Parker et al., "Auditory Oddball Responses Across the Schizophrenia-Bipolar Spectrum and their Relationship to Cognitive and Clinical Features."

Supplemental Methods:

Recruitment: Subjects were recruited at Psychosis and Affective Research Domains and Intermediate Phenotypes (PARDIP) and Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) consortium sties: University of Georgia and Augusta University, Beth Israel Deaconess Hospital, Harvard Medical School, University of Chicago, UT Southwestern Medical School, and Institute of Living/Hartford Hospital and Yale School of Medicine, and followed previously published approaches (1). For recruitment of B-SNIP1 subjects used in the replication portion, please see (1). Clinically stable participants were recruited via community advertisements, linked community facilities and programs, and local National Alliance on Mental Illness-type organizations. All subjects provided written informed consent before participation. This study was approved by Institutional Review Boards at each data collection and analysis site.

Patients had a diagnosis of schizophrenia (SZ), schizoaffective disorder (SAD), or bipolar disorder with a history of psychosis (BDP) or no history of psychosis (BDNP) based on the Structured Clinical Interview for DSM-IV-TR (SCID) (2). Medical history, Positive and Negative Syndrome Scale (3), Young Mania Rating Scale (4) , Montgomery-Asberg Depression Rating Scale (MADRS) (5), Birchwood Social Functioning Scale (6), and Global Assessment of Functioning scale (Axis V of DSM-IV) were acquired by trained Masters- or Doctoral-level clinicians. Presence of serious medical or neurological illness, mental retardation, head trauma with >30 minutes unconsciousness, current substance use ascertained by history as well as urine screens on day of testing, abuse in the past 3 months, and dependence within 6 months or extensive history of drug dependence (based on SCID) were criteria for exclusion. Healthy persons were free of any lifetime psychotic or chronic mood disorders and a family history of psychotic or BP disorders in first-degree relatives. Clinical information and diagnoses were reviewed and confirmed at diagnostic consensus meetings including senior psychiatrists/psychologists and the clinician who conducted the structured interviews at each site. All possible efforts were made to collect all clinical, cognitive, and EEG measures within 1 month after confirmation of inclusion into the study.

Clinical Rater Training and Maintenance: Clinical raters went through extensive training and certification prior to contributing ratings to the study, as well as ongoing training throughout the course of the study. Initial competency was established by on site didactic training for all clinical assessments and data collection procedures (SCID-I/P, SIDP-IV, YMRS, MADRS, PANSS, SFS, SBS, clinical history and demographics), followed by a pencil and paper competency evaluation (100% accuracy required), and finally the establishment of inter-rater reliability. Inter-rater reliability was accomplished using a train-to-criterion protocol with recorded patient interviews (for symptom scales all total scores were required to be within 2 points of the standardized score and all individual item scores were required to be within 1 point of the standardized score; for diagnostic assessments 100% agreement was required for the primary diagnosis). Remediation and additional training was provided as needed on a case-by-case basis until competency was achieved; clinical raters were not otherwise allowed to contribute data to the study. In order to maintain competency and reduce "drift," in-person didactic re-training sessions were conducted annually and inter-rater reliability established at 6 month intervals. Additionally, monthly diagnostic consensus calls (SCID-I, SIDP, SBS) were held throughout the course of the study, allowing for ongoing assessment monitoring and training (1).

Comparison between B-SNIP1 and B-SNIP2 Subjects: Subjects from B-SNIP1 overlap with Ethridge et al. and Clementz et al. (7; 8) and each step of quality control was completed using the exact steps as outlined in the main text. Following identical steps used in the main text, ERP PCA components

were identified for Standard (Frontal) and Target (Frontal and Parietal) trials using the combined B-SNIP1 and B-SNIP2 samples. In order to compare responses between studies, each ERP time point was standardized by using the mean and standard deviation from all subjects across all time points for each ERP component from each study. A direct comparison between of the mean ERP response of B-SNIP1 and the new subjects from B-SNIP2 as performed by group. Figure one is a straightforward illustration of the similarity of ERP morphologies by DSM diagnosis illustrating the strong replication of auditory oddball ERP findings across the psychosis spectrum. For each group in both studies (BDNP was not included since BDNP was not collected during B-SNIP1), the mean ERP response from -100 to 600 ms from B-SNIP1 was correlated with the mean ERP response from B-SNIP2.

Additionally, group by study ANOVAs were calculated on each 20 ms time bin from -100 to 600 ms. Calculations from G*power indicated the group x study ANOVAs with n=1761 are able to capture Cohens f-effect sizes in the .07-.09 range (.8-.99 power, alpha=.05). All ANOVA p-values within each component were adjusted using a false discovery rate method (9). This is identical to the procedure used in the group by sex ANOVA used in the primary text. There were no significant group by study interactions at any time-bins from any of the ERP components.

95% Confidence intervals of the effect size for the group x study interactions were calculated across time bins for each component using a bootstrapping procedure (bootstrap=5000 iterations; uncorrected for multiple comparisons) (10). The average f-effect size for the group x study interactions were Standards ERP =.044, Targets Frontal ERP=.039, Targets Parietal ERP=.045. A Cohen's f-effect size of .1 indicates a small effect size. See Figure S3.

Equivalence contrast tests were calculated on the total study samples (B-SNIP1 vs B-SNIP2), Healthy comparison groups, and all psychosis subjects for each ERP component across time bins (uncorrected for multiple comparisons). Equivalence testing demonstrates whether mean differences between groups are small enough that the differences can be considered clinically unimportant and that they can be treated as equivalent. A clinically significant threshold was set at ± .1 common language effect size. Common language effect size corresponds to the probability of that a random score from group A will be larger than a random score from group B. A value of .5 indicates that the two samples are identical. The 90% CI of each contrast was calculated using a bootstrapping procedure (bootstrap=5000 iterations) (10; 11). Consistent with the main factor of "study" from the ANOVA results, the average contrast value across time bins for the "total sample" were: Standards ERP =.52, Targets Frontal ERP=.51, Targets Parietal ERP=.49. See Figure S3.

