Brief Potentially Ictal Rhythmic Discharges in Critically Ill Adults

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Continuous electroencephalography (CEEG) monitoring is used increasingly to assess brain function in critically ill patients. Substantial efforts have been made to standardize critical care EEG terminology and to associate EEG patterns with clinical course and outcome.1-5 One of the main indications for CEEG is to detect electrographic seizures. Most electroencephalographers use a definition of seizures that includes a minimal duration of 10 seconds,2-7 which reflects the typical duration of partial seizures in patients with chronic epilepsy.8-10 Rhythmic ictal-appearing patterns lasting less than 10 seconds have been described in neonates under different acronyms: brief rhythmic discharges (BRDs), brief electroencephalography rhythmic discharges (BERDs), and brief ictal rhythmic discharges (BIRDs).11-13 In neonates, these patterns encompass discharges of any frequency, including less than 4 Hz, because they are common in this age group. Rhythmic delta activity and periodic discharges with a frequency of less than 4 Hz are common in critically ill patients but are usually not considered to be ictal.3,5 Ictal discharges in children and adults often have a higher frequency than those in neonates. The occurrence of brief rhythmic discharges with a frequency higher than 4 Hz has never been studied in these older age groups.

In this study, we sought to investigate the prevalence, significance, and prognostic implication of these discharges. In addition, we propose the acronym B(I)RDs (brief potentially ictal rhythmic discharges; the parentheses in the acronym indicate that their ictal nature is equivocal) in a group of critically ill patients.

IMPORTANCE Brief potentially ictal rhythmic discharges, termed B(I)RDs, have been described mainly in neonates, and their significance in adults remains unclear.

OBJECTIVE To describe the incidence of B(I)RDs in critically ill patients and investigate their association with seizures and outcome.

DESIGN, SETTING, AND PARTICIPANTS We reviewed the records of prospectively identified patients with B(I)RDs and patients serving as controls matched for age (±5 years) and primary diagnosis.

MAIN OUTCOMES AND MEASURES The prevalence of seizures during continuous electroencephalography and functional outcome, as measured by the Glasgow Outcome Scale, were determined.

RESULTS We identified B(I)RDs in 20 patients (2%). The pattern most often consisted of very brief (1-3 seconds) runs of sharply contoured theta activity without obvious evolution. All patients with B(I)RDs had cerebral injury, and in cases with a single focal lesion (11 [55%]), B(I)RDs were localized in the same region in all but 2 cases (18%). Patients with B(I)RDs were more likely to have seizures during continuous electroencephalography than were patients without B(I)RDs (15 of 20 [75%] vs 10 of 40 [25%]; P < .001), and 9 patients with B(I)RDs (60%) had only subclinical seizures. Brief potentially ictal rhythmic discharges were identified before seizures in all but 1 case (93%) and ceased in all 12 cases (80%) in which seizures were controlled. Patients with B(I)RDs tended to have a worse outcome than controls (16 [80%] vs 25 [63%]); however, this finding was not statistically significant.

CONCLUSIONS AND RELEVANCE Brief potentially ictal rhythmic discharges in critically ill patients are associated with a high prevalence (75%) of electrographic seizures and might serve as an early predictor of seizures during subsequent monitoring. A larger prospective study is needed to better understand their clinical and prognostic significance.
Methods

Study Design and Population
The present study was approved by the institutional review board of Yale University. From our prospective database on 1135 patients who received CEEG between July 1, 2011, and February 28, 2013, we identified 19 records in which the occurrence of B(I)RDs, defined as very brief (<10 seconds) lateralized runs of rhythmic activity with a frequency greater than 4 Hz, was mentioned. In addition, we selected 101 records in which the occurrence of such discharges was not mentioned. Two authors (J.Y.Y. and N.G.) reviewed the entire EEG recording of these 120 patients. The presence of B(I)RDs was confirmed in the 19 patients who were mentioned in the EEG report. In addition, B(I)RDs were identified in 1 of 101 individuals for whom the discharges were not mentioned in the report, bringing the number of cases to 20. The control group consisted of the 100 patients for whom we confirmed the absence of B(I)RDs and comprised 60 randomly selected controls and 40 matched controls. The 60 randomly selected controls were used exclusively to determine the sensitivity of EEG readers in identifying B(I)RDs. The 40 controls matched to cases for primary diagnosis and age (±5 years) with a 2:1 ratio were included in the sensitivity analysis and used for further comparisons with the cases.

