SUPPLEMENTARY MATERIAL: Diminished Variability of Alpha and Beta Band-limited Power as a Neural Signature in Schizophrenia

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1 Supplementary Methods

1.1 Study cohort information

All participants in the SZ group had a diagnosis of the condition according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) [1]. Clinical assessment including diagnosis and evaluation of psychiatric symptoms via the PANSS [2] were performed by trained psychiatrists. Exclusion criteria for both groups included history of stroke, intellectual disability, history of epilepsy, substance abuse, and history of head injury with loss of consciousness for over ten minutes. Furthermore, presence or history of any mental disorder according to DSM-5 was an exclusion criterion for HC participants, while presence of an additional condition besides SZ resulted in exclusion from the patient group. Members of the patient cohort were on medication at the times of EEG recordings and PANSS assessment. For more details on medication and symptom characteristics in the SZ group, please see Table 1 in [3].

1.2 Surrogate data testing

We utilized the phase randomization technique introduced by Theiler and coworkers [4]. In that, we took the original, 30-second (pre-processed) EEG time series, performed Fourier transformation, and then randomized the phases before inverse Fourier transformation. Therefore, if observed changes in spectral dynamics were a consequence of nonlinearity, we should see reduced temporal variability of alpha BLP in the surrogate time series. For every participant, a set of $n = 100$ surrogates were generated and we repeated the sliding window analysis on these surrogate datasets focusing only on $\sigma(\alpha\text{-}BLP^{EC}_{mixd})$. Presence of nonlinearity was statistically confirmed, if a z-test indicated with $p < 0.05$ certainty that the true spectral index ($\sigma(\alpha\text{-}BLP^{EC}_{mixd})$) did not come from the same distribution as those obtained from surrogates.

1.3 Confirmation analysis and dataset

We analyzed the dataset made available by Olejarczyk & Jernajczyk [5], containing recordings from 14 patients with paranoid SZ and 14 age- and sex-matched HC individuals. We limited our analysis on $\sigma(\alpha\text{-}BLP^{EC}_{mixd})$ due to the inherit charactristics of the published EEG data. Namely, EEG was collected from 19 cortical locations according to a standardized 10-20 montage EEG data, sampled at 250 Hz. The published data was band-pass filtered with a high-pass filter at 1 Hz and a low-pass filter at 45 Hz. This ultimately reduced the available frequency range for IRASA decomposition with the current parameter settings, as applying a resampling with factor $h = 2.6$ would have introduced the filtering effects at about 20 Hz [6]). Additionally, clinical (PANSS scores) and demographic was unavailable for the sample in [5]). These characteristics prevented us to replicate our exact analysis pipeline on this dataset.

1.4 Correlation analyses regarding medication

Correlation analyses between global EEG indices and CPZ equivalent dose values were carried out along similar considerations as described in the main text. Only global EEG indices that showed significant between-group differences in SZ were included in this analysis. While the goal was to assess correlation between EEG markers and CPZ, other confounders such as age, sex, years in education and disease duration were regressed out from both EEG indices and CPZ values. Investigating the relationship between PANSS scores and CPZ was conducted according to the same principles.

References

[1] Association, A.P., *et al.*: Diagnostic and Statistical Manual of Mental Disorders: DSM-5. American psychiatric association, ??? (2013)

[2] Kay, S.R., Fiszbein, A., Opler, L.A.: The positive and negative syndrome scale (panss) for schizophrenia. Schizophrenia bulletin **13**(2), 261–276 (1987)

[3] Racz, F.S., Farkas, K., Becske, M., Molnar, H., Fodor, Z., Mukli, P., Csukly, G.: Reduced temporal variability of cortical excitation/inhibition ratio in schizophrenia. Schizophrenia **11**(1), 20 (2025)

[4] Theiler, J., Eubank, S., Longtin, A., Galdrikian, B., Farmer, J.D.: Testing for nonlinearity in time series: the method of surrogate data. Physica D: Nonlinear Phenomena **58**(1-4), 77–94 (1992)

[5] Olejarczyk, E., Jernajczyk, W.: Graph-based analysis of brain connectivity in schizophrenia. PloS one **12**(11), 0188629 (2017)

