# Sonification of Seizures: Music to Our Ears*



**Victoria A. McCredie, MBChB, PhD**
Interdepartmental Division of Critical Care Medicine
University of Toronto;
Department of Critical Care Medicine
Toronto Western Hospital
University Health Network; and
Krembil Research Institute
Toronto Western Hospital
Toronto, ON, Canada

The increasing use of electroencephalography (EEG) to monitor brain function in critically ill patients has uncovered that seizure activity occurs frequently in patients both with and without acute brain injury. The majority of seizures (> 90%) (1) in the ICU are in fact subclinical or nonconvulsive and may occur in more than 30% of high-risk patients (2). Many patients remain comatose or confused after generalized convulsive status epilepticus making it a challenge to differentiate a postictal state or medication-induced encephalopathy from ongoing subclinical seizure activity without EEG monitoring (3). EEG is the only diagnostic tool that can definitely establish the diagnosis of nonconvulsive seizures (NCSz) or nonconvulsive status epilepticus when clinical signs of seizures are absent. However, the technical requirements and constraints of electrophysiology monitoring in the ICU, including the availability of EEG technicians and neurophysiologists to interpret studies, are obstacles to its full application in many ICUs. Potential solutions to reduce this burden on resources include educational initiatives for nonexperts (4), simplified montages with reduced electrode placement (5), automated seizure recognition programs (6), and quantitative EEG display tools (7). Predominantly, these solutions seek to simplify the acquisition and interpretation of raw EEG waveforms to facilitate visual detection of seizures, but what if we could listen to the brain to hear seizures?

In this issue of *Critical Care Medicine*, Vespa et al (8) report the use of a simplified 10-electrode headband converting EEG data to sound to detect seizures. The use of sound to monitor physiology is not a new concept in medicine: consider the use of variable-pitch pulse tones in pulse oximeters to identify oxygen desaturation. The idea of EEG sonification was first described in 1934 when Edgar Adrian described the transformation of EEG data into sound (9). The study by Vespa et al (8) tests a new EEG system called "Rapid-EEG" that uses advanced algorithms to translate low-frequency EEG signals into the audible range modulating a voice-like synthesized sound. This multicenter cohort study assessed changes in the physicians' diagnostic and therapeutic decision-making based on the use of the "Rapid-EEG" system. Conducted in five academic hospitals in the United States, the study by Vespa et al (8) compared conventional seizure management (i.e., 29 trainees and 8 attending neurologists relying solely on clinical judgment) versus decision-making guided by "Rapid-EEG". The major indication for EEG was altered mental status, and most patients were admitted with status epilepticus, intracranial hemorrhage, or altered mental status of unknown cause. Using a 2-minute standardized assessment of EEG data (listening to EEG sound for 30 s from each hemisphere and reviewing visual waveforms for 60 s), the "Rapid-EEG" system had a significant impact on physicians' diagnostic suspicion for seizures. Overall, physicians changed their diagnostic decision in 40% of cases, with 33% downgrading their suspicion for seizures. This subsequently resulted in changes to treatment decisions in 20% of cases, with 13% changing their decision to not escalate antiseizure treatment after accessing the "Rapid-EEG" data. Compared with a majority consensus of three epileptologists evaluating the same EEG data, the sensitivity of physicians' seizure diagnosis significantly increased from 78% to 100% after the use of "Rapid-EEG" and specificity significantly increased from 64% to 89%.

Beyond evaluating changes in physicians' diagnostic and therapeutic decision-making, the study by Vespa et al (8) illustrates the ongoing challenges to obtain timely EEG monitoring in the ICU, potentially delaying treatment. The Neurocritical Care Society and the European Society of Intensive Care Medicine consensus statements recommend EEG to rule out NCSz in brain-injured and comatose ICU patients without primary brain injury and urgent EEG (within 60 min) in status epilepticus who do not return to functional baseline within 1 hour after antiseizure medication (10, 11). However, the timely acquisition of EEG in the ICU remains a huge challenge in many centers. In the study by Vespa et al (8), the median time to conventional EEG setup in five modern academic centers was still 4 hours (interquartile range [IQR] 2–8 hr), not including specialist interpretation (8). Most hospitals struggle to meet these society recommendations, and as such, EEG continues to be underutilized in the ICU (12). In many smaller ICUs, EEG

*See also p. 1249.

