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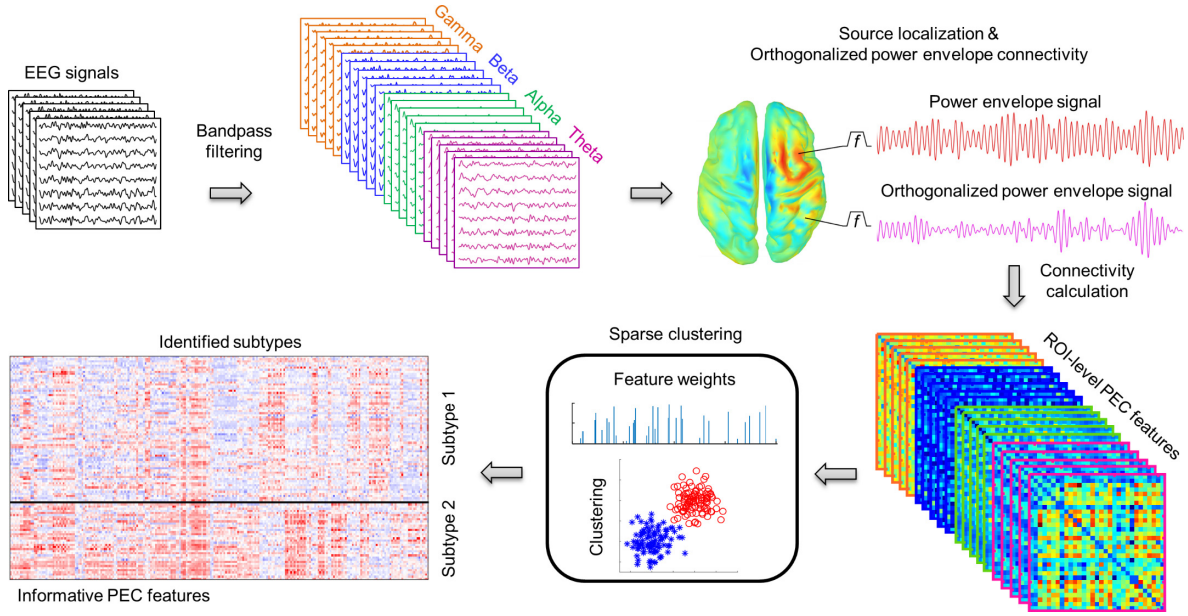
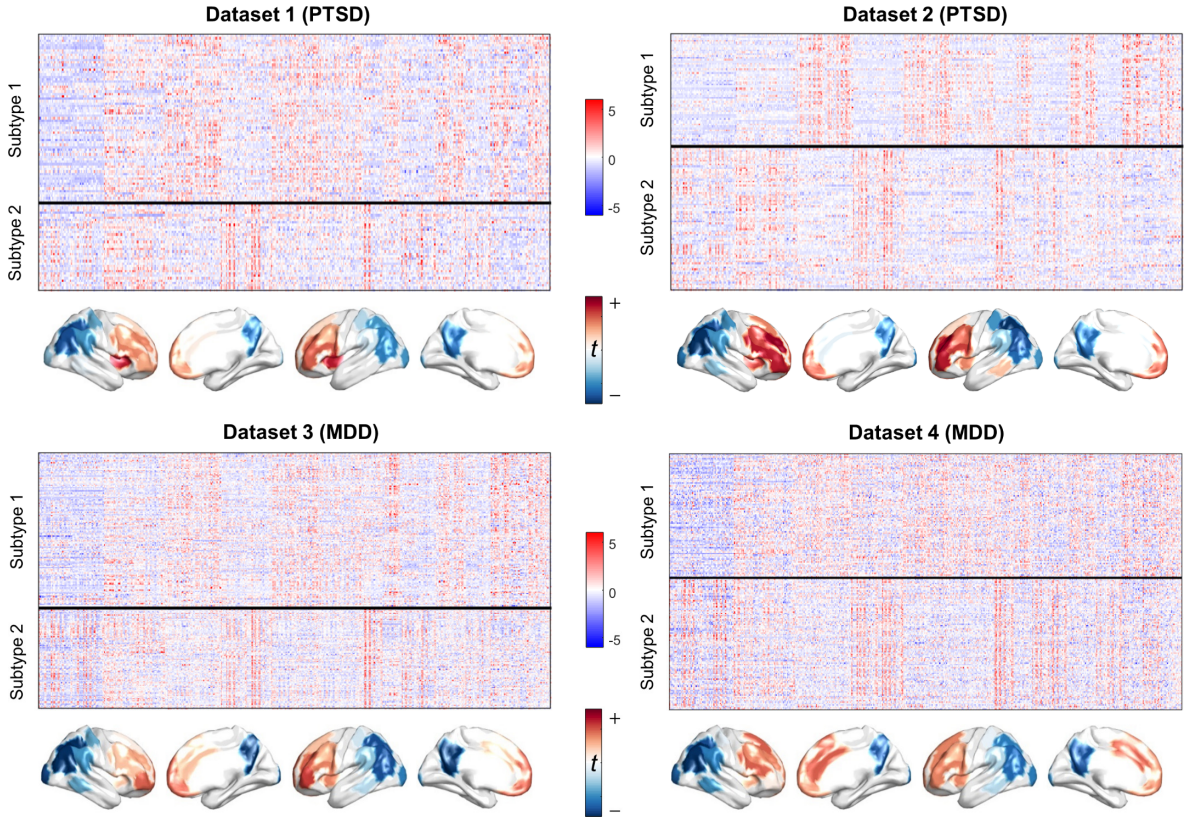
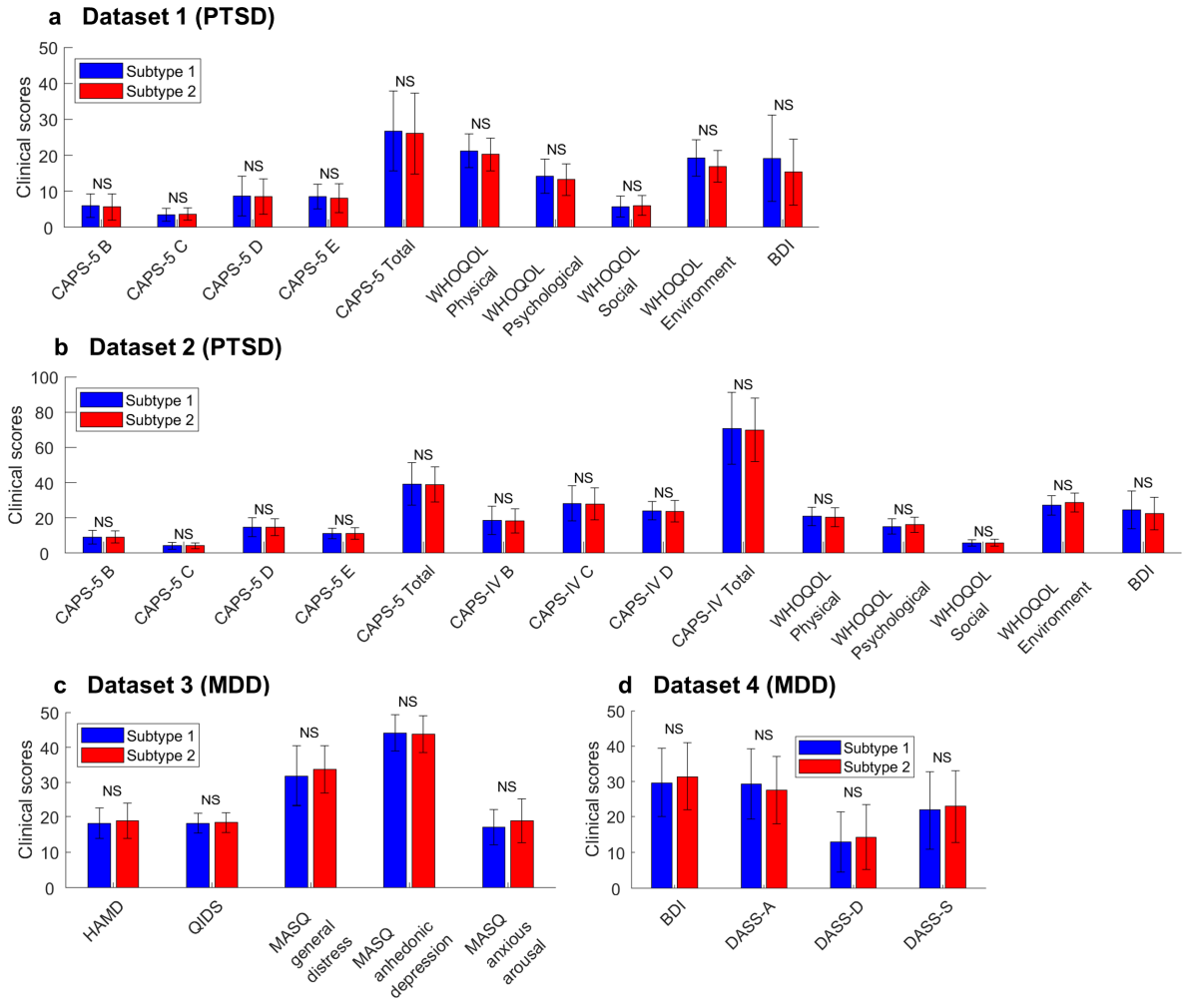
Supplementary Figure 1 | Illustration of our developed subtyping framework. Channel-space EEG signals were first bandpass filtered into four canonical frequency bands: theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (31–50 Hz). Source localization was performed to convert the channel-space EEG into the source-space signals. Power envelope signal of each vertex was calculated based on analytical signal derived by wavelet transform and orthogonalized for all other vertices. PEC was calculated as the Pearson's correlation coefficient between the power envelopes at each pair of vertices, followed by the Fisher's r-to-z transformation. Regional pairwise PEC features were further extracted by averaging PEC values over all corresponding vertex pairs. Sparse clustering was then employed to achieve a data-driven approach to explore the potentially important PEC biomarkers for discovering neurophysiological subtypes.