[6] Racz, F.S., Farkas, K., Stylianou, O., Kaposzta, Z., Czoch, A., Mukli, P., Csukly, G., Eke, A.: Separating scale-free and oscillatory components of neural activity in schizophrenia. Brain and behavior **11**(5), 02047 (2021)

Supplementary Figures

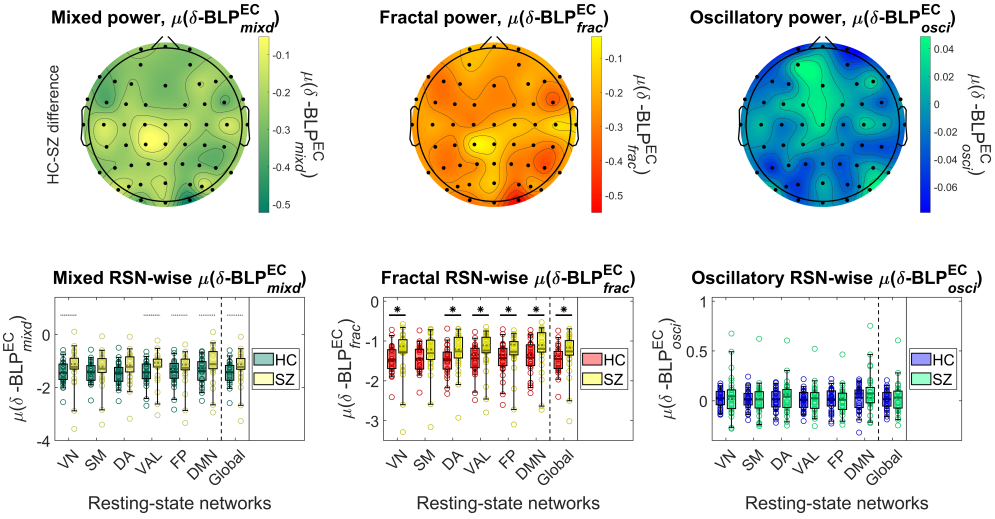

Fig. 1 Difference between average eyes-closed (EC) delta band-limited power (BLP) between healthy control (HC) and schizophrenia (SZ) groups in mixed (left), fractal (middle) and oscillatory (right) spectra. Top panels show the whole-brain topology of HC-SZ with negative values indicating HC¡SZ, while lower panels illustrate results on the level of resting-state networks (RSNs). Asterisk symbols indicate significant HC vs. SZ difference ($p < 0.05$, adjusted).

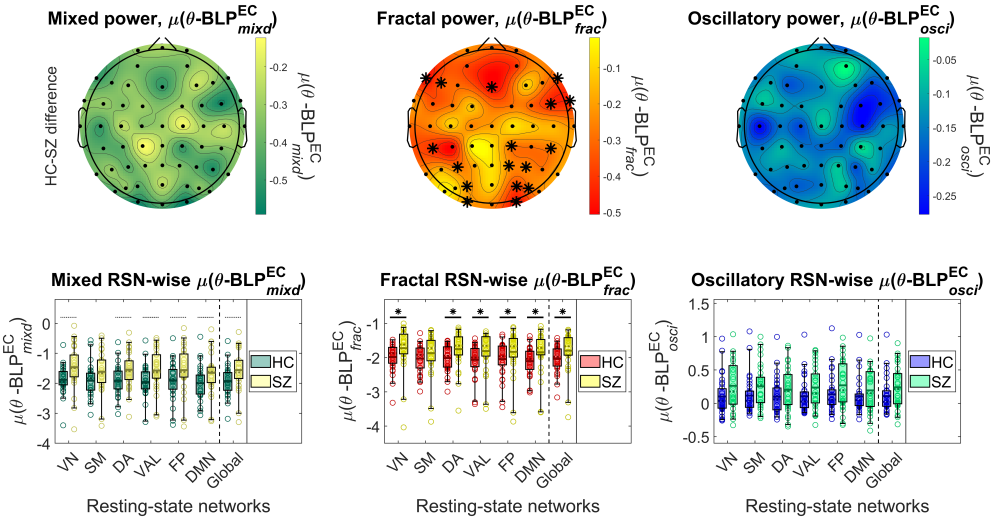

Fig. 2 Difference between average eyes-closed (EC) theta band-limited power (BLP) between healthy control (HC) and schizophrenia (SZ) groups in mixed (left), fractal (middle) and oscillatory (right) spectra. Top panels show the whole-brain topology of HC-SZ with negative values indicating HC<SZ, while lower panels illustrate results on the level of resting-state networks (RSNs). Asterisk symbols indicate significant HC vs. SZ difference ($p < 0.05$, adjusted).

