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Termination patterns of stimulus-induced rhythmic, periodic, or ictal patterns and spontaneous electrographic seizures

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HIGHLIGHTS

- Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) are difficult to distinguish from spontaneous seizures.
- We identified a termination pattern of SIRPID activity, distinct from that of spontaneous seizures.
- The termination pattern has high accuracy for distinguishing SIRPIDs from spontaneous seizures.

ABSTRACT

Objective: To investigate the ability of the evolution and termination patterns to distinguish stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) from spontaneous electrographic seizures, a challenge to the neurophysiologist and clinician.
Methods: We screened the prospectively collected database of patients undergoing continuous EEG (cEEG) and identified 25 cases of SIRPIDs. We compared patients with SIRPIDs to 25 patients with spontaneous seizures. Two experienced neurophysiologists graded the termination pattern of both on fast fourier transform (FFT) as "abrupt" or "sputtering."
Results: The identification of a "sputtering" or cyclical tapering pattern accurately discriminated SIRPIDs from spontaneous seizures with 88% sensitivity and 87% specificity, yielding a positive predictive value of 82% for SIRPIDs when the pattern was present (negative predictive value 87% when the sputtering termination was not seen). Similarly, the identification of an "abrupt" termination pattern identified clinically determined seizures with 84% sensitivity and 88% specificity.
Conclusions: The termination pattern quickly and accurately distinguishes SIRPIDs from spontaneous seizures, suggesting that at least some SIRPIDs have an underlying mechanism distinct from that of spontaneous seizures.
Significance: If validated in other studies, the use of evolution and termination patterns to classify EEG patterns as epileptiform seizures versus SIRPIDs will help guide treatment of these patients.

1. Introduction

Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) are rhythmic, periodic, or ictal-appearing patterns consistently elicited by stimulation of the patient (i.e. suctioning, physical examination of the patient, noxious stimulation, or sudden ambient noise) (Hirsch et al., 2004). They are a relatively common finding in the critically ill, with reported prevalence of 10–34% (Braksick et al., 2016; Hirsch et al., 2004; Ong et al., 2012). The reported causes of SIRPIDs include intracerebral hemorrhage, traumatic brain injury, anoxic brain injury, metabolic disturbances, and drug toxicity amongst other etiologies (Braksick et al., 2016). There is a high (27–51%) (Braksick et al., 2016; Hirsch et al., 2004) prevalence of spontaneous seizures reported in these patients; however, seizure onset locations have no relation to SIRPID locations in the majority of cases when both are seen (Hirsch et al., 2004). One recent multicenter study found no increased incidence of seizures in patients with stimulus-induced activity, once the underlying EEG pattern was taken into account (Rodriguez Ruiz et al., 2017). Both SIRPIDs and ictal activity may

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respond to benzodiazepines (Kaplan and Duckworth, 2011); however, so do other well-defined EEG patterns like triphasic waves (Fountain and Waldman, 2001). Under the ACNS standardized terminology, the phenomenon of stimulus-induced patterns is delineated by adding "SI" to a descriptive term such as generalized rhythmic delta activity or lateralized periodic discharges (Hirsch et al., 2013); however, to refer to the group of stimulus-induced patterns in this paper, we will follow other recent publications (Alvarez et al., 2013; Braksick et al., 2016; Van Straten et al., 2014) and use the term SIRPIDs.

SIRPIDs are often difficult to differentiate from spontaneous seizure activity; raw EEG alone may not be able to distinguish between nonconvulsive seizure activity and metabolic or drug-induced patterns (Brenner and Schaul, 1990; Hirsch et al., 2004), and the correlation of the onset of every rhythmic, periodic, or potentially ictal pattern in a 24-h EEG record with video data to assess for a provoking stimulus is time-consuming, and hence costly. Whether, and how aggressively, SIRPIDs should be treated pharmacologically is unclear (Hirsch et al., 2008), as is whether all SIRPIDs truly represent an epileptic process. The mechanism underlying the pattern seen in SIRPIDs has not been defined, although propagation from a deep seizure focus (Kaplan and Duckworth, 2011) or the thalamocortical activation of a hyperexcitable cortex have been suggested (Hirsch et al., 2008, 2004). The significance of SIRPIDs also remains to be better described; prior work has shown no independent increase in mortality with SIRPIDs, although they are often associated with other electrographic markers of poor outcome (Braksick et al., 2016). In addition, whether SIRPIDs represent a form of abnormal reactivity is unclear; some studies have treated SIRPIDs and reactivity as different processes (Braksick et al., 2016) and found that patients with SIRPIDs with an otherwise unreactive EEG have a worse prognosis than patients with SIRPIDs with EEG reactivity (Braksick et al., 2016).

