University of Cincinnati

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I, Cameron W. Thomas, hereby submit this original work as part of the requirements for the degree of Master of Science in Clinical and Translational Research.

It is entitled:
Altering time compression algorithms of amplitude-integrated electroencephalography display improves neonatal seizure detection

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Altering time compression algorithms of amplitude-integrated electroencephalography display improves neonatal seizure detection

A thesis submitted to the
Graduate School
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Master of Science
in
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by
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Abstract

Objectives

Primary objective: Determine the aEEG time compression algorithm which maximizes sensitivity and specificity for the identification of neonatal seizures.

Secondary objectives: 1) Quantify the effect of prior EEG reading experience on user sensitivity and specificity of aEEG for identification of neonatal seizures. 2) Identify the contribution of concurrent unprocessed single-channel raw EEG tracing to the final sensitivity and specificity of aEEG.

Methods

Full, neonatal montage, conventional EEG (cEEG) recordings from 24 neonates >36 weeks gestation and < 28 days of life were obtained. Representative 6 hr segments of cEEG including a mix of normal brain activity and abnormal seizure activity were converted to amplitude integrated EEG (aEEG) using Stellate Harmonie® software. Six different aEEG formats were created: 6cm display per hour live recording, 12cm/hr and 24cm/hr each presented with and without accompanying unfiltered single channel cEEG tracing. Two readers with extensive experience interpreting cEEG and two without that experience interpreted each study. Each reader’s results were compared to the interpretation of the original neonatal cEEG by an expert in neonatal electrophysiology. Comparisons were used to generate sensitivity, specificity and classification accuracy for each reader and method. A theoretical clinical model assessed the impact of detected differences on clinical decision making.
Results

Twenty four 6 hour recordings were presented in 6 different formats to each reader. Thus, each reader interpreted 864 hours of aEEG. When combining studies and readers, sensitivity improved from 39% to 53% when aEEG compression decreased from 6cm/hr to 24cm/hr. When aEEG was accompanied by unfiltered single channel cEEG tracing sensitivity improved from 30% to 55% as aEEG compression was reduced. Specificities improved with reduced compression from 70% to 77% with no accompanying cEEG and ranged from 82%-90% with accompanying unfiltered cEEG signal though trend was downward with reduced compression due to increased false positives. Classification accuracy improved from 53% to 70% as aEEG compression was reduced and unfiltered cEEG signal was included for interpretation.

When data was analyzed by reader type, readers with extensive experience interpreting cEEG outperformed readers without extensive experience interpreting cEEG in 81% of direct comparisons. The readers were equal in 9.5% of direct comparisons, and the inexperienced readers outperformed the experienced readers in 9.5%, of which 7% was accounted for by a single test format (24cm/hr without unfiltered cEEG) in which experienced readers identified a higher number of false positives.

Clinical decision modeling showed that experienced readers made about one less error in interpretation per 6hr recording.

Conclusions

Our study confirms that decompressing traditional aEEG signal from 6cm/hr to 12cm/hr or 24cm/hr improves the sensitivity and specificity as well as the classification accuracy of aEEG.
When readers with extensive experience in conventional EEG are available, adding raw tracing
to the aEEG generally enhances these effects.

Given the potential shortcomings of aEEG, it is best used as part of a comprehensive clinical
monitoring protocol where cEEG and expert neurologic interpretation of neurophysiologic data
are available when clinical suspicion combined with aEEG monitoring identifies suspected
seizure activity.
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A special thanks to my family – especially to Michelle for her patience and unwavering support throughout all the long years of my educational path – Yes Michelle, I think I am finally done!
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Altering time compression algorithms of amplitude-integrated electroencephalography display improves neonatal seizure detection