Electroencephalography
Two authors (J.Y.Y. and N.G.) reviewed the entire EEG recording for each patient in our study population and controls for the occurrence of seizures, periodic and rhythmic discharges, and background EEG, including state changes, posterior dominant rhythm, sleep transients, and reactivity as defined in the American Clinical Neurophysiology Society’s Standardized Critical Care EEG Terminology.

We defined B(I)RDs as very brief (<10 seconds) lateralized runs of rhythmic activity greater than 4 Hz, with or without evolution. Given the short duration of these events, the presence of evolution in frequency, shape, amplitude, and spread to other electrodes or of a sharply contoured shape was not considered necessary but was recorded. Seizures were defined according to published criteria. Briefly, seizures had to last more than 10 seconds and meet 1 of the following criteria: (1) repetitive spikes, sharp waves, or spike/sharp-wave and slow-wave complexes with a frequency greater than 3 Hz; (2) repetitive rhythmic waves with either incrementing onset, decrementing offset, and/or postdischarge slowing or attenuation; or (3) repetitive spikes, sharp waves, or spike/sharp-wave and slow-wave complexes with a frequency of 3 Hz or less and significant improvement in clinical state or EEG background after administration of an antiepileptic drug. We recorded the time of occurrence of the first B(I)RD and the first seizure during monitoring. We also quantified the prevalence of B(I)RDs during the first 12 hours of monitoring according to the American Clinical Neurophysiology Society’s Standardized Critical Care EEG Terminology.

Clinical Variables
Clinical data collection included demographics, main neurologic diagnoses, history of epilepsy, neurologic examination at the time of CEEG (categorized as alert and oriented, awake but abnormal, stuporous, and comatose), and functional outcome (using the Glasgow Outcome Scale: 1 indicates dead; 2, persistent vegetative state/minimally conscious state; 3, severe disability; 4, moderate disability; and 5, mild disability). The location of the brain injury was retrieved from the imaging reports. The size of ischemic strokes and intraparenchymal hemorrhages on the day closest to the onset of CEEG monitoring was calculated, using the ABC/2 (ie, measures in the x, y, and z axes, respectively) score on diffusion-weighted magnetic resonance images for strokes and computed tomography images for hemorrhages.

Statistical Analysis
The Fisher exact test was used to assess group differences in categorical variables, and the Mann-Whitney test was used to assess group differences in numeric variables. When appropriate, multivariate logistic regression was performed to assess the independent effect of multiple variables. P < .05 was considered statistically significant. Statistical analysis was performed using MATLAB (MathWorks; http://www.mathworks.com).

Results

Prevalence of B(I)RDs and Sensitivity of EEG Readers
We retrospectively identified B(I)RDs in 20 (10 males; median age, 65 years) of 1135 patients (2%) who underwent CEEG monitoring between July 1, 2011, and February 28, 2013. These 20 cases comprised all 19 cases for which the reports mentioned their occurrence and 1 of 101 cases for which the report did not mention them. The sensitivity of detection and reporting of B(I)RDs was 95% (95% CI, 86%-98%) and the specificity was 100% (95% CI, 96%-100%). The demographic and clinical data are summarized in Table 1.

EEG Characteristics of B(I)RDs
The typical frequency for B(I)RDs was in the theta, alpha, and beta frequency bands in 14 (70%), 3 (15%), and 3 (15%) cases, respectively. Typical duration was 1 to 3 seconds. Most (17 of 20 [85%]) B(I)RDs were sharply contoured except in the theta frequency band in 2 patients (10%) and the beta frequency band in 1 patient (5%), which were sinusoidal. None of the B(I)RDs showed obvious evolution. The B(I)RDs were unifocal except in 1 patient who had bilateral independent foci. Eleven foci were located over the left hemisphere and 10 were over the right hemisphere. Thirteen foci were anterior (frontal, frontotemporal or anterior temporal, and temporal), and 7 were posterior (parietal, temporoparietal, parieto-occipital, or occipital). The B(I)RDs occurred regardless of the stage of arousal in all patients. Thirteen patients (65%) showed evidence of state changes, including 7 individuals (35%) with stage N2 sleep transients. Typical examples of B(I)RDs are shown in Figure 1A and
The frequency of B(I)RDs during the first 12 hours of recording was between 1 per 10 seconds and 1 per minute in 6 cases (30%), between 1 per minute and 1 per hour in 12 cases (60%), and less than 1 per hour in 2 cases (10%). B(I)RDS were not reliably identified on quantitative EEG panels using a typical display resolution of 1 hour per screen.

