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Supplementary materials

Materials and methods

Diagnoses summary

Supplementary Table 1. Diagnoses summary[a]

Diagnoses[b]	Deletion (n = 20)	Duplication (n = 8)
ADHD	**4**	**1**
Anxiety disorders including OCD and Phobia	**-**	**2**
Articulation Disorder	**9**	**1**
Other Disruptive Behaviour Disorder (Conduct/Oppositional)	**3**	**2**
Developmental Coordination Disorder	**12**	**3**
Enuresis Disorder	**2**	**-**
Language Disorders	**8**	**4**
Learning Disorder	**1**	**1**
Intellectual Disability (MR)	**4**	**-**
Seizures/Epilepsy	**3**	**1**

[a]Comorbidities or more than one diagnoses are present in this sample.
[b]Seizure / epilepsy diagnoses data were extracted from the nrrg.csv file; all other diagnoses data were found in the diagnosis_summary.csv file.

Psychometric assessments (CNV groups only)

ADOS-CSS

Among the assessments used to collect phenotypic data was the Autism Diagnostic Observation Schedule (ADOS; Gotham *et al.,* 2007), a standardised measure commonly used to assess ASD-related behaviours. Based on raw total scores of the ADOS, calibrated severity scores (CSS; Gotham *et al.,* 2009) were then calculated to assess the severity of ASD-behavioural symptoms. Data from six DEL and one DUP carriers are missing.

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 one DEL carrier is missing.

Stimuli and procedure

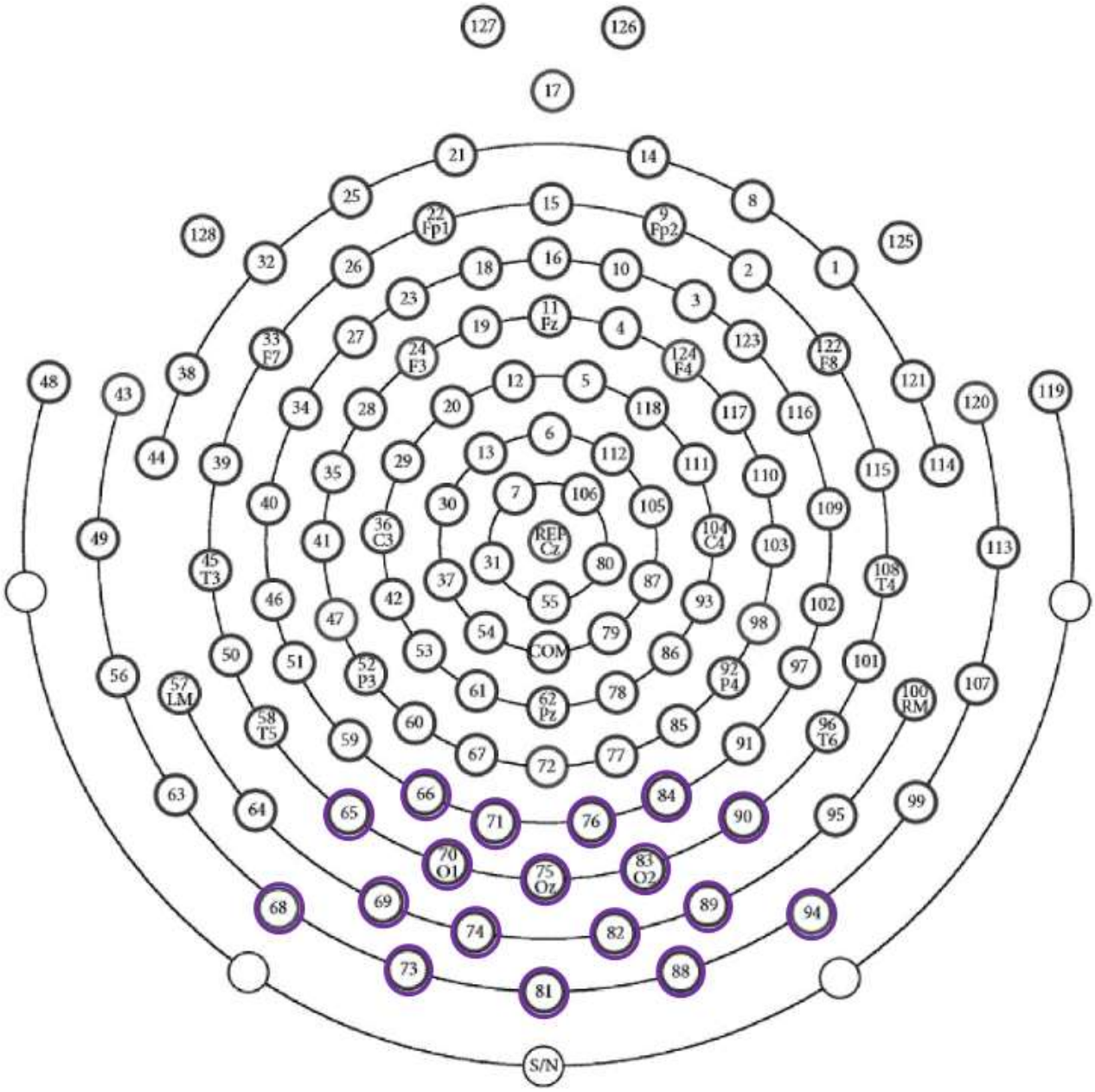
The presented stimuli consisted of black and white high contrast checkerboards of 99% with an average luminance of 80 cd/m^2, and a phase reversal rate of 2 Hz (i.e. phase reversing from black to white and white to black twice per second). The size of the checker was ~60 arcminute with a spatial frequency of 0.5 cycles/degree. Participants were seated ~60 cm from a Tobbii T60 eye tracking monitor (Tobii Technology, Sweden) that was 34.7 cm wide. Infant participants were seated on their caregiver's lap. The stimulus was presented on the monitor by running the E-Prime software (Psychology Software Tools, Pittsburgh, PA) in a dark room that was sound-attenuated and electrically shielded. Binocular eye gaze was monitored to ensure phase-reversal occurred as long as the participant's fixation gaze on the stimulus lasted for a minimum of 100 ms. Phase-reversal was paused when the participant's gaze was not fixated towards the stimulus. Depending on the participants' attentiveness and patience during the sessions, up to 150 trials were presented.