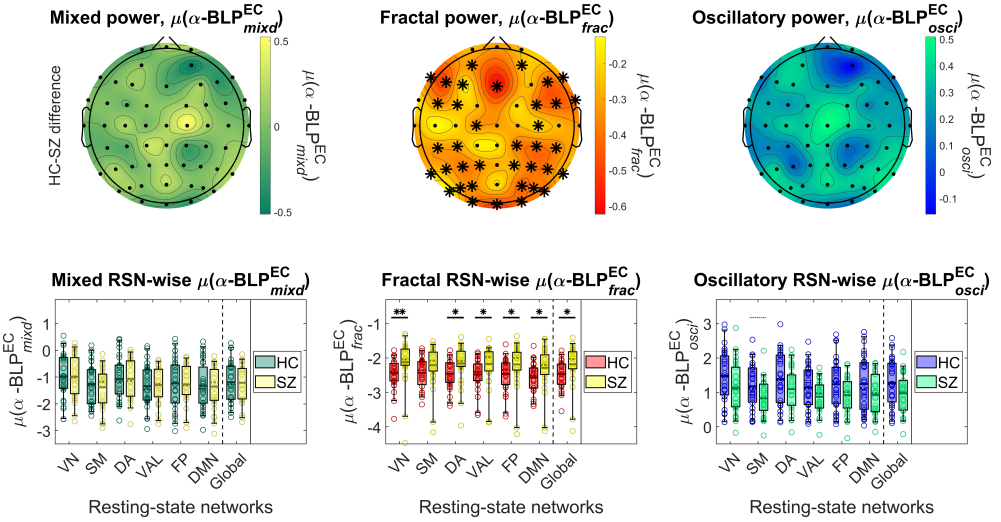

Fig. 3 Difference between average eyes-closed (EC) alpha band-limited power (BLP) between healthy control (HC) and schizophrenia (SZ) groups in mixed (left), fractal (middle) and oscillatory (right) spectra. Top panels show the whole-brain topology of HC-SZ with negative values indicating HC¡SZ, while lower panels illustrate results on the level of resting-state networks (RSNs). Asterisk symbols indicate significant HC vs. SZ difference (*: $p < 0.05$, **: $p < 0.01$, adjusted).

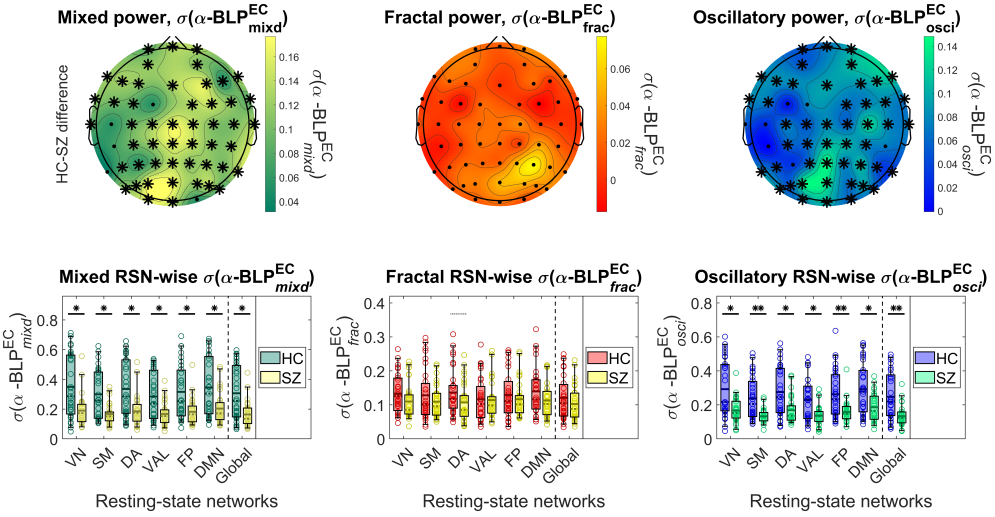

Fig. 4 Difference in temporal variance of eyes-closed (EC) alpha band-limited power (BLP) between healthy control (HC) and schizophrenia (SZ) groups in mixed (left), fractal (middle) and oscillatory (right) spectra. Top panels show the whole-brain topology of HC-SZ with negative values indicating HC<SZ, while lower panels illustrate results on the level of resting-state networks (RSNs). Asterisk symbols indicate significant HC vs. SZ difference (*: $p < 0.05$, **: $p < 0.01$, adjusted).

