

Optimizing seizure detection by quantitative EEG in paediatric refractory status epilepticus

^{1,2}Junjie HUANG, ³Gita KRISHNASWAMY, ¹Jocelyn LIM, ¹Nazima Binte SAHUL HAMED, ¹Simon LING, ¹Terrence THOMAS, ^{1,3}Derrick CHAN

¹Department of Paediatric Medicine, KK Women's and Children's Hospital, Singapore; ²Duke-NUS Graduate Medical School, Singapore; ³Office of Clinical Sciences, Duke-NUS Graduate Medical School

Abstract

Background & Objective: Continuous electroencephalography (cEEG) is valuable in the diagnosis and management of refractory status epilepticus (RSE) but requires intensive skilled interpretation. Density spectral array (DSA) is a quantitative analytic tool used to screen cEEG recordings for seizures. This study aims to determine the optimal amplitude setting and to compare the use of single-average-trendgraph display and eight-trendgraph display in seizure detection with DSA. **Methods:** Five excerpts from pediatric cEEG recordings with RSE were identified. In Phase 1 of the study, each of 4 readers determined the DSA amplitude setting one most preferred for each excerpt, and marked all seizures in one excerpt using one's preferred setting. Inter-rater agreement in seizure detection was measured. In Phase 2, readers marked all seizures in all excerpts, first using single-average-trendgraph display, and then using eight-trendgraph display after a wash-out period. Intra-rater agreement in seizure detection between the two display methods was calculated. **Results:** In Phase 1, DSA readers' choice of preferred amplitude settings varied widely but inter-rater agreement in seizure detection was high. In Phase 2, seizure detection using single- and eight-trendgraph displays showed high agreement with each other and, where they disagreed, single-average-trendgraph was more sensitive. Additionally, low seizure-to-background amplitude ratio in EEG recordings was associated with worse detection sensitivity/specificity.

Conclusions: DSA amplitude settings do not affect seizure detection. Single-trendgraph display is comparable to eight-trendgraph display in screening cEEG for seizures. Seizure detection with DSA performs better in cEEG recordings with high seizure-to-background amplitude ratio.

Keywords: Density spectral array, continuous EEG monitoring, seizure detection, refractory status epilepticus, pediatric, critical care

INTRODUCTION

Refractory status epilepticus (RSE) is defined as status epilepticus that continues for at least one hour despite first- and second-line anticonvulsant therapy. RSE is a neurological emergency which necessitates intubation and transfer to intensive care unit (ICU) for aggressive seizure management.¹ RSE carries a high morbidity and mortality.^{1,2} Continuous EEG (cEEG) monitoring is an important tool for the diagnosis and management of SE and RSE in the critical care setting. It enables clinicians to titrate anticonvulsants to achieve seizure control and burst-suppression on EEG³, while limiting doses to minimize side effects and complications.^{3,4} Non-convulsive status epilepticus has been reported in 48% of patients treated for convulsive

status epilepticus⁵ and 8% of comatose patients.⁶ Continuous EEG can detect non-convulsive seizures.⁷

Given the advantages of cEEG monitoring, recent years have seen an increase in its use for critically ill children.⁷ Nonetheless, there are several important drawbacks. Firstly, the large amount of data generated can be overwhelming for manual analysis. Secondly, it requires trained EEG technologists to maintain high-quality recordings and electroencephalographers to review the data⁴, with review seldom done in real time.⁷ The third disadvantage is the associated high costs for equipment and personnel.⁴

One solution to address these disadvantages is the development of quantitative EEG analysis. Density spectral array (DSA), also known

as compressed spectral array (CSA) or color density spectral array (CDSA) is an analytic tool which decomposes raw EEG data by fast-Fourier transform to generate time-compressed trendgraph(s) with x-axis being time, y-axis being frequency, and color dimension representing amplitude.^{8,9} As seizures typically manifest as increased frequency and amplitude on EEG, these appear as coherent patterns on DSA (Figure 1).⁸

DSA is available in many commercial EEG software packages. The literature on the utility of DSA in critically ill patients and/or refractory status epilepticus has described its sensitivity and specificity of seizure detection across experienced and DSA-naïve readers employing eight-trendgraph displays. However, there are no standardized amplitude settings or display settings.⁸⁻¹⁰ Further studies on average-trendgraph displays and how best to utilize them have also been independently recommended.^{8,9}

The primary aim of this study was to determine the optimal amplitude settings for seizure identification on DSA displays in children with RSE. Secondary aims included determining intra-rater agreement in seizure detection between single-average-trendgraph (1TG) display and eight-trendgraph (8TG) display in children with RSE, as well as comparing the sensitivity and specificity of seizure detection with 1TG display and that with 8TG display in children with RSE.

METHODS

We conducted a two-phase study: Phase 1 to find the optimal amplitude setting for seizure identification on DSA displays and Phase 2 to compare the use of 1TG display and 8TG display. The same set of cEEG recordings were used for both experiments.