EEG recording and pre-processing prior to current study

EEG was continuously recorded using a 128 channel HydroCel Geodesic Net-Version 1 (Electrical Geodesics Inc., Eugene, OR, USA). The signal was amplified with a NetAmps 300 amplifier and digitised at a sampling rate of 500 Hz. A total offset of 34 ms was present and consistent for all participants. The offset resulted from both an 18 ms amplifier offset (due to the anti-alias filters within the amplifier) and 16 ms DIN offset (due to a delay between the stimulus trigger and stimulus visual onset on the monitor). Because this offset was consistent for all participants, it is not expected to drive group differences. In addition, the time window for the P1 component used for this study has a wide range (60-140 ms post-stimulus onset), which accounted for this offset and captured the P1 response.

A number of pre-processing steps were conducted offline using NetStation software prior to obtaining the data for the current study. Firstly, the data were filtered with a bandpass of 0.3-30 Hz. Secondly, the data were segmented into epochs 400 ms long (100 ms baseline and 300 ms post-stimulus). Baseline correction was applied. 'Bad' channels, i.e. channels which recorded a noisy EEG signal were removed. Channels were defined as bad if they: were missing; measured EOG from around the eyes, had amplitude ± 150 μV; contained artifacts in 100% of trials. By hand-edit, trials were marked bad if more than 12 channels were bad (not including missing or eye channels). Trials with eye blinks, eye movements, large clusters of bad channels, muscle artefacts, or excessive drift, were rejected. Bad channels were replaced using interpolation techniques. Channels (including interpolated channels) were referenced to an average reference.

EEG channel selection



Supplementary Fig 1. 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. For power and SNR analyses, the channels circled in purple were averaged.

Supplementary Table 2. Channels selected for C1, P1, N1, and timecourse variability primary analyses based upon criterion 1 (peak channel for P1 responses).

All three groups (n = 39)	**Control (n = 11)**	**Deletion (n = 20)**	**Duplication (n = 8)**
58 [1]	62 [1]	58 [1]	71 [1]
62 [1]	71 [2]	69 [1]	73 [1]
69 [1]	74 [2]	70 [1]	74 [1]
70 [1]	75 [3]	71 [1]	75 [1]
71 [4]	76 [2]	74 [2]	81 [1]
73 [1]	99 [1]	75 [4]	82 [1]
74 [5]		76 [2]	84 [1]
75 [8]		81 [1]	99 [1]
76 [4]		82 [4]	
81 [2]		83 [2]	
82 [5]		90 [1]	
83 [2]			
84 [1]			
90 [1]			
99 [2]			

The frequency of subjects for which each channel was selected is noted in brackets. Reported as channel number [frequency].

Supplementary Table 3. Channels selected for C1, P1, N1, and timecourse variability supplementary analyses based upon criterion 2 (peak channel unique for each component).

