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**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

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# Spontaneous Neural Activity Relates to Psychiatric Traits in 16p11.2 CNV Carriers: An Analysis of EEG Spectral Power and Multiscale Entropy

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**Abstract**

Copy number variations (CNV) at the 16p11.2 chromosomal region are rare high-risk CNVs associated with various clinical features and psychiatric disorders including intellectual disability, developmental delays, and autism spectrum disorder. No study to date has investigated whether spontaneous neural activity is altered for 16p11.2 CNV carriers and whether this relates to psychiatric traits. The aim of this study is to examine the impact of 16p11.2 deletions (del) and duplications (dup) on spontaneous neural activity and its relationship to psychiatric problems. EEG was previously collected as part of the Simons Searchlight initiative. Using spectral power (delta, theta, alpha, and beta frequency bands), complexity index (CI), and multiscale entropy analysis techniques, we analyzed frontal resting-state EEG data collected from 22 16p11.2 del carriers, 14 dup carriers, and 13 controls. We then examined associations between neural activity and psychiatric traits, measured with the Child Behavior Checklist. Results indicated that EEG entropy was higher for del and dup compared to controls, respectively, at all timescales. CI was also higher for del and dup compared to controls. Theta power of 16p11.2 dup carriers was higher than controls. A strong association was found between entropy at higher timescales and anxiety problems. In addition, a strong correlation was found between theta power and pervasive developmental problems. Atypical spontaneous neural activity is implicated in 16p11.2 CNVs. With higher entropy or theta power, psychiatric traits increase in severity. Our findings provide evidence of the link between genotype, neural activity, and phenotypes in 16p11.2 CNVs.

***Keywords:*** 16p11.2 Copy Number Variants, Rare Genetic Syndromes, CBCL, EEG, Resting-State, Entropy.

## Introduction

Deletions (del) and duplications (dup) of the 16p11.2 chromosomal region (~600 kb breakpoints 4–5) are pathogenic copy number variations (CNVs) that increase the risk of developing one or more of the possible associated disorders and difficulties (Shinawi et al., 2010; D'angelo et al., 2016; Hanson et al., 2015; Niarchou et al., 2019). The consequences of this CNV are heterogenous as they vary from one individual to another in their severity and phenotypes (Girirajan and Eichler, 2010; Niarchou et al., 2019), including intellectual disability, developmental delays, autistic and other psychiatric traits. Evidence suggests that 16p11.2 CNV carriers additionally present with atypical neural activity in response to various sensory, sensorimotor, and social stimuli (see **Table 1** for a summary of this work). Overall, anomalies were identified in M/EEG signal features of event-related potentials (and its variability) and power at alpha and beta frequencies, evoked by different events. These studies are pioneering works investigating M/EEG activity in this rare CNV, however further work is necessary to assess features detectable from spontaneous neural activity, using conventional and other promising techniques, such as multiscale entropy (MSE). Entropy features may serve as reliable endophenotypes informing prognosis and treatment progression in 16p11.2 CNV carriers.

Atypical M/EEG entropy has been implicated in various psychiatric disorders that are associated with 16p11.2 CNVs (for a review, see Chu et al., 2017; Takahashi, 2013; Yang and Tsai, 2013), but has not yet been investigated in individuals who have either a deletion or a duplication at this chromosomal region. With MSE analysis (Costa et al., 2002; Costa et al., 2005), in particular, it is possible to quantify the level of entropy or irregularity of moment-to-moment patterns of amplitudes in the signal across different scales. Higher entropy indicates higher irregularity in the signal, while lower entropy indicates a more regular, predictable pattern. Interestingly, both higher and lower entropy have been found in psychiatric disorders (relative to typical controls) in a manner that is task- (e.g., Mišić et al., 2015), scale-, and brain region-dependent (e.g., Ghanbari et al., 2015). For example, compared to controls, higher entropy was found in ASD at higher scales in the occipital, parietal, and temporal areas at resting-state (Takahashi et al., 2016), while lower entropy at higher scales was found in a face and chair detection task (Catarino et al., 2011) in the same brain areas. In addition, Milne et al. (2019) found lower overall entropy in ASD at resting-state across all scales and brain regions. Other psychiatric disorders, associated with 16p11.2

CNVs, that have shown atypical MSE include epilepsy and seizures (Bosl et al., 2017; Lu et al., 2015), attention deficit hyperactivity disorder (ADHD, Chenxi et al., 2016), Schizophrenia (Takahashi et al., 2010), and Alzheimer's (Yang et al., 2013; Mizuno et al., 2010).