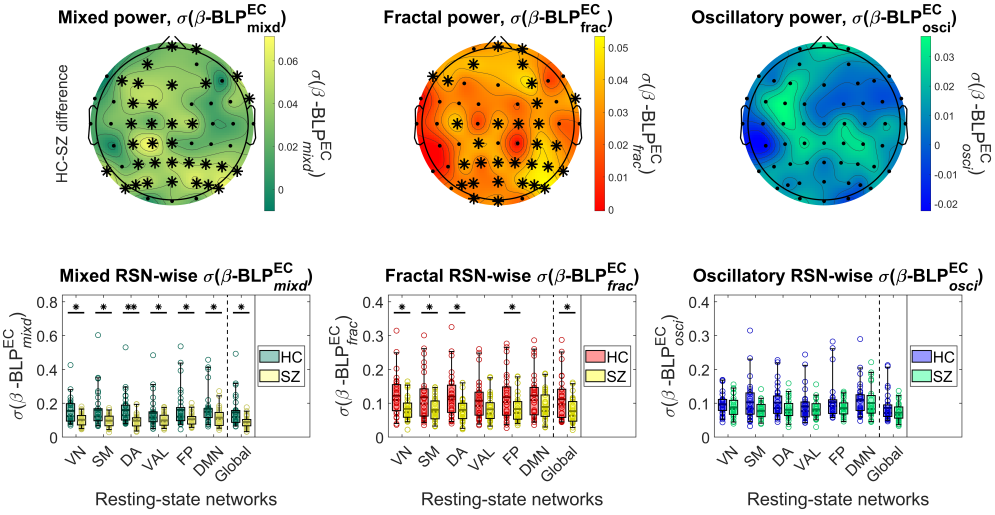

Fig. 5 Difference in temporal variance of eyes-closed (EC) beta band-limited power (BLP) between healthy control (HC) and schizophrenia (SZ) groups in mixed (left), fractal (middle) and oscillatory (right) spectra. Top panels show the whole-brain topology of HC-SZ with negative values indicating HC<SZ, while lower panels illustrate results on the level of resting-state networks (RSNs). Asterisk symbols indicate significant HC vs. SZ difference (*: $p < 0.05$, **: $p < 0.01$, adjusted).