Research Site Effects: In order to ensure consistent EEG recordings across research center sites, a number of steps were taken. Each site had identical EEG equipment and software in order to collect data. Every year, multiple pilot subjects went to each research center and completed the OB EEG task under identical conditions as the research participants. This allowed for the researchers to harmonize potential differences in EEG set-up, data collection, and presentation of the stimuli. Additionally, after the data had been pre-processed, age-adjusted, and was ready for final analysis, a group by site ANOVA was performed on each 20-ms bin from -100 to 600 ms for each ERP component. No significant group by site interactions were found. This is consistent with (12; 13) which examined other auditory paradigms using overlapping research participants.

EEG Recording: Electroencephalogram (EEG) was continuously recorded from 64 silver/silver chloride sensors (impedance <10 kΩ; QuikCap, Compumedrics Neuroscan, El Paso, Texas), positioned according to the standard 10-10 EEG system with mastoids and CB1/2 locations to provide greater sampling below the canthomeatal line, with nose reference and forehead ground. Recordings were amplified (12,500X) and digitized (1000 Hz) using Neuroscan ACQUIRE and SynAmps2 recording systems (Compumedics Neuroscan).

EEG Processing: EEG data were pre-processed following previously published methods (7; 12–14). Raw EEG data were inspected for bad sensors and artifacts. Bad sensors were interpolated (no more than 5% for any subject) using spherical spline interpolation (BESA 5.3; MEGIS Software, Grafelfing, Germany). Data were transformed to an average reference and down-sampled to 500 Hz and digitally band pass filtered from .5 Hz to 55 Hz (zero-phase filter; roll-off: 6 and 48 dB/octave, respectively). Blink and cardiac artifacts were minimized using independent component analysis (EEGLAB 13.6) (15). EEG data on each trial were then segmented into 1250-ms epochs extending from 250 ms before to 1000 ms after trial onset. Trials containing activity ±75 mV at any sensor were eliminated from further processing. Since our previous study (7) confirmed similar percentages of correct responses (~90%) to target trials across patient groups, all artifact-free target trials were included in subsequent analyses (7). At least 50% of trials were accepted for all included subjects with no significant difference between groups on number of usable trials. Data from included trials were averaged for each subject to create a 64-sensor grand average ERP. Each ERP was baseline adjusted using the 100 ms pre-stimulus period (see Figure 1 and 2).

Frequency principal component analysis: In order to identify frequency bands of interest we performed a frequency principal component analysis (fPCA) using the following steps: power values from each time-bin from 0 to 600 ms were averaged for standards and targets. All subjects' data were concatenated to create a matrix of 50 variables (3-52 Hz) and (t * n) x 64 observations (where t is trial type and n is the number of subjects; t=2 (standards and targets); n=1078). An fPCA was carried out on the matrix with promax (oblique) vector rotation and Kaiser normalization (16). Scree tests identified three components accounting for greater than 95% of the variance across subjects and sensors. The three resulting fPCA components were: (i) low (3-13 Hz); (ii) beta (14-29 Hz); and (iii) gamma (30-52 Hz) frequencies (see Figure S1). This result is highly consistent with previous results from B-SNIP1 (7) and captures the cortically relevant frequency bands resolvable with EEG (17). Each fPCA component weight was multiplied by each subject's grand average time-frequency data at each time bin, summed across frequencies, and divided by the plus sum of the component weights, reducing the waveform from 50 frequencies (3-52 Hz) to three frequency bands. This resulted in 6 total waveforms (three standard and three target). For each frequency component, all sensors were averaged to create one time-frequency waveform (Figure 3). Each time-frequency waveform was then standardized across all subjects, so frequency data are displayed in standardized Power values.

Multivariate Canonical and Correlational Analyses: A canonical discriminant analysis (CDA) is similar to PCA, but uses pooled within-group covariance matrices and pits group means as variables and measurements as observations (18; 19). Thus, the n^groups-1 functions are extracted, which are uncorrelated and maximize group differences. CDA creates a linear combination of the predictors that have the highest possible within-group (see figure 4a). The p-value presented in the main text is associated with the Chi-square statistic, which is testing the null hypothesis that: the function, and all functions that follow, have no discriminating ability. This is part of the standard output in SPSS. Additionally, it is possible to examine group mean differences of the function scores using traditional statistics like ANOVAs and post-hoc tests, which are included in tables S2 and s3. The correlation between each discriminant function and the 26 EEG variables are listed in table S4 so that the interested reader can see how individual EEG variables are related to the overall discriminant functions.

The canonical correlational analyses we used for comparing the EEG variables and Cognitive variables/ EEG variables and Clinical variables are similar to a CDA, but instead of creating functions that are uncorrelated and maximize group differences, it creates a linear combination latent function pairs for each data set (i.e. 1 Neural and 1 Cognitive) that are maximally correlated with each other, but uncorrelated with the any of the other latent function pairs. The number of latent pairs is based on the data set with the fewest variables (n=6 for both CCAs in the main text). The p-value statistic presented in the text is based off of the F-value from the Wilks' Lambda multivariate test with a null hypothesis that

the two sets of variables are not linearly related. In tables S5 and S6 we also have the structure matrices that list the correlation between each latent pair and the variables that went into each function so that the interested reader can see how individual variables are related to the function pairs.

Supplemental Analyses to identify restricted list of measures: Each of the 26 variables were submitted to linear discriminant analysis (LDA) with group as the dependent variable (HC, BDNP, BDP, SAD, and SZ). EEG variables that minimized overall Wilks' lambda at $p < .05$ were entered in a stepwise fashion, leaving a parsimonious selection of neural measures that differentiated groups. Then, to ensure that identified ERP and TF variables contributed to reliable and stable group separations, a jackknife procedure was performed by submitting 95 % of the total sample (n = 1024, sampling without replacement) to an LDA 1000 times. EEG Components consistently identified (>50% of procedures) across iterations were then used in a canonical discriminant analysis (identical to the main analysis in the paper). The results follow an identical pattern as the CDA that used all 26 variables, although with marginally smaller effect sizes. A Pearson correlation between the CDA variates used in the main paper and the CDA variates using the reduced number of EEG variables were: Variate 1: r=.96; Variate 2: r=.79; Variate 3: r= .75. See table S12 and S13 for Jackknife results and the mean responses of each variate by group.