In clinical interpretation of a number of continuous video-EEGs (cEEGs), we noted that a "sputtering" or cyclical tapering pattern, consisting of alternating periods of the SIRPIDs with lower-power periods without discharges, was apparent at the termination of SIRPIDs. This pattern was easily visualized on a fast Fourier transform (FFT) display of quantitative EEG. To determine whether this evolutionary pattern can distinguish SIRPIDs from seizures, we retrospectively compared EEGs from prospectively collected patients with SIRPIDs and prospectively collected patients with seizures.

2. Methods

2.1. Subjects

We screened the database of all patients who underwent 24-h video-EEG monitoring at Johns Hopkins Hospital from 5/2014–8/2016 for clinically identified SIRPIDs. The stimulus-induced nature of the relevant pattern was confirmed with video review (when video was available) or with annotations on EEG indicating stimulation or interaction with the patient. We then identified an equal number of consecutive patients from the database who had spontaneous seizures (but no SIRPIDs) on continuous video-EEG. We collected patient information including age, sex, reason for hospitalization, location in hospital, presence of systemic infection, CNS infection, recent neurosurgery, stroke, intracranial hemorrhage, prior seizures, number of antiepileptic drugs (AEDs), disposition at discharge, and number of AEDs at discharge. Twenty-five patients with SIRPIDs were identified, and 25 consecutive patients with spontaneous seizures were used for comparison.

2.2. EEG data recording and processing

Continuous EEG and video were digitally recorded by using 21 electrodes placed according to the International 10–20 system (or 9 electrodes in a reduced montage, when surgical site prevented all electrodes from being placed: Fp1, Fp2, T3, T4, C3, C4, O1, O2, and Cz) using Nihon Kohden EEG-1200 machines and software (Tokyo, Japan). Clinical review occurred at least twice daily.

We processed all EEGs on Persyst 12 (Prescott, AZ) and identified the clinically determined seizure or SIRPID pattern on the quantitative EEG FFT panels. Two neurophysiologists (blinded to the clinical diagnosis) graded the termination of any seizure-like pattern on a clip of these FFT panels (from the seizure or SIRPID) as either an "abrupt" or a "sputtering/cyclical tapering" termination (Figs. 1 and 2).

2.3. Analysis

We compared clinical characteristics of patients with seizures and with SIRPIDs using a Wilcoxon rank-sum test or chi-squared test as appropriate with Stata 13 (College Station, TX). Descriptive statistics are reported as median (interquartile range [IQR]) for continuous variables and as percentages for categorical variables. In order to account for the likelihood that patients with seizures were triaged to neurology or neurocritical care locations in the hospital, for the comparison of hospital location where SIRPIDs were identified, we used a chi-square test to compare SIRPID hospital locations with the locations of all 24-h video EEG monitoring performed over one year. A p-value of 0.05 was considered significant.

2.4. Inter-rater reliability

We calculated the inter-rater reliability (Kappa) score for EEG grading using Stata 13. We then calculated the sensitivity and specificity and the positive and negative predicted values for the termination pattern identifying SIRPIDs versus seizures.

3. Results

3.1. Ability to distinguish spontaneous seizures from SIRPIDs

The identification of a "sputtering" or cyclical tapering termination pattern of the abnormal activity on FFT (Fig. 1) accurately discriminated SIRPIDs from spontaneous seizures with 88% sensitivity and 87% specificity, yielding a positive predictive value of 82% for SIRPIDs when the pattern was present (negative predictive value 87% when the sputtering termination was not seen). Similarly, the identification of an "abrupt" termination pattern (Fig. 2) identified clinically determined seizures with 84% sensitivity and 88% specificity.

3.2. Inter-rater reliability

The inter-rater agreement (Kappa) for classification of the termination pattern was 0.64 (substantial agreement (Landis and Koch, 1977)), which is within the upper range of published inter-rater agreement for ICU pattern modifier agreement (Mani et al., 2012).

3.3. Clinical characteristics in patients with SIRPIDs and seizures

SIRPIDs were significantly more likely to be identified in patients on a non-neurological unit than a neurological unit when compared to the locations of all patients undergoing continuous