Scan for Extended Content

Poster 2.432

Spectral electroencephalogram abnormalities across development in patients with Dravet syndrome

Colenbier N,[1] Neuray C,[2] Vereycken E,[1] Vanhollebeke G,[1] Zoteva V,[1] Ticho B,[3] Parkerson KA,[3] van Mierlo P[1]

[1]Clouds of Care NV, Ghent, Belgium;
[2]Centre for Cognitive Neuroscience, Salzburg, Austria;
[3]Stoke Therapeutics, Inc., Bedford, MA, USA.

Key Findings

1. Dravet syndrome is characterized by EEG abnormalities, particularly in the δ-band (1–4 Hz).
2. EEG δ-power is elevated in patients with Dravet syndrome compared with neurotypical controls.
3. δ-power decreases with age but remains persistently higher in patients with Dravet syndrome compared with neurotypical controls.
4. Additional research is needed to study the potential of δ-power to assess treatment efficacy.

American Epilepsy Society Annual Meeting 2025
December 5–9, 2025 | Atlanta, GA

Introduction

- Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy. More than 90% of DS cases are caused by voltage-gated sodium channel α subunit 1 (*SCN1A*) variants that result in 50% $Na_V1.1$ sodium channel expression, causing refractory seizures and significant developmental, cognitive, and behavioral impairments that impact quality of life.[1–7]
- In children and adolescents, increased electroencephalogram (EEG) δ-power activity during wakefulness may be associated with developmental impairment and reduced cognitive performance.[8,9]
- This study examined the differences in EEGs between patients with DS and neurotypical control participants (NCPs) and evaluated the potential of spectral power in assessing disease modification.

Methods

- Spectral power from routine clinical EEG recordings of patients with DS and age-matched NCPs were compared.
- DS data were from the baseline visit of patients with DS aged 2–18 years enrolled in the MONARCH and ADMIRAL Phase 1/2a studies.
- NCP data were from epilepsy-unrelated EEGs recorded at Saint-Luc University Hospital (Brussels, Belgium).
- All data were acquired in a clinical setting using the international 10-20 system.
- Fifteen minutes of preprocessed data were used to compute power spectra (1–32 Hz, log-scaled) using Morlet wavelet decomposition.
- Absolute power values were averaged across electrodes and log-transformed to decibels (dB).
- Statistical analyses were performed within a general linear model (GLM):

$$P \sim 1 + GENOTYPE + AGE + GENOTYPE{:}AGE$$

where P is the log-transformed power at a given frequency, AGE is a patient's age log_2-transformed and mean-centered, and GENOTYPE indicates DS or NCP.

- Group differences across frequencies (1–32 Hz) were tested using clustered permutation t-tests with threshold-free cluster enhancement (10,000 iterations) to account for multiple comparisons and inter-frequency correlations.
- For developmental trajectory analyses, δ-band (1–4 Hz) power was averaged and modeled using the same GLM or a variant with fewer fixed factors to assess genotype-by-age interactions, and genotype age-corrected changes.

Results

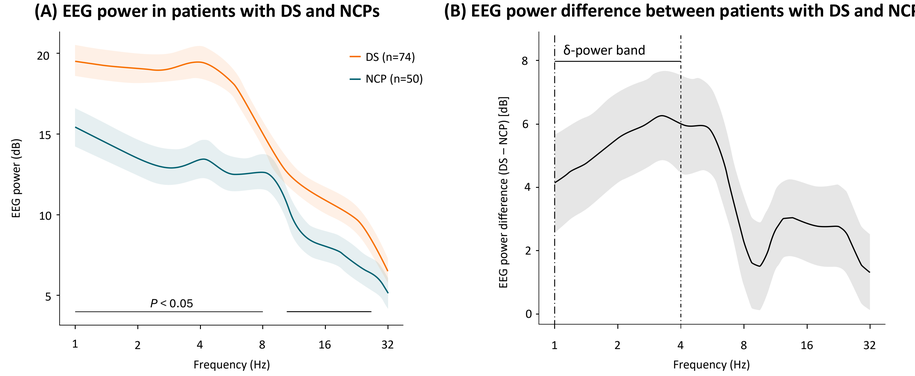
Baseline characteristics

- The analyses included 74 patients with DS (median age 9.0 years; 50% female) and 50 age-matched NCPs (median age 8.0 years; 50% female).