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Supplemental Tables:

Table S1: B-SNIP1 Sample Characteristics

B-SNIP1 Characteristics

	HC	BDP	SAD	SZ	Total	t-test comparing averages of B-SNIP1 and B-SNIP2	*p*
N	223	174	134	218	749		
Mean age	37.37	35.68	36.52	34.53	36.00	t(1758)=-2.43*	.02
Age SD	12.31	12.90	12.32	12.44	12.51		
Sex (% F)	57	58	58	31	50		
Illness duration						t(1064)=-8.09***	<.001
Mean	N/A	16.46	15.77	13.72	15.15		
SD	N/A	12.32	10.97	12.01	11.90		
Years of Formal Education						t(1722)=-2.32*	.02
Mean	15.23	14.26	13.13	12.83	13.93		
SD	2.57	2.36	2.19	2.22	2.56		
Ethnicity (% Hispanic)	10	8	13	9	10		
Race (%)							
AA	24	18	33	44	30		
AE	0	0	0	0	0		

AS	4	2	1	2	2		
CA	67	77	60	50	63		
NH	0	0	0	0	0		
MR	2	1	5	3	3		
OT/UNK	2	2	1	2	2		
Global Assessment of Function (GAF)						t(1626)=-1.70	.09
N	219	173	132	217	741		
M	86.89	60.99	49.24	49.34	63.14		
SD	6.37	12.47	11.96	12.16	19.36		
Birchwood Social Functioning Scale (SFS)						t(1492)=-.13	.90
N	157	135	107	166	565		
M	157.18	134.04	120.00	122.76	134.50		
SD	16.51	22.64	25.27	24.24	26.70		
BACS Verbal Memory						t(1673)=3.81***	<.001
N	216	171	130	208	725		
M	-.12	-.42	-1.08	-1.02	-.62		
SD	1.11	1.25	1.38	1.34	1.33		
BACS Digit Sequencing						t(1672)=.92	.36
M	-.13	-.51	-.92	-1.31	-.70		
SD	1.13	1.08	1.16	1.12	1.22		
BACS Token Motor						t(1642)=5.01***	<.001
M	0.00	-.88	-1.35	-1.33	-.83		

SD	1.05	1.21	1.10	1.23	1.28		
BACS Verbal Fluency						t(1669)=-.69	.49
M	.13	-.17	-.55	-.81	-.33		
SD	1.05	1.19	1.21	1.13	1.20		
BACS Symbol Coding						t(1672)=-2.33*	.02
M	.05	-.92	-1.41	-1.44	-.87		
SD	1.04	1.09	1.13	1.10	1.25		
BACS Tower of London						t(1672)=1.15	.25
M	.03	-.15	-.70	-.80	-.38		
SD	1.12	1.09	1.28	1.45	1.30		
Positive and Negative Syndrome Scale (PANSS) Positive						t(1045)=-2.59*	.01
N	N/A	171	132	211	514		
M	N/A	12.55	17.53	16.95	15.64		
SD	N/A	4.33	5.04	5.48	5.46		
PANSS Negative						t(1044)=-2.63*	.01
N	N/A	171	132	211	514		
M	N/A	12.19	15.59	16.84	14.97		
SD	N/A	3.98	5.01	5.75	5.41		
PANSS General						t(1046)=-.51	.61
N	N/A	171	132	212	515		
M	N/A	28.58	34.47	32.97	31.90		
SD	N/A	8.04	8.62	8.82	8.84		

PANSS Total						t(1043)=-1.97*	.049
N	N/A	171	132	210	513		
M	N/A	53.32	67.59	66.72	62.48		
SD	N/A	13.81	16.00	16.96	16.98		
Montgomery-Åsberg Depression Rating Scale (MADRS)						t(1049)=-3.08**	.002
N	N/A	170	131	209	510		
M	N/A	10.59	14.08	8.66	10.69		
SD	N/A	9.60	10.18	7.92	9.35		
Young Mania Rating Scale (YMRS)						t(1050)=-9.73***	<.001
N	N/A	171	131	210	512		
M	N/A	5.11	6.55	5.71	5.73		
SD	N/A	5.75	6.22	5.64	5.85		

Note. SZ = schizophrenia, SAD = schizoaffective disorder, BDP = bipolar I disorder with psychotic features.

*$p < .05$, **$p < .01$, ***$p < .001$. t-tests were performed excluding the BDNP sample from B-SNIP2.

Table S2: Group EEG Values (Age-corrected Standardized Voltage) and Effect sizes relative to the Healthy comparison group.

		HC		BDNP		BDP		SAD		SZ			BDNP	BDP	SAD	SZ
	Average F-Value (4,1068)	Mean	STD	Mean	STD	Mean	STD	Mean	STD	Mean	STD		Glass Delta			
Standards ERP P50 (60-80 ms)	3.62	-.089	.76	.341	.92	-.018	.71	.005	.74	.035	.88		.569	.095	.124	.165
Standards ERP N100 (80-140 ms)	14.23	-1.636	.91	-1.399	.96	-1.458	.97	-1.094	.93	-1.162	.93		.260	.195	.594	.519
Standards ERP Rising P200 (140-200 ms)	6.69	.842	1.14	.677	1.02	.451	1.03	.880	1.09	.893	.90		-.144	-.341	.034	.045
Standards ERP Late P200 (200-280 ms)	9.50	1.282	.97	.976	.90	1.044	.81	.882	.86	.871	.73		-.314	-.244	-.410	-.421
Standards ERP Late (520-600 ms)	3.11	.100	.44	-.066	.43	.034	.40	-.001	.37	.009	.40		-.379	-.151	-.230	-.207
Standards LOW Early/Mid (20-340 ms)	1.18	.869	.54	.818	.51	.685	.49	.585	.55	.585	.52		-.095	-.342	-.530	-.530
Standards BETA Early (20-160 ms)	5.85	1.231	.70	1.285	.73	.993	.64	.932	.72	.967	.76		.077	-.341	-.427	-.377

