16	34	3.54		
Precentral Gyrus	L	-60	4	26	3.54		
Temporal Pole	R	52	16	-30	3.54		
Premotor Cortex	L	-12	-12	54	3.43		
Precentral Gyrus	L	-48	0	30	3.43		
Postcentral Gyrus	L	-64	-16	26	3.43		
Supramarginal Gyrus	R	68	-44	14	3.43		
Superior Temporal Gyrus	R	64	-24	-2	3.43		
Temporal Pole	R	60	8	-18	3.43		
Postcentral Gyrus	L	-24	-32	66	3.35		
Primary Motor Cortex	L	-4	-24	54	3.35		
Primary Somatosensory Cortex	R	36	-24	46	3.35		
Temporal Pole	L	-48	12	-34	3.35		
Primary Motor Cortex	R	36	-24	54	3.29		
Premotor Cortex	L	-4	-16	50	3.29		

N.B. Only values exhibiting $Z \geq 3.09$ ($p < .001$) are reported. Actual thresholding was conducted with voxelwise and clusterwise permutation at $Z > 2.33$, and cluster $p < .05$.

Table S5 (cont'd). Local maxima (8mm minimum distance) associated with level 1 group contrast, using Gaussian Random Field Theory.

		MNI Coordinates					
Region	**L/R**	**x**	**y**	**z**	***Z***	***mm*^{3}**	**p_k**
Primary Somatosensory Cortex	R	44	-32	46	3.29	133,248	.0005
Superior Temporal Gyrus	R	60	4	-10	3.29		
Precentral Gyrus	R	48	0	30	3.24		
Supplementary Motor Area	R	8	-8	62	3.19		
Precentral Gyrus	R	12	-16	54	3.19		
Primary Somatosensory Cortex	R	28	-28	50	3.19		
Middle Temporal Gyrus	R	56	-44	10	3.19		
Postcentral Gyrus	L	-12	-36	70	3.15		
Postcentral Gyrus	R	20	-32	66	3.15		
Inferior Parietal Lobule	R	40	-24	38	3.15		
Posterior Insula	L	-36	-12	14	3.15		
Posterior Insula	R	40	0	18	3.12		
Premotor Cortex	R	12	-16	78	3.09		
Middle Insula	R	40	4	2	3.09		
Thalamus	L	-12	-20	14	3.72	27,328	.0061
Pallidum	L	-12	4	2	3.72		
Thalamus	L	-12	-12	2	3.72		
Amygdala	L	-24	-8	-14	3.72		
Hippocampus	L	-28	-32	-14	3.72		
Temporal Fusiform Cortex	L	-36	-36	-18	3.72		
Cerebellum, VI	L	-36	-48	-30	3.72		
Putamen	R	24	0	14	3.54		
Thalamus	R	16	-12	10	3.54		
Hippocampus	L	-24	-36	-2	3.54		
Subiculum	L	-12	-36	-2	3.54		
Temporal Occipital Fusiform Gyrus	L	-32	-52	-18	3.54		
Putamen	L	-24	12	2	3.43		
Midbrain	L	-8	-36	-10	3.43		
Pallidum	L	-20	-4	-2	3.35		
Caudate	L	-20	8	18	3.24		
Putamen	L	-24	12	-6	3.19		
Caudate	R	16	8	22	3.09		
Hippocampus	R	32	-28	-14	3.72	14.528	.0167
Amygdala	R	24	-4	-22	3.72		
Inferior Temporal Gyrus	R	48	-20	-22	3.72		
Hippocampus	R	28	-20	-18	3.54		
Temporal Occipital Fusiform Gyrus	R	40	-40	-18	3.54		
Occipital Fusiform Gyrus	R	36	-76	-14	3.15		
Putamen	R	28	-12	-2	3.12		

N.B. Only values exhibiting $Z \geq 3.09$ ($p < .001$) are reported. Actual thresholding was conducted with voxelwise and clusterwise permutation at $Z > 2.33$, and cluster $p < .05$.

Table S6. Local maxima associated with level 2 group contrasts using Gaussian Random Field Theory for multiple comparisons correction.