**Etiology of B(I)RDs**

All patients with B(I)RDs had evidence of cerebral injury (Table 1), and all but 1 patient had acute brain injuries. Tumor and stroke were the most common sources of the injury. The location and severity of brain injury was comparable in both groups (Table 1). One patient, who presented with “new-onset seizures,” was found to have a T2/fluid-attenuated inversion recovery signal abnormality of the right hippocampus and was thought to have had undiagnosed epilepsy for approximately 7 years. Four patients (20%) had a history of epilepsy, which did not differ significantly from the incidence in the control group.

**Abnormalities in Neuroimaging**

Results of brain imaging performed in all 20 patients with B(I)RDs (16 underwent magnetic resonance imaging and 4 underwent computed tomography) were abnormal. In cases with a single focal lesion (11 [55%]), B(I)RDS were localized in the same region in all but 2 patients (18%). One of these patients had an acute left thalamic hemorrhage with intraventricular hemorrhage, and B(I)RDS were identified in the left frontotemporal and right parieto-occipital regions. The other patient had a systemic infection, magnetic resonance imaging showed a tiny punctate infarct in the right frontal white matter, and B(I)RDS were seen over the right posterior region.

The brain injury was reported to involve the cerebral cortex in 14 of 20 patients with B(I)RDs (70%) and 27 of 40 controls (68%). The size of ischemic stroke (median [range], 26 [10-42] cm³ vs 40 [4-75] cm³ in the B(I)RDs and control groups, respectively) and intraparenchymal hemorrhage (12 [9-38] cm³ vs 12 [4-34] cm³ in the B(I)RDs and control group) were similar in both groups.
The patient presented with a new-onset, generalized tonic-clonic seizure and failure to regain full consciousness postictally. A, A 10-second electroencephalogram (EEG) page showing a very brief run of sharply contoured, intermittent rhythmic theta activity (brief potentially ictal rhythmic discharge) over the left anterior region (boxed areas). B and C, Two 10-second EEG pages showing the onset of an electrographic seizure from the left anterior region (boxed areas). High- and low-pass filters were set at 1 and 70 Hz, respectively. The notch filter was off.
Figure 2. Electroencephalogram Recordings of a Woman in Her Mid-70s With Anoxic Brain Injury After Cardiac Arrest

The injury resulted from a cardiac arrest. A, A 10-second electroencephalogram (EEG) page showing 2 very brief runs of sinusoidal rhythmic beta activity (brief potentially ictal rhythmic discharges) over the right anterior region (boxed areas). B and C, Two 10-second EEG pages showing the onset of an electrographic seizure starting from the right anterior region and spreading to the right hemisphere (boxed areas). High- and low-pass filters were set at 1 and 70 Hz, respectively. The notch filter was off.
Association With Acute Seizures and Lateralized Periodic Discharges on EEG

Patients with B(I)RDs were more likely to have seizures during CEEG than were patients without B(I)RDs (15 of 20 [75%] vs 10 of 40 [25%]; P < .001). Of these 15 patients, 9 individuals (60%) had only subclinical seizures. In the control group, 7 patients (70%) had only subclinical seizures. Seizures often started with a morphology similar to that of B(I)RDs and within the same region (same electrode contacts). Representative cases are shown in Figure 1B and Figure 2B.

In 14 of 15 patients (93%) with B(I)RDs and seizures, B(I)RDs preceded the onset of the first seizure. In 15 of 20 patients (75%), B(I)RDs were identified within the first hour of CEEG monitoring, but only 5 patients (25%) had seizures within this hour. Of the 15 patients with B(I)RDs in the first hour, only 3 patients (20%) had seizures within this hour.

The risk of seizures associated with B(I)RDs was similar across the different locations of B(I)RDs (10 of 13 [77%] for anterior B(I)RDs and 5 of 7 [71%] for posterior B(I)RDs). Seizures responded to treatment in 12 of the 15 patients with B(I)RDs (80%); in all 12 cases, B(I)RDs ceased after the seizures had been controlled.