Selection and interpretation of cEEG recordings

Clinical recordings from paediatric patients admitted to KKH and who had undergone cEEG monitoring were identified from the hospital EEG database. We evaluated the recordings of paediatric patients aged 1-16 with a diagnosis of RSE and who had cEEG recordings of at least 12 hours' duration. All EEGs were recorded using the International 10-20 System; Neurofax EEG-1200 (Nihon Kohden) EEG machines; sampling rate: 500 Hz; high-frequency filter: 70 Hz; low-frequency filter: 0.53 Hz; 19-inch monitor; resolution 1280 x 1024 pixels.

The digital scalp cEEG recordings of five different patients were analyzed. One 12-hour excerpt was obtained from each of the five

patients' recordings and de-identified. The five excerpts consisted of raw 19-channel EEG tracings recorded from electrodes placed according to the International 10-20 System and displayed in common referential montage with averaged A1-A2 (Aav) reference. The raw EEG tracings of the five excerpts were subjected to manual analysis by an experienced clinical electroencephalographer (DC). The exact start and end of each seizure were marked directly on the digital recording (DC). This formed the gold standard for comparison with DSA seizure screening and for calculation of sensitivity and specificity.

The five raw EEG excerpts were transformed into DSA trendgraphs using Neurofax EEG-1200 software (Nihon-Kohden). Two sets of trendgraphs were generated: 1.) a 1TG display, where the averaged signal of all 19 EEG channels was shown in a single trendgraph, and 2.) an 8TG display, where each trendgraph represented one of the following channels: Fp1-Aav, Fp2-Aav, C3-Aav, C4-Aav, T3-Aav, T4-Aav, O1-Aav, O2-Aav. Trendgraphs were displayed at a time scale of one hour per strip with settings as seen in Figure 1C.

Establishing standard settings for DSA (Phase 1)

In this initial phase, only the 1TG display was used. Four readers participated in the determination of optimal settings for DSA reading: two experienced EEG technologists with minimal prior exposure to DSA (Readers 1 and 2) and two experienced electroencephalographers with prior experience with DSA (Readers 3 and 4).

Single trendgraphs of the five cEEG excerpts were presented to each reader. Readers were informed that the recordings were from patients admitted to the ICU for RSE. No other clinical information regarding the patients or recordings was provided. Raw EEG tracings and all original annotations were hidden from view. Readers were asked to select a preferred amplitude setting and then identify seizures in one excerpt (Excerpt 1) using the amplitude setting they had respectively chosen. One of the investigators (JH) provided the readers with scripted instructions for the determination of the optimal amplitude setting for each cEEG excerpt (Figure 2). No additional teaching about DSA interpretation was given to the readers. The range of amplitudes covered by the color scale was adjusted by changing the "maximum voltage" to values between 0.1 to 100 μ V. The order of presentation of the DSA excerpts to each reader was unique, having been created with a random number generator. To