Control (n = 11)			**Deletion (n = 20)**			**Duplication (n = 8)**		
C1	**P1**	**N1**	**C1**	**P1**	**N1**	**C1**	**P1**	**N1**
91 [1]	99 [1]	89 [1]	97 [1]	90 [1]	99 [2]	94 [1]	99 [1]	99 [1]
81 [1]	76 [2]	85 [1]	96 [2]	83 [2]	96 [1]	83 [1]	84 [1]	94 [2]
75 [2]	75 [3]	83 [1]	94 [1]	82 [4]	94 [2]	82 [1]	82 [1]	90 [1]
74 [1]	74 [2]	82 [1]	91 [1]	81 [1]	93 [1]	75 [1]	81 [1]	88 [1]
73 [1]	71 [2]	81 [1]	88 [1]	76 [2]	88 [1]	73 [1]	75 [1]	76 [1]
71 [2]	62 [1]	75 [1]	83 [2]	75 [4]	84 [2]	65 [1]	74 [1]	56 [2]
57 [1]		71 [1]	82 [1]	74 [2]	82 [1]	60 [1]	73 [1]	
56 [1]		68 [1]	74 [1]	71 [1]	76 [1]	56 [1]	71 [1]	
		65 [1]	73 [2]	70 [1]	74 [1]			
		56 [2]	71 [1]	69 [1]	73 [2]			
			68 [3]	58 [1]	71 [1]			
			57 [1]		70 [2]			
			56 [2]		65 [1]			
			51 [1]		56 [2]			

The frequency of subjects for which each channel was selected is noted in brackets. Reported as channel number [frequency].

Alpha and beta power variability

The fast Fourier transform of the full length of each single trial data (200 datapoints) for each participant was computed using the 'fft' matlabTM function and divided by the number of datapoints. The signal was first zero-padded, to form a total of 1000 timepoints, and subtracted from the mean signal amplitude (this is done to remove the direct current signal). In addition, a taper was applied to the data, specifically, a hanning window, using the 'hann' Matlab function. Power spectral density (PSD) was then computed by squaring the absolute of the Fourier coefficients then multiplying by two to account for the negative frequencies. Given the parameters of the data, i.e. sampling rate of 500 Hz and 200 datapoints (corresponding to 400 ms) epoch lengths, the frequency resolution was 2.5 Hz. Absolute and relative power were computed for the alpha (8-14 Hz) and beta (14-30 Hz) frequency ranges. Using the 'trapz' Matlab function, trapezoidal integration for each range was conducted to obtain the absolute power of single trials. Prior to obtaining the relative power, the total spectral power was defined as the entire range between 1-30 Hz. Relative alpha and relative beta power were subsequently calculated as the ratio of alpha and beta power, respectively, to total power on each trial. To analyse power variability, again the MAD of single-trial absolute and relative alpha and beta power was found for each participant. Mean absolute and relative alpha and beta power were measured to facilitate comparisons with other studies. These analyses were conducted using in-house code (code available upon request) derived from codes shared by Dr Mike X. Cohen (Cohen, 2014) with functions from the EEGlab toolbox (Delorme and Makeig, 2004).

Signal-to-noise ratio

SNR can generally be defined as the ratio of post-stimulus signal strength to the pre-stimulus signal strength (the latter traditionally termed as noise), and is usually expressed in decibels. To compute the visual evoked potential SNR, the squared root-mean-square-amplitude (rms) of the post-stimulus signal was divided by the squared rms of the pre-stimulus signal and converted into decibels. The 'post-stimulus period' was taken from 0 ms to 100 ms post stimulus onset, and the 'pre-stimulus period' was from -100 ms to 0 ms relative to stimulus time. This ensured that equal temporal segments of data before and after stimulus presentation necessary to compute the SNR were obtained. The current study followed the same SNR formula used in Butler *et al.* (2017) to compute SNRs:

$$SNR_{db} = 10 * log_{10}\left(\frac{rms_{post-stimulus}}{rms_{pre-stimulus}}\right)^2$$

Where *rms* is the root-mean-square amplitude.

This formula is also embedded as a function in MATLAB 'snr' version R2016a (The MathWorks Inc.). The SNR from the mean of occipital and parietal channels was computed for each trial and then averaged across trials and compared between groups.

Results

Correlations between IQ, ADOS-CSS, and EEG measures in 16p CNV

Supplementary Table 4. Correlations between IQ, ADOS-CSS, and EEG measures in 16p CNV.