Lateralized periodic discharges (LPDs) were more frequent in patients with B(I)RDs than in controls, but this difference was not significant (11 of 20 [55%] vs 14 of 40 [35%]; P = .17). In patients with B(I)RDs and LPDs, B(I)RDs occurred independently of LPDs in 8 of 11 cases (73%) but co-localized to the same region (Figure 3). Lateralized periodic discharges persisted after seizures were controlled in 15 of the 16 patients (94%) with LPDs and seizures. The distinctive morphology of B(I)RDs in 3 patients with coexisting LPDs with superimposed fast activity is shown in Figure 3B. Patients with LPDs were more likely to have seizures during CEEG than were patients without LPDs (16 of 25 [64%] vs 7 of 35 [20%]; P = .001). In multivariate analysis, both B(I)RDs and LPDs were independently associated with a higher risk of seizures (Table 2). Nine of the 11 patients (82%) with B(I)RDs and LPDs had seizures.

Clinical Correlates of B(I)RDs

Thirteen patients (65%) with B(I)RDs were comatose or stuporous at the time of CEEG. This proportion was higher than that in controls, although the difference was not statistically significant (18 of 40 [45%]; P = .52) (Table 1). No clinical manifestations were observed during B(I)RDs in any patient.

Outcome

We observed that LPDs and seizures were associated with a worse outcome at discharge (Table 3). Although patients with B(I)RDs tended to have a worse outcome than controls (16 [80%] vs 25 [63%]), this finding was not statistically significant.

Discussion

In this retrospective case-control study of prospectively identified critically ill patients undergoing CEEG, we studied the cross-sectional prevalence of B(I)RDs and their relationship to seizures, location of brain injury, and outcome. We identified B(I)RDs in 20 of 1135 patients (2%). The sensitivity and specificity of EEG readers to report these discharges were 95% and 100%, respectively, thus indicating that the prevalence we report is a valid estimate. The pattern most often consisted of 1- to 3-second runs of sharply contoured theta activity but did not show obvious evolution. All patients but one had an acute brain injury. Brief potentially ictal rhythmic discharges, similar to LPDs, were independently associated with a significantly higher risk of seizures during CEEG (15 of 20 patients [75%] with B(I)RDs and 16 of 25 patients [64%] with LPDs). Most seizures in these patients were nonconvulsive (eg, electrographic only). Brief potentially ictal rhythmic discharges were identified before seizures in all but one case. Although the outcome was worse in patients with B(I)RDs than in those without B(I)RDs, this finding was not significant. Seizures and LPDs were both independently associated with worse outcome, as previously described.

The EEG criteria for the definition of electrographic seizures usually include a minimal duration of 10 seconds. Well-known exceptions to that rule are absence and myoclonic seizures. It is uncommon for complex partial seizures to last less than 10 seconds, but simple partial seizures as short as 3 seconds have been reported.

The existence of very brief rhythmic discharges similar in morphology to ictal discharges is well established in the neonatal EEG literature, as reviewed by Shewmon. These discharges have been described using several acronyms, including B(I)RDs (brief ictal or interictal rhythmic discharges), which lacks specificity; BERDs (brief electrographic rhythmic discharges), which implicitly suggests that these represent nonconvulsive seizures; and BIRDs (brief ictal or interictal rhythmic discharges), which we favor. Shewmon used the BIRDs acronym because the “I” could indicate both ictal and interictal. Based on our results and results from prior studies, it is manifest that B(I)RDs are closely related to seizures, even if they do not meet the duration and evolution criteria for seizures. A similar pattern of very brief and focal intermittent rhythmic activity has been described in scalp EEG recordings of patients with focal cortical dysplasia. Interestingly, these intermittent runs corresponded to continuous fast rhythmic spiking, sometimes with evolution, seen on electrocorticography. We thus suggest that B(I)RDs be used as an acronym for brief potentially ictal rhythmic discharges, with the parentheses within the acronym indicating that their ictal nature is equivocal.

