

This is a repository copy of Spontaneous neural activity relates to psychiatric traits in 16p11.2 CNV carriers: An analysis of EEG spectral power and multiscale entropy.

White Rose Research Online URL for this paper: https://eprints.whiterose.ac.uk/167679/

Version: Supplemental Material

Article:

Al-Jawahiri, R., Jones, M. orcid.org/0000-0002-4580-7559 and Milne, E. orcid.org/0000-0003-0127-0718 (2021) Spontaneous neural activity relates to psychiatric traits in 16p11.2 CNV carriers: An analysis of EEG spectral power and multiscale entropy. Journal of Psychiatric Research, 136. pp. 610-618. ISSN 0022-3956

https://doi.org/10.1016/j.jpsychires.2020.10.036

Article available under the terms of the CC-BY-NC-ND licence (https://creativecommons.org/licenses/by-nc-nd/4.0/).

Reuse

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: https://creativecommons.org/licenses/

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk https://eprints.whiterose.ac.uk/

Supplementary Information

Diagnosis	dup (n = 14)	del (n = 22)
ADHD	2	3
Coordination disorder	6	12
Language disorder	5	9
Learning disorder	2	1
Intellectual disability	3	4
Behaviour disorder	2	3
Borderline intellectual functioning	3	2
ASD	3	3
Enuresis disorder		1
Articulation disorder	1	8
Reactive attachment disorder	1	
Anxiety/OCD/Phobia	2	
Seizures/epilepsy	4	7

Table S1: Diagnoses in 16p11.2 CNV carriers.

Comorbidities or more than one diagnoses are present in this sample.

Seizure / epilepsy diagnoses data were extracted from the nrrf.csv file; all other diagnoses data were found in the diagnosis_summary.csv file.

ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; OCD, obsessive compulsive disorder

EEG recording and pre-processing prior to current study

EEG was recorded using a 128 channel HydroCel Geodesic Net (Electrical Geodesics Inc., Eugene, OR, USA). The signal was amplified with a NetAmps 300 amplifier and digitised at a sampling rate of 500 Hz. Spontaneous EEG was collected for 2 to 12 minutes during which participants rested and watched silent videos on a Tobii T60 eye-tracking monitor (Tobii Technology, Sweden; Note that eye-tracking data was not collected). The monitor was 34.7 cm wide and was positioned at a distance of ~ 60 cm from the participants' seat. Infant participants were seated on their caregiver's lap.

EEG data were previously pre-processed offline, using NetStation software, by collaborators of the SVIP project. A number of pre-processing steps were conducted prior to obtaining the data for the current study. The data were filtered with 1 Hz high pass and 60 Hz notch filter. Missing channels and eye channels were marked bad. Also, excessively noisy channels were marked bad and replaced using interpolation techniques. Channels (including interpolated channels) were referenced to an average reference.

The channels selected for the current study



Fig. S1. Electrical Geodesics Inc. (EGI) 128-channel hydrocel sensor net – **version 1.** The correspondence between the EGI 128 sensor net and the international 10–20 system. The channels circled in green were selected for analyses.

Behavioural and psychiatric assessments

Child Behaviour Checklist for Ages 1.5-5 (CBCL)

Child Behavior Checklist for ages 1.5-5 (CBCL) and IQ participant data were accessed from the Simons VIP Phase 1 16p11.2 dataset at SFARI Base

(http://www.sfari.org/resources/sfari-base). The CBCL/1.5-5 (Rescorla, 2005) is an assessment of parent or caregiver report of behavioral and psychiatric problems in preschool children. The assessment contains 99 statements, which describes child problems, such as 'aches or pains without medical cause' and 'acts too young for age'. The respondent is asked to indicate whether the statements are 'not true' [0], 'somewhat or sometimes true' [1], or 'very true or often true' [2], either presently or within the past two months. The CBCL/1.5-5 identifies the following seven empirically-based syndromes based on the summed scores of items of the respective syndrome: aggressive behavior, anxious/depressed, attention problems, emotionally reactive, somatic complaints, withdrawn, and sleep problems. The CBCL/1.5-5 also yields five DSM-oriented categories: affective problems, anxiety problems, attention deficit/hyperactivity problems, pervasive developmental problems, and oppositional defiant problems. In addition, two aggregate broad-band scales can be derived by grouping items that comprise certain syndromes; these two global groupings are labelled as internalizing problems and externalizing problems. Finally, the sum of all CBCL 1.5-5 items yields a 'total problems' score. The clinical range for the syndromes and DSM-oriented scales is defined as T-scores \geq 70, and the borderline clinical range is T-scores between 65 and 69. For the broadband and total problems scores, the clinical range is T-scores \geq 64, and the borderline range is T-scores between 60 and 63. For the current paper, T-scores of each DSM-oriented scale and T-scores of the syndromic scale 'sleep problems' were taken for correlational analyses with the EEG measures of interest. Data from nine del carriers are missing. CBCL severity in the current del sample is shown in Table S2.