**Key Words:** electroencephalography; electroencephalography sonification; intensive care medicine; nonconvulsive seizures

Dr. McCredie disclosed that she does not have any potential conflicts of interest.



**DOI: 10.1097/CCM.0000000000004483**

monitoring is simply unavailable due to prohibitive costs and limited resources. Impressively, the median time to Rapid-EEG setup was 5 minutes (IQR, 4–10 min) and may represent a possible solution to provide EEG monitoring in these situations because nonneurophysiologist staff can set up and monitor the system without specialist input.

Although the study by Vespa et al (8) illustrates the possible advantages of EEG sonification to aid physician decision-making, a few limitations must be considered. First, the study by Vespa et al (8) included neurologists and neurology trainees, possibly limiting generalizability to ICUs without this expertise. This decision was likely guided by the model of neurocritical care that is common in the United States, where neurologists primarily treat these patients. Outside of the United States, many of these patients are cared for in general ICUs with intensivist-led models of care. Second, the Rapid-EEG system uses a limited 10-electrode headband, compared with conventional 21-electrode EEG montage. In general, there is a lack of robust studies on the diagnostic utility of simplified EEG montages in the ICU. The full standardized EEG montage (the International 10–20 system consisting of 21 electrodes) was created to facilitate comparisons across centers and readers (13) and is the current standard for EEG acquisition and interpretation. However, with the increasing demand for EEG in the ICU, a reduced number of electrodes varying in both total number of electrodes and montage configuration have gained popularity. A prior study by Young et al (5) showed that a simplified four-channel ICU bedside monitoring system with a subhairline montage had a sensitive of 68% and specificity of 98% to detect seizures, compared with a standard EEG machine using the international 10–20 system of electrode placement. More recently, a study by Westover et al (14) evaluated an eight-channel EEG configuration with 10 electrodes covering the lateral circumference of the scalp, the same configuration employed by the "Rapid-EEG" system. A conventional full montage was digitally reduced to 10 electrodes to ensure the same time frame and electrode placement were compared. When adjusting for access to ancillary information such as spectral trending, video information, and clinical information for the conventional EEG interpretation, the sensitivity and specificity of the simplified EEG for seizure detection was 98% and 100%, respectively. Overall, the optimal montage and number of electrodes to record EEG in the ICU are still uncertain. However, considerations should include the requirement to record high-quality data against the practicality of placing many electrodes in a resource-limited and time-constrained environment and the potential costs for recording and interpreting data. The small potential loss in sensitivity may be acceptable if the use of a smaller number of electrodes dramatically increases the feasibility of monitoring and thus increasing access for many more at-risk patients.

The present study by Vespa et al (8) does not answer the question of whether EEG sonification alone is a sufficiently accurate diagnostic tool to preclude visual EEG review (8). At best, it would seem that this technology would allow for the widespread screening of at-risk patients. The addition of EEG sonification data to a simplified visual EEG montage was used as a combined intervention in this current study by Vespa et al (8). However, a prior study by Parvizi et al (15) did explore the supplementary use of the EEG sonification method to visual assessment. After a 4-minute training video, nonexperts (34 medical students) assessed 84 visual and audio tests in random order, demonstrating improved sensitivity for seizures and seizure-like activity (generalized periodic discharges, lateralized periodic discharges, triphasic wave, or burst suppression) by listening to EEG sound, rather than visual presentation. The sensitivity of medical students' seizure diagnostic capabilities was 76% ± 19% using an 18-channel visual presentation of EEG samples. After listened to single-channel sonified EEG samples for 15 seconds, students were able to detect seizures with a high degree of sensitivity (98% ± 5%) compared with the reference standard of visual assessment by senior epileptologists.