To our knowledge, no study has investigated whether EEG neural activity is altered for 16p11.2 CNVs at rest, using either entropy-based approaches or conventional analyses of spectral power. As frontal resting-fMRI activity has been implicated in 16p11.2 del and linked with cognitive and social traits (Bertero et al., 2018), the current study will focus on frontal neural activity and its link to psychiatric traits in 16p11.2 CNVs. Thus, the purpose of the current study is twofold: 1) To determine whether frontal spontaneous neural activity, indexed by EEG power and entropy, in 16p11.2 CNVs is altered compared to controls; 2) To establish whether this spontaneous neural activity is related to psychiatric traits in 16p.11.2 del.

## Methods and Materials

### Data source

The dataset was obtained from the Simons Foundation Autism Research Initiative (SFARI), specifically the Simons Searchlight initiative, previously named Simons Variation in Individuals Project (SVIP, The simons vip consortium, 2012). Datasets collected as part of Simons Searchlight, which include 16p11.2 CNV data, are available to approved researchers via the data request process (https://www.sfari.org/resource/simons-searchlight/). For this study, data of individuals with 16p11.2 deletion, the reciprocal duplication, and typically developing individuals were obtained from SFARI. Participant identification, recruitment, and inclusion/exclusion criteria of Simons Searchlight have been described previously (see The simons vip consortium, 2012; Jenkins et al., 2016; LeBlanc and Nelson, 2016). Briefly, eligibility criteria consisted of having a deletion or duplication of the 16p11.2 region. Exclusion criteria consisted of having any other pathogenic CNVs or known genetic syndromes. The control participants analyzed in this study did not undergo the Simon's VIP battery of assessments. LeBlanc and Nelson (2016) recruited the control group independently through the Boston Children's Hospital participant registry. The group consisted of typical individuals without any neurological or developmental disorders.

### Ethical approval

The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The local institutional ethical review board reviewed and approved the secondary analyses presented here. Our request to obtain access to phenotypic and imaging data on SFARI Base was approved after submitting the required information and signing the joinder to the researcher distribution agreement (https://www.sfari.org/resource/sfari-base/). SFARI obtained initial ethical approval for the SVIP (IRB of record: Columbia University Medical Center, The simons vip consortium, 2012). As part of the SVIP, approval was obtained for data collection on individuals with 16p11.2 deletions or duplications and for their de-identified data to be shared with approved researchers.

### Participants

Data from a total of 53 participants were obtained (n = 14 control, 25 del, and 14 dup). Participants identified as extreme outliers for the respective entropy and power analyses were excluded (n = 1 control and 3 del for MSE and CI analyses; n = 2 control, 3 del, 2 dup for power analyses). Therefore, 49 participants (n = 13 control, 22 del, and 14 dup) were

analyzed using entropy analyses, and 46 participants were analyzed using power analyses (n = 12 control, 22 del, and 12 dup). Participant information (of those included in the entropy group analyses) relating to age, sex, CNV inheritance, number of diagnoses, and IQ scores are reported in **Table 2**.

The diagnoses in the current sample are listed in **Supplementary Table S1**. Information regarding current medication was extracted from the SFARI medication questionnaire; four CNV carriers were currently taking medication for anxiety, ADHD, and epilepsy/ seizures. There was no significant age difference between the three groups ($\chi^2(2) = 1.50$, $p = 0.472$); and no association between group and sex ($\chi^2(2) = 0.36$, $p = 0.834$). Other than age and sex, participant details and phenotypic data were not available for the control group. Therefore, IQ comparisons between del and dup with controls, respectively, were not possible.

**EEG recording and pre-processing**

EEG data collection and some pre-processing were conducted prior to the current study by collaborators of SVIP, as described in **Supplementary Information**. Briefly, using a 128 channel HydroCel Net (Electrical Geodesics Inc., Eugene, OR, USA), EEG was collected for 2 to 12 minutes during which participants rested and watched silent videos on a monitor. Infant participants were seated on their caregiver's lap. Additional pre-processing steps were conducted by the current authors after obtaining the dataset. For each participant, a channel was identified as 'bad' (not suitable for further analyses) if more than 10% of its datapoints were outside of the predefined range [-150 uV, 150 uV]. If a particular channel was bad for more than 11 participants, then the channel was removed for all participants. Under this criterion, 38 channels out of 128 channels were not used for main analyses or as input channels for interpolation where required. From the remaining channels, 27 frontal channels were selected for analysis (**Supplementary Fig. S1**). The frontal channels marked as bad, for the respective participant, were removed and interpolated. On average, two channels [range: 0, 13] were interpolated per participant. The signal was then detrended by removing the linear trend in the data. (Note that embedded in the sample entropy function described later, the mean is subtracted and divided by the standard deviation of the signal prior to computing sample entropy).