Patients with DS demonstrate elevated EEG δ-power

- Across the 1–32 Hz spectrum, children with DS showed broadly increased EEG power compared with NCPs, with significant differences at most frequencies (P<0.05) except within the α (9–11 Hz) and γ (31–32 Hz) ranges.
- The EEG spectral power change was most pronounced in the δ-band (1-4 Hz) ranging from 4.13 to 6.00 dB higher in patients with DS than in NCPs frequencies (P<0.05) (**Figure 1**).

Figure 1. Characterization of spectral power in patients with DS and NCPs.

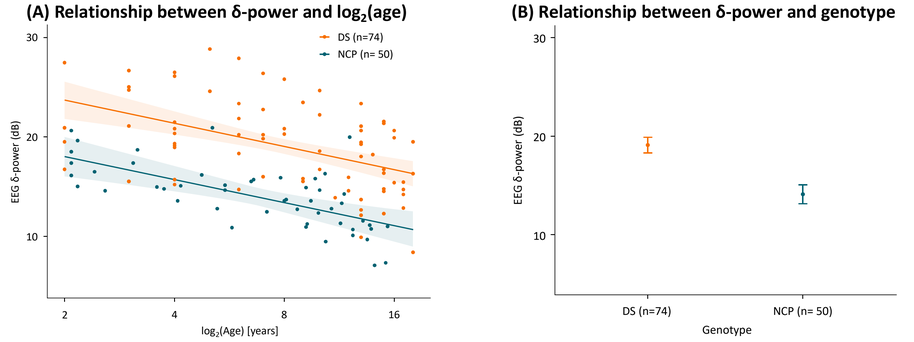


Shaded areas represent 95% confidence intervals. dB, decibel; Hz, hertz.

EEG δ-power decreases with age but remains persistently higher in DS

- Analysis of developmental trajectories revealed that δ-power decreased over time as age increased in both groups (DS: −2.34 dB/log_2(age), P<0.001; NCP: −2.33 dB/log_2(age), P<0.001) without a significant difference in slope (difference: −0.01 dB/log_2(age), P=0.983) (**Figure 2A**).
- Despite age-related decline, δ-power was consistently elevated in DS compared with NCPs (5.02 dB higher; P<0.001), indicating persistent electrophysiological abnormalities beyond age-expected levels (**Figure 2B**).

Figure 2. Spectral δ-power differences between patients with DS and NCPs.



Developmental trajectories were derived using a GLM. Shaded areas or error bars represent 95% CIs. CI, confidence interval; dB, decibel; EEG, electroencephalogram.

References: 1. Hattori J *et al. Epilepsia* 2008; 49 (4): 626–633. 2. Gil-Nagel A *et al. Sci Rep* 2023; 13 (1): 3355. 3. Bechi G *et al. Epilepsia* 2012; 53 (1): 87–100. 4. Zuberi SM *et al. Epilepsia* 2022; 63 (6): 1349–1397. 5. Villas *N et al. Epilepsy Behav* 2017; 74: 81–86. 6. Sinoo C *et al. Epilepsy Behav* 2019; 90: 217–227. 7. Brunklaus A *et al. Epilepsia* 2011; 52(8): 1476–1482. 8. Kulandaivel K *et al. Epilepsy Behav* 2011; 20 (4): 700–705. 9. Doval S *et al. Brain Topogr* 2024; 37: 1068–1088.

Disclosures: Shareholders: Clouds of Care (CN, PvM). Employment: Clouds of Care (NC, GV, VZ, EV), Stoke Therapeutics (BT, KAP).
Acknowledgments: This study was supported by Stoke Therapeutics. We thank research staff, investigators, and participants. Medical writing and editorial assistance were provided by Tanmay Chavan, PhD of Porterhouse Medical US and were funded by Stoke Therapeutics according to Good Publication Practice guidelines.