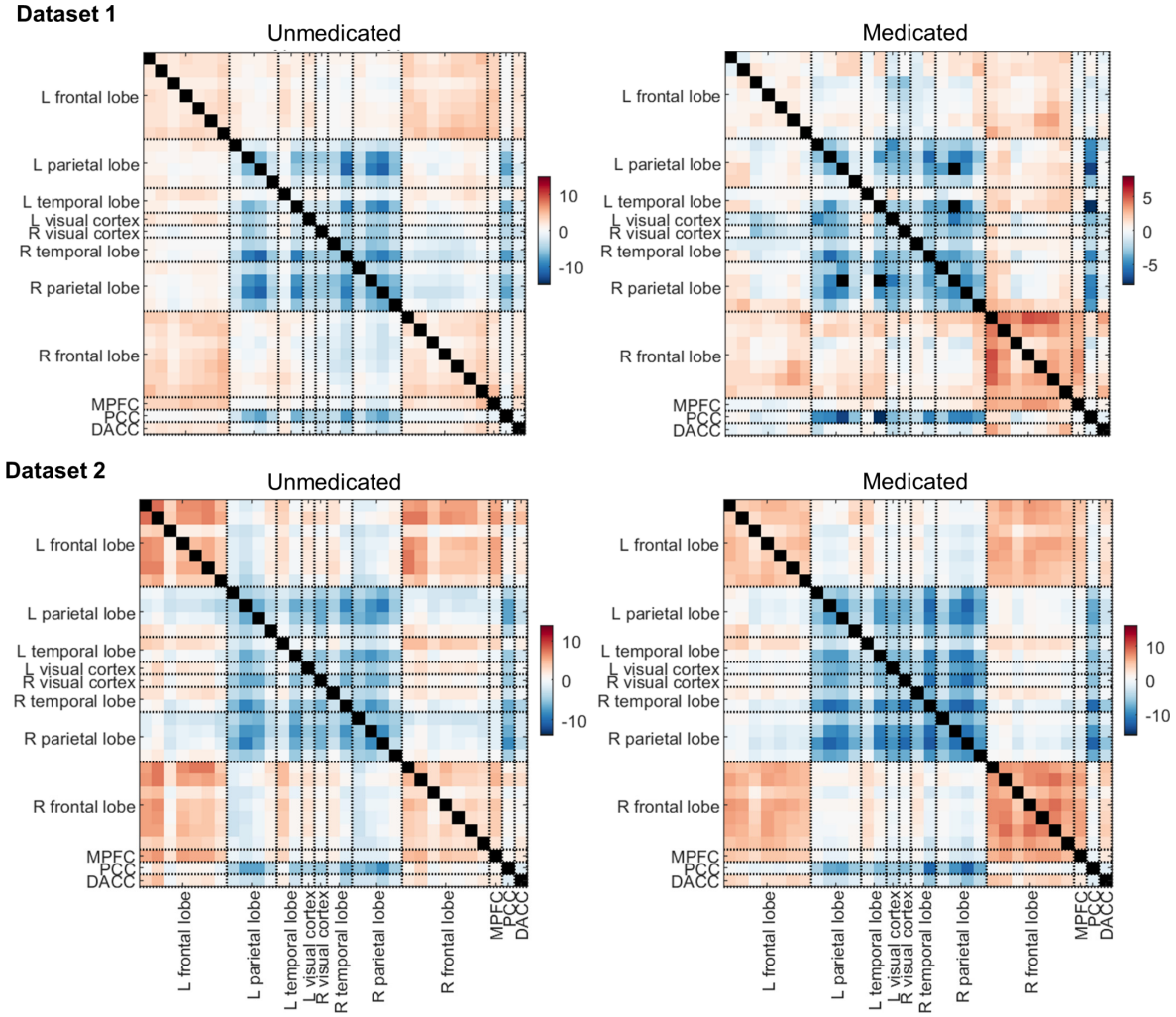
Supplementary Figure 2 | PEC feature distribution ordered by subtypes for each of the four datasets. The PEC difference between the subtypes is also visualized on the surface with t values obtained by two-sample t-test (subtype 1 versus subtype 2). The regional t-value was averaged for each ROI across all ROIs.



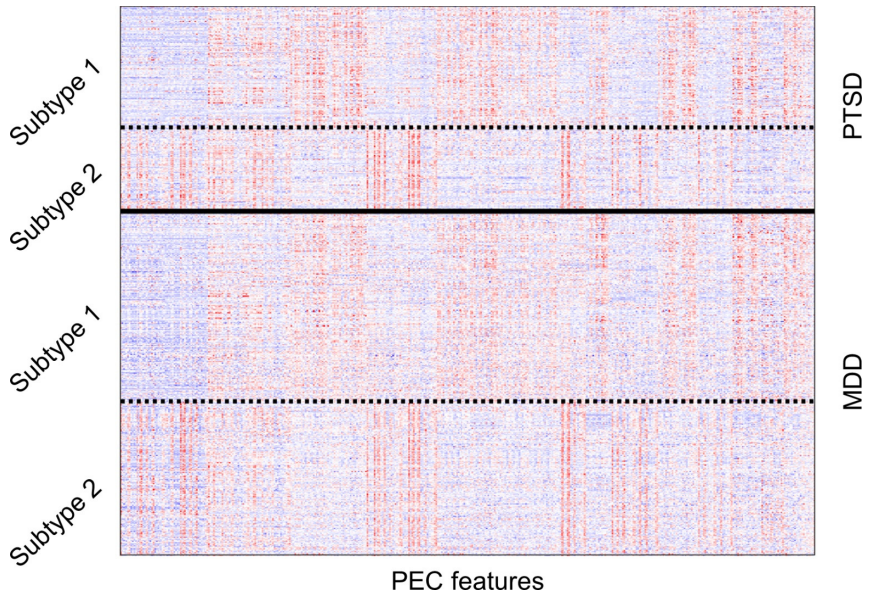
Supplementary Figure 3 | Baseline clinical score difference between the discovered subtypes. No significant difference (FDR corrected) in baseline clinical scores was found between the two subtypes. CAPS = Clinician-administered PTSD Scale, WHOQOL = World Health Organization Quality-of-life Scale, BDI = Beck Depression Inventory, HAMD = Hamilton Depression Rating Scale, QIDS = Quick Inventory of Depressive Symptomatology, MASQ = Mood and Anxiety Symptoms Questionnaire, DASS = Depression, Anxiety and Stress Scale. All error bars represent the standard deviation and NS denotes not significant.