Region	L/R	MNI Coordinates x	y	z	*Z*	mm^3	p_k
C1a vs. C1b							
Inferior Temporal Gyrus	R	60	-48	-18	3.72	8,128	0.0200
Middle Temporal Gyrus	R	64	-40	-6	3.43		
Angular Gyrus	R	60	-60	18	3.01		
Lateral Occipital Cortex	R	60	-60	10	2.97		
Middle Temporal Gyrus	R	68	-48	-2	2.85		
Lateral Occipital Cortex	R	56	-60	-6	2.47		
Inferior Temporal Gyrus	R	64	-56	-14	2.44		
C2a vs. C2b							
Frontal Opercular Cortex	R	48	16	2	3.43	20,480	$1.8x10^{-6}$
Orbitofrontal Cortex	L	-16	20	-14	3.35		
Subgenual Cingulate Cortex	L	-8	20	-2	3.24		
Middle Insular Cortex	R	44	4	-2	3.12		
Caudate	L	-16	24	-6	3.09		
Superior Temporal Gyrus	R	44	-12	-14	3.06		
Orbitofrontal Cortex	L	-28	20	-14	3.01		
Ventromedial Prefrontal Cortex	R	12	32	-14	2.99		
Temporal Pole	R	48	12	-6	2.97		
Superior Temporal Gyrus	R	36	0	-18	2.93		
Ventromedial Prefrontal cortex	L	-12	40	-14	2.86		
Planum Temporale	R	64	-16	6	2.69		
Heschl's Gyrus	R	48	-16	10	2.59		
Anterior Insular Cortex	R	32	12	-14	2.59		
Putamen	L	-16	16	-6	2.55		
Orbitofrontal Cortex	R	8	12	-26	2.41		
Subgenual Cingulate Cortex	R	8	24	-18	2.40		
Nucleus Accumbens	L	-8	12	-10	2.35		
Cerebellum	R	12	-68	-34	3.43	7,616	0.0153
Cerebellum, VIIb	R	36	-64	-50	3.19		
Cerebellum, Crus II	R	28	-64	-42	3.04		
Cerebellum, Crus II	R	8	-80	-42	2.89		
Cerebellum, VIIb	R	16	-76	-46	2.58		
Cerebellum, VI	R	12	-72	-18	2.47		
Cerebellum, Crus II	L	-8	-76	-42	2.36		
Middle Frontal Gyrus	L	-52	20	38	3.19	6,656	0.0348
Inferior Frontal Gyrus	L	-36	32	10	2.75		
Inferior Frontal Gyrus	L	-52	36	14	2.72		
Middle Frontal Gyrus	L	-48	28	38	2.69		
Superior Temporal Gyrus	L	-40	-12	-10	3.04	6,528	0.0390
Temporal Pole	L	-48	8	-6	2.93		
Amygdala	L	-28	-4	-14	2.89		
Superior Temporal Gyrus	L	-68	-32	18	2.55		
Temporal Pole	L	-48	12	-14	2.47		
Superior Temporal Gyrus	L	-68	-36	6	2.37		
Heschl's Gyrus	L	-48	-12	6	2.35		

N.B. Only values exhibiting $Z \geq 2.33$ ($p < .01$) are reported. Actual thresholding was conducted at $Z > 1.65$, cluster $p<.05$.

Table S7. Local maxima ($Z \geq 2.33$) associated with level 3, C1 group contrasts using Gaussian Random Field Theory for multiple comparisons correction.

Region	L/R	MNI Coordinates x	y	z	*Z*	mm^3	p_k
C1a1 vs. C1a2							
Lingual Gyrus	L	-8	-68	-6	3.29	33,408	$3.9x10^{-9}$
Intracalcarine Cortex	L	-12	-80	6	3.15		
Lateral Occipital Cortex	R	48	-72	-18	3.15		
Intracalcarine Cortex	L	-8	-80	14	3.09		
Lateral Occipital Cortex	L	-12	-78	46	3.06		
Temporal Occipital Fusiform Cortex	R	36	-56	-18	2.95		
Occipital Pole	R	16	-88	42	2.88		
Precuneus	R	12	-60	26	2.76		
Lingual Gyrus	R	12	-68	-10	2.58		
Precuneus	-	0	-76	50	2.56		
Cerebellum, Crus I	R	40	-76	-22	2.56		
Cuneus	-	0	-80	30	2.53		
Lingual Gyrus	R	8	-84	-6	2.45		
Lateral Occipital Cortex	L	-28	-72	26	2.39		
Lateral Occipital Cortex	L	-24	-64	34	2.38		
Occipital Pole	R	28	-96	22	2.37		
Occipital Fusiform Cortex	R	28	-76	-2	2.35		
C1b1 vs. C1b2							
Frontal Pole	R	36	44	-10	3.29	12,928	0.0013
Temporal Pole	R	44	16	-22	3.29		
Anterior Insular Cortex	R	36	20	-6	3.19		
Frontal Pole	R	40	44	2	3.09		
Pallidum	R	16	4	2	3.09		
Temporal Pole	R	36	16	-30	2.91		
Orbitofrontal Cortex	R	20	28	-14	2.76		
Nucleus Accumbens	R	8	8	-8	2.63		
Putamen	R	28	-12	2	2.40		
Anterior Insular Cortex	R	32	12	-14	2.40		
Superior Parietal Lobule	R	32	-52	38	3.43	12,672	0.0015
Superior Parietal Lobule	R	24	-64	62	3.24		
Supramarginal Gyrus	R	48	-32	46	2.93		
Supramarginal Gyrus	R	48	-36	54	2.88		
Superior Parietal Lobule	R	20	-52	54	2.69		
Superior Parietal Lobule	R	32	-48	54	2.65		
Angular Gyrus	R	48	-52	54	2.59		
Lateral Occipital Cortex	R	12	-64	66	2.57		
Superior Parietal Lobule	L	-40	-44	50	3.72	10,752	0.0052
Postcentral Gyrus	L	-32	-36	46	3.15		
Superior Parietal Lobule	L	-4	-60	70	2.7		
Superior Parietal Lobule	L	-24	-48	70	2.42		
Superior Parietal Lobule	L	-16	-52	70	2.37		
Cerebellum, VIIb	L	-28	-68	-58	3.72	7,680	0.0425
Cerebellum, Crus II	L	-24	-64	-38	3.01		
Cerebellum, VI	L	-28	-64	-30	2.71		
Cerebellum, VIIb	L	-40	-48	-50	2.6		