Standards GAMMA Early (20-100 ms)		5.38		1.444	.88	1.649	1.01	1.106	.92	1.198	.95	1.227	1.03		.232	-.383	-.279	-.246
Standards GAMMA Mid (180-200 ms)		3.48		-.257	.73	-.011	.75	-.117	.75	-.130	.84	-.085	.87		.337	.191	.174	.235
Standards GAMMA Mid-2 (220-260 ms)		3.89		-.331	.72	-.078	.80	-.227	.74	-.181	.86	-.125	.85		.350	.145	.208	.286
Targets Frontal ERP N100 (80-140 ms)		8.60		-.768	.64	-.667	.69	-.578	.60	-.461	.65	-.518	.67		.158	.298	.483	.393
Targets Frontal ERP P2/N2 (140-240 ms)		6.18		.337	.87	.535	.83	.229	.87	.649	.77	.466	.74		.227	-.123	.357	.148
Targets Frontal ERP P3a (280-360 ms)		5.67		.629	1.17	.131	.97	.291	1.03	.335	.93	.359	.96		-.425	-.288	-.251	-.230
Targets Frontal ERP Late (420-580 ms)		5.33		-.589	.77	-.702	.91	-.641	.79	-.421	.76	-.314	.70		-.146	-.067	.218	.356
Targets Parietal ERP N100 (60-140 ms)		4.75		-.846	.44	-.778	.43	-.871	.42	-.743	.37	-.712	.36		.156	-.058	.235	.308

Targets Parietal ERP N200 (140-260 ms)		13.16		-.866	.63	-.573	.59	-.777	.56	-.537	.56	-.499	.50		.468	.143	.525	.586
Targets Parietal ERP Early P300b (320-420 ms)		9.47		1.241	1.00	1.018	.97	.956	.95	.772	.81	.867	.81		-.222	-.284	-.467	-.373
Targets Parietal ERP Late P300b (420-600 ms)		5.52		.701	.71	.633	.66	.514	.69	.450	.66	.438	.57		-.096	-.262	-.352	-.369
Targets LOW Early (40-160 ms)		6.22		.742	.67	.736	.70	.533	.65	.518	.68	.445	.73		-.009	-.311	-.335	-.443
Targets LOW Mid (160-300 ms)		15.14		.928	.73	.685	.78	.627	.68	.544	.75	.437	.78		-.333	-.414	-.528	-.675
Targets LOW Late (300-440 ms)		12.92		.396	.73	.231	.70	.141	.63	.053	.66	-.003	.68		-.227	-.350	-.471	-.548
Targets BETA Mid (140-220 ms)		4.34		.548	.87	.621	1.02	.378	.79	.262	.83	.336	.80		.085	-.196	-.330	-.244
Targets BETA Late (420-560 ms)		4.26		-.609	.76	-.577	.82	-.493	.76	-.397	.85	-.379	.85		.043	.153	.279	.303
Targets GAMMA		3.44		-.067	.83	.234	.99	.078	.88	.056	1.00	.131	.97		.365	.176	.149	.239

Mid (140-180 ms)																
Targets GAMMA Mid-2 (240-280 ms)		2.91		-.185	.91	.111	1.01	-.081	.88	-.029	.98	-.004	1.06		.324	.113	.171	.198
Targets GAMMA Late (340-600 ms)		3.71		-.309	.82	-.077	.93	-.116	.84	-.118	.97	-.078	.98		.283	.236	.233	.282
CDA Variate 1:		75.48		.528	.94	.002	.76	.062	.90	-.572	.82	-.510	.83		-.556	-.493	-1.164	-1.099
CDA Variate 2:		18.34		.027	1.00	.846	.99	-.414	.97	-.034	.84	.048	.98		.818	-.440	-.060	.021
CDA Variate 3:		12.84		.129	.99	-.503	.99	-.376	1.04	.125	.98	.084	.89		-.641	-.512	-.003	-.045

Table S3: Post-Hoc comparisons for each EEG and CDA variable:

Tukey's B Homogenous Subgroups	
Standards ERP P50 (60-80 ms)	HC/BDP/SAD/SZ < BDNP
Standards ERP N100 (80-140 ms)	HC/BDP/BDNP < BDNP/SZ < SZ/SAD
Standards ERP Rising P200 (140-200 ms)	BDP/BDNP < BDNP/HC/SAD/SZ
Standards ERP Late P200 (200-280 ms)	SZ/SAD/BDNP/BDP < HC
Standards ERP Late (520-600 ms)	BDNP/SAD/SZ/BDP < SAD/SZ/BDP/HC
Standards LOW Early/Mid (20-340 ms)	SADSZ/BDP < BDP/BDNP < BDNP/HC
Standards BETA Early (20-160 ms)	SAD/SZ/BDP < HC/BDNP
Standards GAMMA Early (20-100 ms)	BDP/SAD/SZ < SAD/SZ/HC < HC/BDNP
Standards GAMMA Mid (180-200 ms)	HC/SAD/BDP/SZ/BDNP
Standards GAMMA Mid-2 (220-260 ms)	HC/BDP/SAD/SZ < BDP/SAD/SZ/BDNP
Targets Frontal ERP N100 (80-140 ms)	HC/BDNP < BDNP/BDP/SZ < BDP/SZ/SAD
Targets Frontal ERP P2/N2 (140-240 ms)	BDP/HC/SZ < HC/SZ/BDNP < SZ/BDNP/SAD
Targets Frontal ERP P3a (280-360 ms)	BDNP/BDP/SAD/SZ < SAD/SZ/HC
Targets Frontal ERP Late (420-580 ms)	BDNP/BDP/HC < BDP/HC/SAD < SAD/SZ
Targets Parietal ERP N100 (60-140 ms)	BDP/HC/BDNP < HC/BDNP/SAD < BDNP/SAD/SZ
Targets Parietal ERP N200 (140-260 ms)	HC/BDP < BDNP/SAD/SZ
Targets Parietal ERP Early P300b (320-420 ms)	SAD/SZ/BDP/BDNP > BDNP/HC
Targets Parietal ERP Late P300b (420-600 ms)	SZ/SAD/BDP/BDNP < BDP/BDNP/HC
Targets LOW Early (40-160 ms)	SZ/SAD/BBDP < BDNP/HC
Targets LOW Mid (160-300 ms)	SZ/SAD/BDP < SAD/BDP/BDNP < HC

Targets LOW Late (300-440 ms)	SZ/SAD/BDP < SAD/BDP/BDNP < BDNP/HC
Targets BETA Mid (140-220 ms)	SAD/SZ/BDP < SZ/BDP/HC < BDP/HC/BDNP
Targets BETA Late (420-560 ms)	HC/BDNP/BDP/SAD/SZ
Targets GAMMA Mid (140-180 ms)	HC/SAD/BDP/SZ < SAD/BDP/SZ/BDNP
Targets GAMMA Mid-2 (240-280 ms)	HC/BDP/SAD/SZ/BDNP
Targets GAMMA Late (340-600 ms)	HC/SAD/BDP/SZ/BDNP
CDA Variate 1:	HC < BDP/BDNP < SZ/SAD
CDA Variate 1:	BDP < SAD/HC/SZ < BDNP
CDA Variate 1:	BDNP/BDP < SZ/SAD/HC