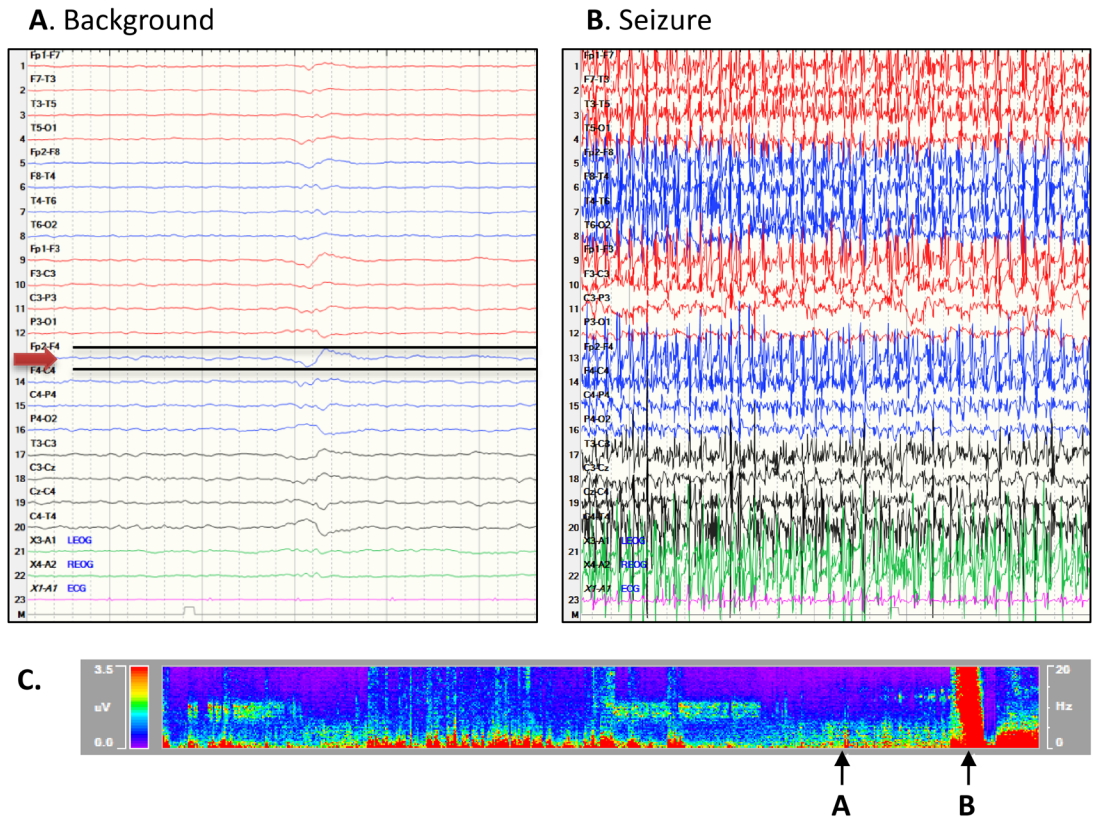


Figure 1. **A & B.** EEG tracings of the two time points indicated by arrows in C. Low-frequency filter, 0.53 Hz; high-frequency filter, 70 Hz; montage, AP bipolar; time constant, 0.3 sec; speed, 30 mm/sec; sensitivity, 20 μ V. Panel A also illustrated the measurement of crest-to-trough amplitude for each channel on the raw EEG tracings -- the distance between the two black lines would be the crest-to-trough amplitude for the channel indicated by the red arrow. **C.** Single-average-trendgraph DSA display showing an episode of seizure in a continuous background. Arrow B shows an area of “hot zone” (high voltage; color spectrum) across the whole frequency range (0-20 Hz, Y-axis), which reflects a drastic increase in both the amplitude and the frequency of the raw EEG tracings of an ictal episode. Trendgraph shows averaged signal from a 19-channel, common referential montage with averaged A1-A2 (Aav) reference.

evaluate intra-rater agreement, one of the five excerpts was randomly selected to be presented twice, non-consecutively). The readers were blinded to the sequence of the excerpts and were not informed of the duplication. Once the readers had selected their preferred amplitude settings, they were asked to identify seizures in one excerpt (Excerpt 1) using the amplitude setting they had chosen. At his/her perceived optimal amplitude setting for this excerpt, the reader reviewed the whole 12-hour DSA display and marked any epoch suspected to be seizures. Marking was accomplished by placing a *single-pixel wide* annotation marker at the onset and offset of each suspected seizure event.

Seizure detection in ITG versus 8TG displays (Phase 2)

The composition of the readers was different

in Phase 2, with 4 DSA readers participating: two experienced electroencephalographers who routinely used DSA to supplement manual EEG analysis (Readers a and b; senior readers), as well as two pediatric neurology registrars/senior residents with minimal prior exposure to DSA (Readers c and d; junior readers).

A one-hour, structured training session was conducted with the four readers to standardize interpretation. The maximal voltage was set at the standardized value of 3.5 μ V. The DSA readers were shown examples of DSA patterns including continuous background, burst-suppression background, seizures, as well as common artifacts, in both display methods described in Section 2.1. The corresponding raw EEG tracings were displayed simultaneously to facilitate understanding and pattern association. In addition, a hardcopy of DSA atlas (see Appendix), which