## Behavioral and psychiatric assessments

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 CBCL yields the following categories based on the summed scores of items of the respective category: affective problems, anxiety problems, attention deficit/hyperactivity problems, pervasive developmental problems, oppositional defiant problems, and sleep problems. For this paper, T-scores of each category were taken for correlational analyses with the EEG measures of interest. Data from nine del carriers are missing. See **Supplementary Information** for details regarding the CBCL assessment and the CBCL severity levels in the current sample (**Supplementary Table S2**), in addition to details regarding the previously conducted IQ assessments.

## EEG measures

### *Multiscale entropy*

Multiscale entropy (MSE) analysis was performed on scales 1-20 for a continuous EEG signal of 60,000 data-points (2 minutes; 500 Hz sampling rate). From the whole signal of length <10 minutes, the chosen two-minute segment range was from 8000 to 68,000 data-points. (This range allows the exclusion of the first 16 seconds of recording in order to avoid potentially contaminated data due to participant movement and other artifacts while the participant became settled at the start of the session. Visual inspection of the data suggested that 'noise' was often present within the first 16 seconds of recording). The following software and toolboxes were used for the analyses, MATLAB (The MathWorks Inc.), EEGlab toolbox (Delorme and Makeig, 2004), and multiscale entropy toolbox (http://www.psynetresearch.org/tools.html) (Liang et al., 2014). The MSE method measures sample entropy (Richman and Moorman, 2000) on multiple time scales (see **Supplementary Information**, Costa et al., 2002, 2005). MSE consists of two main steps as follows. Based on previous M/EEG studies (e.g., Takahashi et al., 2016; Ghanbari et al., 2015) and recommendations by Richman and Moorman (2000), the following MSE parameters were chosen: $m$ was set to 2 and $r = 0.2$. MSE was first determined for each channel and then averaged over the frontal region, in line with Takahashi et al. (2016). Entropy of scales 1-20 was averaged into four bins: scales of 1-5, 6-10, 11-15, and 16-20. The data was further

reduced for correlation analyses; Entropy was averaged into two 'bins' of scales 1-10 and 11-20.

***Complexity index***

The complexity index (CI) is another measure of entropy as described by Costa et al. (2005). For each channel, CI was computed by estimating the area under the MSE curve via integrating entropy values of all scales by using a trapezoidal numerical integration via the 'trapz' function in MATLAB. The average CI was then calculated over channels at the frontal region.

***Power spectral density***

Power spectral density (PSD) of each channel was computed using the 'pwelch' MATLAB function. The signal was first detrended and subtracted from the mean signal amplitude. In accordance with Welch's method, the signal (60,000 data-points or 2 minutes) was divided into segments of equal length (2-second segments in this case) with a 50% overlap. Given a sampling rate of 500 Hz and N = 1000 data-points per segment, the resultant frequency resolution was 0.5 Hz. Each segment was windowed with a Hamming window and modified periodograms (PSDs of each Hamming window) were estimated. The final PSD was obtained by averaging the periodograms of all segments. Absolute and relative power were then computed for the following frequency bands: delta [2-4 Hz], theta [4-8 Hz], alpha [8-14 Hz], and beta [14-30 Hz]. Absolute power of each frequency band was obtained via the trapezoidal integration method, using the 'trapz' MATLAB function. Prior to obtaining the relative power, the total spectral power was defined as the entire range between 1-50 Hz (the upper limit was set to avoid the frequency range effectively removed by a notch filter applied at 60 Hz). Relative power at each frequency band was subsequently calculated as the ratio of power of the respective frequency band to the total spectral power defined earlier. Relative power of each frequency band was respectively averaged over the frontal region.

