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# Amplitude integrated electroencephalography for neonatal seizure detection: an alternative opinion to the 2025 Cochrane review

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Amplitude-integrated electroencephalography (aEEG) is widely used in neonatal intensive care units for bedside neuromonitoring, seizure detection, prognostication, and guidance of therapeutic hypothermia. A recent Cochrane systematic review comparing aEEG with conventional video-electroencephalography (cEEG) questioned the value of aEEG for neonatal seizure detection. However, careful interpretation of these findings is warranted. This commentary highlights key methodological limitations of the review, including the inclusion of studies without raw EEG display, heterogeneity in electrode configurations, inconsistent reporting of interpreter expertise, and variable seizure definitions. These factors likely bias pooled estimates toward underestimating the performance of modern aEEG systems when used according to contemporary standards. We emphasize that aEEG should not be evaluated as a substitute for cEEG, but as a complementary bedside modality. Beyond seizure detection, aEEG provides clinically meaningful information through background assessment, early prognostication in hypoxic–ischemic encephalopathy, and longitudinal trend monitoring, particularly in settings where cEEG is unavailable. We conclude that dismissing aEEG technology based on methodologically limited comparisons risks undervaluing an important and pragmatic neuromonitoring tool. Future research and guidelines should prioritize optimized application, standardized protocols, training, and integration with emerging analytic approaches, including artificial intelligence, to support equitable neonatal neurocritical care worldwide.

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## IMPACT:

- aEEG has been widely used in Neonatal Intensive Care Units (NICUs) for bedside neuromonitoring of critically ill newborns, focusing on seizure detection, prognostication, and eligibility for therapeutic hypothermia.
- A Cochrane Review published in August 2025 compared aEEG to conventional video-electroencephalography and questioned the value of aEEG for seizure detection.
- Numerous methodologic limitations were present in the review, including the use of studies without a raw EEG signal display, heterogeneity in electrode configurations, inconsistent interpreter expertise, and different seizure definitions.
- In sensitivity analyses presented in the Cochrane review, studies that incorporated raw EEG tracings showed higher sensitivity and specificity for seizure detection compared to those relying solely on the compressed aEEG.
- When used with raw EEG signal display, standardized protocols, and trained readers, aEEG provides reliable and clinically meaningful information and is critical in settings where cEEG is not available. Future studies should optimize its application and integrate aEEG into multimodal neuroprotection strategies.

Amplitude-integrated EEG (aEEG) is frequently used in Neonatal Intensive Care Units (NICUs) around the world for neuromonitoring of high-risk newborns for seizure detection, neuroprediction, selection of patients for therapeutic hypothermia, and monitoring patients at high risk of brain injury, including preterm infants.<sup>1</sup> A recent Cochrane review by Rakshashbhavankar et al. performed a meta-analysis comparing aEEG with conventional video-

electroencephalography (cEEG) for neonatal seizure detection and questioned the value of aEEG.<sup>2</sup> Systematic reviews are indispensable to evidence-based medicine; however, this meta-analysis illustrates the challenges and pitfalls of pooling heterogeneous data and reaches conclusions that misrepresent the established role of aEEG monitoring in clinical practice.

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Several limitations undermine the ability to draw meaningful conclusions from this Cochrane review:

- First, only half of the studies incorporated raw EEG traces alongside the compressed aEEG trend display; this is a major methodological limitation given the fact that all modern aEEG systems display the raw, unprocessed EEG trace. Modern aEEG devices are essentially limited-montage EEG systems with aEEG trends. Without the raw EEG, one cannot reliably identify short-duration and focal seizures, as well as common recording artifacts that resemble EEG seizures.<sup>3,4</sup> This reduces the diagnostic accuracy and biases results toward underperformance of aEEG compared to the reference standard cEEG. Indeed, in the sensitivity analysis presented in the Cochrane review, studies that incorporated raw EEG signals versus those relying solely on the compressed aEEG showed higher sensitivity (0.75, 95% CI 0.64–0.84 vs. 0.68, 95% CI 0.45–0.84) and specificity (0.85, 95% CI 0.74–0.92 vs. 0.73, 95% CI 0.20–0.99) compared with those relying solely on the compressed aEEG trend for detection of seizures.
- Second, interpreter expertise was inconsistently reported. Only three of the 16 included studies reported aEEG training, while 10 of the 16 reported aEEG experience. It is well established that insufficient user expertise markedly reduces accuracy and increases false positives,<sup>3,5,6</sup> thereby conflating human performance with technological capability. The accuracy of any neurophysiological tool is heavily dependent on education and training, and failing to stratify results by interpreter expertise risks attributing operator-related variability to the method itself.
- Third, there was considerable heterogeneity in electrode configuration, recording duration, and outcome definitions. Compared to the standard two-channel aEEG recordings, four studies relied on single-channel recordings, and two did not specify the number of channels. Some included studies used short monitoring windows that were insufficient to capture the dynamic and evolving nature of neonatal seizures. Moreover, variability in the definition of a “seizure” across studies further complicated pooled estimates of sensitivity and specificity.<sup>7</sup>
- Fourth, the authors’ concluding statement, that “Studies are required to evaluate if the combination of aEEG and clinical observation is better than clinical observation alone” is unacceptable. This is already well-known and has been summarized in previous systematic reviews.<sup>8</sup> Indeed, a major impetus for the development of aEEG was the low sensitivity and specificity of unaided clinical, bedside diagnoses of neonatal seizures. The review implicitly supports clinical observation alone as an acceptable comparator to aEEG, despite overwhelming evidence that most neonatal seizures are electrographic-only and therefore undetectable at the bedside.<sup>9,10</sup> Reliance on observation alone is outdated and risks undertreatment of electrographic-only seizures, as well as overtreatment of abnormal movements mimicking clinical seizures.