Table S4: CDA Results and Structure Matrix:

Function	Eigenvalue	% of Variance	Canonical Correlation
CDA-1	.288	64.5	.473
CDA-2	.078	17.4	.268
CDA-3	.051	11.5	.221

Test of Function(s)	Wilks' Lambda	Chi-square	df	Sig.
1 through 4	.666	431.339	104	<.001
2 through 4	.858	163.018	75	<.001
3 through 4	.924	83.745	48	.001

CDA Structure Matrix:	CDA-1	CDA-2	CDA-3
Standards ERP P50 (60-80 ms)	-.113	.311	-.335
Standards ERP N100 (80-140 ms)	-.452	.027	.066
Standards ERP Rising P200 (140-200 ms)	-.05	.219	.569
Standards ERP Late P200 (200-280 ms)	.378	-.027	.161
Standards ERP Late (520-600 ms)	.19	-.148	.249
Standards LOW Early/Mid (20-340 ms)	.44	.213	.033
Standards BETA Early (20-160 ms)	.322	.335	.027
Standards GAMMA Early (20-100 ms)	.193	.458	.091
Standards GAMMA Mid (180-200 ms)	-.153	.076	-.252
Standards GAMMA Mid-2 (220-260 ms)	-.186	.125	-.175

Targets Frontal ERP N100 (80-140 ms)	-.352	-.139	-.088
Targets BETA Late (420-560 ms)	-.227	-.084	.027
Targets Frontal ERP P2/N2 (140-240 ms)	-.23	.27	.24
Targets Frontal ERP P3a (280-360 ms)	.213	-.056	.454
Targets Frontal ERP Late (420-580 ms)	-.245	-.013	.399
Targets Parietal ERP N100 (60-140 ms)	-.248	.193	.205
Targets Parietal ERP N200 (140-260 ms)	-.502	.253	-.007
Targets Parietal ERP Early P300 (320-420 ms)	.373	.094	.137
Targets Parietal ERP Late P300 (420-600 ms)	.313	.154	.082
Targets LOW Early (40-160 ms)	.31	.233	.064
Targets LOW Late (300-440 ms)	.437	.124	.152
Targets LOW Mid (160-300 ms)	.483	.087	.213
Targets BETA Mid (140-220 ms)	.241	.232	-.06
Targets GAMMA Mid (140-180 ms)	-.142	.107	-.255
Targets GAMMA Mid-2 (240-280 ms)	-.143	.13	-.177
Targets GAMMA Late (340-600 ms)	-.19	.006	-.228

Table S5: CCA Cognition Structure Matrix

COGNITION		NEURAL	
BACS: Verbal Memory	.70	Standards ERP P50 (60-80 ms)	-.23
BACS: Digit Sequencing	.65	Standards ERP N100 (80-140 ms)	-.52
BACS: Token Motor	.64	Standards ERP Rising P200 (140-200 ms)	-.02
BACS: Verbal Fluency	.60	Standards ERP Late P200 (200-280 ms)	.33
BACS: Symbol Coding	.89	Standards ERP Late (520-600 ms)	.16
BACS: Tower of London	.68	Standards LOW Early/Mid (20-340 ms)	.54
		Standards BETA Early (20-160 ms)	.32
		Standards GAMMA Early (20-100 ms)	.10
		Standards GAMMA Mid (180-200 ms)	-.29
		Standards GAMMA Mid-2 (220-260 ms)	-.28
		Targets Frontal ERP N100 (80-140 ms)	-.42
		Targets Frontal ERP P2/N2 (140-240 ms)	-.25
		Targets Frontal ERP P3a (280-360 ms)	.26
		Targets Frontal ERP Late (420-580 ms)	-.27
		Targets Parietal ERP N100 (60-140 ms)	-.42
		Targets Parietal ERP N200 (140-260 ms)	-.49
		Targets Parietal ERP Early P300 (320-420 ms)	.48
		Targets Parietal ERP Late P300 (420-600 ms)	.44
		Targets LOW Early (40-160 ms)	.46
		Targets LOW Mid (160-300 ms)	.63

	Targets LOW Late (300-440 ms)	.62
	Targets BETA Mid (140-220 ms)	.21
	Targets BETA Late (420-560 ms)	-.19
	Targets GAMMA Mid (140-180 ms)	-.26
	Targets GAMMA Mid-2 (240-280 ms)	-.24
	Targets GAMMA Late (340-600 ms)	-.31

Table S6: CCA Clinical Structure Matrix

CLINICAL		NEURAL	
PANSS Positive	-.34	Standards ERP P50 (60-80 ms)	-.13
PANSS Negative	-.34	Standards ERP N100 (80-140 ms)	.24
PANSS General	.12	Standards ERP Rising P200 (140-200 ms)	.46
MADRS	.48	Standards ERP Late P200 (200-280 ms)	-.05
YOUNG MANIA	.23	Standards ERP Late (520-600 ms)	.15
Social Functioning	.36	Standards LOW Early/Mid (20-340 ms)	-.31
		Standards BETA Early (20-160 ms)	-.16
		Standards GAMMA Early (20-100 ms)	.03
		Standards GAMMA Mid (180-200 ms)	.19
		Standards GAMMA Mid-2 (220-260 ms)	.14
		Targets Frontal ERP N100 (80-140 ms)	.34
		Targets Frontal ERP P2/N2 (140-240 ms)	.14
		Targets Frontal ERP P3a (280-360 ms)	.16
		Targets Frontal ERP Late (420-580 ms)	.51
		Targets Parietal ERP N100 (60-140 ms)	.36
		Targets Parietal ERP N200 (140-260 ms)	.29
		Targets Parietal ERP Early P300 (320-420 ms)	-.35
		Targets Parietal ERP Late P300 (420-600 ms)	-.32
		Targets LOW Early (40-160 ms)	-.16
		Targets LOW Mid (160-300 ms)	-.20
		Targets LOW Late (300-440 ms)	-.23

	Targets BETA Mid (140-220 ms)	.03
	Targets BETA Late (420-560 ms)	.24
	Targets GAMMA Mid (140-180 ms)	.15
	Targets GAMMA Mid-2 (240-280 ms)	.09
	Targets GAMMA Late (340-600 ms)	.08