**Statistical analyses**

Permutation tests (Rodgers, 1999) were conducted to investigate whether there were group differences in neural activity in the frontal region between del/control, dup/control, and del/dup comparisons. This was conducted, as described previously in Al-Jawahiri et al. (2019). To account for multiple comparisons, the false discovery rate (FDR) was controlled using the Benjamini-Hochberg procedure, with $q < 0.05$. We also applied the permutation approach to Spearman's correlation analyses to examine whether age, IQ, and psychiatric

traits (i.e., CBCL) impact neural responses in 16p11.2 CNV. All the outcomes were corrected by controlling the FDR using the Benjamini-Hochberg procedure, with $q < 0.05$. Correlation permutation tests between age and neural responses were performed separately for del, dup, and control groups (initial sample size: n = 14 control, n = 14 dup, n = 25 del). Prior to conducting analyses, outliers were identified, using Cook's distance, for the respective correlation pairs and removed (control: median number of outliers = 2, range = [1, 2]; dup: median = 1.5, range = [1, 2]; del: median = 2.5, range = [2, 3]). As IQ and CBCL data were either not available or insufficient for the control and dup groups (n = 14 prior to excluding outliers for IQ vs EEG measures' correlations for dup), correlation permutation analyses were conducted for only the del group (n = 25). However, there were some missing IQ (n = 3) and CBCL (n = 9) data for del. Outliers from the remaining IQ (n = 22) and CBCL (n = 16) data were removed (median number of outliers = 2; range = [0, 4]) prior to conducting analyses.

## Results

### Multiscale entropy

Significant group differences ($p \leq 0.033$) were found in entropy at all the respective scales (i.e., 1-5, 6-10, 11-15, and 16-20) in the frontal region (**Table 3**; **Fig. 1A**). Specifically, entropy was higher in both del and dup than controls. No significant differences in entropy were found between del and dup.

### Complexity index

CI was significantly higher for del and dup compared to controls, respectively ($p \leq 0.033$), at the frontal region (**Table 3**; **Fig. 1B**). No significant difference in CI was found between del and dup.

### Power spectral density

**Fig. 2** shows the average spectra used to derive the relative power for each group. Group differences in relative power within each frequency band (delta, theta, alpha, and beta) at the frontal region were examined (significance threshold at $p \leq 0.004$, **Table 3**, **Fig. 1C**). Theta power was significantly higher in dup than in controls (**Fig. 1D**). No other significant differences in power were found between the three groups.

### The impact of age on MSE and power

Due to the wide age range of participants, we assessed the impact of age on EEG measures of interest. Correlation permutation tests were performed separately for del, dup, and control groups. Specifically, correlations were performed between age and the following EEG measures: lower scale entropy (1-10) and higher scale entropy (11-20); power of delta, theta, alpha, and beta bands (significance threshold at $p \leq 0.025$ for MSE measures and $p \leq 0.013$ for power measures). No significant correlations were found between age and any of these EEG measures at the frontal region in any group (**Supplementary Table S3**).

### The relationship between EEG activity and psychiatric traits

Correlation permutation tests were performed to examine correlations between MSE (i.e., 1-10 and 11-20 scales; **Fig. 3A**) and power measures (**Fig. 3B**) against psychiatric traits (i.e., CBCL and IQ) in the del group (**Table 4**). Due to the small sample size, the dup group was not included in this analysis. A strong correlation was found between entropy at higher scales (scales 11-20) and anxiety problems (significance threshold at $p \leq 0.004$). A strong

correlation was also found between theta power and pervasive developmental problems (significance threshold at $p \leq 0.002$). Overall, with higher entropy or power, psychiatric traits, i.e., anxiety and pervasive developmental problems, increase in severity in del. No other significant correlations were found between any of the EEG measures and CBCL subscales or IQ.

**The relationship between entropy and power**

The EEG signal is information-rich and, thus, it can be challenging to perfectly isolate certain features and determine all possible influences from other features in the signal. Nevertheless, in recognition of the possible interplay between entropy and power features, we have conducted correlation permutation tests to examine this, separately for each group (significance threshold at $p \leq 0.033$, corrected for multiple comparisons). Specifically, the power measures of interest for this post-hoc analysis in the current study are theta and alpha power as the former was correlated with anxiety in del and showed group differences in dup compared to controls. The latter, i.e., alpha power, has been found to be a dominant frequency impacting entropy in eyes-open resting-state paradigms (Kosciessa et al., 2020). Here, entropy variables were collapsed into two categories: lower scales (1-10) and higher scales (11-20) – consistent with the earlier correlation analyses in this study (see **Supplementary Fig. S2** for correlation analyses with entropy collapsed into four categories scales 1-5, 6-10, 11-15, 16-20). Results (**Fig. 4**) showed moderate to strong positive correlations between entropy, at lower scales and higher scales, and alpha power for the del, dup, and controls groups, respectively. For del, there were also moderate positive correlations between entropy, at lower and higher scales, and theta power. Overall, the results suggest that alpha and, to a lesser extent, theta power may impact on entropy levels at all scales. Therefore, it is important to note that entropy group differences, identified earlier, are not solely due to signal features of entropy. Other factors, such as alpha and theta power, may have contributed to the different presentation of entropy in each group (despite no group differences in alpha power).