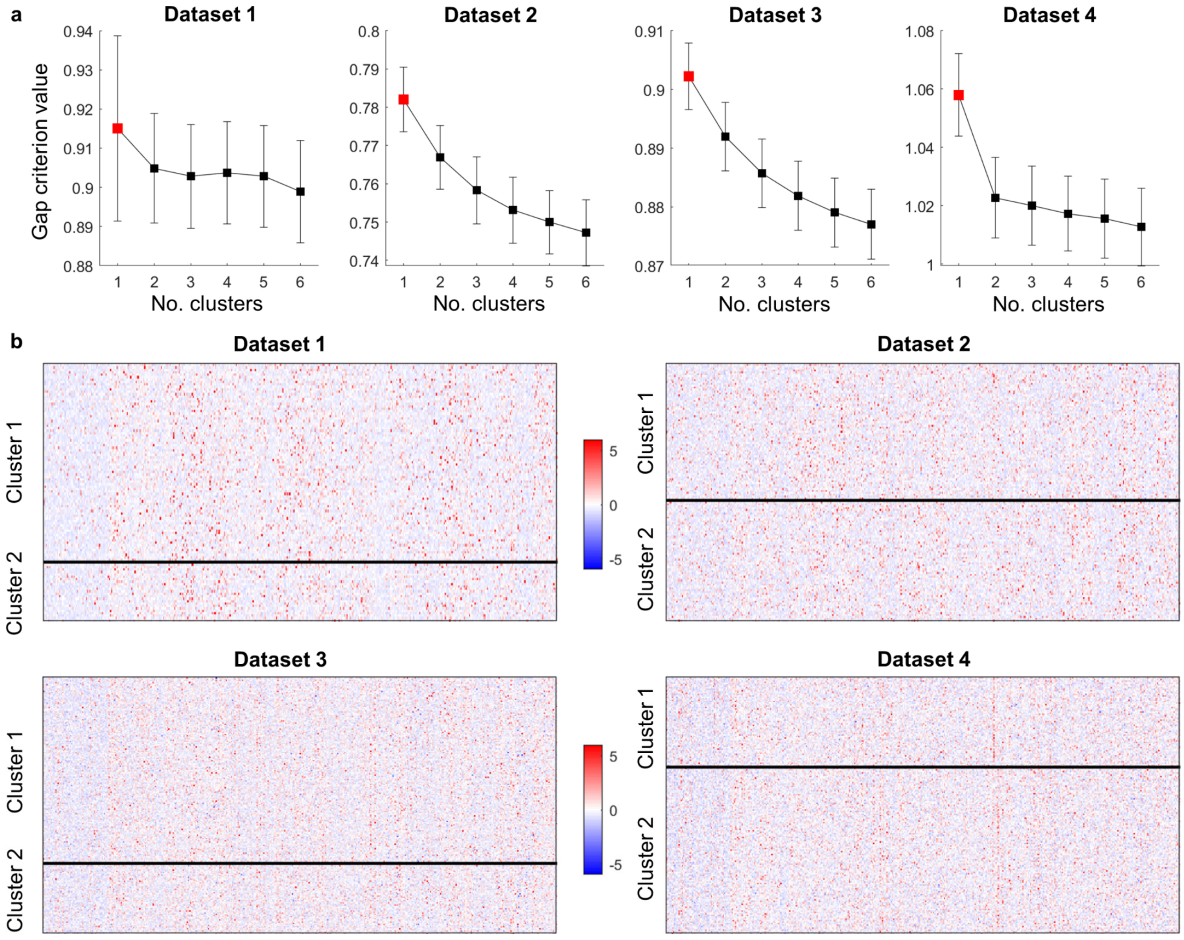
Supplementary Figure 4 | PEC difference between the two subtypes (subtype 1 vs. subtype 2, two-sample t-test with FDR correction) for unmedicated and medicated patients, respectively.



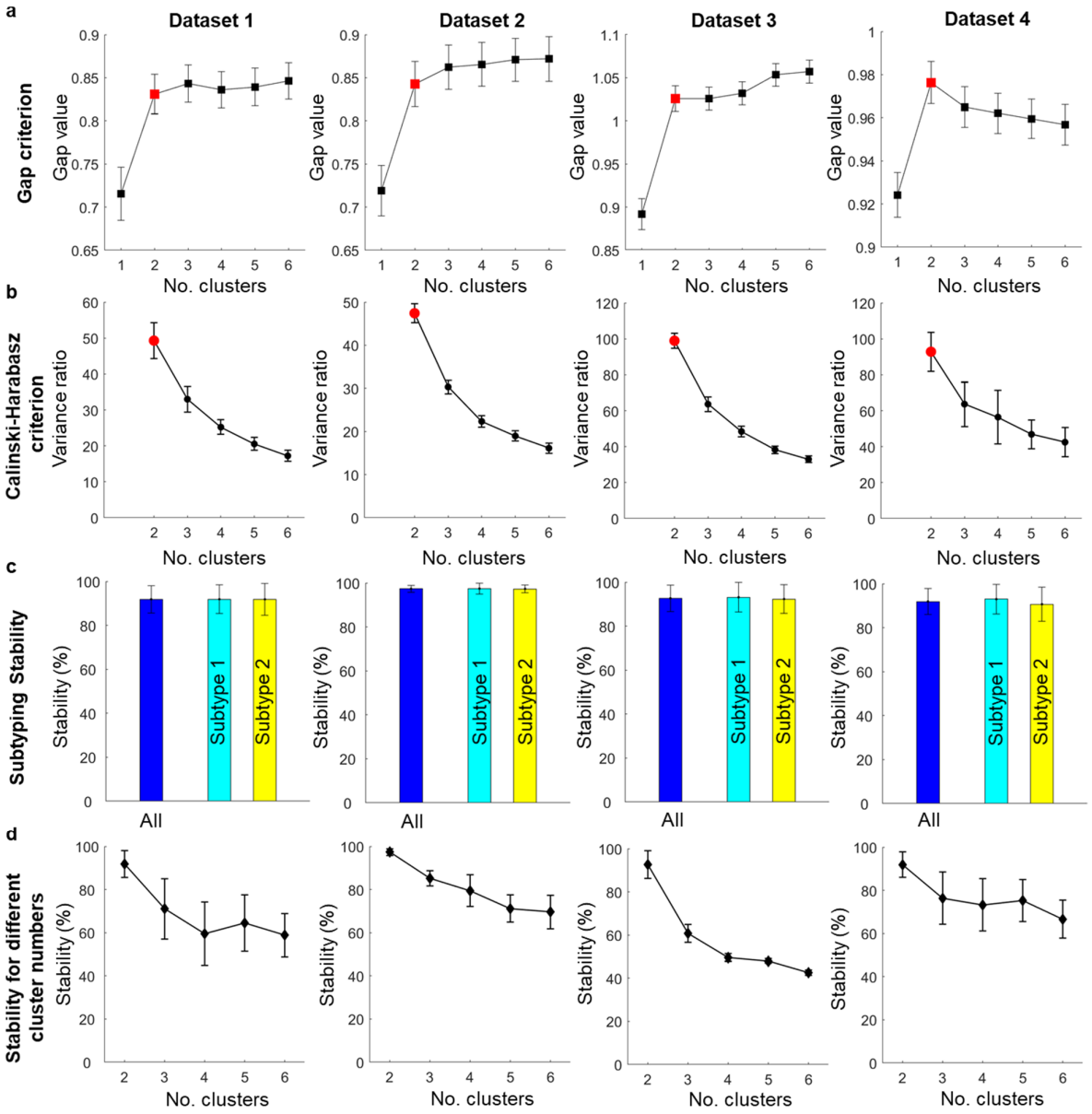
Supplementary Figure 5 | Subtype PEC pattern derived by clustering on patients combining across all four datasets.



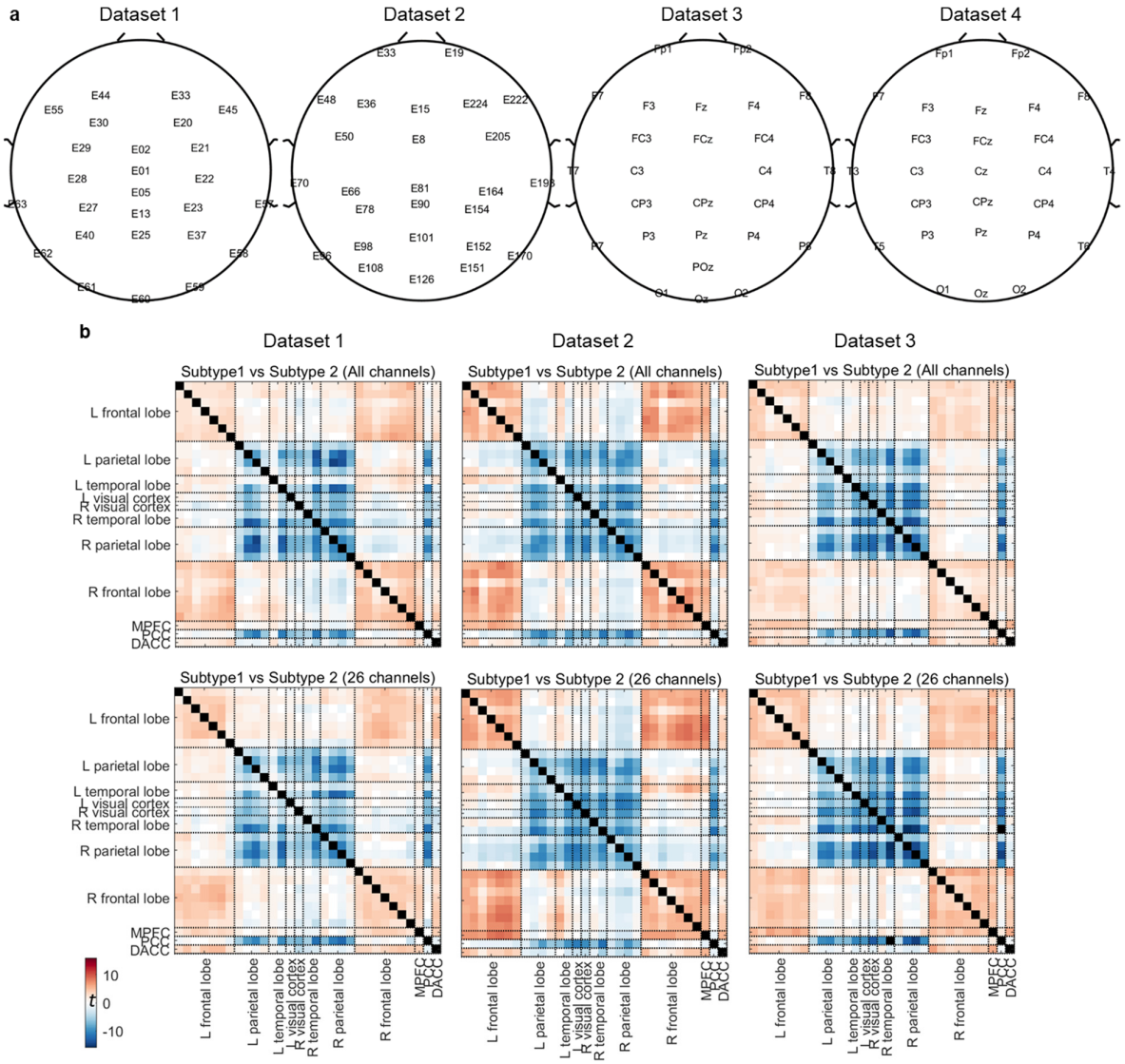
Supplementary Figure 6 | Clustering using randomly permuted PEC features across subjects. **a**, Gap criterion values in using different numbers of clusters. **b**, Feature patterns obtained by clustering with two clusters on randomly permuted PEC features.



