

RHYTHMS IN EPILEPSY RECORDED BY THE RNS SYSTEM

Circadian and ultradian patterns of epileptiform discharges differ by seizure-onset location during long-term ambulatory intracranial monitoring.

SPENCER, ET AL. *EPILEPSIA*, 2016.

Multi-day rhythms modulate seizure risk in epilepsy.

BAUD, ET AL. *NATURE COMMUNICATIONS*, 2018.

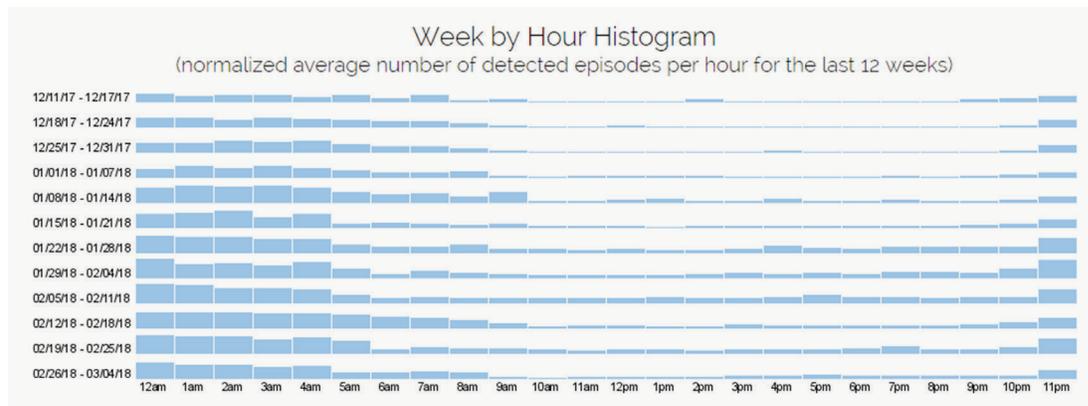
SUMMARY

- Even though seizures are typically brief events that occupy a fraction of a patient's life (~0.05%), their unpredictability is a major contributor to epilepsy-related disability¹
- Chronic electrographic data collected by the RNS System indicates that >90% of patients demonstrate a robust circadian (24-hour) pattern
- RNS System stored epileptiform activity also indicates that patients exhibit unique multi-day rhythms (20-30 days) within which seizures occur directly prior to peak activity

BACKGROUND

In addition to therapeutic benefits, the RNS System is the only device that provides long-term recordings of neural activity at the seizure focus/foci. Examples of the type of data provided by the RNS System include:

- Electrocorticographic recordings of sample baseline, interictal, and ictal activity
- Continuous counts of electrographic events and other epileptiform activity over days, months, and years



Histogram showing counts of electrographic events recorded by the RNS System. This information is available to physicians through the PDMS (Patient Data Management System).

RNS System data terminology used here:

- **Detection:** irregular epileptiform activity detected by the RNS System
- **Long episode:** a specific type of detection trigger (lasting longer than a pre-specified time period) that often represent electrographic seizures



KEY RESULTS²

Circadian Patterns (Spencer, et al. *Epilepsia*, 2016) N=134:

- >90% of patients demonstrated a robust circadian (24-hour) pattern in electrographic activity
- “Detections” showed a strong circadian pattern that peaked during normal sleep hours (Figure 1), regardless of the region of seizure onset
- “Long episode” rhythmicity varied by the region of seizure onset (Figure 2)
 - For the frontal and temporal neocortical regions they were nocturnally predominant
 - For the mesial temporal regions they were more evenly distributed throughout the day
- A deeper understanding of electrographic rhythmicity may be helpful for patient management, such as informing decisions about timing of medication doses or behavior counseling

Figure 1

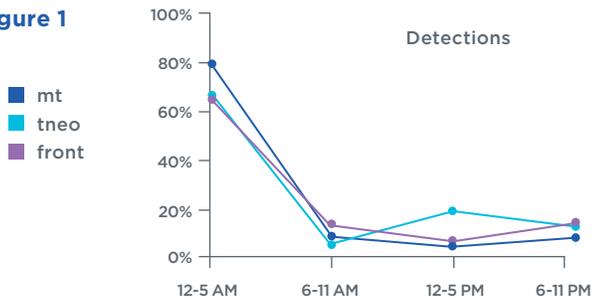
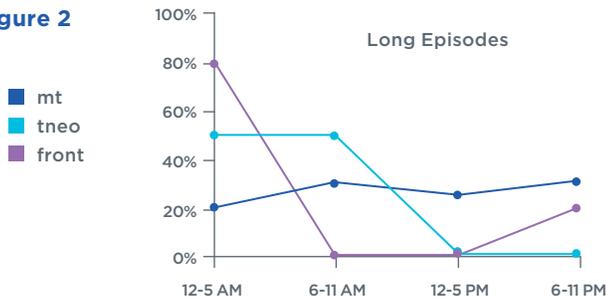


Figure 2



Footnotes

1. Epilepsy Innovation Institute (Ei2) 2016 Community Survey of >1000 epilepsy patients
2. These were retrospective analyses, and were not powered to drive conclusions of clinical significance. N values are small and caution must be taken when interpreting results.



SPENCER



BAUD



The RNS System is an adjunctive therapy for adults with refractory, partial onset seizures with no more than 2 epileptogenic foci. See important prescribing and safety information in the RNS[®] System labeling. Refer to the labeling for a description of the RNS[®] System and its components, indications for use, contraindications, warnings, cautions, adverse events and instructions for use. The manuals are available at www.NeuroPace.com

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Multi-day (“multidien”) Patterns (Baud, et al. *Nature Communications*, 2018) N=37:

- In addition to daily (circadian) rhythms of epileptiform activity, slower, multi-day (multidien) rhythms were observed in all studied patients (Figure 3)
- Multidien rhythms are most commonly 20–30 days in length, and are found in men and women
- The exact period of the multidien cycle is variable across patients but relatively stable over months to years within each patient
- Seizures tend to occur on the rising phase of the multidien rhythm, just before the peak (Figure 4); similarly, seizures preferentially occur at certain phases of the circadian rhythm
- The fact that seizures are more or less likely to occur at different phases of the underlying circadian and multidien rhythms means that these rhythms may provide biomarkers of seizure risk, which could help determine the timing of seizures

Figure 3

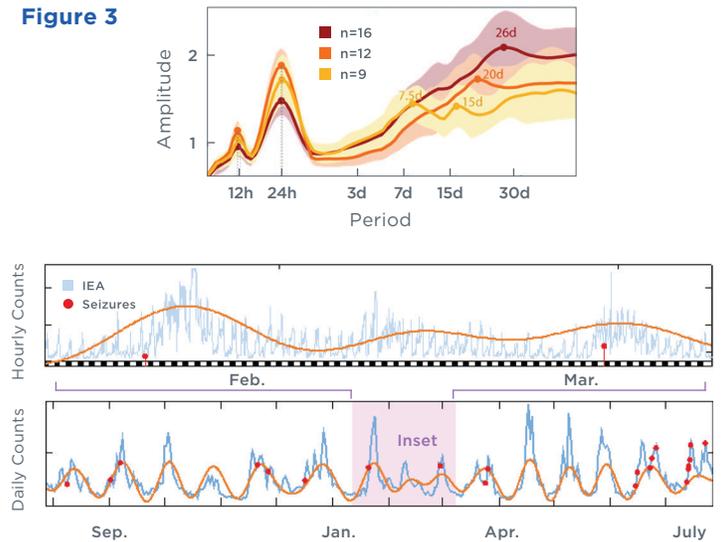


Figure 4