## Discussion

The aims of the current study were 1) to determine whether frontal spontaneous neural activity, as revealed by EEG power and MSE, in 16p11.2 CNVs is altered compared to controls; and 2) to examine links between spontaneous neural activity and psychiatric traits in 16p11.2 del. The main findings are 1) MSE and CI were higher for 16p11.2 CNVs (i.e., del and dup) than controls at all respective scales over the frontal region; 2) Theta power was higher for dup compared with controls; 3) In del, strong associations were found between MSE and anxiety problems, and between theta power and pervasive developmental problems as measured with the CBCL. Together, these results suggest atypical frontal spontaneous neural activity that seems to strongly reflect or impact on certain psychiatric traits.

Taking the ESSENCE approach of considering interrelated psychiatric disorders together (Gillberg, 2010), certain commonalities emerge in neural entropy between these disorders and 16p11.2 CNVs. We have shown similar neural changes in a genetic condition that underpins various psychiatric disorders, thus suggesting a mechanism for which genetic conditions could lead to these diagnoses or psychiatric traits. Notably, the current study found higher entropy in 16p11.2 CNVs at both lower and higher scales compared to controls, as jointly reflected by CI and MSE analyses. This is reminiscent of findings previously reported in relation to ASD and absence epilepsy (Bosl et al., 2017) where an overall higher entropy at resting-state was also found compared to controls. Findings from many other studies, though, suggest that it is more common in psychiatric disorders for there to be scale-dependent variations in the level of entropy, compared to controls. Higher spontaneous frontal entropy has been more frequently observed at higher scales in particular (ASD, Ghanbari et al., 2015; Schizophrenia, Takahashi et al., 2010; Alzheimer's, Yang et al., 2013; Mizuno et al., 2010). This implies that psychiatric disorders, in the aforementioned studies, showed atypical long-range spontaneous neural connectivity involving the frontal region, as it has been suggested that neural entropy at lower and higher scales respectively reflect local/shorter-range and longer-range neural connectivity (McDonough and Nashiro, 2014; Vakorin et al., 2011). In contrast, findings in the current study may indicate a disruption in both shorter- and longer-range neural connectivity involving the frontal region and spontaneous neural activity in general.

Our findings additionally implicate theta power in 16p11.2 dup. Interestingly, although we found higher entropy in both 16p11.2 del and dup compared to controls, higher theta power was observed solely in dup. This could indicate that entropy, relative to power, is a more sensitive measure useful for capturing certain properties of neural information processing in 16p11.2 del, not possible by conventional power analyses alone. Notably, this finding of higher theta is consistent within the literature of a range of psychiatric disorders (e.g., Schizophrenia, ADHD) and genetic syndromes (e.g., Angelman syndrome, Frohlich et al., 2019; Newson and Thiagarajan, 2018; Wang et al., 2013). Higher power at lower frequencies in these disorders and 16p11.2 dup may indicate a similar dysfunction or compensatory mechanism that affects psychiatric traits shared among these disorders. Theta power has been commonly regarded as implicating memory processes (Berens and Horner, 2017). In this study, higher theta was associated with higher severity in pervasive developmental problems, which could be affected by disruptive learning and memory processes.