Background

Over the last decade, amplitude integrated electroencephalography (aEEG) has gained popularity as a means of monitoring cerebral function in at-risk neonates. Particular emphasis has been placed upon identification of seizures in neonates with clinically identifiable spells which suggest possible underlying seizure activity, as well as identification of clinically silent seizures in those neonates presumed to be at highest risk for this type of event, such as asphyxiated infants. Neonatal seizures are frequently subtle, but may also occur in the absence of clinical signs or symptoms, particularly after initial treatment with standard antiepileptic medications such as phenobarbital.\(^1,2\) Electrographic seizures identified by continuous standard electroencephalography (EEG) or aEEG, are associated with poor neurodevelopmental outcomes, although causality has not been clearly established.\(^3-5\) Until more information is available, monitoring and treatment for subtle and subclinical seizures is generally thought to be beneficial for the care of these infants.

Continuous traditional 11 electrode neonatal EEG monitoring is often not available in community or even tertiary-care Level III Neonatal Intensive Care Units because of high equipment costs, the time-intensive nature of reading continuous standard EEG and limited availability of healthcare providers with the expertise necessary to perform and interpret continuous EEG.\(^6,7\) Amplitude-integrated EEG (aEEG), also known as Cerebral Function Monitoring (CFM) has developed as a potentially viable alternative. Through a series of steps, the signal from two central electrodes (single channel), easily placed by minimally trained providers, is acquired, filtered and compressed resulting typically in signal output display in which 6 cm of display is equivalent to one hour of real time.
recording. This display allows seizure recognition by visualization of changes in amplitude patterns over time.\textsuperscript{7,8} Although aEEG can detect the majority of seizures in term infants, it may not correctly identify seizures that are brief or focal, especially if the focal epileptogenic zone occurs far from the centrally placed electrodes.\textsuperscript{9,10} The utility of aEEG is further hindered by the incorrect identification of artifact as seizures which is more likely to occur in aEEG than with continuous standard EEG.\textsuperscript{9} These inaccuracies probably result from both the time compression and the use of only two electrodes.\textsuperscript{11} Additional display of the single-channel raw EEG tracing improves sensitivity.\textsuperscript{9}

**Objectives**

*Primary objective:* Determine the aEEG time compression algorithm which maximizes sensitivity and specificity for the identification of neonatal seizures.

*Secondary objectives:* 1) Quantify the effect of prior EEG reading experience on user sensitivity and specificity of aEEG for identification of neonatal seizures. 2) Identify the contribution of concurrent unprocessed single-channel raw EEG tracing to the final sensitivity and specificity of aEEG.

**Hypothesis**

Decompressing traditional aEEG signal and viewing aEEG with concurrent unprocessed single channel raw EEG will improve sensitivity and specificity of aEEG in neonatal seizure detection. This effect will be enhanced by prior reader experience with interpreting conventional EEG.
Specific Aims

1) Compare sensitivity and specificity of standard format aEEG which displays 6cm of digital signal output per hour of live recording with alternative time compression formats of 12cm/hour of live recording and 24cm/hour live recording with and without unprocessed single channel EEG.

2) Analyze seizure identification data in all aEEG formats according to prior reader experience interpreting conventional EEG.