The study by Vespa et al makes a significant contribution to the ongoing efforts to improve access to real-time EEG acquisition and reduce time to diagnosis (8). The novel use of a simplified EEG montage paired with sonification system may be valuable in the acute assessment of patients with suspected NCSz, leading to more accurate diagnostic decision-making and increasing physicians' confidence in their diagnostic and therapeutic plans. A simplified system like "Rapid-EEG" appears to be a way to expand EEG monitoring to ICUs without expertise in EEG acquisition and interpretation, and the decreased sensitivity compared with conventional EEG monitoring is better than a situation where there is no monitoring. Further studies are needed to understand if the findings of the current study by Vespa et al (8) are generalizable across different disciplines of medicine. Future large-scale studies should also seek to validate the feasibility and utility of this Rapid-EEG system in nonacademic centers where solutions to improve access to EEG are needed. Whether a simplified EEG system like this can help physicians manage patients in the community setting, enabling EEG setup when technicians are unavailable, and deferring transfer to a tertiary neurologic center is unknown. As the impact of brain dysfunction on critical illness outcomes is increasingly recognized, and evidence suggests a clear association between electrographic seizure burden, neuronal injury and poor neurologic outcomes (16, 17), technological innovations such as the "Rapid-EEG" system are needed to facilitate pragmatic clinical trials to understand if the urgent treatment of NCSz and nonconvulsive status epilepticus improves long-term neurocognitive outcomes.

## REFERENCES


1. Claassen J, Mayer SA, Kowalski RG, et al: Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology* 2004; 62:1743–1748
2. Limotai C, Ingsathit A, Thadanipon K, et al: How and whom to monitor for seizures in an ICU: A systematic review and meta-analysis. *Crit Care Med* 2019; 47:e366–e373
3. DeLorenzo RJ, Waterhouse EJ, Towne AR, et al: Persistent nonconvulsive status epilepticus after the control of convulsive status epilepticus. *Epilepsia* 1998; 39:833–840

4. Citerio G, Patruno A, Beretta S, et al; Continuous Quantified EEG in NeuroIntensive Care (CrazyEEG) Group: Implementation of continuous qEEG in two neurointensive care units by intensivists: A feasibility study. *Intensive Care Med* 2017; 43:1067–1068
5. Young GB, Sharpe MD, Savard M, et al: Seizure detection with a commercially available bedside EEG monitor and the subhairline montage. *Neurocrit Care* 2009; 11:411–416
6. Din F, Lalgudi Ganesan S, Akiyama T, et al: Seizure detection algorithms in critically Ill children: A comparative evaluation. *Crit Care Med* 2020; 48:545–552
7. Stewart CP, Otsubo H, Ochi A, et al: Seizure identification in the ICU using quantitative EEG displays. *Neurology* 2010; 75:1501–1508
8. Vespa PM, Olson DM, John S, et al: Evaluating the Clinical Impact of Rapid Response Electroencephalography: The DECIDE Multicenter Prospective Observational Clinical Study. *Crit Care Med* 2020; 48:1249–1257
9. Lutters B, Koehler PJ: Brainwaves in concert: The 20th century sonification of the electroencephalogram. *Brain* 2016; 139:2809–2814
10. Claassen J, Taccone FS, Horn P, et al; Neurointensive Care Section of the European Society of Intensive Care Medicine: Recommendations on the use of EEG monitoring in critically ill patients: Consensus statement from the neurointensive care section of the ESICM. *Intensive Care Med* 2013; 39:1337–1351
11. Le Roux P, Menon DK, Citerio G, et al; Neurocritical Care Society; European Society of Intensive Care Medicine: Consensus summary statement of the international multidisciplinary consensus conference on multimodality monitoring in neurocritical care: A statement for healthcare professionals from the neurocritical care society and the european society of intensive care medicine. *Intensive Care Med* 2014; 40:1189–1209
12. Park A, Chapman M, McCredie VA, et al: EEG utilization in Canadian intensive care units: A multicentre prospective observational study. *Seizure* 2016; 43:42–47
13. The ten twenty electrode system: International federation of societies for electroencephalography and clinical neurophysiology. *American Journal of EEG Technology* 1961; 1:13–19
14. Westover MB, Gururangan K, Markert MS, et al: Diagnostic value of electroencephalography with ten electrodes in critically ill patients. *Neurocrit Care* 2020 Feb 7. [online ahead of print]
15. Parvizi J, Gururangan K, Razavi B, et al: Detecting silent seizures by their sound. *Epilepsia* 2018; 59:877–884
16. Vespa PM, McArthur DL, Xu Y, et al: Nonconvulsive seizures after traumatic brain injury are associated with hippocampal atrophy. *Neurology* 2010; 75:792–798
17. Payne ET, Zhao XY, Frndova H, et al: Seizure burden is independently associated with short term outcome in critically ill children. *Brain* 2014; 137:1429–1438

