Raw Versus Processed EEG: Which One is Better?

Automated Long-Term EEG Review: Fast and Precise Analysis in Critical Care Patients.

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BACKGROUND: Ongoing or recurrent seizure activity without prominent motor features is a common burden in neurological critical care patients and people with epilepsy during ICU stays. Continuous EEG (CEEG) is the gold standard for detecting ongoing ictal EEG patterns and monitoring functional brain activity. However CEEG review is very demanding and time consuming. The purpose of the present multirater, EEG expert reviewer study, is to test and assess the clinical feasibility of an automatic EEG pattern detection method (Neurotrend). METHODS: Four board certified EEG reviewers used Neurotrend to annotate 76 CEEG datasets à 6 h (in total 456 h of EEG) for rhythmic and periodic EEG patterns (RPP), unequivocal ictal EEG patterns and burst suppression. All reviewers had a predefined time limit of 5 min (± 2 min) per CEEG dataset and were compared to a predefined gold standard (conventional EEG review with unlimited time). Subanalysis of specific features of RPP was conducted as well. We used Gwet's AC_1 and AC_2coefficients to calculate interrater agreement (IRA) and multirater agreement (MRA). Also, we determined individual performance measures for unequivocal ictal EEG patterns and burst suppression. Bonferroni-Holmes correction for multiple testing was applied to all statistical tests. RESULTS: Mean review time was 3.3 min (± 1.9 min) per CEEG dataset. We found substantial IRA for unequivocal ictal EEG patterns (0.61–0.79; mean sensitivity 86.8%; mean specificity 82.2%, $p < 0.001$) and burst suppression (0.68–0.71; mean sensitivity 96.7%; mean specificity 76.9% $p < 0.001$). Two reviewers showed substantial IRA for RPP (0.68–0.72), whereas the other two showed moderate agreement (0.45–0.54), compared to the gold standard ($p < 0.001$). MRA showed almost perfect agreement for burst suppression (0.86) and moderate agreement for RPP (0.54) and unequivocal ictal EEG patterns (0.57). CONCLUSIONS: We demonstrated the clinical feasibility of an automatic critical care EEG pattern detection method on two levels: (1) reasonable high agreement compared to the gold standard, (2) reasonable short review times compared to previously reported EEG review times with conventional EEG analysis.

Commentary

The use of continuous EEG (cEEG) monitoring has been invaluable in detecting nonconvulsive seizures (NCS) and nonconvulsive status epilepticus (NCSE) in critically ill patients. Approximately 20% of patients undergoing cEEG are noted to have NCS or NCSE (1, 2). In the last decade, with the increasing realization of the frequency of seizures in critically ill patients, there has been a greater than 4-fold increase in the number of cEEG studies being performed (3). Most patients undergo cEEG for 24 to 48 hours, and if seizures are detected, monitoring is often extended (4). This monitoring generates a lot of data that must be interpreted and reported frequently throughout the monitoring cycle.

A cEEG study that is 24-hours long generates 5760 "pages" of EEG when viewed on a digital monitor at 15 sec/page (5). When every page is reviewed at a fast pace of 5 pages/sec, a 24-hour data sample requires almost 20 minutes. If abnormalities or complexities are present, the review must be slowed; the time requirement then increases. In a recent study, experienced electroencephalographers required, on average, 38 minutes to review a typical 24-hour cEEG (6).

Quantitative analysis of the EEG (qEEG) offers one way to increase the speed of review of cEEG data. QEEG involves mathematic processing of the EEG data. The software used for qEEG analysis typically uses several instruments that analyze the data differently; each instrument is used for looking at different aspects of the EEG (5, 7). The analysis is displayed on a graphic user interface (GUI) to make interpretation easier. QEEG has been used for EEG analysis for many decades. In its earliest days, it was used to detect features in routine EEGs that might not be visible upon raw review (8). Approximately 20 years ago, a joint American Academy of Neurology (AAN) and American Clinical Neurophysiology Society (ACNS) report noted possible value of qEEG in analysis of the EEG in the epilepsy-monitoring unit, intensive care unit, and operating room (9). Several qEEG analysis software packages are now available, and many EEG machine companies provide built-in analysis software as well.

A recent study by Koren and colleagues (10) evaluated the ability of an automated analysis software called NeuroTrend

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(NT) in assisting with cEEG data review. They evaluated 24-hour cEEG recordings from 20 patients. Six of the patients had a normal recording while the others had rhythmic or periodic patterns (RPP; periodic discharges [PDs], rhythmic delta activity [RDA] or seizures). The PDs and RDA were classified according to the classification proposed by the ACNS (11). Seizures and status epilepticus (SE) were defined per the Salzburg criteria (12). Each 24-hour cEEG recording was broken down into four 6-hour segments; of these 80 segments, four had to be discarded due to artifacts, leaving 76 segments to be analyzed. Four reviewers with "moderate experience" were given 2 hours of instructions on how to analyze the NT obtained data and how to classify the RPP. They had 5 minutes to review each 6-hour segment of NT obtained data; they had access to raw EEG if needed. This NT obtained analysis was compared with a "gold standard," which was two EEG reviewers with "substantial …experience." The gold standard reviewers did not have access to NT obtained data, and they reviewed only the raw EEG without a time limit. The interrater agreement (IRA) for the various RPP between the four reviewers using NT obtained data and the gold standard was determined.