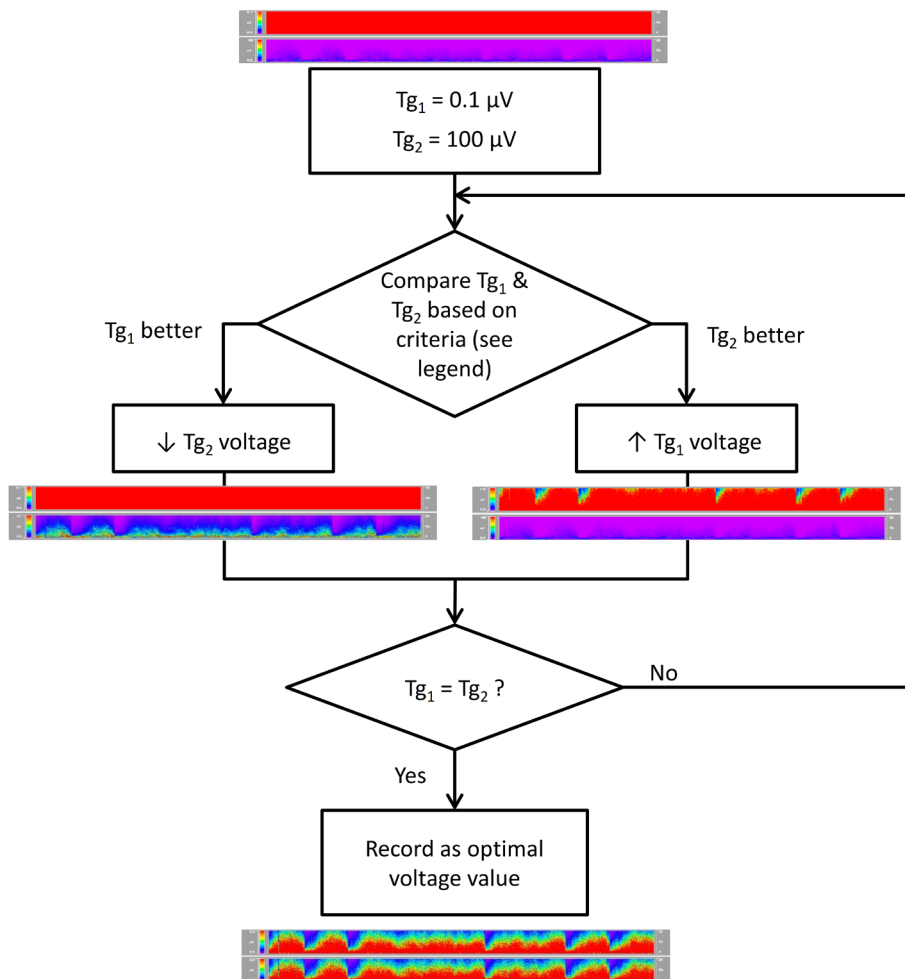


Figure 2. For each EEG excerpt, a pair of DSA trendgraphs (denoted as Tg_1 and Tg_2) were displayed, one on top of the other. The two trendgraphs were identical to each other except for their amplitude settings. To start with, the maximal voltages of the two trendgraphs were set at two extreme values, Tg_1 being $0.1 \mu V$, and Tg_2 being $100 \mu V$. Each reader was asked to visually compare the two trendgraphs and select one based on the following criteria: 1) better differentiation of differences in frequency/amplitude; and 2) better ability to detect electrographic seizures, if any. Based on his/her decision, the chosen trendgraph remained, while the maximum voltage of the other trendgraph would be adjusted toward the value of the chosen one (i.e. if Tg_1 was chosen, the voltage of Tg_2 would be adjusted down, and vice versa). A new round of comparison would be carried out with the new pair, and again a selection was made. This process was repeated until the two voltage values converged on a single number, which would then be recorded as the perceived optimal amplitude setting for this excerpt by this reader.

contains examples either the same as or similar to those shown on screen, was given to each reader.

To compare the use of the two display methods, each DSA reader went through two interpretation sessions individually. The two sessions were separated by a wash-out period of at least one week to minimize recall from the first session. DSA settings used were the same as those used in the training session.

In Session I, they were asked to mark all seizure

events in the five cEEG excerpts by viewing only the 1TG display; in Session II, the same task was performed but with only the 8TG display. Seizure marking was done in similar ways as in Section 2.2. The order of presentation of the DSA excerpts to each reader was unique, having been created with a random number generator. The readers were blinded to the sequence of the excerpts.

The seizure-to-background amplitude ratio (SBAR) was calculated to reflect the signal-to-

noise ratio of each recording. Background and seizure amplitudes in the five cEEG excerpts were measured from raw EEG tracings in common referential montage with Aav reference. Background amplitude in each cEEG excerpt was sampled from ten 10-second epochs randomly selected from seizure-free periods. The amplitude between the highest crest and the lowest trough in each channel was measured in each epoch and the highest value recorded. These were then averaged to give the background amplitude. Seizure amplitude from the five excerpts was sampled, measuring maximum amplitude in five randomly selected seizures from each excerpt (except for Excerpt 3 where only two seizures were present). The seizure amplitudes were measured and averaged in the same way as the background. Discontinuous EEG tracings were further characterized in terms of the low-amplitude suppression component of burst-suppression patterns, by averaging the durations of ten randomly selected inter-burst intervals (IBI) to give an averaged IBI length.

This study was approved by the Centralized Institutional Review Board of KKH.

Statistical analysis

Statistical analyses were performed using IBM SPSS Version 19. Fleiss κ , a measure of agreement among multiple raters was calculated using SAS Version 9.2.

Mean amplitudes of seizures and EEG background were compared using two-tailed Student's t-test, with level of significance of 0.05.

In Phase 1, inter-rater and intra-rater agreement of the optimal amplitude setting for each excerpt were measured by the intraclass correlation coefficient (ICC) and Pearson correlation, respectively. For seizure identification on Excerpt 1, the 12 hours of data were divided into 15-minute intervals, and inter-rater agreement on whether an interval contained any seizure activity was assessed by the kappa statistic κ .

In Phase 2, each excerpt was again divided into 15-minute intervals. Intra-rater agreement between 1TG display and 8TG display was measured by weighted κ .

In both phases of the study, sensitivity and specificity of correctly identifying the presence of seizure activity in any given 15-minute interval were calculated against gold standard manual analysis.

McNemar's test was performed to compare the sensitivity and specificity between 1TG and 8TG displays.

RESULTS

Phase 1

DSA readers differed substantially in their choice of optimal amplitude settings (Table 2). The intra-class correlation coefficient was -0.23 ($p = 0.91$), signifying practically no inter-rater agreement above chance. In contrast, intra-rater agreement for a given excerpt was high, as shown by a Pearson correlation coefficient of 0.99 ($p = 0.001$). The inter-rater agreement (assessed by κ) in seizure identification was calculated to determine the effect of the choice of amplitude setting on the readers' ability to detect seizures. The detection sensitivity/specificity of the readers was also determined. Despite use of different amplitude settings, agreement between every pair of readers was substantial, with Cohen's κ of 0.67 or higher; the two electroencephalographers (Readers 3 and 4) even showed perfect agreement (Cohen's $\kappa = 1.00$). Overall Fleiss κ (a measure of agreement among multiple raters) was 0.81, which was almost perfect. Sensitivity of seizure detection was very high, especially for Readers 3 and 4 (Table 2). Specificity was 100% for all readers. Overall, amplitude settings did not have a large impact on seizure detection on DSA within a wide range of values.