Methods

Study files were created from neonatal EEG recordings obtained using the Stellate Harmonie® EEG system for 28 term or near-term (>36 weeks gestational age) neonates (<1 month of age) referred for prolonged inpatient EEG studies at Cincinnati Children’s Hospital Medical Center (CCHMC) between April 2008 and October 2009. Neonatal EEGs were performed in CCHMC neonatal or pediatric intensive care units as deemed clinically necessary by the treating physicians using standard continuous neonatal EEG technique and 11 electrode application. The selected studies included a characteristic mix of normal brain activity and abnormal seizure activity. All studies were de-identified and randomized by a computer application specialist not otherwise involved in the study. Representative six hour segments of the recordings were converted to aEEG from C3, C4, P3 and P4 electrodes using Stellate Harmonie® software. File duration was selected for purposes of uniformity and to prevent readers from correlating files by unique length. Employing varying time compression algorithms, six different formats of aEEG output display were produced: 6 cm/hour, 12 cm/hour and 24cm/hour of live recording each presented with and without a single channel of unprocessed EEG tracing. Each block of alternative formats was also randomized to prevent correlation across formats.
An experienced Pediatric/Neonatal Epileptologist interpreted the conventional EEG tracings from which the aEEGs were created and documented the timing, duration and number of electrographic seizures in each recording. This served as the gold standard to which aEEG interpretation was compared. Readers of the aEEG studies included the previously mentioned Pediatric/Neonatal Epileptologist as well as a Neonatal Neurologist with extensive EEG reading experience, a Neonatologist, a Neonatology Fellow and a Neonatal Intensive Care nurse. These persons were selected as they were felt to be relevant personnel who would potentially use this technology in the course of standard clinical care. Prior to analyzing the recordings, each reader completed a brief tutorial explaining aEEG and providing representative samples of normal and abnormal tracings. For each aEEG tracing presented, readers were asked to identify the number of suspected electrographic seizures as well as their time and duration. This information was later cross-checked with the gold standard reader event log to ensure that all identified events were accurately classified (e.g. to determine if events were true positive, false positive, true negative, false negative).

Finally, a clinical decision making model was designed to assess the impact of aEEG interpretation on possible treatment decisions. In this model, for each hour of recording a theoretical decision to start anti-epileptic medications was made if a seizure was identified by the reader. Thus, a false positive could result in inappropriate initiation of medical therapy and a false negative could result in a missed opportunity to treat current seizure activity and/or possibly prevent future seizures.

All readers were blinded to patient identity and any patient clinical information not contained in the EEG. Furthermore, video files from the EEG were separated from the created aEEG files and could not be referenced. Files were made the same length and were presented in random order within each format group to prevent cross-correlation between formats. No recent EEG studies were used in
the study to prevent readers from correlating studies with recent clinical interactions or experiences involving study subjects from whom recordings were obtained.

**Statistical Methods**

Randomized block ANOVA (analysis of variance) analysis was performed to calculate the number of aEEG recordings needed to power the study. Based on the number of readers, the various aEEG formats to be interpreted and the ability to detect a fifteen percent difference between methods with a probability of type I error of < 0.05, seventeen study subjects were required to give appropriate statistical power to the study. To give further power to the study and to allow for inconsistencies in study quality or duration, an additional 7 studies were included for a total of twenty four studies.

Analyses were conducted using linear mixed models. Fixed effects included time compression, presence or absence of single channel conventional EEG, and physician training background (extensive experience reading conventional EEG or no experience reading conventional EEG). Random effects included study subject and reader nested within physician training background. The number of seizures identified by aEEG was compared to the gold standard number of identified seizures to calculate sensitivity, specificity and classification accuracy. Using Least Squares Means (LSMeans), each alternative display format was compared to the typical 6cm/hr format to confirm that any detected difference in sensitivity, specificity and classification accuracy, defined as the proportion of correct decisions, was statistically significant. Each alternative display format was not compared to every other alternative display format as clinical relevance was diminished when comparing readers of varying backgrounds with varying study formats instead of comparing readers within a format, or formats by reader. By only comparing each alternative display format to the typical 6cm/hr format,
complex interaction terms were also minimized. To ensure the most conservative interpretation of any detected differences, the Bonferroni correction was used to adjust for the multiple tests.

Data for the clinical decision making model was obtained using a generalized linear model with binomial regression. The False Discovery Rate (FDR) was used to adjust for the various comparisons.

Results

Twenty eight neonatal EEG files met selection criteria during the study period. Four of the studies were excluded from analysis due to inadequate study length, significant disruptions in the recording, or problematic artifact in leads from which the aEEG file were created. Twenty four recordings of 6 hours duration, including recordings with and without seizure activity, were presented in 6 different file formats to each reader. Thus, each reader was required to interpret a total of 864 hours of aEEG recording. The least experienced reader had substantial inconsistency in interpreting the recordings resulting in reader classification accuracy consistently below 50%. These aberrancies introduced interaction terms into the data that were otherwise absent and thus a determination was made to exclude this data from the final analysis.

