AQ1

Rapid Response Electroencephalography for Urgent Evaluation of Patients in Community Hospital Intensive Care Practice

Moussa Yazbeck, Parveen Sra, Josef Parvizi

ABSTRACT

INTRODUCTION: Limited access to specialized technicians and trained neurologists results in delayed access to electroencephalography (EEG) and an accurate diagnosis of patients with critical neurological problems. This study evaluated the performance of Rapid Response EEG System (RR-EEG), which promises fast EEG acquisition and interpretation without traditional technicians or EEG-trained specialists. METHODS: The new technology was tested in a community hospital intensive care unit in Northern California. Three physicians (without previous training in EEG) were trained by the manufacturer of the RR-EEG and acquired EEG without the help of any EEG technicians. Time needed from order to EEG acquisition was noted. Quality of EEG and diagnostic information obtained with the new EEG technology were evaluated and compared with the same information from conventional clinical EEG system. **RESULTS:** Ten patients were tested with this new EEG technology, and 6 of these patients went on to have conventional EEGs when the EEG technicians arrived at the site. In these cases, the conventional EEG was significantly delayed (11.2 ± 3.6 hours) compared with RR-EEG $(5.0 \pm 2.4 \text{ minutes}; P < .005)$. Use of RR-EEG helped clinicians rule out status epilepticus and prevent overtreatment in 4 of 10 cases. Rapid Response EEG and conventional EEG systems yielded similar diagnostic information. CONCLUSION: Rapid Response EEG can be set up by nurses, and diagnostic information about the presence or absence of seizures can be appreciated by nurses. The RR-EEG system, compared with the conventional EEG, did not require EEG technologists and enabled significantly faster access to diagnostic EEG information. This report confirms the ease of use and speed of acquisition and interpretation of EEG information at a community hospital setting using an RR-EEG device. This new technology has the potential to improve emergent clinical decision making and prevent overtreatment of patients in the intensive care unit setting while empowering nursing staff with useful diagnostic information in real time and at the bedside.

Keywords: Ceribell EEG, electroencephalography, new EEG procedure, new technology, nonconvulsive seizure, rapid response, seizure, status epilepticus

Subclinical seizures, including nonconvulsive status epilepticus (NCSE), are prevalent in critically ill patients. Approximately 10% to 20% of intensive care unit (ICU) patients are subject to seizures, and

Questions or comments about this article may be directed to AQ2 Josef Parvizi, MD PHD, at jparvizi@stanford.edu. Stanford University Medical Center, Stanford, CA.

Moussa Yazbeck, MD, John Muir Health, Walnut Creek, CA.

Parveen Sra, MPH, John Muir Health, Walnut Creek, CA.

This study was funded by a research grant from Ceribell Inc (Mountain View, California) to John Muir Health.

This article was presented as a poster at NCS 16th Annual Meeting on September 26, 2018, in Boca Raton, FL.

AQ3 Dr Parvizi is the co-founder of Ceribell and has founder shares in the company. The other authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jnnonline.com).

Copyright © 2019 American Association of Neuroscience Nurses

DOI: 10.1097/JNN.000000000000476

90% of the seizures in critically ill patients are nonconvulsive and can only be diagnosed with EEG monitoring.¹⁻⁵ Accumulating data have shown that prolonged nonconvulsive seizures lead to permanent brain injury.^{6–14} Given the very high risks of missing nonconvulsive seizures, clinicians tend to treat patients with a relatively high risk of nonconvulsive seizures empirically with anticonvulsant treatment, something that was clearly seen in a recent study at a tertiary medical center.¹⁵ Although there is no documented evidence for it, it is reasonable to assume that empiric antiepileptic drug (AED) treatment may be especially prevalent in community hospital settings where conventional electroencephalography (EEG) is not easily accessible. The practice of empiric treatment may have undesirable consequences because treatment with sedation agents and antiepileptic medications (or AEDs) increases the risk of intubation and other adverse events, which may prolong hospitalization. Furthermore, without EEG, it is difficult to confirm whether the given dose of AED is sufficient.

Current EEG technologies require dedicated technicians for setup, neurologists for review, and financial support from the institution for equipment and infrastructure. As a result, many community hospitals do not have EEG capability, and patients with suspected seizures must be transferred to another institution with 24/7 EEG infrastructure or treated empirically.