Table S2: CBCL severity in 16p11.2 del.

	Affective problems	Anxiety problems	Pervasive developmental	ADHD	Oppositional defiant	Sleep problems
	50	51	66	64	52	59
	70	50	51	52	50	88
	63	54	70	64	59	51
	56	57	66	50	52	51
	50	50	50	50	50	50
	60	60	86	57	64	56
	50	50	50	51	50	50
	60	50	68	57	59	59
	52	50	51	50	50	50
	77	57	77	67	52	70
	52	51	59	64	55	51
	70	50	66	52	51	50
	67	50	72	57	50	56
	51	50	59	54	50	62
	77	70	72	76	80	88
	72	70	72	71	73	64
Frequency of carriers in the borderline or clinical range.	6	2	10	3	2	3

Data from nine deletion carriers are missing. Bold indicates T-scores > 64, i.e., borderline clinical or clinical range.

IQ

Based on the participants' age, intellectual and cognitive ability was measured either with the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), the Mullen Scales of Early Learning (Mullen, 1995), or the Differential Ability Scales – Early Years & School Age (DAS-II; Elliott, 2007). Standard scores for full-scale IQ, verbal IQ, and non-verbal IQ were obtained from SFARI. Data from three del carriers are missing.

MSE methodology

1) From the original EEG time-series, multiple time-series { $x_1, x_2, ..., x_N$ } are constructed through a coarse graining process. The process involves averaging neighbouring data-points within non-overlapping windows which increase in length as per the determined scale factor (i.e., from 1 to 20 scales in the current study, where 1 signifies the original timeseries and 20 refers to a window size of 20 data-points). The length of the constructed timeseries, therefore, corresponds to N/ τ , where N is the length of the original time-series and τ is the scale factor. The below equation describes the coarse-graining process; Each element, j, of a coarse-grained time-series { $y(\tau)$ } is calculated as such:

$$y_j^{(\tau)} = (1/\tau) \sum_{i=(j-1)\tau+1}^{j\tau} x_i, \quad 1 \le j \le N/\tau$$

2) Then, SampEn is calculated for each coarse-grained time-series $\{y(\tau)\}$. SampEn measures the regularity of a signal: low entropy signifies high regularity and high entropy indicates irregularity (and possibly high complexity). SampEn is defined as the negative natural logarithm of the conditional probability that within a given time-series $\{y(\tau)\}$, similar sequences of data-points of length m will still match at m+1, while excluding self-matches. SampEn, therefore, is calculated according to the equation: SampEn (m, r, N) = - ln (A/B)

Where *m* denotes sequence length; *r* is the similarity criterion or the tolerance range – two data-point sequences are considered matched if their amplitude falls within the similarity criterion, which is usually defined as 20 percent multiplied by the standard deviation of the original time-series; *N* is the length of the original time-series.

A = the number of matched pairs for m+1/ the number of all probable pairs for m+1

B = the number of matched pairs for m/ the number of all probable pairs for m

Table S3: Correlations between MSE, power, and age.

	del	control	dup
		Age	
MSE lower scale	0.06	-0.18	0.14
MSE higher scale	-0.17	-0.24	0.18
δ	-0.09	0.69	0.18
θ	-0.17	0.30	-0.13
α	-0.34	-0.29	0.22
β	0.39	-0.60	0.11

The reported values correspond to Spearman's rank correlation coefficient. All results are non-significant.



The relationship between alpha, theta and entropy timescales 1-5, 5-10, 11-15, 16-20

Fig. S2. The relationship between power (theta and alpha) and entropy (timescales 1-5, 6-10, 11-15, 16-20). Heat maps showing correlations (Spearman's r coefficient) between power and entropy. Asterisk indicates significant results.

References

- Elliott, C., 2007. Differential Ability Scales–Second edition (DAS-II) Harcourt Assessment. San Antonio, TX.
- Mullen, E.M., 1995. Mullen scales of early learning. AGS Circle Pines, MN.
- Rescorla, L.A., 2005. Assessment of young children using the Achenbach System of Empirically Based Assessment (ASEBA. Mental Retardation and Developmental Disabilities Research Reviews 11(3), 226-237.
- Wechsler, D., 1999. Wechsler abbreviated intelligence scale. San Antonio: The Psychological Corporation.