Commentary

Can electrophysiological assessments of brain function be useful to the intensive care physician in daily clinical practice?

Pierre C Pandin

Assistant Professor, Anesthesiology and Critical Care, Erasmus Hospital, Free University of Brussels, Brussels, Belgium

Corresponding author: Pierre C Pandin, ppandin@ulb.ac.be

Published online: 15 November 2004
This article is online at http://ccforum.com/content/8/6/437

Critical Care 2004, **8:**437-439 (DOI 10.1186/cc3011)

Related to *Research* by Yppärilä *et al*., see page 513

Abstract

Changes in electroencephalogram parameters and auditory event-related potentials, induced by interruption to propofol sedation in intensive care patients, provide a number of electrophysiological measures that can be used to assess neurological function accurately. Studies of electroencephalogram parameters suggest that power spectral estimation, as root mean square power, is more useful and precise than spectral edge frequency 95% in evaluating the functional integrity of the brain. When such parameters are used to evaluate neurological function, in particular the N100 and mismatch negativity components, a precise assessment of a patient's readiness to awaken from a pharmacologically induced coma (such as sedation) can be obtained. In terms of ease of use, however, it is more difficult to establish whether N100 or mismatch negativity is superior.

Keywords auditory event-related potentials, coma, electroencephalogram, evoked potentials, intensive care

Introduction

Can electrophysiological assessments of brain function be useful to the intensive care physician in their daily clinical practice? The study reported by Yppärilä and coworkers [1] sheds some light on this issue. First, it should be emphasized that collaborations between intensive care physicians and electrophysiologists, particularly in this highly specialized context, lead to the publication of reports that have considerable scientific merit. Neurologists and neurophysiologists have for some time encouraged intensive care physicians to bring techniques of electrophysiological evaluation to the intensive care unit (ICU), pointing out that the concepts on which they are based yield solid and reliable patient assessment methods that have become increasingly less abstract over the years [2]. Nevertheless, widespread understanding and acceptance of these procedures, specifically within the ICU, are lacking.

Although evaluation of electroencephalogram (EEG) parameters and event-related potential (ERP) components in order to assess neurological function is perfectly valid from a clinical perspective, the vast majority of intensive care physicians do not incorporate these electrophysiological measurement tools into their daily clinical practice, primarily because they are unaware that such techniques can be highly useful. The challenge over the next few years will therefore be to educate intensive care physicians on how to routinely employ electrophysiological evaluation methods, which not only have been made easier to conduct but also have been integrated into existing critical care monitoring systems. Efforts directed at promoting widespread use of electrophysiological assessment techniques in the ICU will need to be supported on one hand by dual neurological and pharmacological evaluation methods, and on the other hand by ongoing clinical application of the EEG and ERP assessment methods, as described by Yppärilä and coworkers [1]. The report is of particular interest because the findings illustrate so well the complementary relationship that exists between EEG and ERP electrophysiological evaluation techniques. They also offer greater precision regarding the

AEP = auditory evoked potential; EEG = electroencephalogram; ERP = event-related potential; ICU = intensive care unit; MMN = mismatch negativity; RMS = root mean square; SEF95 = spectral edge frequency 95%.

influence of sedation on brain function than do earlier findings reported by Sneyd [3] and Engelhardt [4] and their groups.

In the patients studied, the use of auditory evoked potentials (AEPs) offered greater precision than EEG parameters in evaluating neurological function because responses to stimulation of specific populations, or groups, of neurones could be identified. In contrast, EEG parameters, because of their simplified yet increasingly quantitative nature [5,6], permit electrical activity of the brain to be observed at any given moment. In the investigation conducted by John and coworkers [6], EEG parameters were useful for monitoring the depressive action induced by sedative and anaesthetic agents.

Electroencephalogram parameters: power is more precise than frequency

The findings reported by Yppärilä and coworkers [1] effectively illustrate the difference between the EEG parameters chosen: root mean square (RMS) power, representing the total power of the signal; and spectral edge frequency 95% (SEF95), representing the frequency below which 95% of the power in the EEG spectrum resides. The investigators also addressed the relative value of each type of EEG parameter in terms of the precision with which it could measure the neurological effects of propofol sedation; they demonstrated that evaluations of brain function using RMS power and SEF95 parameters correlated positively with assessments obtained using traditional electrophysiological evaluation methods. In addition, RMS power was found to increase significantly in magnitude on cessation of propofol, indicating resumption of brain function, but this was not the case for SEF95 values.