Table S7: Medications Associations

	Antipsychotics		Antidepressants		Lithium		Anticonvulsants		Stimulants		Anxiolytics	
	r	p	r	p	r	p	r	p	r	p	r	p
Standards ERP P50 (60-80 ms)	-.057	.148	.096*	.015	.032	.422	-.034	.384	-.001	.977	.016	.691
Standards ERP N100 (80-140 ms)	.114**	.004	.062	.118	.072	.069	.013	.734	-.059	.139	.033	.405
Standards ERP Rising P200 (140-200 ms)	.049	.213	-.063	.110	.055	.161	.025	.532	-.009	.825	-.024	.544
Standards ERP Late P200 (200-280 ms)	-.153**	.000	-.067	.090	.046	.246	-.069	.081	.003	.940	-.095*	.016
Standards ERP Late (520-600 ms)	-.039	.321	-.081*	.041	-.006	.886	-.021	.593	-.043	.278	-.074	.060
Standards LOW Early/Mid (20-340 ms)	-.064	.108	.020	.606	.066	.096	.013	.751	.078*	.048	.044	.262
Standards BETA Early (20-160 ms)	-.028	.475	.027	.501	.047	.237	-.010	.795	.092*	.020	.081*	.041
Standards GAMMA Early (20-100 ms)	.016	.689	.027	.499	.017	.676	.002	.968	.065	.098	.037	.352
Standards GAMMA Mid (180-200 ms)	-.040	.312	.008	.847	.023	.565	.004	.921	.014	.723	.004	.912
Standards GAMMA Mid-2 (220-260 ms)	-.028	.475	.009	.827	.022	.570	.013	.748	-.023	.555	-.055	.167
Targets Frontal ERP N100 (80-140 ms)	.069	.080	.046	.245	-.001	.972	-.030	.450	-.056	.155	-.022	.586
Targets BETA Late (420-560 ms)	.069	.083	.097*	.014	.032	.413	.008	.846	-.009	.813	.049	.219
Targets Frontal ERP P2/N2 (140-240 ms)	-.006	.888	-.119**	.003	.045	.260	-.081*	.040	-.013	.738	-.010	.791
Targets Frontal ERP P3a (280-360 ms)	.138**	.000	-.044	.264	-.049	.213	.015	.706	-.003	.936	.019	.627

Targets Frontal ERP Late (420-580 ms)	.098*	.013	-.051	.195	-.070	.076	.108**	.006	-.018	.658	-.042	.291
Targets Parietal ERP N100 (60-140 ms)	.188**	.000	-.016	.695	-.074	.061	.100*	.011	.029	.470	.085*	.031
Targets Parietal ERP N200 (140-260 ms)	-.026	.517	-.022	.570	.055	.162	-.062	.116	.045	.252	.018	.640
Targets Parietal ERP Early P300 (320-420 ms)	-.035	.381	.020	.607	.115**	.003	-.035	.378	.013	.747	.047	.238
Targets Parietal ERP Late P300 (420-600 ms)	-.044	.271	.007	.851	.062	.116	.016	.689	.121**	.002	.061	.121
Targets LOW Early (40-160 ms)	-.066	.097	.007	.855	.050	.205	-.043	.277	.077	.051	.030	.445
Targets LOW Late (300-440 ms)	-.075	.058	-.015	.696	.080*	.044	-.023	.567	.072	.069	.017	.671
Targets LOW Mid (160-300 ms)	-.051	.197	-.027	.499	.079*	.045	-.029	.465	.087*	.028	.078*	.049
Targets BETA Mid (140-220 ms)	.044	.262	-.045	.250	.015	.704	.024	.545	.055	.168	.056	.153
Targets GAMMA Mid (140-180 ms)	-.051	.200	.000	.992	.051	.200	-.014	.720	-.012	.760	-.047	.231
Targets GAMMA Mid-2 (240-280 ms)	-.023	.569	.022	.574	.052	.191	-.019	.639	-.032	.416	-.019	.630
Targets GAMMA Late (340-600 ms)	-.041	.302	.021	.603	.036	.366	-.022	.572	-.034	.395	-.028	.476

Note. Uncorrected Spearman correlations with on/off status and EEG measures. *p<.05, ** p<.01 two tailed

Table S8: Medication details by group

	HC	SZ	SAD	BDP	BDNP
% with medication information	99	96	99	98	99
% on any medication	48	88	93	91	91
Total medication count- mean	1.11	3.99	4.78	4.61	5.11
Total medication count- SD	1.66	2.89	3.49	3.89	4.00
Psychotropic count- mean	.07	2.22	2.66	2.73	2.78
Psychotropic count- SD	.35	1.44	1.66	1.99	1.62
% on psychotropic medication	6	88	90	88	92
% on antipsychotic	0	84	79	65	39
% on first generation AP	0	21	14	1	2
% on second generation AP	0	72	71	65	39
% on antidepressant	3	43	52	44	60
% on tricyclic	0	1	2	2	9
% on MAOI	0	0	0	0	2
% on SSRI	2	32	40	26	34
% on other antidepressant	1	19	22	29	35
% on mood stabilizer	1	22	46	65	68

% on lithium	0	5	12	23	26
% on anticonvulsant	1	18	40	50	51
% on anxiolytic/sedative/hypnotic	2	15	21	28	37
% on anticholinergic/antiparkinsonian	0	22	16	3	2
% on stimulant	1	1	5	6	11
% on other psychotropic	0	6	6	10	15

Table S9

Differences in medication status between clinical groups

	Statistic	*p*
Total medications	$F(3) = 2.64^{*}$	.048
Total psychotropic medications	$F(3) = 4.12^{**}$	.007
On antipsychotic	$x^2(3) = 6.55^{***}$	<.001
On antidepressant	$x^2(3) = 8.53^{*}$	.04
On SSRI	$x^2(3) = 9.09^{*}$	.03
On mood stabilizer	$x^2(3) = 85.83^{***}$	<.001
On lithium	$x^2(3) = 36.51^{***}$	<.001
On anticonvulsant	$x^2(3) = 52.87^{***}$	<.001
On anxiolytic/sedative/hypnotic	$x^2(3) = 18.58^{***}$	<.001
On anticholinergic/ antiparkinsonian	$x^2(3) = 37.93^{***}$	<.001

Note. $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Table S10

Lithium dosage information by clinical group

	SZ	SAD	BDP	BDNP	F(3)	*p*
N on lithium with data	7	18	31	13		
Mean dose	678.57	822.78	922.58	865.38	.74	.53
Dose SD	513.04	34.39	446.484	352.60		

Note. Doses are reported in mg/day.