Evidence from a previous study (Takahashi et al., 2010) suggests that higher entropy might relate to atypical dopaminergic and/or serotonergic activity – both systems associated with anxiety and cognitive processes. Specifically, Takahashi et al. (2010) studied EEG MSE activity in drug-naïve schizophrenia participants, pre- and post-treatment with antipsychotics, and compared MSE with typical controls. Takahashi et al. (2010) found increased entropy at higher scales in fronto-centro-temporal areas in schizophrenia (pre-treatment) compared to typical controls. This is somewhat similar to the findings in the current study as higher entropy was found at higher scales (but also lower scales) in the frontal region in 16p11.2 CNVs compared to controls. Notably, Takahashi et al. (2010) also found that this higher entropy in schizophrenia was lowered to the control participants' level in fronto-central areas in response to antipsychotic treatment. In other words, the observed atypically high entropy observed in schizophrenia was reversed in response to medications that act on attenuating dopaminergic and, to a lesser extent, serotonergic activity. Thus, the identified atypical neural entropy in 16p11.2 CNVs, in the current study, along with the observed strong links between neural activity and psychiatric traits, could, therefore, signify a dysregulation in multiple neurotransmitter systems including dopamine and serotonin, in 16p11.2 CNVs.

Future work should examine whether these EEG features are similarly present in 16p11.2 CNV mouse models by conducting parallel human and mouse studies. If common conserved EEG features are identified cross-species, the mouse model can be used to

investigate the reversibility of these features and associated phenotypes/ pathophysiology. In addition, parallel studies could examine whether these EEG features are indeed endophenotypes that reflect particular dysregulations in dopaminergic or serotonergic activity – thus paving the way to identifying potential drug treatments.

As is typical of EEG studies of rare CNVs and genetic syndromes, key limitations include the small sample size and therefore the lack of examination of possible confounding factors such as seizure susceptibility/epilepsy (**Table S1**) and current medication use. Nevertheless, analyses in this study were based on group averages and conservative significance thresholds. Despite this, it is important to highlight that it would be valuable to support the current findings by replicating the results in future samples. Another limitation of this, and CNV studies in general, is the complexity of CNV screening, which may generate false-positive or false-negative results for pathogenic CNV. In addition, inclusions of unknown benign versions of the same CNV, based on the allelic background, are also possible.

Overall, the current study established that 16p11.2 CNVs present with atypical resting-state neural activity as revealed with entropy and power measures. Neural entropy levels were consistently higher in the frontal region for 16p11.2 CNVs relative to controls at all scales. Therefore, we speculate that this implicates interactions between local and long-range neural processing at resting-state networks. Higher theta power was additionally identified in 16p11.2 dup carriers. Whether reflecting a compensatory or dysfunctional mechanism, neural activity in 16p11.2 CNVs was strongly associated with psychiatric traits, namely, anxiety and pervasive developmental problems. Thus, this study presents the first evidence of links between the 16p11.2 CNV genotype, spontaneous neural activity, and psychiatric phenotypes.

**Acknowledgments**

We are grateful to all of the families at the participating Simons Variation in Individuals Project (Simons VIP) sites, as well as the Simons VIP Consortium. We appreciate obtaining access to phenotypic and imaging data on SFARI Base. Approved researchers can obtain the Simons VIP population dataset described in this study (https://www.sfari.org/resource/simons-vip/) by applying at https://base.sfari.org/. We would like to thank Dr. Jocelyn J. LeBlanc, Dr. Charles A. Nelson, and research staff members at Boston Children's Hospital and Harvard Medical School for their contributions in generating this data.

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**Figure legends**

**Fig. 1. Group differences in entropy and power.** Error bars representing 95% confidence intervals. Subfigure (**A**) shows entropy group differences across scales collapsed into four categories. Subfigure (**B**) shows group distributions of CI. Subfigure (**C**) shows power group differences in delta, theta, alpha, and beta bands. Subfigure (**D**) shows group distributions of theta power. Asterisks in subfigures (**B**) and (**D**) indicate significant results.

**Fig. 2. Power spectral densities of each group.** The power spectrum was used to estimate the relative power of delta, theta, alpha, and beta for each participant. Shaded region representing standard error.

**Fig. 3. Correlations between EEG activity and psychiatric traits in del.** Radar plots displaying associations (Spearman's r coefficient) between **(A)** entropy (lower scales 1-10 and higher scales 11-20) and CBCL traits, and **(B)** power (delta, theta, alpha, and beta) and CBCL traits. Asterisks indicate significant correlations.

**Fig. 4. Correlations between entropy and power.** Heatmaps displaying associations (Spearman's r coefficient) between entropy (lower scales 1-10 and higher scales 11-20) and power (theta and alpha) for each group. Asterisks indicate significant correlations.

Power spectral densities of each group. The power spectrum was used to estimate the relative power of delta, theta, alpha, and beta for each participant. Shaded region representing standard error.