Sensitivity and classification accuracy generally improved as time compression algorithms were altered from the conventional 6cm/hr to less compressed formats of 12cm/hr or 24cm/hr (Table I). This pattern was true whether or not a raw single channel unfiltered EEG signal accompanied the aEEG tracing and if studies were combined for analysis, or if studies containing seizure events were analyzed separately. Specificity improved as time compression was reduced when raw single channel unfiltered EEG was absent, but diminished with reduced time compression when raw single channel unfiltered EEG was included, or in recordings where there were no seizures
captured (Table I). However, as a group, the specificity values were still better with raw single channel unfiltered EEG signal present than when it was absent.

**Table I: Sensitivity, Specificity and Classification Accuracy—All Readers**

<table>
<thead>
<tr>
<th>Speed</th>
<th>Raw</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>CA</th>
<th>Raw</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>CA</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>6</td>
<td>-</td>
<td>0.39</td>
<td>1</td>
<td>0.70</td>
<td>1</td>
<td>0.53</td>
<td>1</td>
<td>0.39</td>
<td>1</td>
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<tr>
<td>12</td>
<td>-</td>
<td>0.50</td>
<td>0.0082</td>
<td>0.70</td>
<td>0.0220</td>
<td>0.60</td>
<td>0.0572</td>
<td>0.50</td>
<td>0.0082</td>
</tr>
<tr>
<td>24</td>
<td>+</td>
<td>0.53</td>
<td>0.0007</td>
<td>0.77</td>
<td>0.0392</td>
<td>0.66</td>
<td>0.0003</td>
<td>0.53</td>
<td>0.0007</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>0.30</td>
<td>0.0421</td>
<td>0.90</td>
<td>&lt;0.0001</td>
<td>0.65</td>
<td>0.0008</td>
<td>0.30</td>
<td>0.0421</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>0.52</td>
<td>0.0018</td>
<td>0.82</td>
<td>0.0002</td>
<td>0.69</td>
<td>&lt;0.0001</td>
<td>0.52</td>
<td>0.0018</td>
</tr>
<tr>
<td>24</td>
<td>+</td>
<td>0.55</td>
<td>&lt;0.0001</td>
<td>0.82</td>
<td>0.0002</td>
<td>0.70</td>
<td>&lt;0.0001</td>
<td>0.55</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Speed: cm/hr
Raw: (−) indicates no single channel unfiltered EEG accompanied recording.
(+ ) indicates that single channel unfiltered EEG was present
CA – classification accuracy
LSMean – least squares means
‡- denotes p-values where Bonferroni correction reveals that the value is above the threshold for statistical significance

When seizure identification was analyzed by reader type (Table II), prevailing trends within reader sub-groups were similar to those discussed when all readers were analyzed together (Table I). Again, sensitivity and classification accuracy generally improved as time compression algorithms were altered from the conventional 6cm/hr to less compressed formats of 12cm/hr or 24cm/hr. This trend was manifest with or without a raw single channel unfiltered EEG signal accompanying the aEEG tracing and if studies were combined for analysis, or if studies containing seizure events were analyzed separately. Exceptions to this pattern occurred in the sensitivity of seizure classification by readers with extensive conventional EEG reading experience (Table II). When reading in the 24cm/hr format, this group of readers had sensitivities of 0.45 at 24cm/hr compared to 0.50 at 12cm/hr. Despite being lower than the sensitivity at 12cm/hr, the sensitivity at 24cm/hr was significantly better than at the traditional 6cm/hr compression algorithm. Additionally, though both 12cm/hr and 24cm/hr with accompanying raw single channel unfiltered EEG signal had much better sensitivity than the
conventional 6cm/hr format, the 12cm/hr and 24cm/hr sensitivities were almost identical. Specificity trends showed more variability. For readers with extensive conventional EEG reading experience, 12cm/hr formats were least specific when considered either with or without accompanying raw single channel unfiltered EEG signal.