As shown in Table 1, Excerpt 1 had a continuous background, whereas the rest had burst-suppression background with IBI of variable lengths. The excerpts varied in the number of seizures they contained; overall, seizure activity was found in about half of all 15-minute intervals. In terms of seizure and background amplitudes, Excerpts 1 and 2 had high SBAR, whereas the rest had low ratios that were closer to 1.

Phase 2

Intra-rater agreement between 1TG display and 8TG display was very good for five excerpts combined in three out of four readers – weighted κ were 0.50, 0.85, 0.80, and 0.87 for Readers A to D, respectively (Supplementary Table 1). SBAR impacted on individual results, with almost perfect intra-rater agreement in excerpts with high SBAR (Excerpts 1 and 2), and much lower intra-rater agreement in those with low SBAR (Excerpts 3 to 5).

The detection sensitivity and specificity of the two display methods were comparable. Sensitivity in 1TG display and in 8TG display was 78-100% and 68-97%, respectively; specificity was 56-99% and 57-100%, respectively. When they differed, 1TG display tended to be more sensitive whereas 8TG display was more specific (Figure 3).

Table 1: Characteristics of the cEEG recording excerpts in terms of patients, backgrounds, and seizures

	Excerpt 1	Excerpt 2*	Excerpt 3	Excerpt 4*	Excerpt 5	Total
Patients	16	2	15	2	5	NA
Age	16	2	15	2	5	NA
Gender	Male	Male	Male	Male	Female	NA
Diagnosis	Likely FIRES	FIRES	FIRES	FIRES	New onset RSE	NA
EEG background	Continuous	Burst-suppression	Burst-suppression	Burst-suppression	Burst-suppression	NA
IBI length[†]	NA	37.5 (14-374)	3.3 (1.0-6.5)	2.1 (0.4-5.9)	22 (4.0-393)	NA
Seizure type	Generalized	Generalized	Generalized	Generalized	Generalized & focal	NA
Number of seizure episodes	41	6	2	97	98	244
Number (percentage) of intervals containing seizures	30 (63%)	6 (13%)	1 (2%)	44 (92%)	35 (73%)	116 (48%)
Total number of intervals	48	48	48	48	48	240
Seizure amplitude**	472 ± 48	461 ± 41	1081 ± 88	694 ± 143	491 ± 79	NA
Background amplitude**	274 ± 61	195 ± 33	1300 ± 67	550 ± 94	511 ± 227	NA
Seizure:background amplitude ratio	1.72	2.36	0.83	1.26	0.96	NA
Student <i>t</i>-test (<i>p</i>-value)^{††}	< 0.001	< 0.001	0.15	0.09	0.82	NA

FIRES, febrile infection-related epilepsy syndrome; IBI, inter-burst interval; NA, not applicable

* Excerpt 2 & 4 were taken from recordings of the same patient.

† Values shown are median (range) in seconds.

** Values shown are mean ± SD in μV .

†† Student *t*-test was done to compare mean amplitudes of seizures and EEG background.

Table 2: Perceived optimal amplitude settings chosen by DSA readers for different cEEG excerpts in terms of maximal voltage (μV) and the corresponding sensitivity and specificity of seizure detection in Excerpt 1

	Reader 1		Reader 2		Reader 3		Reader 4	
		Repeat		Repeat		Repeat		Repeat
Excerpt 1	100	–	3	–	8	–	50	50
Excerpt 2	20	–	2	–	2.5	–	50	–
Excerpt 3	90	–	8	–	9	–	60	–
Excerpt 4	90	90	3.5	–	5	–	60	–
Excerpt 5	80	–	1.5	4	6	3.5	60	–
Sensitivity, % (95% CI)	93.3 (76.5-98.8)		73.3 (53.8-87.0)		100 (85.9-100)		100 (85.9-100)	
Specificity, % (95% CI)	100 (78.1-100)		100 (78.1-100)		100 (78.1-100)		100 (78.1-100)	

CI, confidence interval

In excerpts with high SBAR, 100% sensitivity (Figure 4A) and 100% specificity (Figure 4B) were observed in almost all readers. In contrast, when SBAR was low (i.e. when seizures had similar amplitudes as the EEG background they were found in), detection sensitivity and specificity became less consistent among readers (Figures 3 & 4).

DISCUSSION

This first study of DSA spectrographic settings in cEEG demonstrates that seizure detection sensitivity and specificity is independent of amplitude settings, despite readers' wide range of preferred settings. We found wide variation in preferred amplitude settings among DSA readers but high inter-rater agreement and high sensitivity/specificity in seizure detection between

DSA readers in recordings with a high SBAR. This suggests that amplitude setting in DSA does not affect seizure detection within a wide range of values. In view of this finding in Phase 1, an apparently arbitrary amplitude setting of $3.5 \mu\text{V}$ was used as maximum voltage for Phase 2 without fear of its effect on validity of the results.