The recently developed Rapid Response EEG (RR-EEG) system offers EEG acquisition by anyone without previous training in conventional EEG systems. It can be set up in minutes by nurses or physicians or any other user and significantly shortens setup time compared with conventional EEG.¹⁵ Rapid Response EEG also provides on-device EEG waveform visualization and therefore enables bedside evaluation. The device records and transmits EEG in real time (using WiFi) to a cloud portal (purchased license required), which enables remote evaluation of the visual EEG waveforms by trained neurologists. For credentialing purposes, board certification in clinical neurophysiology or epilepsy is needed for formal interpretation of the EEG.

Besides visual EEG displays on the device and in the cloud reviewing portal, the RR-EEG system also offers a so-called brain stethoscope function that allows the user to listen to the sound of the EEG and differentiate between seizure and seizurelike activity (rhythmic or periodic discharges) versus nonseizure or non-seizurelike patterns. Normal EEG patterns are heard as monotone white noise, whereas abnormal EEG fluctuations caused by seizure discharges are heard as rhythmic sharp fluctuations in tone. In a recent study, the brain stethoscope function was validated.¹⁶ Medical students and nurses without previous EEG training listened to EEG sounds and performed with high sensitivity for seizures (95%–98%) as well as high specificity for seizure and seizurelike activity (82%–84%).¹⁶ In another study, the RR-EEG system was used by neurocritical care fellows in 35 neuro-ICU patient cases within a large academic hospital setting. After using the brain stethoscope function, physicians reevaluated their clinical suspicion for seizure and decision for additional treatment.¹⁵ The current study was designed prospectively to replicate the feasibility and performance of the RR-EEG system in a community hospital ICU, where conventional EEG capability is limited.

Methods Patient Population

Adult patients (\geq 18 years) with an altered mental status (ie, Glasgow Coma Scale score \leq 14) were enrolled in the neuro-ICU during a 5-month period. Patients were deemed at risk for nonconvulsive seizures or NCSE. Conventional EEGs were performed for a subset of 6 patients as their standard-of-care procedures. This study was approved by the institutional review board, and patients' guardians and families were required to be present at the bedside and sign written informed

Call out here

consent (which limited the recruitment of subjects hence only 10 subjects in 5 months).

Rapid Response EEG Device

An RR-EEG System (Ceribell Inc, Mountain View, California) was applied to the patient per manufacturer's instructions. The RR-EEG system consists of a portable 8-channel EEG monitoring recorder that connects to a 10-lead headband (Figure 1). The system records and F1 displays visual EEG waveforms on the device, sonifies EEG signal in real time with a brain stethoscope function, and transmits EEG records wirelessly to a cloud server for remote reading stations. The headband is placed around the head with leads 5 and 10 nearest the occiput and the headband fastening in the front over the forehead. Odd-numbered leads are on the left, and even-numbered leads are on the right. Because the device has 10 electrodes, 8 channels of visual EEG are displayed in bipolar montage, similar to the lateral channels of the double-banana montage. The brain stethoscope function converts EEG signals into sounds without any time compression (ie, speeding up the playback). Sonification is applied to 1 temporal channel on each side.

Physician Evaluation for Seizures

After obtaining consent, the treating physician used available clinical information at the time of bedside evaluation, rated suspicion for nonconvulsive seizure in each case, and decided whether the patient needed treatment with additional AEDs.

After application of the RR-EEG device by ICU staff, the physician listened to 30 seconds of EEG sound from each hemisphere and reevaluated suspicion for seizure and AED treatment decision. Then, the physician visually reviewed the EEG waveforms displayed on the RR-EEG device at the bedside and again reevaluated suspicion for seizure and AED treatment decision. The physician evaluation procedure is illustrated in Supplementary Figure 1 (Supplemental Digital Content 1, available at http://links.lww.com/JNN/A196).

After the physician evaluated seizure suspicion and treatment decisions for the patients, EEG recording with the RR-EEG device was then continued for up



Note. The system consists of a handheld recording device connected to a 10-lead headband with wet electrodes. The recording device displays and records the EEG waveform and converts the EEG to sound using a proprietary conversion algorithm.

to 12 hours. If conventional EEG became available per standard of care or if disconnection was needed for any other reason, the Rapid Response device was disconnected. Clinical team members (physician and nurse) also rated their experience related to the ease of use of the Rapid Response recording device and headband.