N.B. Only values exhibiting $Z \geq 2.33$ ($p < .01$) are reported. Actual thresholding was conducted at $Z > 1.65$, cluster $p < .05$.

Table S8. Local maxima ($Z \geq 2.33$) associated with level 3, C2A group contrast using Gaussian Random Field Theory for multiple comparisons correction.

Region	L/R	MNI Coordinates x	y	z	Z	mm^3	p_k
C2a1 vs. C2a2							
Precuneus	-	0	-60	58	3.29	8,512	0.0045
Lateral Occipital Cortex	L	-16	-72	46	2.82		
Precuneus	R	4	-68	30	2.79		
Precuneus	L	-4	-60	38	2.49		
Temporal Pole	L	-36	8	-46	3.54	8,448	0.0047
Inferior Frontal Gyrus	L	-52	20	-6	3.24		
Orbitofrontal Cortex	L	-28	28	-6	3.04		
Temporal Pole	L	-36	16	-46	3.01		
Orbitofrontal Cortex	L	-44	24	-18	2.83		
Orbitofrontal Cortex	L	-36	16	-18	2.79		
Orbitofrontal Cortex	L	-28	16	-14	2.61		
Temporal Pole	L	-52	20	-26	2.58		
Orbitofrontal Cortex	L	-28	24	-14	2.47		
Orbitofrontal Cortex	L	-24	8	-14	2.35		
Orbitofrontal Cortex	R	48	28	-18	3.54	7,808	0.0083
Temporal Pole	R	52	20	-18	3.54		
Inferior Frontal Gyrus	R	52	24	-6	3.43		
Anterior Insular Cortex	R	32	16	-14	3.35		
Orbitofrontal Cortex	R	32	24	-14	3.19		
Orbitofrontal Cortex	R	16	20	-18	2.72		
Caudate	R	16	28	-6	2.68		
Putamen	R	24	8	-10	2.66		
Putamen	R	32	0	-10	2.43		
Lateral Occipital Cortex	R	40	-68	18	3.24	6,720	0.0221
Lateral Occipital Cortex	R	28	-72	22	3.06		
Lateral Occipital Cortex	R	24	-72	42	3.04		
Lateral Occipital Cortex	R	28	-80	38	2.88		
Lateral Occipital Cortex	R	20	-68	50	2.66		
Lateral Occipital Cortex	R	36	-80	26	2.6		
Lateral Occipital Cortex	R	44	-84	26	2.54		

N.B. Only values exhibiting $Z \geq 2.33$ ($p < .01$) are reported. Actual thresholding was conducted at $Z > 1.65$, cluster $p < .05$.

Table S9. Local maxima ($Z \geq 2.33$) associated with level 3, C2B group contrast using Gaussian Random Field Theory for multiple comparisons correction.