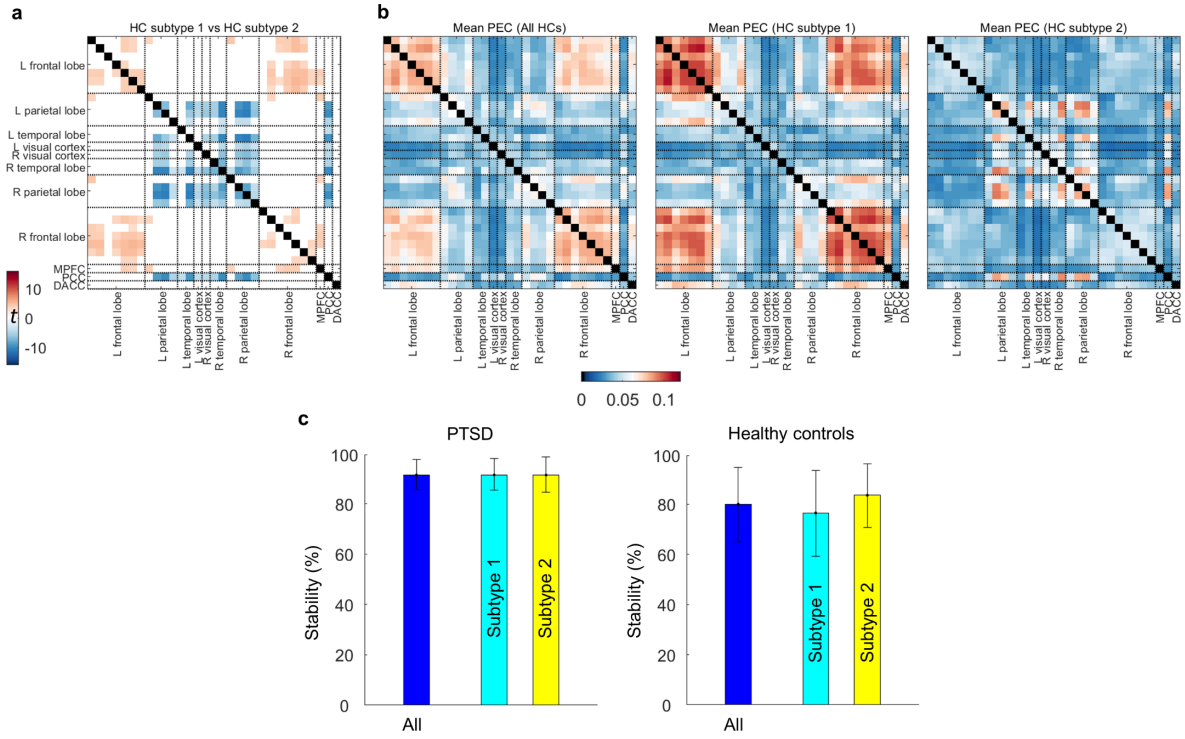
Supplementary Figure 7 | PEC-based clustering evaluation analysis for different independent datasets. **a**, Gap statistic criterion values in using different numbers of clusters (The best criterion values are marked in red). **b**, Variance ratios in using different numbers of clusters based Calinski-Harabasz criterion (The best criterion values are marked in red). **c**, Cluster assignment stability evaluated by repeating clustering 100 times by randomly leaving 10% subjects out. **d**, Cluster assignment stability in using different numbers of clusters. All error bars indicate standard deviation.



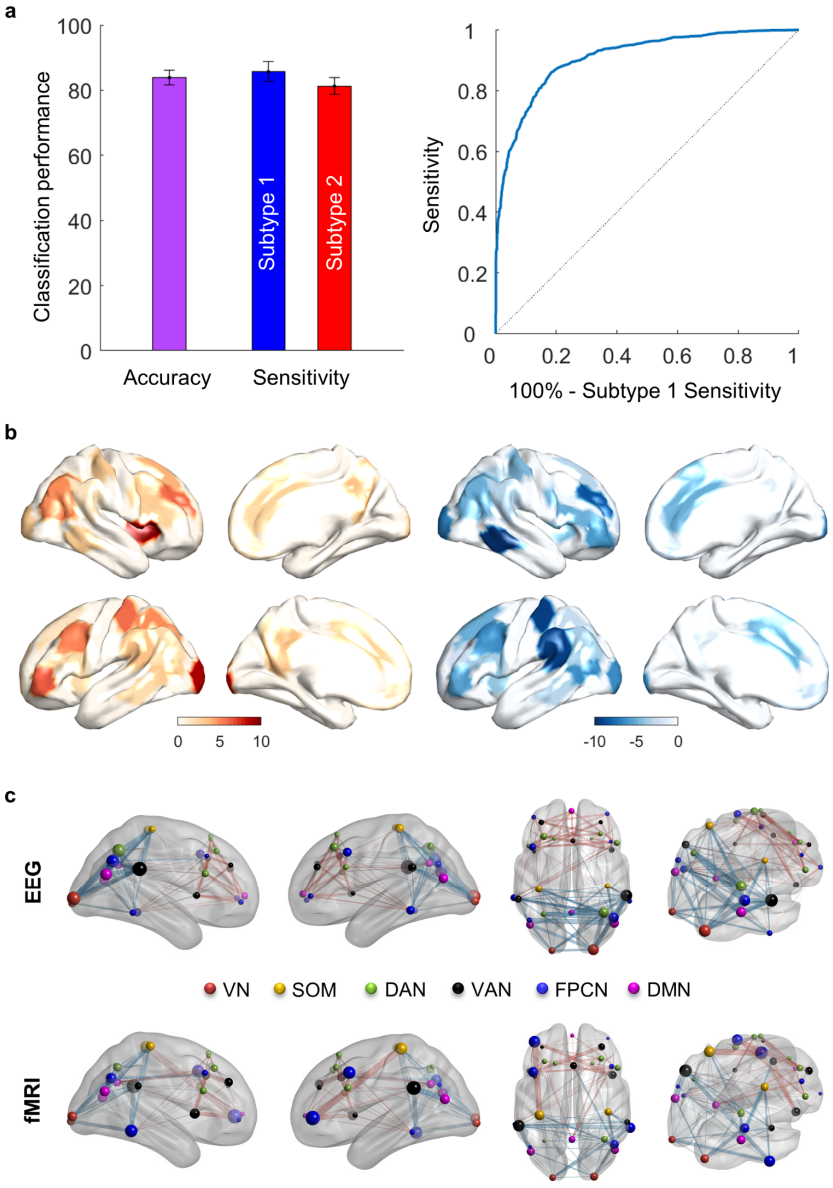
Supplementary Figure 8 | Comparison of PEC patterns obtained using 26 channels that are comparable across datasets versus using all channels. **a**, Channel montages. For dataset 1 - 3, the channel montages show the downsampled 26 channels that are most close to those of dataset 4. **b**, PEC differences (two-sample t-test with FDR correction) between the two subtypes derived from dataset 1 – 3 for using all channels and the downsampled 26 channels, respectively.