Statistical Analysis

The study primary end points were clinicians' seizure suspicion and treatment decision based on RR-EEG data. Secondary end points were EEG setup time and ease of use of the RR-EEG system. In patients with conventional EEG recordings, setup time and diagnostic data were compared with those of the RR-EEG system. Descriptive analysis was performed. P values were calculated for categorical data (seizure suspicion and treatment decision) and for continuous data (time to EEG) using t test parametric comparisons.

Results

Ten patients were recruited for the study. The mean age was 59.7 years, and 50% were female. Median Glasgow Coma Scale score was 9. Five patients were sedated, 8 patients were intubated, and 9 of 10 patients were preemptively treated with antiepileptic medications. Four patients presented with subarachnoid hematoma or other intracranial hemorrhage. The demographic information and patient clinical characteristics are described in Supplemental Table 1 (Supplemental Digital Content 2, available at http://links.lww.com/JNN/A195).

Before the use of the RR-EEG, the treating physician assessed the risk for nonconvulsive seizure based on patient medical history and clinical presentation. In 5 patients, seizure suspicion was high, and the physician's decision was to add additional AEDs. In the other 5 cases, the physician's suspicion for seizure was low, and the physician was not planning to add additional AEDs.

Rapid Response EEG was used for all 10 patients. After listening to EEG sounds (30 seconds of the left and right hemispheres, respectively), the treating physician reevaluated his or her seizure suspicion and treatment decision. In the 5 high-suspicion cases, 4 assessments were changed to low or no seizure suspicion and treatment was deescalated; 1 patient remained in the high-suspicion category. All 5 low-suspicion cases remained of low suspicion for seizure, and the physician would not add additional AED treatment. The changes in physician diagnostic decision after using the brain stethoscope function are shown in Supplemental Table 2 (Supplemental Digital Content 3, available at http:// links.lww.com/JNN/A197), and the changes in treatment decision are illustrated in Supplemental Figure 2 (Supplemental Digital Content 4, available at http:// links.lww.com/JNN/A198).

After listening to the EEG sound, the treating physician also reviewed RR-EEG waveforms on the handheld device. Seizure suspicion and treatment decision after the visual EEG review did not change from the postsonification evaluations. Conventional EEG was performed for 6 patients as part of their standard of care. For the patient who had high seizure suspicion post sonification, conventional EEG showed artifact obscuring the right frontal and central leads, leaving the diagnosis inconclusive. No electrographic seizure was noted in the other 5 conventional EEG recordings that lasted for 40 to 60 minutes each—suggesting a 5 of 5 concordance between the Rapid Response and conventional EEG diagnoses.

Rapid Response EEG was significantly faster than conventional EEG in setup time (P < .001). The mean setup time for RR-EEG was 5.0 \pm 2.4 minutes. For the patients who also had conventional EEG performed as part of their standard of clinical care per hospital procedure, it took the conventional EEG 11.2 \pm 3.6 hours because of challenges in obtaining EEG on weekends and after hours. Of the 6 conventional EEG, 5 cases were ordered after regular hours. The average arrival time for these cases were 12.29 ± 2.29 hours.

Clinical team members rated their experience related to the ease of use of the RR-EEG recording device and headband. In a scale of 1 to 5, with 1 being "very easy" and 5 being "very difficult," the average ease of use of the headband and the device was rated as 1.9 ± 1.0 and 1.6 ± 0.8 , respectively. This showed that the RR-EEG device was easy to use.

Discussion

The current study aimed to evaluate the feasibility and performance of the RR-EEG system to detect seizures in a community hospital ICU, where conventional EEG was not available 24/7. Our data from 10 ICU patients showed that the RR-EEG system can help physicians evaluate the presence or absence of hemispheric or generalized NCSE by listening to the sound of the EEG at the bedside. Our results also demonstrated that the RR-EEG system significantly reduced time to EEG acquisition and led to a significant change in treatment decisions, especially with the potential to reduce unnecessary additional treatment in those who are not actively seizing.