Perhaps the most striking finding when analyzing the data by reader type (Table II) is the great consistency with which readers with extensive experience interpreting conventional EEG outperform those without extensive experience. Of 42 possible comparisons, experienced EEG readers outperform inexperienced readers 34 times (81% of comparisons), sometimes by very large margins. The readers are equivalent in 4 comparisons (9.5% of comparisons) and the inexperienced readers outperform the experienced readers in 4 comparisons (9.5% of comparisons), 3 of which are within the same format, 24cm/hr without accompanying raw single channel unfiltered EEG.

**Clinical Decision Making Paradigm**

The Clinical Decision Making Paradigm creates a framework from which the data previously discussed in Tables I and II can be given clinical meaning. A theoretical model was created in which a clinician would round on the patient hooked up to aEEG at hourly intervals. At the end of each hour aEEG was reviewed and the clinician would make a decision regarding treatment with seizure medications. If a seizure was identified, treatment would commence. If no seizure was identified, the clinician would return in one hour to review the next block of recording. For each subsequent hourly review, a decision would again be reached regarding initiating (or escalating if treatment was previously commenced) treatment or deferring treatment. Thus for each format and each patient within the format, there were 6 decision points.
Table II: Sensitivity, Specificity and Classification Accuracy—Analyzed by Reader Experience

Reading Conventional EEG

<table>
<thead>
<tr>
<th>Readers WITH extensive conventional EEG reading experience</th>
<th>Readers WITHOUT extensive conventional EEG reading experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=24</td>
<td>ONLY STUDIES WITH SEIZURE EVENTS N=13</td>
</tr>
<tr>
<td>Speed</td>
<td>Raw</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>0.50</td>
</tr>
<tr>
<td>24</td>
<td>0.45</td>
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<tr>
<td>6</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
</tr>
<tr>
<td>24</td>
<td>+</td>
</tr>
</tbody>
</table>

Based on this scenario a correct clinical decision would be to initiate seizure medications if any seizure or seizures was/were identified in the preceding hour. Another correct decision would be to defer starting medications if no seizures had been identified in the previous hour. Conversely, incorrect decisions would include starting seizure medications for an event that was not a seizure (artifact), or failing to start seizure medications for an event that was a seizure and was not identified correctly. Using this scenario and correcting for multiple comparisons demonstrates that when comparing aEEG methods within the Clinical Decision Making Paradigm, 12cm/hr and 24cm/hr without raw tracing are superior to 6cm/hr without raw tracing (Table III). When compared to the 6cm without raw tracing format, other formats such as 6cm/hr with raw tracing, 12cm/hr with raw tracing and

Speed is in cm/hr
Raw: (–) indicates no single channel unfiltered EEG accompanied recording; (+) indicates that single channel unfiltered EEG was present
CA – classification accuracy
RMSE – root mean square error
24cm/hr with raw tracing trend toward significance but do not meet the pre-established threshold. In the model there is little difference when 12cm/hr modalities and 24cm/hr modalities are compared to each other.

Table III: Comparison of aEEG methods (derived from Clinical Decision Making Paradigm)

| Primary Method | Primary Raw | Comparison Method | Comparison Raw | Estimate | Pr > |t| | i | FDR |
|----------------|-------------|-------------------|----------------|----------|-----------------|---|---|---|
| 6              | -           | 24                | -              | -0.7751  | 0.0001          | 1 | 1 | 1 |
| 6              | -           | 12                | -              | -0.4477  | 0.0102          | 2 | 1 | 2 |
| 6              | -           | 6                 | +              | -0.3954  | 0.0229          | 3 | 0 | 3 |
| 6              | +           | 12                | +              | -0.301   | 0.1012          | 5 | 0 | 5 |
| 6              | +           | 24                | +              | -0.2483  | 0.1736          | 6 | 0 | 6 |
| 12             | -           | 24                | -              | -0.3274  | 0.0793          | 4 | 0 | 4 |
| 12             | -           | 12                | +              | -0.2487  | 0.1796          | 7 | 0 | 7 |
| 12             | +           | 24                | +              | 0.05268  | 0.7788          | 9 | 0 | 9 |
| 24             | -           | 24                | +              | 0.1314   | 0.4898          | 8 | 0 | 8 |