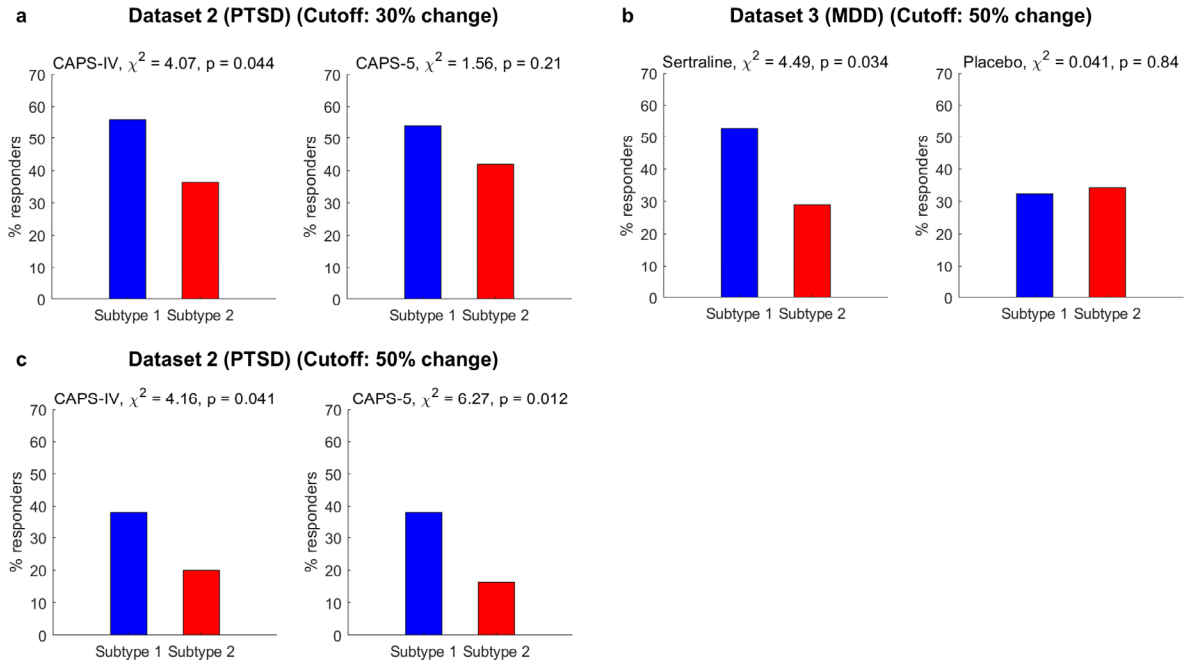
Supplementary Figure 9 | Subtype PEC patterns derived by clustering on healthy controls (HC) of dataset 1. **a**, PEC difference (two-sample t-test with FDR correction) between the two identified subtypes. **b**, Mean PEC matrices for all HCs, subtype 1, and subtype 2, respectively. **c**, Clustering stability assessed on PTSD and HC groups, respectively. The subtyping stability of healthy controls (80.1%) was significantly lower (Wilcoxon rank sum statistical test: z=2.3, p=0.02) than that of PTSD (91.9%) as well as more variable (coefficient of variation in healthy controls: 16.0, and in patients: 6.2). The error bars indicate standard deviation.



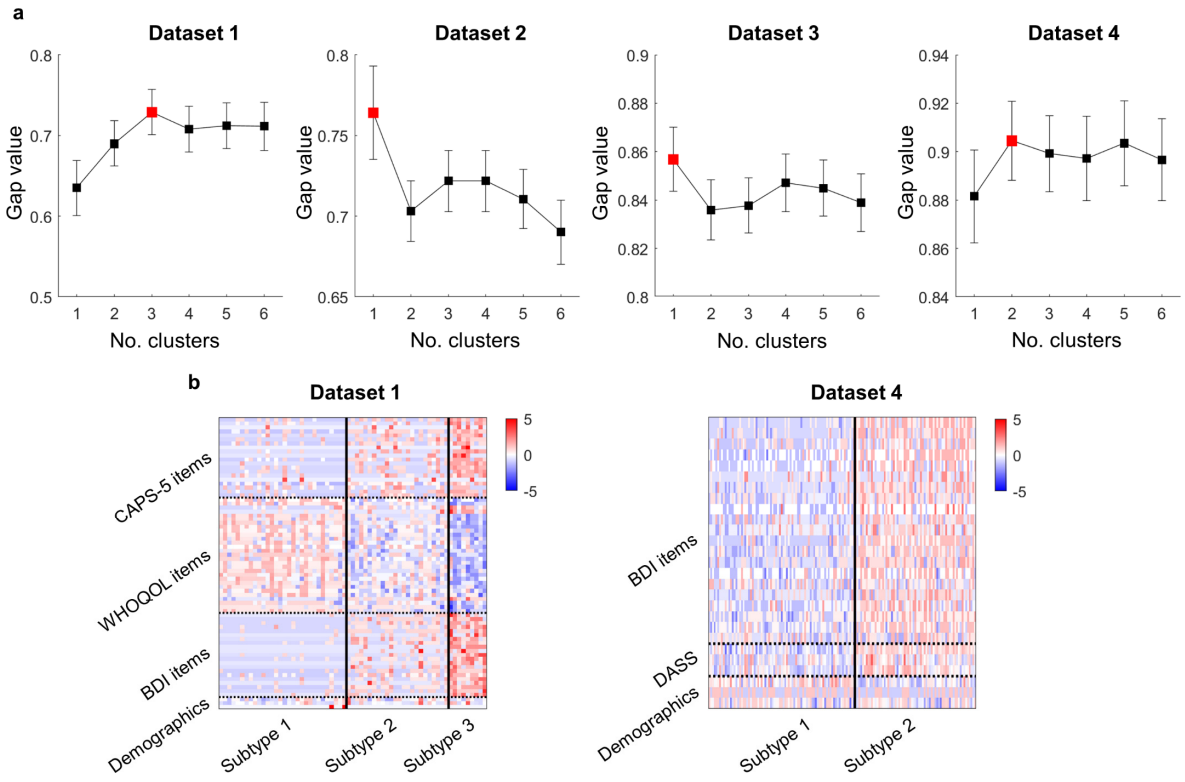
Supplementary Figure 10 | Subtype discriminability assessed using resting-state fMRI. A linear classifier was trained using a relevance vector machine[1,2] with pooled resting-state fMRI data to distinguish the two EEG-connectivity defined subtypes. Classification performance was evaluated using a 10x10 fold cross-validation. **a**, Our classifier with rsfMRI connectivity features was able to distinguish the two EEG-connectivity defined subtypes with an accuracy of 83.9% (permutation test, p<0.0001), a sensitivity of 85.7% in detecting subtype1 and 81.2% in detecting subtype 2. The error bars indicate standard deviation. **b**, The most discriminative features involved regions of FPCN, VAN, and visual network. **c**, Overlapping connections between EEG PEC and fMRI connectivity classifier profiles in distinguishing the two EEG subtypes.



