Seizure 19 (2010) 580–586

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Feasibility of online seizure detection with continuous EEG monitoring in the intensive care unit

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ARTICLE INFO

Article history:
Received 16 March 2010
Received in revised form 8 August 2010
Accepted 2 September 2010

Keywords:
Coma
Continuous EEG
Epilepsy monitoring
Intensive care unit

ABSTRACT

Introduction: Continuous EEG (cEEG) is of great interest in view of the reported high prevalence of non-convulsive seizures on intensive care units (ICUs). Here, we describe our experiences applying a seizure warning system using cEEG monitoring.
Methods: Fifty comatose ICU patients were included prospectively and monitored. Twenty-eight patients had post-anoxic encephalopathy (PAE) and 22 had focal brain lesions. A measure of neuronal interactions, synchronization likelihood, was calculated online over 10 s EEG epochs and instances when the synchronization likelihood exceeded a threshold where marked as seizures.
Results: Five patients developed seizures. Our method detected seizures in three patients, in the other patients seizures were missed because of they were non-convulsive and had a focal character. The average false positive rate was 0.676/h.
Discussion: This is our first attempt to implement online seizure detection in the ICU. Despite problems with artifacts and that we missed focally oriented seizures, we succeeded in monitoring patients online. Given the relatively high occurrence of seizures, online seizure detection with cEEG merits further development for use in ICUs.

1. Introduction

In modern intensive care units (ICUs) almost all of a patient's vital functions are continuously monitored. However, facilities for monitoring brain function are still missing in most ICUs, despite recommendations in the literature.[1–4] Unfortunately, neurological function of these patients, who are mostly intubated and sedated, is therefore only intermittently assessed (scoring the Glasgow Coma Scale and pupillary light reactions), often by ICU-nurses. These 'neurochecks' are discontinuous and subject to inter- and intra-observer variations, even when carried out by experts.[5]

The importance of brain function monitoring is stressed by the fact that the neurological complication rate is high in comatose patients.[6] An objective of cerebral monitoring is to recognize early changes in brain function and thus prevent secondary injury. Recognition of seizures is essential, since most seizures in the ICU occur without clear clinical manifestations, a phenomenon called non-convulsive seizures (NCS).[7] NCS can only be detected by electroencephalography (EEG). It has been proven that continuous EEG (cEEG) has a contributing impact on medical decision-making in 82% of monitored neurological patients.[5] Since the use of cEEG, NCS are being recognized more frequently and are associated with an unfavorable outcome[2,8–10] (see Table 1 for an overview). cEEG is the only method to monitor the brain's electrical activity as a surrogate for brain function, and the only way to detect NCS. Almost all studies concerning cEEG in the ICU are performed in a few centers, mostly in the USA (Table 1).

To deal with the shortcomings of EEG monitoring, several recommendations have been proposed in the literature. Firstly, it is recommended to review cEEG at least twice a day.[4] Secondly, it is suggested to train ICU-nurses in basic principles of EEG. In this way expertise is partly transported to the ICU.[5,11] Although this might be an option for specialized neurological ICUs, in general ICUs this expert training is too time-consuming in relation to the number of patients. Besides, in a study in which ICU bedside caregivers had been educated in identifying epileptiform discharges, recognition of seizure patterns still remained low.[12] Thirdly, certain basic

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doi:10.1016/j.seizure.2010.09.007

Table 1
Series of continuous EEG monitored patients. Prevalence of acute seizures.

Study	Center	Design	Patients	Monitoring type	Inclusion criteria	Seizures (%)
Jordan[37]	Jordan Neuroscience Inc, San Bernardino, CA, USA	Retrospective	100	cEEG (length?)	ICU patients (no PAE)	29% (65% NCSE)
Young et al.[38]	University of Western Ontario, Canada	Retrospective	350	EEG	Comatose ICU patients	11.7% epileptiform activity
Jordan[5]	Jordan Neuroscience Inc, San Bernardino, CA, USA	Retrospective	124	cEEG (length?)	NICU patients	35% (76% NCSE)
Litt et al.[39]	Sinai Hospital Baltimore, USA	Retrospective	239	EEG	NICU patients	11% NCSE
Privitera et al.[40]	University of Cincinnati, USA	Prospective	198	EEG (emergency)	Unconscious patients	34%
Jaitly et al.[41]	Medical College of Virginia, USA	Prospective	180	cEEG	SE	–[a]
DeLorenzo et al.[42]	Medical College of Virginia, USA	Prospective	164	cEEG (min. 24 h)	After CSE	48%
Vespa et al.[10]	University of California, Los Angeles, CA, USA	Prospective	94	cEEG (3.5–11.5 days)	Adult TBI	22%, 6 pt SE (57% NC)
Towne et al.[8]	Medical College of Virginia, USA	Retrospective	236	min. 30 min EEG	ICU pts, comatose, no clinical seizure activity ook PAE pt	8% NCSE
Claassen et al.[9]	Colombia University, New York, USA	Retrospective	570	cEEG	Unconscious patients	19% (92% NC)
Pandian et al.[43]	Mayo Clinics, Rochester, USA	Retrospective	105	Video-cEEG (1–17 days)	ICU patients, also CSE	–[a]
Young and Doig[11]	University of Western Ontario, Canada	Prospective	55	cEEG	Comatose patients	20%
Ronne-Engstrom et al.[44]	University Hospital Uppsala, Sweden	Prospective	70	cEEG	TBI	33%
Ponten et al. (2010)[b]	VU University Medical Center	Prospective	50	cEEG	Comatose patients	10% (4% NC)