Speed is in cm/hr
Raw: (–) indicates no single channel unfiltered EEG accompanied recording; (+) indicates that single channel unfiltered EEG was present
i- denotes ranking of Pr > |t| value in preparation for FDR
FDR – false discovery rate used to account for multiple comparisons. When value is 1, corresponding Pr > |t| is statistically significant

The Clinical Decision Making Paradigm can also be used to compare reader type. If a reader without extensive experience interpreting conventional EEG is compared to a reader with extensive experience and each reader is presented with an aEEG recording accompanied by single channel raw EEG signal, the experienced reader will make one less error in clinical judgment to start or defer seizure medications (Table IV) over the six possible decision points previously described in the Clinical Decision Making Paradigm. This represents an almost 17% reduction in interpretation errors. If experienced readers are then compared solely as to whether they are interpreting the aEEG with or without accompanying single channel raw EEG signal, the error reduction is about half of that produced when comparing reader types (Table IV) suggesting that only a portion of the advantage enjoyed by the experienced reader can be explained by their presumably better understanding of the raw signal.
**Table IV: Comparison of aEEG readers (derived from Clinical Decision Making Paradigm)**

| Primary Reader | Primary Raw | Comparison Reader | Comparison Raw | Estimate | Pr > |t| | i | FDR |
|----------------|-------------|-------------------|----------------|---------|-------|----|----|----|
| -              | +           | +                 | +             | -0.9824 | 0.0004 | 1  | 1  |
| +              | -           | +                 | -             | -0.5422 | 0.0008 | 2  | 1  |
| -              | -           | -                 | +             | 0.2004  | 0.154  | 3  | 0  |
| -              | +           | -                 | -             | -0.2398 | 0.3766 | 4  | 0  |

Raw: (−) indicates no single channel unfiltered EEG accompanied recording; (+) indicates that single channel unfiltered EEG was present

Reader: (−) indicates that reader DOES NOT HAVE extensive experience in reading conventional EEG; (+) indicated that reader HAS extensive experience in reading conventional EEG.

i- denotes ranking of Pr > |t| value in preparation for FDR

FDR – false discovery rate used to account for multiple comparisons. When value is 1, corresponding Pr > |t| is statistically significant