The mean time to review each NT obtained 6-hour dataset was 3.3 minutes and 12 minutes per patient (4 6-hour datasets). The review time for the "gold standard" reviewers was not provided. The IRA for RPP with the gold standard was substantial for two reviewers and moderate for the other two. For unequivocal ictal patterns, the IRA was higher, and the mean sensitivity for detecting these patterns was 86.8% (range, 68.4–97.4%) while the specificity was 82.2% (range, 68.4–92.1%). The IRA for burst-suppression patterns was 96.7% (range, 93.3–100%) and specificity was 76.9% (73.9–79.6%). The sensitivity for detecting various periodic discharges was less than that for detecting seizures.

This study is the latest to show that qEEG provides a valuable adjunct to cEEG review. The average time to review a 24-hour dataset was 12 minutes. This is comparable to a study by Moura and colleagues (6) that found that it took 8 minutes to review a 24-hour dataset with qEEG (obtained using different software). Raw EEG review of the same dataset averaged 38 minutes. Similarly, Haider and colleagues (13) noted that raw EEG review took an average of 19 minutes per 6-hour dataset compared with qEEG enhanced raw EEG review that took 14.5 minutes and qEEG only review that took 6 minutes. None of the studies advocated using qEEG without the ability to review raw EEG.

While quicker cEEG review is certainly advantageous, it cannot be at the expense of accuracy for detecting seizures and other features of interest. In this study, using the NT qEEG software developed by the Austrian Institute of Technology (Seibersdorf, Austria), the sensitivity for detecting seizures was on average 86.8%, but the range of the four reviewers was quite wide (68.4–97.4%). Other commercial qEEG software packages have also been evaluated. Sierra-Marcos and colleagues (14) reported that the Persyst12 qEEG software developed by the Persyst Corporation (San Diego, CA) had a sensitivity of 76.1% in detecting seizures from 98 intensive care unit recordings. Haider and colleagues (13) used an older version of the same software, Persyst11, and found the mean sensitivity for detecting seizures with qEEG combined with raw EEG review was 63 to 68 percent. Sackellares and colleagues (15) used ICU-ASDA (automated seizure detection algorithm) qEEG software developed by Optima Neuroscience (Alachua, FL) and noted a sensitivity of 90.4% in detecting seizures in intensive care unit EEG datasets. Direct comparison of these commercially available qEEG software packages is not possible as the datasets evaluated, methodology used, and the number of qEEG instruments used was different. Moreover, there are frequent improvements being made to the software, which can change the sensitivity of seizure detection.

The sensitivity of various qEEG instruments in detecting seizures and other EEG patterns (such as PDs and RDA) is determined by comparing with a "gold standard." This gold standard is often raw EEG review by "experienced" reviewers. Depending on the study, the experienced reviewers, in addition to having experience, have either specialized training and/or have passed a certifying examination. While the rationale for using such a paradigm for evaluating new qEEG software is understandable, it does introduce biases that must be recognized.

The gold standard is highly dependent on the "experienced" reviewers. A recent study showed that eight experienced EEG readers had only a moderate IRA (kappa = 0.58) in identifying seizures and an even lower IRA in identifying PDs (kappa = 0.38) (16). Certification by the American Board of Clinical Neurophysiology resulted in a higher IRA, but other board certifications, years of fellowship training or years of practice did not (17). Another factor in raw EEG review that is often not considered is human fatigue. Monotonous raw EEG review can lead to inattention and distraction, leading to missed findings. One can certainly wonder whether the "gold standard" is really golden.

Meanwhile, the qEEG reviewers in various studies typically have had little training in reviewing the qEEG trends being studied (as was the case in this study). They often receive 1 to 2 hours of instruction on how to use the various qEEG instruments and do not know how to manipulate the instruments to improve their ability to detect features of interest. This may negatively affect the sensitivity and specificity of qEEG.

The qEEG instruments are usually tested in a way they are not used clinically. Many studies split large 24-hour datasets into smaller segments. Each segment is evaluated individually. In practice, when a qEEG instrument detects the first seizure, the reader is focused on finding a similar qEEG pattern. Thus, the clinical qEEG review is more focused, quicker, and possibly more accurate. These nuances of the use of qEEG are difficult to replicate in a study designed to show the effectiveness of the instrument.

The need for cEEG continues to increase faster than the number of trained EEG reviewers. Interpretation of these tests is challenging due to the enormous amount of data they contain. While review of every page of EEG has been the standard, whether it is the best way to proceed in the future is being challenged. The use of qEEG instruments allows quicker identification of areas of interest. A combination of raw and qEEG review may be the best to thoroughly and efficiently review these large data sets. One way of doing so is to initially analyze the raw EEG to identify clinically meaningful events, like seizures. The qEEG pattern of these events is noted, and subsequently the qEEG can be reviewed to identify such events and

confirm with raw EEG. Whether such review will take less time than raw EEG review remains to be determined. It is possible that the review time may remain the same or even increase as readers review areas of interest in greater detail and skip over other parts of the EEG.