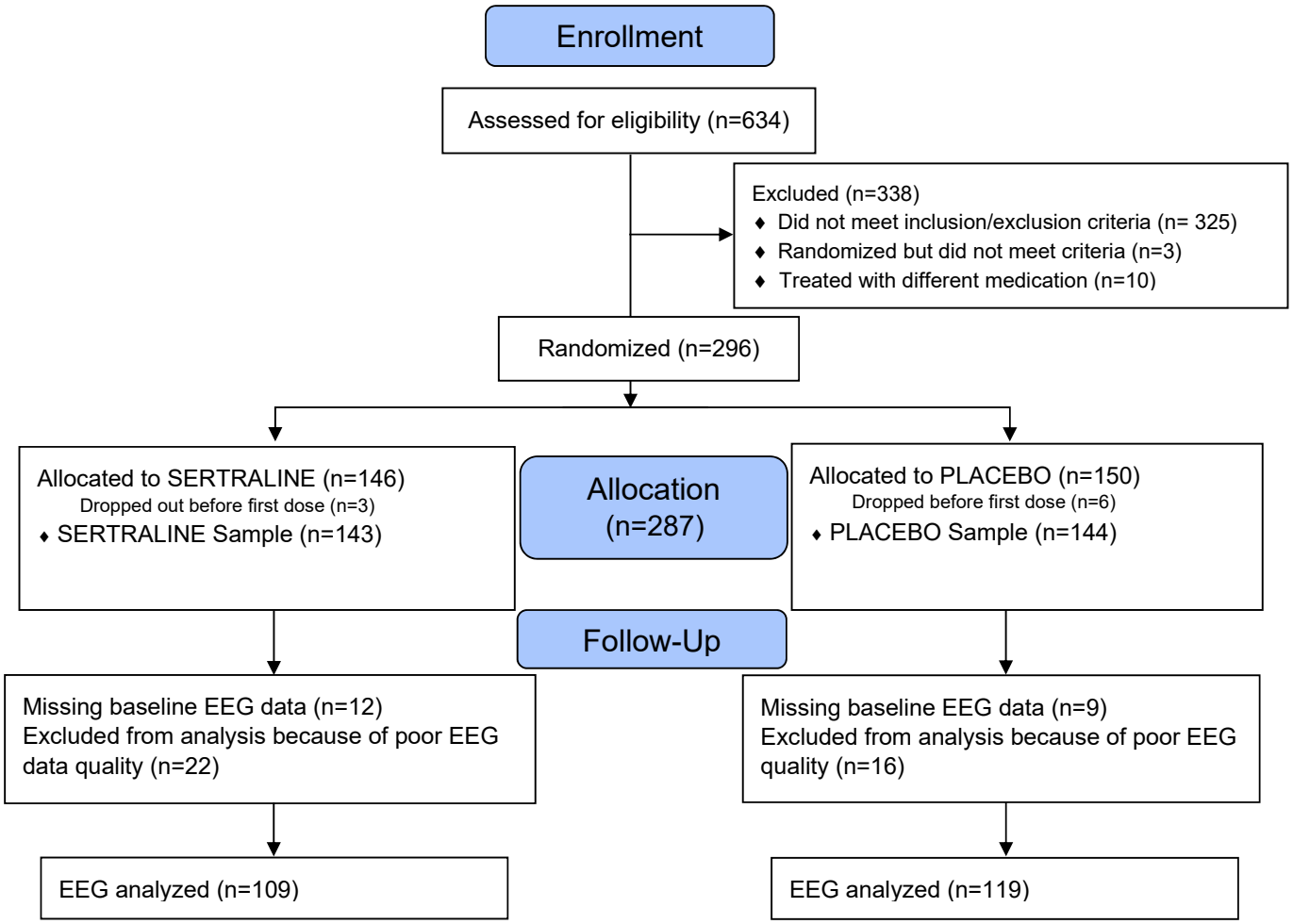
Supplementary Figure 11 | Comparison of treatment responders between the subtypes. Subtype 1 included significantly more responders than those in subtype 2 for both psychotherapy **a** and antidepressant medication **b**. Here, a 30% pre minus post treatment symptom change was used as the cutoff to identify responders in dataset 2 (PTSD) while a 50% change was used as the cutoff in dataset 3 (MDD). **c**, For completeness, we also show the results if using a 50% symptom change cutoff for defining treatment response in PTSD (i.e. to match that used for MDD).



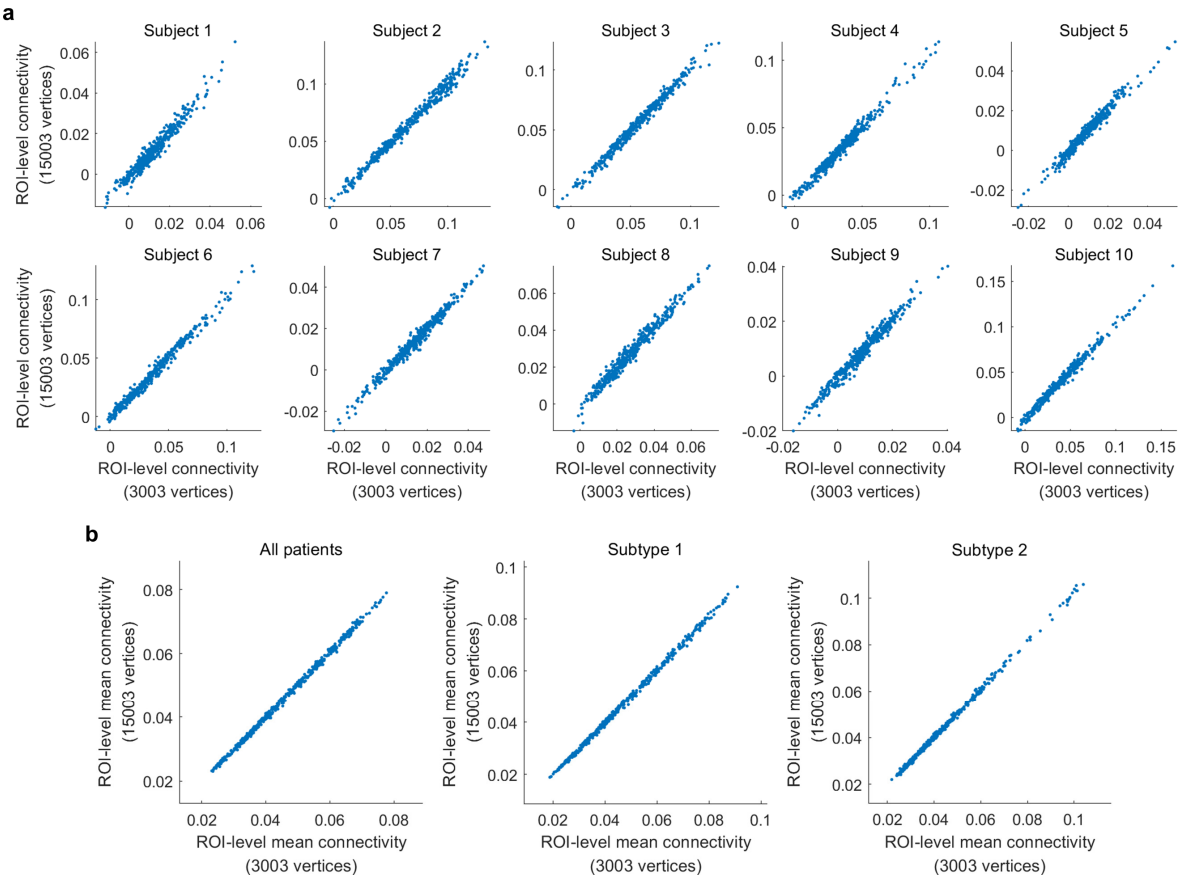
Supplementary Figure 12 | Clustering on baseline clinical scores and typical demographic information alone for different independent datasets. **a**, Gap values calculated using gap statistic criterion using different numbers of clusters for each of the four datasets. The error bars indicate standard deviation. **b**, Clinical subtypes identified for dataset 1 and dataset 4, respectively. CAPS = Clinician-administered PTSD Scale, WHOQOL = World Health Organization Quality-of-life Scale, BDI = Beck Depression Inventory, HAMD = Hamilton Depression Rating Scale, QIDS = Quick Inventory of Depressive Symptomatology, MASQ = Mood and Anxiety Symptoms Questionnaire, DASS = Depression, Anxiety and Stress Scale. Demographic variables included age, gender, and years of education.



Supplementary Figure 13 | EMBARC CONSORT Flow Diagram for the patients included in the subtyping analyses. For this analysis, patients were included (1) regardless of their $HAMD_{17}$ score, and (2) if they had resting-state EEG data of sufficient quality.



Supplementary Figure 14 | Comparison of PEC estimates between using different numbers of vertices. **a**, ROI-level PEC comparison between using 3003 vertices versus 15003 vertices for ten typical subjects. **b**, ROI-level mean PEC comparison between using 3003 vertices and 15003 vertices for all patients, subtype 1, and subtype 2, respectively.



Supplementary Table 1 | Difference of demographics between the two PEC-defined subtypes.

Dataset 1 (PTSD)				
Categorical variables	Subtype 1 (N = 69)	Subtype 2 (N = 37)	X^2 value	p value
Males, No. (%)	66 (95.7)	30 (81.1)	5.99	0.014
Continuous variables, mean (SD)			t value	p value
Age, yr	34.8 (7.6)	32.8 (7.7)	1.28	0.20
Educational attainment, yr	15.6 (2.2)	14.9 (2.3)	1.54	0.13
Dataset 2 (PTSD)				
Categorical variables	Subtype 1 (N = 64)	Subtype 2 (N = 71)	X^2 value	p value
Males, No. (%)	55 (85.9)	57 (80.3)	0.76	0.38
Continuous variables, mean (SD)			t value	p value
Age, yr	46.2 (14.2)	44.1 (12.6)	0.91	0.36
Educational attainment, yr	15.0 (1.8)	14.8 (1.7)	0.56	0.57
Dataset 3 (MDD)				
Categorical variables	Subtype 1 (N = 137)	Subtype 2 (N = 91)	X^2 value	p value
Males, No. (%)	50 (36.5)	28 (30.8)	0.80	0.37
Continuous variables, mean (SD)			t value	p value
Age, yr	39.0 (13.0)	35.9 (13.4)	1.76	0.080
Educational attainment, yr	15.4 (2.5)	15.0 (2.6)	1.18	0.24
Dataset 4 (MDD)				
Categorical variables	Subtype 1 (N = 86)	Subtype 2 (N = 93)	X^2 value	p value
Males, No. (%)	25 (29.1)	64 (68.8)	28.2	<0.0001
Continuous variables, mean (SD)			t value	p value
Age, yr	42.9 (13.0)	43.7 (13.1)	-0.38	0.70
Educational attainment, yr	13.7 (4.1)	14.5 (3.8)	-1.43	0.15
All datasets				
Categorical variables	Subtype 1 (N = 356)	Subtype 2 (N = 292)	X^2 value	p value
Males, No. (%)	196 (55.1)	179 (61.3)	2.57	0.11
Continuous variables, mean (SD)			t value	p value
Age, yr	40.4 (12.9)	40.0 (13.3)	0.45	0.65
Educational attainment, yr	14.9 (2.9)	14.8 (2.8)	0.73	0.47

Supplementary Table 2 | Responsiveness of EEG-connectivity subtypes to psychotherapy treatment, assessed by linear mixed models (group x time interaction) with item-level CAPS scores for dataset 2.