We also showed that 1TG display is comparable to 8TG display in screening for seizures. Many studies utilize 8TG displays in the evaluation of seizures. Multiple trendgraphs lead to increased display complexity. In our study, 1TG display and 8TG display shared high agreement in seizure detection. In situations where the two methods disagreed, 1TG display tended to be more sensitive and less specific than its counterpart (Figure 5). This supports the routine use of 1TG display in clinical practice. Higher sensitivity is desirable in clinical practice, where electroencephalographers

Supplementary Table 3: Weighted κ^* between single-average-trendgraph display and eight-trendgraph display

	Reader A	Reader B	Reader C	Reader D
Excerpt 1	1.00	1.00	0.96	0.96
Excerpt 2	0.95	0.95	1.00	1.00
Excerpt 3	0.004	(94%)	(100%)	(100%)
Excerpt 4	0.15	0.30	0.37	0.64
Excerpt 5	0.55	0.71	0.83	0.81
Combined	0.50	0.85	0.80	0.87

* Numbers in parentheses are concordance rates; weighted κ cannot be calculated for Reader B to D in Excerpt 3 because they have marked the whole excerpt either positive throughout or negative throughout with at least one display method.

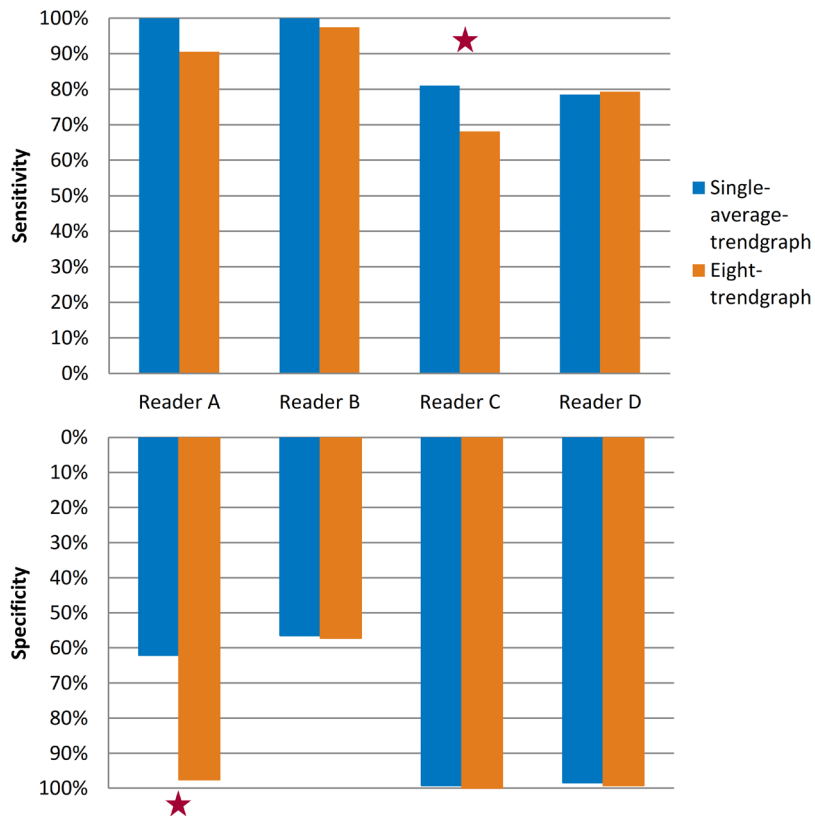


Figure 3. Blinded to the raw EEG tracings, two electroencephalographers (Reader A and B) and two pediatric trainees (Reader C and D) were asked to mark all seizures in five cEEG excerpts, first using single-average-trendgraph (ITG) DSA display, and then using eight-trendgraph (8TG) display after a wash-out period of at least one week. All excerpts were then divided into 15-minute intervals. Sensitivity and specificity of correctly identifying the presence of seizure activity in any given interval was then calculated. Star denotes $p < 0.001$ by McNemar’s test.

use DSA to screen long recordings for concerning epochs suspected to be seizures, and then zoom into the corresponding raw tracings for closer examination. It is important not to miss true seizures on the first pass by DSA, whereas false positives are less serious and can be easily identified by reviewing the raw tracings. 1TG displays enable simultaneous display of the raw EEG tracings on the same screen. It also reduces complexity of the presented information and hence the potential for reader fatigue.

Low SBAR in EEG recordings was associated with worse detection accuracy (either lower sensitivity or lower specificity; refer to Figure 4). In previous studies, some factors identified to impact sensitivity and specificity of seizure detection on quantitative EEG are: short, low amplitude and focal or bilaterally independent seizures.^{9,11} Stewart *et al.* noted that a proportion of the missed seizures “occurred in the context

of abundant interictal epileptiform discharges”.⁹ Akman *et al.* also reported that seizures missed by DSA tended to have lower amplitude and occur in a higher-amplitude background than their successfully-identified counterparts.¹⁰ This present study provides an objective measure – SBAR – that can predict higher risk of missed seizures. Application of this to clinical practice could lead to more effective and targeted use of DSA. Continuous EEG recordings with a high SBAR could be readily screened with DSA while recordings with a low SBAR would be screened with DSA with great caution and awareness of the low sensitivity/specificity.