**Discussion**

In a study comparing aEEG to cEEG published in 2008, Shah et al. calculated the sensitivity and specificity of aEEG when compared to a gold standard of cEEG⁹. In that study, interpretation of 351 total hours of aEEG tracings was performed by two readers each with about 3 years of clinical experience interpreting aEEG. Their study demonstrated that aEEG without the accompanying unfiltered cEEG signal yielded low sensitivities ranging from 27%-56% depending on reader and aEEG format (single or dual channel aEEG). Similar data from our study can be obtained by looking at the 6cm/hr format with no accompanying unfiltered cEEG output. Our sensitivity when combining readers in this format interpreting 864 hours of recording was 39%, confirming Shah’s findings despite our use of readers inexperienced in use of aEEG. The Shah study also demonstrates improvements in sensitivity and specificity when unfiltered cEEG output is viewed simultaneously with aEEG. Their data combining readers and formats showed a sensitivity of 76% and specificity of 78%. Although our study did not match the magnitude of improvements in sensitivity and specificity demonstrated by Shah et al., the improvements were substantial, and the difference in magnitude can be explained by differences in study design and reader experience with cEEG.
In most neonatal intensive care units that use aEEG as a screening tool, there is relatively low reader experience in interpreting aEEG. Our study was designed with this in mind and readers were selected based on what might be typical in an academic setting or a higher level non-academic neonatal intensive care. Neonatologists are often asked to read and interpret aEEG despite lack of formal training in electrophysiology. Neurology readers are familiar with cEEG but often have little to no experience with aEEG, therefore we had great interest in knowing how readers of these backgrounds performed in interpreting real clinical data. In 2004, Rennie et al. published an analysis of aEEG accuracy using non-expert readers\textsuperscript{12}. Their study design differs from ours in several important ways: 1) Substantial portion of pre-term infants included in study cohort (little published data on accuracy of aEEG in preterm infants), 2) Only patients with seizures are included in study (harder to detect number of false positives), 3) Almost all seizures documented in study either start or become generalized (focal seizures are more likely to be missed on aEEG), 4) No unfiltered cEEG signal was viewed concurrently with aEEG. 5) The way in which they created their aEEG began with analog signal and required several unique adaptations that could potentially change the quality and consistency of the recording compared to coherent aEEG systems used in other studies. Despite these shortcomings, the Rennie study shared several important similarities to our study such as the use of non-expert aEEG readers and the analysis of several different compression formats. Their trends at differing compression formats were similar to ours. They compared formats of 6cm/hr, 15cm/hr and 30cm/hr achieving sensitivities of 38%, 54% and 55%. These are remarkably similar to our trends at 6cm/hr, 12cm/hr and 24cm/hr of 39%, 50% and 53%. Their specificity trends of 92%, 75%, and 61% more closely matched our specificity data when unfiltered cEEG channel was viewed simultaneously but this may be a result of differences in study design.

[12]
Recent statements from The American Clinical Neurophysiology Society’s Guideline on Continuous Electroencephalography Monitoring in Neonates are confirmed by our study data.

“Conventional video-EEG monitoring is the gold standard for neonatal seizure detection and quantification and should be used whenever available for seizure detection and differential diagnosis of abnormal appearing, paroxysmal clinical events.”13 Although aEEG may serve a useful purpose as a screening tool and an adjunct to cEEG, “If seizures are suspected on aEEG, ...conventional EEG monitoring, if available, should begin as soon as possible to confirm and refine the electrodiagnosis”13

The clinical effectiveness of aEEG can be enhanced with relatively simple modifications such as decreasing compression from 6cm/hr to 12cm/hr or 24cm/hr. These improvements can be further strengthened by adding raw unfiltered cEEG tracing where there is adequate experience and expertise to interpret the raw data. Amplitude integrated EEG should not be relied upon excessively, especially where clinical suspicion for seizures is high because the sensitivity is low and thus the test is very prone to false negatives no matter the reader. Also caution should be used when using the decompressed formats with raw tracing as there is some tendency toward false positives especially where no seizures are present. The options to change compression and add raw tracing are available on many aEEG platforms currently on the market and these options should guide decisions about purchasing monitoring equipment or design of clinical monitoring protocols.

The consequence of false decisions when relying solely upon aEEG could potentially be high. If seizures were not identified, they could continue unabated causing cytotoxic injury in the developing brain and leading to a decline in clinical status. Also, due to kindling phenomena, as untreated seizures continued, future seizures could become more intractable or difficult to treat. If seizures were
identified incorrectly, incorrect treatment could incur costs associated with seizure medications, higher levels of care, more prolonged hospital stays, poor feeding due to excess sedation, etc.

**Conclusions**

Our study confirms that decompressing traditional aEEG signal from 6cm/hr to 12cm/hr or 24cm/hr improves the sensitivity and specificity as well as the classification accuracy of aEEG. When readers with extensive experience in conventional EEG are available, adding raw tracing to the aEEG generally enhances these effects.

Given the potential shortcomings of aEEG, it is best used as part of a comprehensive clinical monitoring protocol where cEEG and expert neurologic interpretation of neurophysiologic data are available when clinical suspicion combined with aEEG monitoring identifies suspected seizure activity.
Bibliography