Table S11

Chlorpromazine (CPZ) dose equivalents by clinical group

	SZ	SAD	BDP	BDNP	F(3)	*p*
N on antipsychotics with data	143	138	87	19		
Mean dose	725.06	595.72	298.94	264.53	3.69	.01
Dose SD	1217.15	116.95	284.18	275.14		

Note. Doses are reported in mg/day.

Table S12

Jackknife Stepwise Linear Discriminant (95% of the sample)

EEG Variables	Number of times in STEPWISE (1000 Iterations: 95% of Sample)	Percentage in Stepwise Iterations	Average F-Value
Standards ERP Late P200 (200-280 ms)	1000	100	5.88
Targets Frontal ERP P2/N2 (140-240 ms)	1000	100	9.61
Targets Parietal ERP N200 (140-260 ms)	1000	100	18.59
Targets BETA Mid (140-220 ms)	1000	100	5.92
Targets BETA Late (420-560 ms)	1000	100	10.24
Targets LOW Mid (160-300 ms)	998	99.8	8.30
Standards ERP Rising P200 (140-200 ms)	991	99.1	5.31
Standards ERP P50 (60-80 ms)	760	76	3.06
Standards GAMMA Early (20-100 ms)	610	61	3.79
Standards BETA Early (20-160 ms)	582	58.2	7.76
Standards LOW Early/Mid (20-340 ms)	456	45.6	13.04
Targets Frontal ERP N100 (80-140 ms)	358	35.8	2.75
Standards ERP N100 (80-140 ms)	265	26.5	12.83
Targets Frontal ERP P3a (280-360 ms)	219	21.9	5.19
Targets Parietal ERP Early P300 (320-420 ms)	158	15.8	7.49
Targets Frontal ERP Late (420-580 ms)	152	15.2	3.05
Targets Parietal ERP N100 (60-140 ms)	29	2.9	2.53
Standards ERP Late (520-600 ms)	23	2.3	2.54
Targets LOW Early (40-160 ms)	10	1	2.65
Standards GAMMA Mid-2 (220-260 ms)	6	0.6	3.11
Targets LOW Late (300-440 ms)	6	0.6	3.37
Standards GAMMA Mid (180-200 ms)	4	0.4	2.43
Targets GAMMA Late (340-600 ms)	3	0.3	3.87

Targets Parietal ERP Late P300 (420-600 ms)	1	0.1	2.42
Targets GAMMA Mid (140-180 ms)	1	0.1	2.68
Targets GAMMA Mid-2 (240-280 ms)	0	0	N/A

Table s13:
Canonical Discriminant Analysis Variate Means using Top 10 Variables from Table S11. Values are in Standardized Units.

		HC		BDNP		BDP		SAD		SZ		BDNP	BDP	SAD	SZ
	Average F-Value (4,1068)	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Glass Delta			
JK-CDA Variate 1:	69.26	0.50	0.94	0.05	0.81	0.09	0.87	-0.54	0.87	-0.51	0.86	-0.47	-0.44	-1.10	-1.06
JK-CDA Variate 2:	13.32	-0.01	1.00	0.79	1.16	-0.24	0.95	-0.04	0.83	0.01	1.02	0.80	-0.23	-0.03	0.02
JK-CDA Variate 3:	8.35	0.11	0.97	-0.23	0.94	-0.34	0.96	0.15	1.07	0.00	0.97	-0.35	-0.46	0.04	-0.11

Pearson Correlation	**r-value**	**p-value**
CDA-1 vs JK-CDA 1	.96	< .0001
CDA-2 vs JK-CDA 2	.79	< .0001
CDA-3 vs JK-CDA 3	.75	< .0001

Supplemental Figures

Figure S1: Frequency Principal Component Analysis. The PCA factor weights of each component are plotted for each frequency from 3-52 Hz. The three components accounted for >95% of the variance.