That qEEG has a place in cEEG interpretation is now firmly established. It is also clear that it cannot yet replace raw EEG review. Fortunately, several choices of qEEG software are available for clinicians, and each has its virtues. How to marry the use of raw EEG and qEEG in clinical practice should be the focus of subsequent studies.

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References

1. Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology* 2004;62:1743–1748.
2. Swisher CB, Shah D, Sinha SR, Husain AM. Baseline EEG pattern on continuous ICU EEG monitoring and incidence of seizures. *J Clin Neurophysiol* 2015;32:147–151.
3. Ney JP, van der Goes DN, Nuwer MR, Nelson L, Eccher MA. Continuous and routine EEG in intensive care: utilization and outcomes, United States 2005–2009. *Neurology* 2013;81:2002–2008.
4. Gavvala J, Abend N, LaRoche S, Hahn C, Herman ST, Claassen J, Macken M, Schuele S, Gerard E; for the Critical Care EEG Monitoring Research Consortium (CCEMRC). Continuous EEG monitoring: a survey of neurophysiologists and neurointensivists. *Epilepsia* 2014;55:1864–1871.
5. Sinha SR. Quantitative EEG analysis: basics. In: *Continuous EEG Monitoring: Principles and Practice.* (Husain AM, Sinha SR, eds). Switzerland: Springer International Publishing, 2017:173–189.
6. Moura LMVR, Shafi MM, Ng M, Pati S, Cash SS, Cole AJ, Hoch DB, Rosenthal ES, Westover MB. Spectrogram screening of adult EEGs is sensitive and efficient. *Neurology* 2014;83:56–64.
7. Acharya UR, Vinitha Sree S, Swapna G, Martis RJ, Suri JS. Automated EEG analysis of epilepsy: a review. *Knowledge-Based Systems* 2013;45:147–165.
8. Bricolo A, Turazzi S, Faccioli F, Odorizzi F, Sciaretta G, Erculiani P. Clinical application of compressed spectral array in long-term EEG monitoring of comatose patients. *Electroencephalogr Clin Neurophysiol* 1978;45:211–225.
9. Nuwer M. Assessment of digital EEG, quantitative EEG, and EEG brain mapping: report of the American Academy of Neurology and the American Clinical Neurophysiology Society. *Neurology* 1997;49:277–292.
10. Koren JP, Herta J, Furbass F, Pirker S, Reiner-Deitemyer V, Riederer F, Flechsenhar J, Hartmann M, Kluge T, Baumgartner C. Automated long-term EEG review: fast and precise analysis in critical care patients. *Front Neurol* 2018;9:454.
11. Hirsch LJ, LaRoche SM, Gaspard N, Gerard E, Svoronos A, Herman ST, Mani R, Arif H, Jette N, Minazad Y, Kerrigan JF, Vespa P, Hantus S, Claassen J, Young GB, So E, Kaplan PW, Nuwer MR, Fountain NB, Drislane FW. American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version. *J Clin Neurophysiol* 2013;30:1–27.
12. Leitinger M, Beniczky S, Rohracher A, Gardella E, Kalss G, Qerama E, Höfler J, Hess Lindberg-Larsen A, Kuchukhidze G, Dobesberger J, Langthaler PB, Trinka E. Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus–approach to clinical application. *Epilepsy Behav* 2015;49:158–163.
13. Haider HA, Esteller R, Hahn CD, Westover MB, Halford JJ, Lee JW, Shafi MM, Gaspard N, Herman ST, Gerard EE, Hirsch LJ, Ehrenberg JA, LaRoche SM; for the Critical Care EEG Monitoring Research Consortium. Sensitivity of quantitative EEG for seizure identification in the intensive care unit. *Neurology* 2016;87:935–944.
14. Sierra-Marcos A, Scheuer ML, Rossetti AO. Seizure detection with automated EEG analysis: a validation study focusing on periodic patterns. *Clin Neurophysiol* 2015;126:456–462.
15. Sackellares JC, Shiau D-S, Halford JJ, LaRoche SM, Kelly KM. Quantitative EEG analysis for automated detection of nonconvulsive seizures in intensive care units. *Epilepsy Behav* 2011;22:S69–S73.
16. Halford JJ, Shiau D, Desrochers JA, Kolls BJ, Dean BC, Waters CG, Azar NJ, Haas KF, Kutluay E, Martz GU, Sinha SR, Kern RT, Kelly KM, Sackellares JC, LaRoche SM. Inter-rater agreement on identification of electrographic seizures and periodic discharges in ICU EEG recordings. *Clin Neurophysiol* 2015;126:1661–1669.
17. Halford JJ, Arain A, Kalamangalam GP, LaRoche SM, Leonardo B, Basha M, Azar NJ, Kutluay E, Martz GU, Bethany WJ, Waters CG, Dean BC. Characteristics of EEG interpreters associated with higher interrater agreement. *J Clin Neurophysiol* 2017;34:168–173.