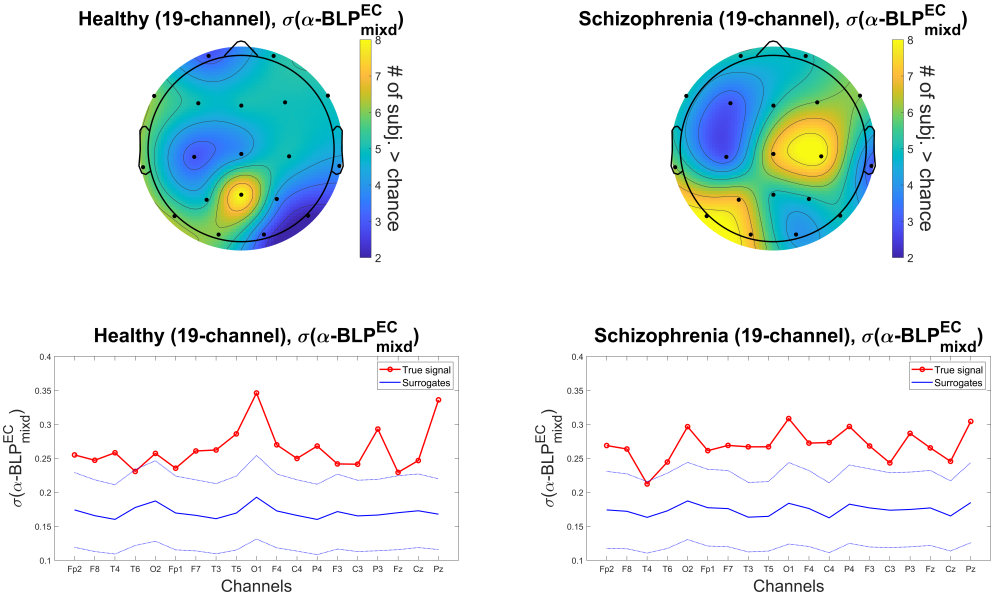

Fig. 6 Results of surrogate data analysis in HC (left) and SZ (right) groups on the 19-channel EEG dataset. Upper panels: number of participants for given locations where nonlinearity could be confirmed. Lower panels: grand average actual $\sigma(\alpha\text{-}BLP^{EC}_{mixd})$ (red) contrasted with those obtained from surrogate data (blue). Continuous line denotes the mean, while dotted line denotes standard deviation from the mean.

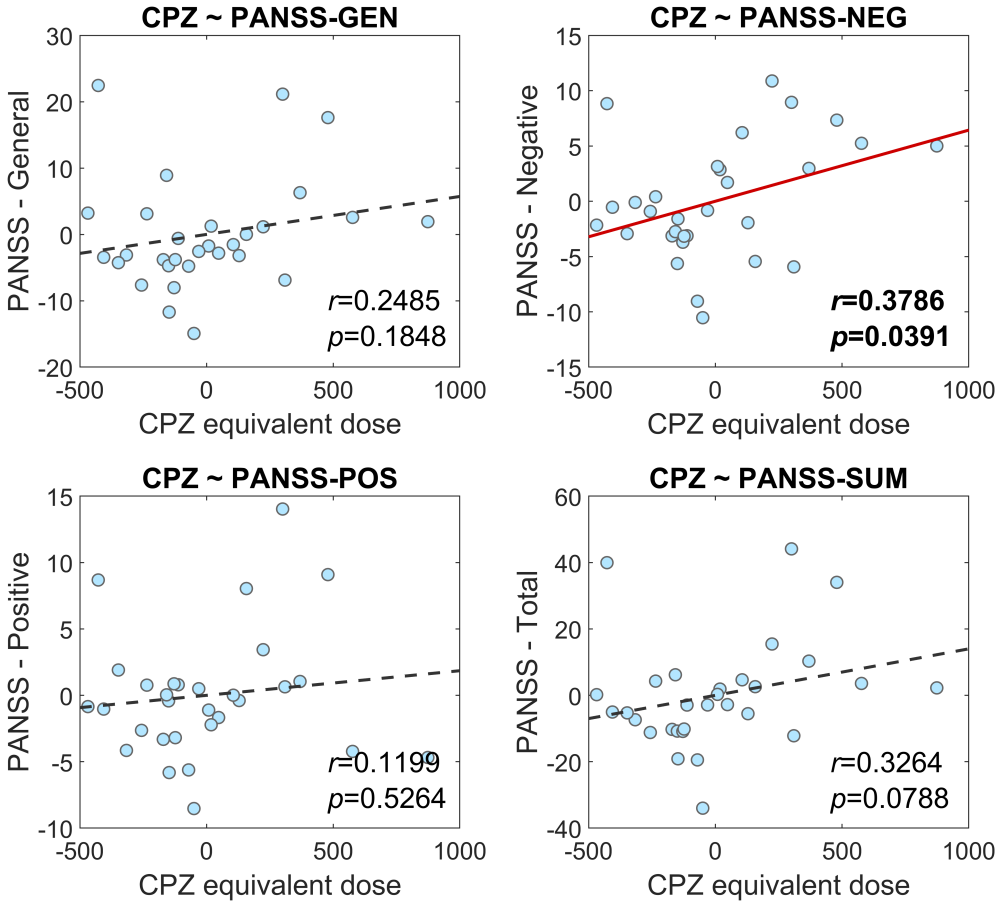

Fig. 7 Correlation analysis between CPZ doses and PANSS scores for general (upper left), negative (upper right), positive (lower left) and all symptoms combined (lower right). A continuous red trend line and bold text indicates significant correlation ($p < 0.05$) between medication and symptoms, while gray dashed line illustrates the trend otherwise. All variables were adjusted for potential confounding effects of age, sex, years in education and disease duration. CPZ: chlorpromazine equivalent dose; PANSS: positive and negative syndrome scale; GEN: general; NEG: negative; POS: positive; SUM: all symptoms combined.