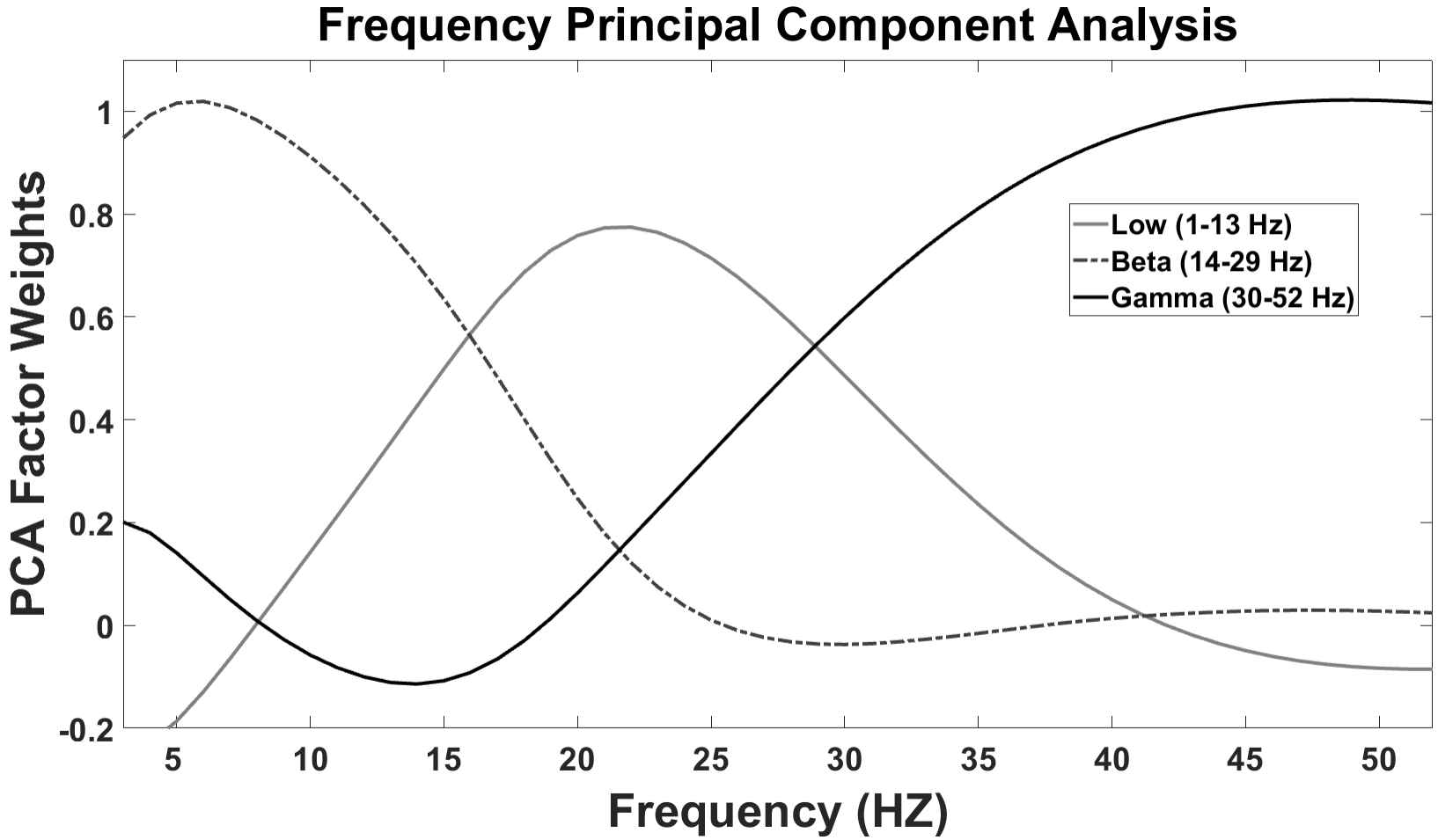
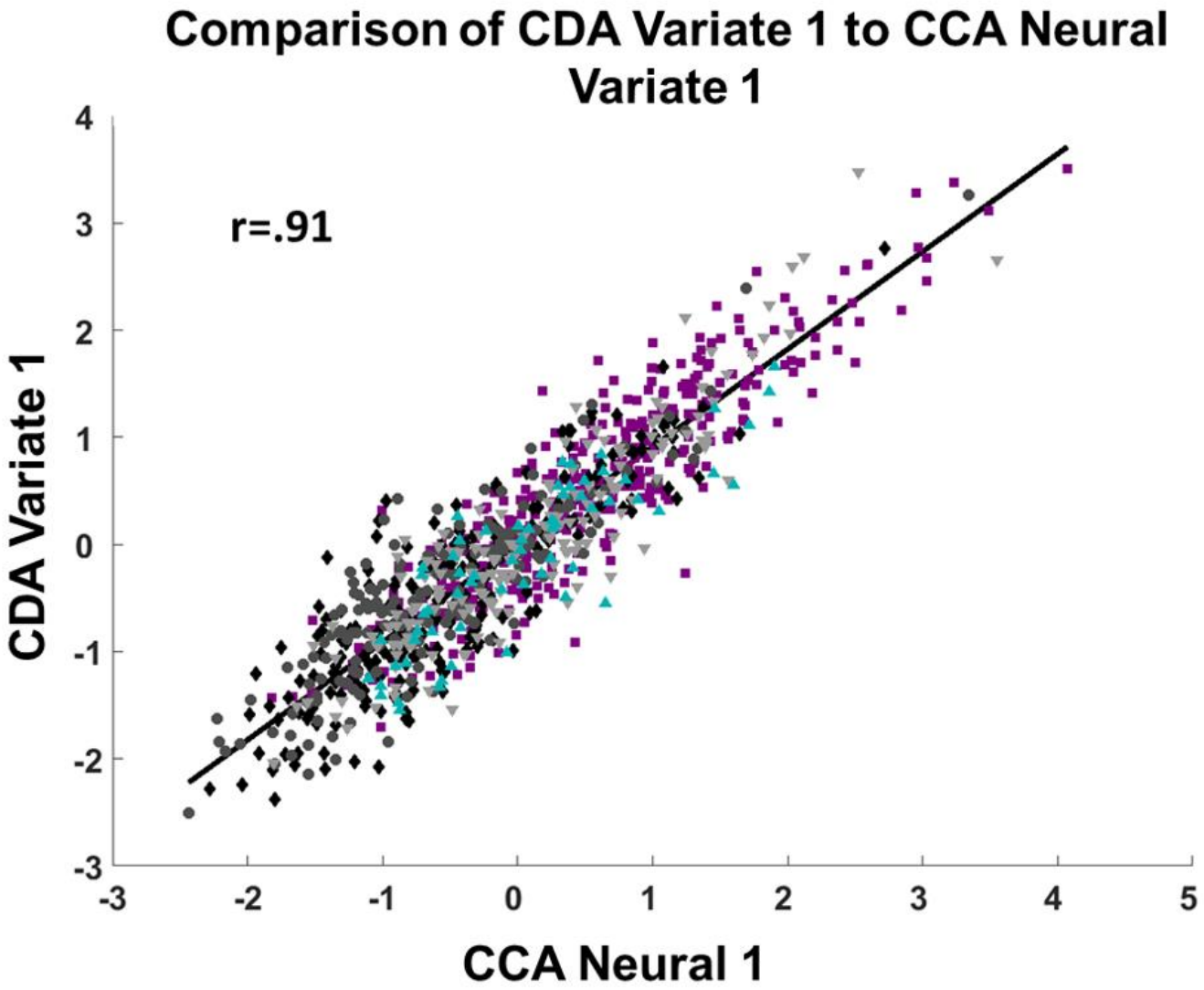


Figure S2: Scatter plot of the CDA neural values in comparison to the CCA neural values. Two-tailed Pearson correlation with a total



n=987.

Figure S3:
Top: **B-SNIP1 vs B-SNIP2 sample group x study effect sizes (95% CI) for each ERP component across each 20 ms time-bin.** An F effect size of .1 indicates a small effect size. No Group x Study p-values were <.05 after FDR correction. Effect size plots are not corrected for multiple comparisons.

Bottom: Total Study, HC, and Psychosis equivalence contrasts in common language effect sizes (90% CI) for each ERP component across each 20 ms time-bin. An effect size of .5 indicates no difference between samples. Contrast= B-SNIP1 – B-SNIP2. Contrasts effect size plots are not corrected for multiple comparisons. See supplemental methods for additional details.