Pediatric neurology registrars (senior residents) with little or no experience in manual EEG interpretation were deliberately included as DSA readers to evaluate the effect of experience in EEG interpretation on DSA analysis. They were able to detect seizures on DSA with very high

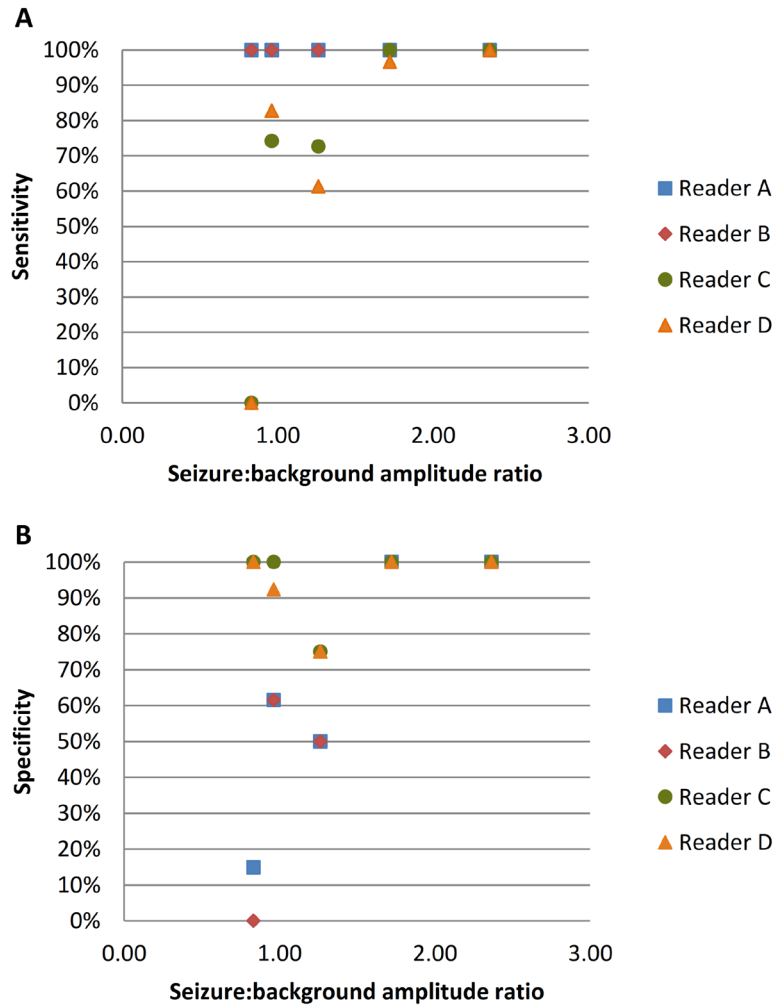


Figure 4. Blinded to the raw EEG tracings, four DSA readers (Reader A to D) were asked to mark all seizures in five cEEG excerpts, using 1TG DSA display. All excerpts were then divided into 15-minute intervals. (A) Sensitivity or (B) specificity of correctly identifying the presence of seizure activity in any given interval was then calculated. This was plotted against the seizure-background amplitude ratio of the cEEG excerpts.

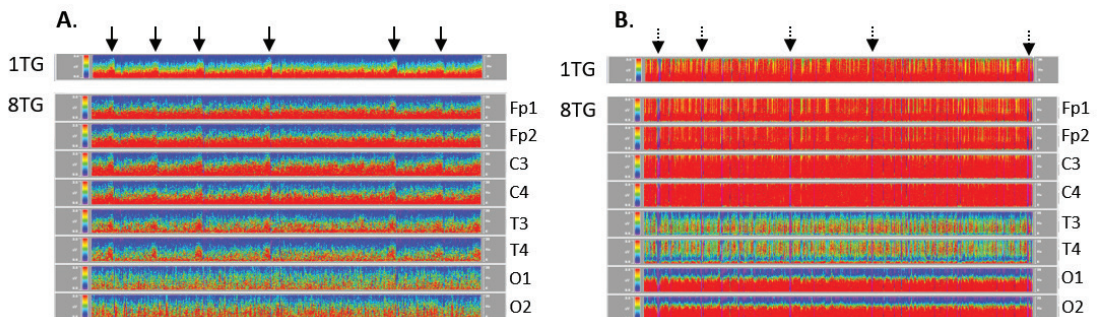


Figure 5. In situations where the two methods disagreed, 1TG display tended to be more sensitive and less specific than 8TG display. In 8TG display, each trendgraph represented one of the following channels: Fp1-Aav, Fp2-Aav, C3-Aav, C4-Aav, T3-Aav, T4-Aav, O1-Aav, O2-Aav. (A) Readers 3 & 5 was able to pick up true seizures (indicated by solid arrows) more confidently with 1TG display than with 8TG; (B) Reader 3 mistook burst-suppression background as seizures (indicated by dotted arrows) with 1TG display but not with 8TG.

sensitivity and specificity for recordings with high SBAR. This shows that DSA can provide real-time cEEG screening capability by non-expert medical personnel (e.g. trainee neurologists, intensivists, or ICU nurses) with adequate sensitivity and specificity. This has value in alerting clinical staff to probable breakthrough seizures or inadequate seizure control in a timely manner. In conjunction with treatment protocols, it can facilitate real-time, out-of-hours seizure detection and permit timely treatment.