ASBL, acute structural brain lesion; EPC, epilepsia partialis continua; TBI, traumatic brain lesion; PAE, postanoxic encephalopathy; NCSE, nonconvulsive status epilepticus; (G)CSE, (generalized) convulsive status epilepticus.
[a] Because of inclusion criteria (status epilepticus) not possible to calculate the prevalence.
[b] Current study.

conditions are needed to make cEEG effective. The ICU is not at all like the standard EEG laboratory. There are many sources of exogenous artifacts (e.g. other electronic devices, manipulation of the patient). Finally, continuous recordings are long-term, which means that the requirements of the apparatus are different with ample opportunity for electrode dislodgment.[13]

The clinical neurophysiologist is not continuously present in the ICU. However, continuous assessment of the EEG to detect seizures is preferred so that treatment can be adjusted immediately. With the appearance of digitally recorded EEG, quantitative analysis can be used for automatic detection of seizure activity; previous studies used for example amplitude integration, compressed spectral array analysis, spike detection methods or the brain symmetry index (BSI).[14–20] Amplitude integrated EEG (aEEG) is widely used to detect neonatal seizures, despite the fact that the accuracy of seizure recognition can be moderate, especially in brief, low amplitude, focally oriented seizures.[15,21] Neonatologists analyze the aEEG signals at the patient's bedside, where in our opinion clinical neurophysiologists should at least be involved in this interpretation, as they are specially trained in EEG reviewing. In a recent study Young et al. compared a four-channel EEG monitoring device with 16 channel EEG recordings and found a sensitivity of 68% and specificity of 98% with visual interpretation of the signals.[22] In our clinic we have experience with another quantitative analysis approach for EEG, namely synchronization likelihood (SL).[23] SL is a nonlinear measure of statistical interdependencies between time series, which has shown to be a promising measure for detecting seizures in neonatal EEGs and frontal lobe epilepsy.[24–26] Furthermore, a retrospective study has shown that the mean SL can distinguish between seizure and non-seizure epochs in comatose ICU patients.[27] We do realize that the SL is most sensitive for generalized synchronization, although we do not know another method sensitive for both very focal and more generalized seizures. The goal of this study is to introduce SL as an online automatic detection method for real-life EEG monitoring, and explore the feasibility of its use, as the system automatically alarms when seizures are suspected, thus providing an opportunity to analyze the cEEG on demand, in a general tertiary university ICU. This procedure will be much more complicated than retrospectively analyzing EEG recordings detecting seizures, nonetheless it is necessary to improve the treatment of critical ill patients suffering from seizures.

2. Materials and methods

2.1. Patient selection

From October 2005 until January 2007, patients with a comatose state due (at least partly) to central neurological damage were enrolled prospectively in this non-blinded, non-randomized observational study. cEEG was performed according the protocol of daily care and treatment at the general tertiary ICU of our hospital (VU University Medical Center). The ethical committee of our hospital gave its approval for this study. Recordings started only at daily working times. Patients were eligible for this study if the following inclusion criteria were met: admission to the ICU, 18 years of age or older, any central neurological damage and coma (GCS < 8). Life expectancy should exceed 24 h, there should be no planned intervention (surgical or diagnostic imaging) in the first 6 h, and electrode placement should be possible. An EEG apparatus as well as an EEG technician had to be available. Patients were selected daily, based on the information on their medical charts and cEEG was started when permission was obtained from the treating intensivist. Patients using sedative drugs were included, as well as patients who underwent mild therapeutic hypothermia (approximately 32 °C) following cardiopulmonary resuscitation, or traumatic brain injury. We registered the following patient characteristics: age, gender, medical history, diagnosis at admission, clinical and neurological examination before and after registration, and (sedative) medication during cEEG (Table 2).