		DEL		DUP	
		IQ	**ADOS-CSS**	**IQ**	**ADOS-CSS**
C1, P1, N1 variability	C1 amplitude (µV)	-0.45	0.38	-0.3	-0.64
	C1 latency (ms)	0.06	0.08	0.54	-0.03
	P1 amplitude (µV)	-0.42	0	-0.49	-0.76
	P1 latency (ms)	-0.27	0.07	-0.7	0.06
	N1 amplitude (µV)	-0.59	0.11	-0.51	-0.52
	N1 latency (ms)	-0.37	-0.01	-0.4	0.52
Power variability	Absolute alpha (μV^2)	-0.67	0.29	-0.07	-0.88
	Relative alpha (%)	-0.1	-0.09	-0.04	-0.7
	Absolute beta (μV^2)	-0.13	0.17	-0.54	-0.39
	Relative beta (%)	0.21	0.05	0.16	0.7
SNR	(dB)	0.02	0.26	0.01	0.33
C1, P1, N1 mean	C1 amplitude (µV)	-0.01	0.23	0.14	0.21
	C1 latency (ms)	-0.49	0.74	-0.09	0.27
	P1 amplitude (µV)	0	-0.11	0.18	-0.21
	P1 latency (ms)	-0.39	-0.02	0.05	0.12
	N1 amplitude (µV)	0.02	0.1	0.17	0.64
	N1 latency (ms)	-0.18	-0.39	-0.46	0.28
Power mean	Absolute alpha (μV^2)	-0.64	0.18	-0.24	-0.88
	Relative alpha (%)	-0.19	-0.14	0.16	-0.7
	Absolute beta (μV^2)	-0.13	0.36	-0.71	-0.76
	Relative beta (%)	0.32	-0.01	0.05	0.76

The reported values correspond to the r coefficient. All results are non-significant. Significance threshold at $p < 0.003$.

Correlations between age and EEG variability and averaged metrics in 16p CNV and control groups

Supplementary Table 5. Correlations between age and EEG variability and averaged metrics in 16p and control groups.

		DEL	Control	DUP
			Age	
C1, P1, N1 variability	C1 amplitude (µV)	0.26	-0.06	-0.23
	C1 latency (ms)	0.27	-0.36	0.02
	P1 amplitude (µV)	-0.37	<0.01	-0.57
	P1 latency (ms)	-0.47	-0.12	0.25
	N1 amplitude (µV)	-0.60	-0.16	-0.51
	N1 latency (ms)	-0.36	-0.18	-0.12
Power variability	Absolute alpha (μV^2)	-0.47	0.11	-0.42
	Relative alpha (%)	-0.30	-0.01	0.14
	Absolute beta (μV^2)	0.47	0.05	-0.38
	Relative beta (%)	0.53	0.28	0.36
SNR	(dB)	-0.15	-0.20	-0.55
C1, P1, N1 mean	C1 amplitude (µV)	0.10	-0.57	0.24
	C1 latency (ms)	-0.39	0.05	0.12
	P1 amplitude (µV)	0.04	0.36	-0.41
	P1 latency (ms)	-0.2	-0.02	0.49
	N1 amplitude (µV)	-0.19	-0.15	0.25
	N1 latency (ms)	-0.25	0.32	0.28
Power mean	Absolute alpha (μV^2)	-0.34	0.11	-0.40
	Relative alpha (%)	-0.25	0.23	0.08
	Absolute beta (μV^2)	0.47	0.05	-0.47
	Relative beta (%)	0.50	0.05	0.54

The reported values correspond to the r coefficient. All results are non-significant. Significance threshold at $p < 0.006$.

Data integrity – correlations between EEG measures and trial number

Supplementary Table 6. Correlations between EEG measures and trial number.

		Trial number
C1, P1, N1 variability	C1 amplitude (μV)	-0.38
	C1 latency (ms)	-0.07
	P1 amplitude (μV)	-0.43
	P1 latency (ms)	0.02
	N1 amplitude (μV)	-0.43
	N1 latency (ms)	-0.25
Power variability	Absolute alpha (μV^2)	-0.14
	Relative alpha (%)	0.09
	Absolute beta (μV^2)	-0.23
	Relative beta (%)	0.13
SNR	(dB)	-0.09
C1, P1, N1 mean	C1 amplitude (μV)	0.14
	C1 latency (ms)	0.05
	P1 amplitude (μV)	-0.06
	P1 latency (ms)	-0.05
	N1 amplitude (μV)	0.28
	N1 latency (ms)	-0.19
Power mean	Absolute alpha (μV^2)	-0.20
	Relative alpha (%)	0.20
	Absolute beta (μV^2)	-0.25
	Relative beta (%)	0.02

The reported values correspond to the r coefficient. All results are non-significant. Significance threshold at $p < 0.006$.

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