Interestingly, when it came to recordings with low SBAR (<1.5), senior readers (Reader a and b) had better sensitivity while junior readers (Readers c and d) had better specificity (Figure 4). A possible explanation for this observation was that, when uncertainty was encountered, junior readers were more cautious and hence more hesitant to label an event as “seizure”, thus preserving specificity at the cost of sensitivity. Senior EEGers should take note to see if such cognitive tendency is consistently observed in junior practitioners in clinical practice, and correct them if appropriate, for the exact same reason that higher sensitivity is desirable in clinical practice as mentioned above.

The limitations of this study are firstly the small sample sizes, in terms of the number and length of cEEG excerpts. This is due to the nature of the study subjects – paediatric patients with refractory status epilepticus who had undergone continuous EEG monitoring. Secondly, this study did not examine the role of frequency settings (in addition to amplitude settings) in seizure detection by DSA, owing simply to the fact that frequency settings could not be changed in the Neurofax EEG-1200 software. It remained to be studied if certain frequency range would give best seizure detection accuracy with DSA. Thirdly, our study design was also artificially strict in blinding of the readers to the raw EEG tracings and concurrent EEG video recordings. In real-life practice, electro-encephalographers can refer to the raw tracings whenever necessary, and continuously refine their DSA interpretation by comparison. Therefore, the true sensitivity and specificity of seizure detection with DSA in clinical practice are probably higher than those estimated in this study. Fourthly, we estimated seizure and background amplitudes by measuring the maximum crest-to-trough amplitude of the waveforms in each 10-second epoch. This is less sophisticated than averaging signals from all parts of the waveforms. However, this is pragmatic as it uses the tools that are routinely used to

measure amplitude during manual interpretation of cEEG in clinical practice. Finally the DSA displays in our system were generated solely from referential montages, unlike the bipolar montages used in some other studies, in order to minimize the risk of cancellation due to in-phase signals in adjacent channels and in line with the system standard settings. The one-hour strips used in this study differ from other studies where the DSA trendgraph of the entire recording is viewed in one screen. The one-hour strip display setting was utilized to remove variation in appearance due to differing recording lengths and standardize the appearance of the peaks.

In conclusion, our study demonstrated that DSA amplitude settings do not affect seizure detection and that single-average-trendgraph display is comparable to eight-trendgraph display in screening cEEG for seizures. We also showed that DSA performs better in cEEG recordings with high seizure-to-background amplitude ratio. Single-trendgraph DSA is an effective seizure screening tool for continuous EEG in pediatric refractory status epilepticus, with higher sensitivity than multiple-trendgraph displays. DSA has the potential to reduce the burden of continuous EEG analysis, increasing accessibility to vulnerable paediatric patients, and enable real-time non-expert detection and treatment of seizures.

ACKNOWLEDGEMENT

We thank Prof Ecosse Lamoreaux of the Academic Medical Research Institute (AMRI@KKH) for his advice in developing the research proposal and design, and Dr Cristelle Chow for her participation in the study.

DISCLOSURE

Financial support: None

Conflict of interests: None

REFERENCES

1. Hunter G, Young GB. Status epilepticus: a review, with emphasis on refractory cases. *Can J Neurol Sci* 2012;39:157-69.
2. Bleck TP. Status epilepticus and the use of continuous EEG monitoring in the intensive care unit. *Continuum (Minneapolis Minn)* 2012;18:560-78.
3. Hyllienmark L, Amark P. Continuous EEG monitoring in a paediatric intensive care unit. *Eur J Paediatr Neurol* 2007;11:70-5.
4. Kurtz P, Hanafy KA, Claassen J. Continuous EEG monitoring: is it ready for prime time? *Curr Opin*

- Crit Care* 2009;15:99-109.
5. DeLorenzo RJ, Waterhouse EJ, Towne AR, *et al.* Persistent nonconvulsive status epilepticus after the control of convulsive status epilepticus. *Epilepsia* 1998;39:833-40.
 6. Towne AR, Waterhouse EJ, Boggs JG, *et al.* Prevalence of nonconvulsive status epilepticus in comatose patients. *Neurology* 2000;54:340-45.
 7. Sanchez SM, Arndt DH, Carpenter JL, *et al.* Electroencephalography monitoring in critically ill children: Current practice and implications for future study design. *Epilepsia* 2013;54(8):1419-27.
 8. Pensirikul AD, Beslow LA, Kessler SK, *et al.* Density spectral array for seizure identification in critically ill children. *J Clin Neurophysiol* 2013;30:371-5.
 9. Stewart CP, Otsubo H, Ochi A, *et al.* Seizure identification in the ICU using quantitative EEG displays. *Neurology* 2010;75:1501-8.
 10. Akman CI, Micic V, Thompson A, *et al.* Seizure detection using digital trend analysis: Factors affecting utility. *Epilepsy Res* 2011;93:66-72.
 11. Dericioglu N, Yetim E, Bas DF, *et al.* Non-expert use of quantitative EEG displays for seizure identification in the adult neuro-intensive care unit. *Epilepsy Res* 2015;109:48-56.