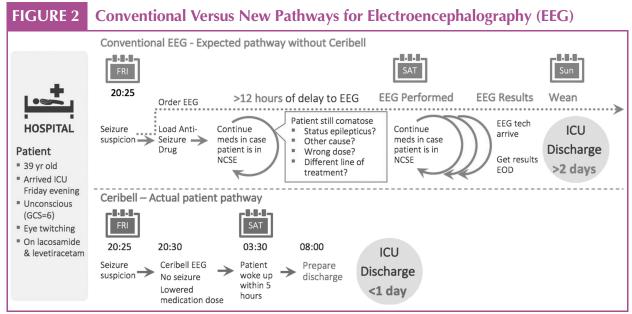
Fast Access to EEG

The RR-EEG system provided rapid acquisition and simplified interpretation of EEG information. The setup time was 5 minutes on average. One factor contributing to delays in acquiring conventional EEG was the unavailability of a trained EEG technician. Of the 6 conventional EEGs performed per hospital standard of care, 5 occurred after regular hours, 4 in the evening and 1 on a weekend. The conventional EEG started in the morning on the next business day in all 5 cases, with an average delay of 12.5 hours. A case study for RR-EEG is presented to highlight the difference in practice between 2 EEG pathways (Figure 2).

By not requiring a dedicated technician to set up the EEG, the RR-EEG system avoids this delay. The device was consistently rated by participating clinicians as easy to use. The brain stethoscope and on-device display provided instant sonification and visual feedback to the clinicians and helped them in their diagnostic decision and treatment plan at the bedside.

Avoid Overtreatment

Early access to EEG information may significantly avoid unnecessary overtreatment of patients and hence liberation from mechanical ventilation sooner and subsequently decreasing length of ICU stay. Although in this study,



Note. This figure illustrates a case for Rapid Response EEG to highlight the difference in practice between 2 EEG pathways. A 39-year-old quadriplegic man who presented to the emergency department with a history of seizure disorder secondary to ruptured AVM was found nonresponsive with eye twitching and eye deviation upward. On admission, his Glasgow Coma Scale score was 6 (1,1,4); computed tomography of the brain was negative for any acute changes. The patient was mildly hypotensive. He received additional levetiracetam, was loaded with valproic acid, and was intubated (with midazolam drip). Conventional EEG was ordered, but EEG technicians were not available after hours. Rapid Response EEG was at the bedside upon the patient's arrival to the intensive care unit (ICU), and the ICU physician set it up within 2 minutes. Rapid Response EEG sonification and visual on-screen EEG traces were evaluated by the ICU physician as negative for seizures. Suspicion for seizures before EEG was high, but it was reduced to "very low" upon sonification and visual review of the patient's EEG at the bedside. Remote EEG interpretation by an epileptologist confirmed the ICU physician's interpretation of the EEG as showing diffuse slowing without any ongoing seizures. The patient's anesthetics were gradually tapered down, and the patient started regaining consciousness and was back to his baseline within 8 hours of admission. He was extubated and transferred to the general ward in the morning. Conventional EEG was performed on the following day in the morning upon technician availability and showed mild diffuse slowing.

9 of the 10 patients were already treated with anticonvulsant medications, use of RR-EEG led to the exclusion of status epilepticus in patients and, as such, prevented additional overtreatment of these patients with high confidence and eventually deescalated treatment when appropriate.

Possible Financial Benefits

Although the financial analysis of using RR-EEG in our hospital was beyond the scope of this study, we are cognizant of several cost-saving opportunities that the use of this new technology could provide. As discussed at length by Kolls and colleagues,¹⁷ having access to EEG in a community hospital leads to reduction in costs and to additional sources of revenue—to name a few, prevention of patient transfers, reduction in length of stay, reduction in the cost of unnecessary intubations or overtreatment, and additional opportunities for new billing revenue and for retention of the patients and increased ICU census.

Limitations of the Study

We recognize that our current study only recruited a very small number of subjects and a larger cohort of patients is needed to address some of the same questions proposed here. Another major limitation of the study is that all subjects recruited to our study had been empirically premedicated with AEDs and we could not find any subject with ongoing seizures. A third limitation of the study pertains to lack of a direct comparison between EEG signals recorded with RR-EEG and with the conventional EEG system. However, a direct comparison of the RR-EEG with 2 of the most prevalent conventional EEG machines was recently published.¹⁸

Conclusion

This study was a mere feasibility study using the new RR-EEG system on 10 patients in a community hospital. Despite the limitations of the study, our findings suggest that the new EEG system has the potential to provide faster access to EEG and help guide treatment decisions (although in this study, 9 of the 10 patients were already treated with anticonvulsant medications) while minimizing the use of EEG technicians and deescalating treatment choices, all of which can ultimately lead to shortening length of stay and lessening cost. This study with a small number of patients serves as a proof-of-concept study documenting that early access to EEG information leads to reliable and correct exclusion of status epilepticus and hence guiding the management of patients at risk for nonconvulsive seizures.