These limitations call into question the conclusions of this meta-analysis. It is not surprising that the reported sensitivity and specificity of published studies varied widely. Importantly, these results should not be interpreted as inherent limitations of aEEG technology, but rather as the obvious consequences of variability of study design, patient characteristics, interpreter experience, and application. It is well known that aEEG provides clinically meaningful and valuable information when it is used according to best practice. Recording should be performed using four electrodes at standardized locations, providing at least two channels with aEEG trends and corresponding raw EEG signals, interpreted by well-trained experts in neonatal EEG.<sup>11,12</sup> At the same time, aEEG

recordings do have intrinsic limitations for seizure detection when compared to cEEG: short or low-amplitude seizures may be missed, and seizures arising from regions distant to electrode placement are less likely to be captured. Accurate interpretation, similar to cEEG interpretation, requires considerable reading expertise, as artifacts can mimic ictal activity.<sup>13,14</sup> These constraints highlight the need for technical rigor and well-trained interpretation in routine clinical use.

In addition to seizure detection, aEEG offers the broader contribution of background interpretation, which may impact the care of critically ill newborns. Robust evidence demonstrates that background patterns within the first 72 h predict outcomes in hypoxic–ischemic encephalopathy (HIE), including in patients receiving therapeutic hypothermia.<sup>15,16</sup> Beyond prognostication, aEEG informs eligibility for cooling, allows long-term trend monitoring, and provides a pragmatic alternative in many settings where cEEG is unavailable.<sup>12</sup> To dismiss aEEG based solely on its seizure detection performance under suboptimal conditions risks disregarding its validated and widely adopted role as a neonatal neuromonitoring tool.

Neuromonitoring of the high-risk neonate is evolving rapidly. New devices which record and interpret neonatal EEG using artificial intelligence and machine-learning algorithms are being introduced into clinical practice. Their relative roles in the context of cEEG and aEEG remain unknown. A constructive way forward requires additional high-quality prospective studies that: (1) standardize electrode configurations and ensure raw EEG signal availability; (2) stratify performance by interpreter expertise; and (3) assess not only diagnostic accuracy but also clinical impact, including time to seizure recognition and response to antiseizure medication treatment. Even in centers with cEEG capability, bedside aEEG continues to have importance, as it allows bedside identification of seizures. Seizure detection algorithms are built into some aEEG devices and newer AI enhanced high performing algorithms will soon be integrated, increasing seizure detection accuracy.<sup>17</sup> Moreover, aEEG has particular importance in resource-limited settings, including many centers in both high-income and low- to middle-income countries where cEEG is often unavailable due to limited pediatric neurophysiology availability and/or limited resources.<sup>18</sup> In these contexts, aEEG may represent the only feasible option for continuous brain monitoring, and optimizing its use can significantly improve timely seizure detection and treatment, helping reduce inequities in neonatal neurocritical care.

In summary, while it is true that cEEG is the reference standard for seizure detection, this Cochrane review underestimates the sensitivity and specificity of modern aEEG technology for neonatal seizure detection due to limitations in the study design in many of the selected studies, as we have highlighted above. The criteria used for comparing aEEG with cEEG, included many studies that lacked access to raw EEG signals, effectively underestimating the established role of modern aEEG devices in neonatal neurocritical care. Clinical observation alone is a markedly limited diagnostic approach and is no longer considered an acceptable comparator. Despite the intrinsic limitations of aEEG compared to cEEG, when applied appropriately, with access to raw EEG signals, standardized protocols, and expert interpretation, aEEG remains a valuable and pragmatic tool. Beyond seizure detection, it provides crucial prognostic information, supports decision-making on the initiation of therapeutic hypothermia, and is an important neuromonitoring tool in settings where cEEG is not readily available. The priority for neonatal neurocritical care should not be to question the value of aEEG, but to refine its application in conjunction with cEEG when available, optimize the education of providers, advocate for the integration of high-performing algorithms and integrate them into multimodal neuroprotection strategies to ensure equitable care for all infants at risk of brain injury, regardless of where they are born.

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GBB is co-founder of University College Cork Spin out company Cergenx Ltd. The remaining authors declare no competing interests.

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