	All Patients		PE		CPT	
CAPS items	F value	p value	F value	p value	F value	p value
CAPS-IV B1	3.55	0.061	3.55	0.063	0.85	0.36
CAPS-IV B2	6.45	0.011	4.93	0.029	2.36	0.13
CAPS-IV B3	1.49	0.22	0.069	0.79	1.46	0.23
CAPS-IV B4	2.33	0.13	2.72	0.10	0.40	0.53
CAPS-IV B5	0.87	0.35	8.88	0.0039	0.32	0.57
CAPS-IV C1	0.82	0.37	0.51	0.48	0.52	0.47
CAPS-IV C2	7.02	0.0086	2.81	0.098	4.48	0.036
CAPS-IV C3	0.55	0.46	0.49	0.49	0.17	0.68
CAPS-IV C4	7.06	0.0084	2.58	0.11	4.78	0.030
CAPS-IV C5	2.80	0.095	0.53	0.47	2.02	0.16
CAPS-IV C6	4.21	0.041	1.27	0.26	2.62	0.11
CAPS-IV C7	0.12	0.73	0.016	0.90	0.15	0.70
CAPS-IV D1	1.63	0.20	0.78	0.38	1.06	0.30
CAPS-IV D2	2.66	0.10	2.41	0.12	0.74	0.39
CAPS-IV D3	10.02	0.0017	7.40	0.0081	5.76	0.018
CAPS-IV D4	2.07	0.15	4.17	0.045	0.17	0.68
CAPS-IV D5	0.33	0.57	1.09	0.30	1.27	0.26
CAPS-5 B1	3.40	0.067	5.68	0.020	0.50	0.48
CAPS-5 B2	4.58	0.033	4.64	0.035	1.53	0.22
CAPS-5 B3	0.30	0.59	0.00007	0.99	0.30	0.58
CAPS-5 B4	0.34	0.56	2.51	0.12	0.24	0.62
CAPS-5 B5	0.93	0.33	12.18	0.00081	0.80	0.37
CAPS-5 C1	0.31	0.58	0.99	0.32	0.054	0.82
CAPS-5 C2	9.07	0.0029	3.60	0.062	6.07	0.015
CAPS-5 D1	0.31	0.58	0.31	0.58	0.12	0.73
CAPS-5 D2	0.10	0.75	2.40	0.13	0.35	0.56
CAPS-5 D3	1.07	0.30	0.23	0.63	0.99	0.32
CAPS-5 D4	3.23	0.073	7.07	0.0096	0.055	0.81
CAPS-5 D5	8.17	0.0046	3.81	0.055	5.06	0.026
CAPS-5 D6	2.39	0.12	0.39	0.54	1.90	0.17
CAPS-5 D7	3.81	0.052	0.76	0.39	2.68	0.10
CAPS-5 E1	2.52	0.11	4.60	0.035	0.089	0.77
CAPS-5 E2	0.41	0.52	1.17	0.28	0.051	0.82
CAPS-5 E3	0.24	0.63	1.72	0.19	0.061	0.81
CAPS-5 E4	1.31	0.25	0.076	0.78	2.24	0.14
CAPS-5 E5	6.99	0.0088	6.76	0.011	3.31	0.071
CAPS-5 E6	0.22	0.64	0.18	0.68	0.22	0.64

Supplementary Table 3 | Responsiveness of EEG-connectivity subtypes to antidepressant medication, assessed by linear mixed models (arm x time interaction) with item-level HAMD scores for dataset 3.

	Subtype 1		Subtype 2	
HAMD items	F value	p value	F value	p value
HAMD-1	8.56	0.0035	1.01	0.32
HAMD-2	12.12	<0.001	0.32	0.57
HAMD-3	7.65	0.0058	0.22	0.64
HAMD-4	1.19	0.28	1.01	0.32
HAMD-5	4.91	0.027	0.00013	0.99
HAMD-6	0.29	0.59	0.00072	0.98
HAMD-7	0.13	0.72	7.19	0.0076
HAMD-8	4.10	0.043	0.26	0.61
HAMD-9	0.74	0.39	1.43	0.23
HAMD-10	0.47	0.49	1.09	0.30
HAMD-11	0.68	0.41	0.0057	0.94
HAMD-12	3.70	0.055	0.011	0.92
HAMD-13	2.23	0.14	0.18	0.67
HAMD-14	0.30	0.58	0.030	0.86
HAMD-15	0.39	0.53	0.25	0.62
HAMD-16	3.81	0.051	1.45	0.23
HAMD-17	0.40	0.53	1.13	0.29

Supplementary Table 4 | Responsiveness of EEG-connectivity subtypes to rTMS treatment, assessed by linear mixed models (group x time interaction) with item-level BDI scores for dataset 4.

	All Patients		10 Hz rTMS at left DLPFC		1 Hz rTMS at right DLPFC	
BDI items	F value	p value	F value	p value	F value	p value
BDI-1	4.22	0.041	5.16	0.025	0.97	0.32
BDI-2	1.74	0.19	3.43	0.066	0.00002	0.99
BDI-3	7.80	0.0055	2.71	0.10	5.01	0.026
BDI-4	0.043	0.83	0.29	0.59	0.012	0.91
BDI-5	0.61	0.44	0.038	0.85	1.08	0.30
BDI-6	3.31	0.070	0.62	0.43	2.33	0.13
BDI-7	0.071	0.79	0.31	0.58	0.015	0.90
BDI-8	0.055	0.81	0.37	0.55	0.72	0.40
BDI-9	0.24	0.63	0.28	0.59	0.044	0.83
BDI-10	2.98	0.085	1.81	0.18	1.33	0.25
BDI-11	0.012	0.91	0.081	0.78	0.043	0.84
BDI-12	4.86	0.028	6.01	0.016	0.83	0.36
BDI-13	0.82	0.37	3.55	0.062	8.25	0.0046
BDI-14	0.57	0.45	3.43	0.067	0.55	0.46
BDI-15	0.79	0.38	1.0	0.32	0.025	0.88
BDI-16	0.068	0.80	0.22	0.64	0.11	0.74
BDI-17	0.018	0.89	0.21	0.65	0.26	0.61
BDI-18	0.053	0.82	1.04	0.31	1.11	0.29
BDI-19	0.0020	0.96	0.79	0.37	0.27	0.61
BDI-20	0.090	0.76	0.31	0.58	0.023	0.88
BDI-21	0.067	0.80	1.17	0.28	0.27	0.61

Supplementary Table 5 | Demographic characteristics and clinical variables of PTSD study dataset 1. Statistics reflect comparisons of PTSD and TEHC groups.

Categorical variables	PTSD (N = 106)	TEHC (N = 95)	X^2 value	p value
Males, No. (%)	96 (90.6)	85 (89.5)	0.07	0.80
Site distribution, % Stanford	32 (30.2)	36 (37.9)	1.33	0.25
Continuous variables, mean (SD)			t value	p value
Age, yr	34.1 (7.6)	32.6 (8.1)	1.31	0.19
Educational attainment, yr	15.3 (2.3)	15.6 (2.1)	-0.89	0.37
CAPS-5 total score	27.2 (10.6)	2.7 (3.6)	18.19	< .001
CAPS-5 subscale B score	6.2 (3.3)	0.5 (1.1)	13.83	< .001
CAPS-5 subscale C score	3.6 (1.7)	0.2 (0.9)	15.09	< .001
CAPS-5 subscale D score	8.8 (5.2)	0.4 (1.0)	13.15	< .001
CAPS-5 subscale E score	8.5 (3.5)	1.6 (2.2)	14.22	< .001
WHOQOL Physical score	20.9 (4.7)	27.4 (3.6)	-9.96	< .001
WHOQOL Psychological score	13.9 (4.6)	19.7 (3.7)	-8.89	< .001
WHOQOL Social score	5.9 (2.8)	8.1 (2.6)	-5.37	< .001
WHOQOL Environment score	18.5 (5.0)	23.8 (4.3)	-7.33	< .001
BDI total score	18.3 (11.6)	3.5 (6.2)	8.99	< .001

Note. CAPS = Clinician-administered PTSD Scale, WHOQOL = World Health Organization Quality-of-life Scale, BDI = Beck Depression Inventory. See Supplementary Table 9 for more details of the clinical scale information.