# Ring Out the Old, Retain With the New*

**Donald B. Chalfin, MD, MS, MPH, FCCP, FCCM**
Visiting Faculty
Jefferson School of Population Health of
Thomas Jefferson University
Philadelphia, PA

Since the turn of the century, we have made great strides in the understanding and recognition of sepsis. We know that sepsis afflicts many critically ill patients and thus it is a leading cause of morbidity and mortality throughout the world, especially among the aged, the immunosuppressed, and those with preexisting comorbidities. We also know that the effects and sequelae from sepsis linger for a long time for those lucky enough to survive, that sepsis is costly, and that after dozens of either equivocal or failed clinical trials of various investigational agents, sepsis is—to say the least—"complex" (1). Yet thankfully, sepsis is now universally recognized as a major public health issue and a frank medical emergency that requires broad awareness, immediate attention, and timely therapeutic intervention (1–4). As a result, patients with suspected sepsis are now being screened, evaluated, and treated earlier than before and likely have greater odds of not only surviving their illness but also surviving with fewer disabilities and residual morbidities (2, 4, 5).

The diagnosis, definition, and recognition of sepsis has always been clinically based although the diagnostic process has been increasingly codified, standardized, and adapted into clinical practice. In 2016, a newer definition of sepsis (Sepsis-3) was developed which differed from the two prior classifications (Sepsis-1 and Sepsis-2), in that it was based upon end-organ dysfunction and the concept of a dysregulated host response to infection versus empirically observed physiologic derangements (1, 6–9). Although Sepsis-3 reflects and captured the latest concepts and the prevailing clinical and scientific thinking, sepsis nevertheless still lacks a diagnostic test, and hence no comparative gold-standard exists. This is a crucial issue in sepsis diagnosis and identification because the newer definition of Sepsis-3 has likely supplanted the older ones in clinical practice, as is often the case when criteria are revised. Yet without a diagnostic standard to enable quantitative comparisons, one cannot determine whether "newer" is indeed "better".

Engoren et al (10), in their study published in this issue of *Critical Care Medicine*, compared the differences between Sepsis-2 and Sepsis-3 in a retrospective, study of 29,459 patients from three large academic medical centers in the United States who had suspected infections, defined as patients who had blood cultures drawn, and were receiving antibiotic therapy. As the authors describe, 62% of all patients were classified as either Sepsis-2 or Sepsis-3, with 44% of patients classified by Sepsis-2 criteria, 44% of patients classified into Sepsis-3, and 23% of patients having both Sepsis-2 and Sepsis-3. Poor agreement was also noted between Sepsis-2 and Sepsis-3, and with respect to patient outcome, observed mortality was 6% in patients with Sepsis-2 only, 10% in patients with Sepsis-3, and 18% in patients classified with both. Among many comparative and joint analyses, not only among Sepsis-2 and Sepsis-3 but also among these and Systemic Inflammatory Response Syndrome and Sequential Organ Failure Assessment components, what particularly stands out is the improved discrimination in

*See also p. 1258.

**Keywords:** sepsis; sepsis-2; sepsis-3; sepsis definitions and criteria; septic shock

Dr. Chalfin received funding from Siemens Healthineers.



**DOI: 10.1097/CCM.0000000000004481**