References

- Friedman D, Claassen J, Hirsch LJ. Continuous electroencephalogram monitoring in the intensive care unit. *Anesth Analg.* 2009; 109(2):506–523.
- Laccheo I, Sonmezturk H, Bhatt AB, et al. Non-convulsive status epilepticus and non-convulsive seizures in neurological ICU patients. *Neurocrit Care*. 2015;22(2):202–211.
- Siddiqui M, Jamil N, Malik A, Bano A, Khan FS, Siddiqui K. Frequency of non convulsive status epilepticus in patients with impaired level of consciousness. *J Pak Med Assoc*. 2009; 59(5):296–298.
- Tomson T, Svanborg E, Wedlund JE. Nonconvulsive status epilepticus: high incidence of complex partial status. *Epilepsia*. 1986;27(3):276–285.
- Zehtabchi S, Abdel Baki SG, Omurtag A, et al. Prevalence of non-convulsive seizure and other electroencephalographic abnormalities in ED patients with altered mental status. *Am J Emerg Med.* 2013;31(11):1578–1582.
- Young GB, Jordan KG, Doig GS. An assessment of nonconvulsive seizures in the intensive care unit using continuous EEG monitoring: an investigation of variables associated with mortality. *Neurology*. 1996;47(1):83–89.
- Jirsch J, Hirsch LJ. Nonconvulsive seizures: developing a rational approach to the diagnosis and management in the critically ill population. *Clin Neurophysiol*. 2007;118(8):1660–1670.
- Krumholz A, Sung GY, Fisher RS, Barry E, Bergey GK, Grattan LM. Complex partial status epilepticus accompanied by serious morbidity and mortality. *Neurology*. 1995;45(8):1499–1504.
- Rabinowicz AL, Correale JD, Bracht KA, Smith TD, DeGiorgio CM. Neuron-specific enolase is increased after nonconvulsive status epilepticus. *Epilepsia*. 1995;36(5):475–479.
- Vespa P, Prins M, Ronne-Engstrom E, et al. Increase in extracellular glutamate caused by reduced cerebral perfusion pressure and seizures after human traumatic brain injury: a microdialysis study. *J Neurosurg*. 1998;89(6):971–982.
- Vespa P, Martin NA, Nenov V, et al. Delayed increase in extracellular glycerol with post-traumatic electrographic epileptic activity: support for the theory that seizures induce secondary injury. *Acta Neurochir Suppl.* 2002;81:355–357.
- Vespa P, Tubi M, Claassen J, et al. Metabolic crisis occurs with seizures and periodic discharges after brain trauma. *Ann Neurol.* 2016;79(4):579–590.
- Williams AJ, Tortella FC, Lu XM, Moreton JE, Hartings JA. Antiepileptic drug treatment of nonconvulsive seizures induced by experimental focal brain ischemia. *J Pharmacol Exp Ther*. 2004;311(1):220–227.
- Krsek P, Mikulecka A, Druga R, et al. Long-term behavioral and morphological consequences of nonconvulsive status epilepticus in rats. *Epilepsy Behav.* 2004;5(2):180–191.
- Hobbs K, Krishnamohan P, Legault C, et al. Rapid bedside evaluation of seizures in the ICU by listening to the sound of brainwaves: a prospective observational clinical trial of Ceribell's brain stethoscope function. *Neurocrit Care*. 2018; 29(2):302–312.
- Parvizi J, Gururangan K, Razavi B, Chafe C. Detecting silent seizures by their sound. *Epilepsia*. 2018;59(4):877–884.
- Kolls BJ, Mace BE, Dombrowski KE. Implementation of continuous video-electroencephalography at a community hospital enhances care and reduces costs. *Neurocrit Care*. 2018;28(2):229–238.
- Kamousi B, Grant A, Woo R. Comparing the quality of signals recorded with Ceribell Rapid Response EEG and conventional clinical EEG system. *Clin Neurophysiol Pract.* 2019;4:69–75.

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES

- AQ1 = Please check if authors name are correctly captured for given names (in red) and surnames (in blue) for indexing after publication.
- AQ2 = Please provide roles/positions of all authors in their respective affiliations.
- AQ3 = Please check whether the conflict of interest statements were appropriately captured.
- AQ4 = EDITOR: Please provide text to be used for a call-out.
- AQ5 = Please spell out AVM.

END OF AUTHOR QUERIES