The prevalence of B(I)RDs in neonatal studies ranges from 17% to 20%. We found a prevalence of 2% in an unselected population of patients who received urgent CEEG. This prevalence is much lower than that of previous studies and is probably explained by the fact that most neonates who benefit from CEEG have a highly epileptogenic brain injury. Similarly, in our study, all patients with B(I)RDs had cerebral injury, most often stroke or tumor. These neurologic insults are also among the most common causes of LPDs. Anticonvulsant drugs prescribed for seizure prophylaxis or clinical seizures before CEEG monitoring may have contributed to lowering the prevalence as well.
A. A man in his mid-70s with papillary thyroid cancer and brain metastases presented with a new-onset seizure. A 10-second electroencephalogram (EEG) page showing a very brief run of sharply contoured, intermittent rhythmic theta activity (brief potentially ictal rhythmic discharges [B(I)RDs]) was noted over the right anterior temporal region (boxed areas). There was simultaneous occurrence of low-amplitude lateralized periodic discharges (LPDs) (underlined) over the right temporal region. B and C. A man in his late 40s with glioblastoma multiforme and focal motor seizures. B. A 10-second EEG page showing the occurrence of a very brief run of sharply contoured theta activity (B(I)RDs) over the left midtemporal region (boxed area) and independent LPDs with fast activity (underlined) over the left posterior quadrant intermittent. C. Similar runs of theta activity were observed in the absence of LPDs (boxed area). High- and low-pass filters were set at 1 and 70 Hz, respectively. The notch filter was off.
B(I)RDs were observed with a similar prevalence over all regions of the head. They resembled seizure onset and occurred in the same region as seizures in a given patient, almost always before the first ictal discharge lasting more than 10 seconds. More practically, the first instance of B(I)RDs occurred in the first hour of recording in 75% of the cases vs only 20% of the seizures. Thus, if B(I)RDs were present on a short EEG recording, it would be important to continue recording (or to treat prophylactically).

B(I)RDs coexisted with LPDs in most cases (11 of 20 [55%]). Although both were associated with a similar risk of seizures, we believe that B(I)RDs represent a different phenomenon than LPDs for the following reasons: (1) LPDs are by definition periodic, whereas B(I)RDs were sporadic; (2) LPDs occur in prolonged runs, usually lasting days, whereas by definition B(I)RDs are very brief; (3) LPDs persisted after seizures when the latter were controlled, whereas B(I)RDs ceased in all patients in whom seizures were successfully treated; (4) LPDs and B(I)RDs can occur in the same patient or they can be seen independently; (5) in 11 patients with both patterns, B(I)RDs occurred independently of LPDs in 8 cases; (6) in patients with LPDs and B(I)RDs, B(I)RDs did not occur consistently with most LPDs as opposed to the low-amplitude, very brief rhythmic activity that is associated with most discharges (termed PLEDs-plus in the past20 and now referred to as +F in the American Clinical Neurophysiology Society’s Standardized Critical Care EEG Terminology4); and (7) B(I)RDs and LPDs were both independently associated with a greater risk of seizure.

So-called benign EEG variants, such as wicket spikes, 14- and 6-Hz positive bursts, and rhythmic temporal theta bursts of drowsiness, can occur as short runs of sharp and rhythmic theta activity and could be mistaken for B(I)RDs, especially in the temporal and temporoparietal regions.11 However, B(I)RDs in critically ill patients occurred regardless of the state (including during stage N2 sleep) and in the absence of normal features of the sleep-wake cycle. In contrast, benign variants have been described21 almost exclusively in otherwise healthy individuals, with the notable exception of the 14- and 6-Hz positive bursts, which have been described in patients with liver failure,22 and especially in children with Reye syndrome.12 No patient in our series had liver failure, and none also exhibit electrographic seizures, a fact that may bias our study. However, the high sensitivity and specificity in reporting B(I)RDs indicate that this is not likely. We defined B(I)RDs as lateralized discharges to avoid including bilateral synchronous activities, such as the posterior dominant rhythm and sleep spindles. Doing so, we have likely overlooked fragments of generalized seizures, which also probably occur.
Conclusions

In this retrospective study of prospectively identified critically ill patients undergoing CEEG, we describe the occurrence of B(1)RDS. These discharges were seen almost exclusively in patients with brain injury and were often, but not always, associated with LPDs and subclinical electrographic seizures. A larger prospective study is required to confirm these findings and to assess whether B(1)RDS are independently associated with a worse outcome after acute brain injury.

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