Supplementary Table 6 | Baseline demographic characteristics and clinical variables of PTSD study dataset 2. Statistics reflect comparisons of the PE and CPT arms.

Categorical variables	PTSD (PE) (N = 44)	PTSD (CPT) (N = 91)	X^2 value	p value
Males, No. (%)	37 (84.1)	75 (82.4)	0.06	0.81
Continuous variables, mean (SD)			t value	p value
Age, yr	47.2 (13.9)	44.1 (13.1)	1.24	0.22
Educational attainment, yr	15.0 (1.6)	14.8 (1.9)	0.74	0.46
CAPS-IV total score	65.6 (20.0)	72.6 (18.2)	-1.96	0.05
CAPS-IV subscale B score	16.7 (6.8)	19.2 (7.6)	-1.97	0.05
CAPS-IV subscale C score	25.5 (10.2)	29.3 (8.9)	-2.14	0.03
CAPS-IV subscale D score	23.5 (6.1)	24.1 (5.6)	-0.55	0.58
CASP-5 total score	37.2 (11.6)	40.0 (10.3)	-1.36	0.18
CAPS-5 subscale B score	8.6 (3.5)	9.4 (3.7)	-1.20	0.24
CAPS-5 subscale C score	4.1 (1.8)	4.3 (1.9)	-0.61	0.54
CAPS-5 subscale D score	13.7 (5.3)	15.2 (4.9)	-1.55	0.13
CAPS-5 subscale E score	10.8 (3.3)	11.2 (3.0)	-0.58	0.56
WHOQOL Physical score	20.8 (4.5)	20.6 (5.7)	0.23	0.82
WHOQOL Psychological score	16.7 (4.0)	15.2 (4.4)	1.63	0.11
WHOQOL Social score	6.5 (1.8)	5.6 (1.9)	2.18	0.03
WHOQOL Environment score	28.4 (5.7)	27.9 (5.4)	0.37	0.71
BDI total score	21.5 (9.1)	24.3 (10.3)	-1.51	0.13

Note. CAPS = Clinician-administered PTSD Scale, WHOQOL = World Health Organization Quality-of-life Scale, BDI = Beck Depression Inventory. See Supplementary Table 9 for more details of the clinical scale information.

Supplementary Table 7 | Baseline demographic characteristics and clinical variables of depression study dataset 3. Statistics reflect comparisons of the Sertraline and Placebo arms.

Categorical variables	Sertraline (N = 109)	Placebo (N = 119)	X^2 value	p value
Males, No. (%)	30 (27.5)	48 (40.3)	4.15	0.04
Continuous variables, mean (SD)			t value	p value
Age, yr	37.1 (13.9)	38.4 (12.6)	-0.77	0.44
Age of onset	16.4 (5.9)	15.9 (5.6)	0.55	0.59
Educational attainment, yr	15.1 (2.6)	15.4 (2.6)	-0.87	0.38
Number of MDE	30.8 (121.3)	45.4 (160.2)	-0.77	0.44
Duration of current episode (mo)	42.7 (74.6)	51.9 (117.9)	-0.70	0.49
$HAMD_{17}$	18.2 (4.7)	18.7 (4.4)	-0.94	0.35
Medication dose	103.5 (32.3)	108.7 (29.7)	-1.18	0.24
QIDS	18.7 (4.7)	17.8 (2.7)	2.28	0.02
MASQ GD score	33.1 (7.6)	32.1 (8.3)	0.91	0.37
MASQ AD score	44.0 (4.3)	43.9 (5.9)	0.15	0.88
MASQ AA score	18.1 (5.8)	17.4 (5.2)	0.97	0.34

Note. MDE = major depression episodes, MASQ = Mood and Anxiety Symptoms Questionnaire; *4 MDD participants (1 placebo, and 3 with sertraline) with no employment status. See Supplementary Table 9 for more details of the clinical scale information.

Supplementary Table 8 | Baseline demographic characteristics and clinical variables of depression study dataset 4.

Characteristic	MDD (N = 179)
Age, mean (SD)	43.3 (13.0)
Males, No. (%)	90 (50.3)
Educational attainment, mean (SD)	14.1 (4.0)
Clinical Assessments	
rTMS protocol	
10 Hz Left aMFG, No. (%)	73 (40.8)
1Hz Right aMFG, No. (%)	106 (59.2)
BDI total score, mean (SD)	30.6 (9.7)
DASS-A, mean (SD)	28.4 (9.8)
DASS-D, mean (SD)	13.6 (8.7)
DASS-S, mean (SD)	22.4 (10.5)

Note. BDI = Beck Depression Inventory, DASS = Depression, Anxiety and Stress Scale. See Supplementary Table 9 for more details of the clinical scale information.

Supplementary Table 9 | Clinical scales used in the study.

Domain	Questionnaire	Description and measures derived
PTSD	Clinician Administered PTSD Scale (CAPS) for DSM IV and DSM 5 past month[3]	Structured clinical interview. Sum of scores for each cluster: Criterion B: Re-experiencing; Criterion C: Avoidance; Criterion D: Negative alterations in cognitions and mood; Criterion E: Alterations in arousal and reactivity; Foreshortened Future (CAPS IV only); and Past moth total score.
	PTSD Checklist (PCL) for DSM IV and DSM 5[4]	Self-report questionnaire assessing the DSM IV and 5 symptoms of PTSD added up to one total score.
Quality of life	WHO Quality of Life Brief questionnaire (WHO-QOL-BREF)[5]	Self-report questionnaire. Scores are derived for 4 subscales: physical, psychological, social, environmental and a measure of overall quality of life.
Depression	Beck Depression Inventory – II (BDI-II)[6]	Self-report questionnaire. Items added up to one total score.
	Hamilton Depression Rating Scale (HAM-D)[7]	Clinician administered rating scale. Items added up to one total scores.
	Quick Inventory of Depressive Symptoms (QIDS-SR-16)[8]	Self-report questionnaire. Items added up to one total scores.
	Depression Anxiety Stress Scales short version (DASS-21)[9]	Self-report questionnaire. Scores are derived for 3 sub-scales: depression (DASS-D), anxiety (DASS-A), and stress (DASS-S).
Mood and Anxiety	Mood and Anxiety Symptom Questionnaire (MASQ)[10]	Self-report questionnaire. Scores are derived for 3 subscales: General distress (GD), Anxious Arousal (AA), Anhedonic Depression (AD)

Statement | Difference between the current findings and our prior reports.

Using resting EEG from dataset 1, we recently established the power envelope connectivity (PEC) method to study the difference in brain connectome profile between PTSD patients and healthy controls[11]. Robust PTSD-related abnormalities were evident in theta-band source-space PEC features and were found to relate to cognitive deficits in these patients. The results from the prior study inspired us to use PEC features measured by EEG, a less expensive but more practical technique, to investigate the intrinsic neurophysiological subtypes. However, the PEC features identified in this study both do not overlap with those in the prior study, and do not differentiate between groups when not considering subtypes. That is, the present manuscript is the corollary of the traditional case-control approach taken in the prior paper.

In another recent paper, we reported on a new computational model, called SELSER[12], tailored for sensor-space EEG and applied it to predict outcome with antidepressant sertraline versus placebo. The SELSER model identified a sertraline-predictive brain signature in major depression (using dataset 3). This method was designed specifically to predict the change in $HAMD_{17}$ clinical score by training a supervised regression model with a known target, and hence differed fundamentally from the unsupervised clustering method presented in our current study. Indeed, the present manuscript and the SELSER paper can be seen as complementary approaches with the prior paper taking a top-down supervised approach and the current one taking a bottom-up unsupervised approach, with both converging on the ability of EEG to predict antidepressant outcome relative to placebo. This convergence, given the large differences in both EEG features (power versus connectivity) and analytic method, speaks to the robustness of the underlying biological findings.

Though these prior reports provided strong support for our current hypothesis about source-space PEC-driven subtypes predictive of different treatments across psychiatric populations, we have studied multiple crucial and challenging issues in the present manuscript. Specifically, we have made the following unique contributions, showing the fundamental differences from the prior reports: (1) Developed a purely data-driven, robust and replicated parcellation of psychiatric phenotypes based only on brain data. The newly designed method provided us an elegant way to characterize the intrinsic data structure and delineate the underlying neurophysiological subtypes for patient stratification; (2) Validated the ability of the identified neurophysiological subtypes in outcome prediction across multiple treatments, including replication of the psychotherapy prediction effect (with a strong effect size), demonstrating their transdiagnostic potential; (3) Established EEG connectivity as a clinically-useful tool for clinical care and drug development in the near term by identifying a previously unknown (but now identified and validated) brain phenotype using a clinic-translatable tool.

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