Region	L/R	MNI Coordinates x	y	z	*Z*	mm^3	p_k
C2b1 vs. C2b2							
Posterior Cingulate Cortex	L	-12	-28	38	3.54	11,584	0.0018
Precentral Gyrus	L	-12	-36	46	3.04		
Precuneus	R	12	-40	46	2.6		
Posterior Cingulate Cortex	R	12	-20	42	2.52		
Posterior Cingulate Cortex	R	16	-32	38	2.52		
Mid Cingulate Cortex	R	4	-12	46	2.4		
Precuneus	R	4	-44	58	2.4		
Supplementary Motor Area	L	-8	-8	46	2.4		
Precuneus	L	-12	-44	50	2.38		
Precentral Gyrus	L	-8	-20	62	2.36		
Precuneus	L	-8	-68	54	2.34		
Cerebellum, Crus II	R	8	-80	-42	3.35	8,960	0.0111
Cerebellum, Crus II	R	4	-84	-26	2.89		
Cerebellum, VIIb	L	-16	-68	-42	2.61		
Cerebellum, Vermis VI	R	4	-68	-26	2.58		
Cerebellum, Crus II	L	-4	-84	-38	2.56		
Cerebellum, Vermis VI	R	4	-78	-26	2.47		
Cerebellum, V	R	12	-60	-18	2.41		
Cerebellum, Crus I	L	-16	-84	-26	2.39		
Cerebellum, Vermis VI	L	-4	-72	-18	2.38		
Lingual Gyrus	L	-4	-88	-22	2.33		
Superior Temporal Gyrus	L	-44	0	-18	3.19	8,640	0.0140
Orbitofrontal Cortex	L	-24	16	-14	3.04		
Putamen	L	-16	16	-6	2.69		
Orbitofrontal Cortex	L	-32	28	-6	2.68		
Anterior Insular Cortex	L	-36	12	-6	2.64		
Middle Insular Cortex	L	-40	-8	-6	2.52		

N.B. Only values exhibiting $Z \geq 2.33$ ($p < .01$) are reported. Actual thresholding was conducted at $Z > 1.65$, cluster $p < .05$.

Supplemental References

1. Fabrigar LR, Wegener DT, MacCallum RC, Strahan EJ (1999): Evaluating the use of exploratory factor analysis in psychological research. *Psychol Methods*. 4:272-299.
2. Henson RK, Roberts JK (2006): Use of Exploratory Factor Analysis in Published Research: Common Errors and Some Comment on Improved Practice. *Educ Psychol Meas*. 66:393-416.
3. Ruscio J, Roche B (2012): Determining the number of factors to retain in an exploratory factor analysis using comparison data of known factorial structure. *Psychol Assess*. 24:282-292.
4. Zwick WR, Velicer WF (1986): Comparison of five rules for determining the number of components to retain. *Psychol Bull*. 99:432-442.
5. Potthoff RF, Tudor GE, Pieper KS, Hasselblad V (2006): Can one assess whether missing data are missing at random in medical studies? *Stat Methods Med Res*. 15:213-234.
6. Gold MS, Bentler PM (2000): Treatments of Missing Data: A Monte Carlo Comparison of RBHDI, Iterative Stochastic Regression Imputation, and Expectation-Maximization. *Structural Equation Modeling: A Multidisciplinary Journal*. 7:319-355.
7. Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE (2012): Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *Neuroimage*. 59:2142-2154.
8. Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, et al. (2013): The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders? *Clinical Psychological Science*.
9. DeYoung CG, Quilty LC, Peterson JB (2007): Between facets and domains: 10 aspects of the Big Five. *J Pers Soc Psychol*. 93:880-896.
10. Cyders MA, Smith GT (2007): Mood-based rash action and its components: Positive and negative urgency. *Pers Individ Dif*. 43:839-850.
11. Mischel W, Ayduk O, Berman MG, Casey BJ, Gotlib IH, Jonides J, et al. (2010): 'Willpower' over the life span: decomposing self-regulation. *Soc Cogn Affect Neurosci*.
12. Belsky J, Pluess M (2009): Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychol Bull*. 135:885-908.
13. Boyce WT, Ellis BJ (2005): Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. *Dev Psychopathol*. 17:271-301.
14. Eklund A, Nichols TE, Knutsson H (2016): Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences*.
15. Roy AK, Gotimer K, Kelly AMC, Castellanos FX, Milham MP, Ernst M (2011): Uncovering putative neural markers of risk avoidance. *Neuropsychologia*. 49:937-944.
16. Krolak-Salmon P, Henaff MA, Vighetto A, Bertrand O, Mauguiere F (2004): Early amygdala reaction to fear spreading in occipital, temporal, and frontal cortex: a depth electrode ERP study in human. *Neuron*. 42:665-676.
17. Bruhl AB, Herwig U, Delsignore A, Jancke L, Rufer M (2013): General emotion processing in social anxiety disorder: neural issues of cognitive control. *Psychiatry Res*. 212:108-115.
18. Olsson A, Nearing KI, Phelps EA (2007): Learning fears by observing others: the neural systems of social fear transmission. *Soc Cogn Affect Neurosci*. 2:3-11.

19. Akitsuki Y, Decety J (2009): Social context and perceived agency affects empathy for pain: An event-related fMRI investigation. *Neuroimage*. 47:722-734.

20. Harrison BJ, Pujol J, López-Solà M, Hernández-Ribas R, Deus J, Ortiz H, et al. (2008): Consistency and functional specialization in the default mode brain network. *Proceedings of the National Academy of Sciences*. 105:9781-9786.

21. Stoppel CM, Boehler CN, Strumpf H, Heinze H-J, Noesselt T, Hopf J-M, et al. (2011): Feature-based attention modulates direction-selective hemodynamic activity within human MT. *Hum Brain Mapp*. 32:2183-2192.

22. Amiez C, Petrides M (2014): Neuroimaging Evidence of the Anatomo-Functional Organization of the Human Cingulate Motor Areas. *Cereb Cortex*. 24:563-578.

23. Moriguchi Y, Ohnishi T, Decety J, Hirakata M, Maeda M, Matsuda H, et al. (2009): The human mirror neuron system in a population with deficient self-awareness: an fMRI study in alexithymia. *Hum Brain Mapp*. 30:2063-2076.

24. McRae K, Gross JJ, Weber J, Robertson ER, Sokol-Hessner P, Ray RD, et al. (2012): The development of emotion regulation: an fMRI study of cognitive reappraisal in children, adolescents and young adults. *Soc Cogn Affect Neurosci*. 7:11-22.

25. Corbetta M, Patel G, Shulman GL (2008): The reorienting system of the human brain: from environment to theory of mind. *Neuron*. 58:306-324.

26. Sherrill KR, Erdem UM, Ross RS, Brown TI, Hasselmo ME, Stern CE (2013): Hippocampus and retrosplenial cortex combine path integration signals for successful navigation. *J Neurosci*. 33:19304-19313.

27. Fan J, Gu X, Liu X, Guise KG, Park Y, Martin L, et al. (2011): Involvement of the anterior cingulate and frontoinsular cortices in rapid processing of salient facial emotional information. *Neuroimage*. 54:2539-2546.

28. Koenigs M, Barbey AK, Postle BR, Grafman J (2009): Superior parietal cortex is critical for the manipulation of information in working memory. *J Neurosci*. 29:14980-14986.

29. Evans DE, Rothbart MK (2007): Developing a model for adult temperament. *Journal of Research in Personality*. 41:868-888.

30. Beck AT, Steer R, Brown G (1996): *Manual for the Beck Depression Inventory II (BDI-II)*. . San Antonio, TX: Psychology Corporation.

31. Whisman MA, Perez JE, Ramel W (2000): Factor structure of the Beck Depression Inventory—Second Edition (BDI-ii) in a student sample. *J Clin Psychol*. 56:545-551.

32. Conners CK, Erhardt D, Sparrow E (1999): *Conners' adult ADHD rating scales: Technical manual*. North Tonawanda, NY: Multi-Health Systems, Inc.

33. Blais A-R, Weber EU (2006): A domain-specific risk-taking (DOSPERT) scale for adult populations. *Judgment and Decision Making*. 1:33-47.

34. Essau CA, Sasagawa S, Frick PJ (2006): Callous-unemotional traits in a community sample of adolescents. *Assessment*. 13:454-469.

35. Davis MH (1983): Measuring individual differences in empathy: Evidence for a multidimensional approach. *J Pers Soc Psychol*. 44:113-126.

36. McCrae RR, Costa Jr PT (2004): A contemplated revision of the NEO Five-Factor Inventory. *Pers Individ Dif*. 36:587-596.

37. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA (1970): *State - Trait Anxiety Inventory*. Menlo Park, CA: Mind Garden, Inc. .

38. Bieling PJ, Antony MM, Swinson RP (1998): The State-Trait Anxiety Inventory, Trait version: structure and content re-examined. *Behav Res Ther*. 36:777-788.

39. Elliott DM, Briere J (1992): Sexual abuse trauma among professional women: Validating the Trauma Symptom Checklist-40 (TSC-40). *Child Abuse Negl*. 16:391-398.

40. Whiteside SP, Lynam DR (2001): The Five Factor Model and impulsivity: using a structural model of personality to understand impulsivity. *Pers Individ Dif*. 30:669-689.