Perhaps monitoring the median EEG frequency would have been more revealing in this particular investigation because the median EEG frequency inherently addresses the distribution of the EEG frequency spectrum around the median [7] – a characteristic that is lacking in SEF95-based EEG assessments [8]. Moreover, the clinical significance of EEG signal power measurement, whether total or relative, has been emphasized in the literature [9,10], making this parameter increasingly simple, stable, and easy to evaluate. Measurement of EEG power parameters is a tool that should certainly be recommended for incorporation into current intensive care practice because it represents a reliable basis for neuromonitoring, which could be used to detect and observe, for example, the evolution of cerebral ischaemia [11] or an epileptic seizure [12], whether generalized or focal, convulsive or nonconvulsive.

Event-related potentials: what is the difference between the N100 and mismatch negativity components?

The N100 component of the AEP appears approximately 100 ms after the onset of a stimulus, thus opening the measurement field to include long lasting AEPs. It is under lied by all the intricacies associated with evoked and spontaneous potentials, exogenous and endogenous [13]. Distinct from the AEPs that preceded it (i.e. those of short and average latencies), long latency AEPs reflect the activation not of a single group of cortical generators, but rather of the concomitant and coordinated interaction of six brain regions; this emphasizes the complexity of the neurological functions to which long latency AEPs, such as N100, correspond. Principally, long latency AEPs are associated with cognitive function.

The mismatch negativity (MMN) component is a contemporary of N100, possessing a latency of approximately 130 ms and a duration of 250–300 ms. The MMN is evoked by nonstandard or unfamiliar auditory stimuli (also called deviant stimuli), which are randomly inserted into a sequence of standard or familiar sound stimuli [14]. Serving as a reflection of the brain's auditory change detection mechanism, the MMN corresponds to an automatic coding process into the sensori-auditory memory, and represents a relatively solid and stable component of it. The MMN offers the unique opportunity to measure sound objectively as it is perceived by the central nervous system. It therefore permits assessment of the auditory capacities of various types of patients, including infants and young children, as well as individuals who are cognitively impaired, unconscious, or even comatose, such as those patients studied by Yppärilä and coworkers [1], who were sedated initially with midazolam and subsequently administered an infusion of propofol.

It is important to note at this juncture that, analogous to the methodologies described by Yppärilä and coworkers [1], the importance of AEP component amplitudes (more than latencies) should be emphasized, and follow-up studies should be conducted to investigate correlations between amplitude values and brain function. Results from these studies will certainly serve as the foundation for development of simplified analytical methods in the future.

From a functional perspective, the N100 and MMN components were particularly interesting because of their ability to indicate and predict when a patient would awake from or reach the end of a coma [15]. Although the MMN appears to be more stable than N100 because of its higher predictive value (estimated to be in the order of 90%), this is not obvious from the findings of Yppärilä and coworkers [1]. Thus, the authors propose several perfectly plausible hypotheses but they are unable to make a definitive statement, and they are drawn to the provisional conclusion that further complementary studies are necessary. They also suggest that more elaborate study protocols should be developed that would address specifically the effects of each relevant drug class (e.g. hypnotics, opiates, etc.) in a more homogenous population.

Conclusion

Although a definitive conclusion is difficult to derive from the results reported by Yppärilä and coworkers [1], their findings

nevertheless have merit because they open the field to more structured investigations. In addition, their findings emphasize the need for combined electrophysiological investigations that measure EEG and ERP parameters, so that optimal precision can be achieved when assesing a patient's neurological state at the end of sedation. Data obtained through combined electrophysiological investigations could eventually supplement the criteria used to withdraw sedation in patients receiving ventilitor assistance, leading to more accurate prediction of the chances of a successful extubation. Finally, let us not forget the importance of bringing EEG and evoked potential measurements into systematic, routine, and perhaps even simplified use in the ICU. This would enable earlier detection of cerebral distress and allow critical intervention while the neuronal lesions are still responsive to treatment, and the tissue damage reversible.

Competing interests

The author(s) declare that they have no competing interests.

References

1. Yppärilä H, Nunes S, Korkhonen I, Partanen J, Ruokonen E: **The effect of interruption of propofol sedation on auditory event-related potentials (ERPs) and electroencephalogram (EEG) in intensive care patients.** *Crit Care* 2004, **8:**R483-R490.
2. Guérit JM: **Medical technology assessment of EEG and evoked potentials in intensive care unit.** *Neurophysiol Clin* 1999, **29:**301-317.
3. Sneyd R, Samra S, Davidson B, Kishimoto T, Kadoya C, Domino E: **Electrophysiological effects of propofol sedation.** *Anesth Analg* 1994, **79:**1151-1158.
4. Engelhardt W, Friess K, Hartung E, Sold M, Dierks T: **EEG and auditory evoked potential P300 compared with psychometric test in assessing vigilance after benzodiazepine sedation and antagonism.** *Br J Anaesth* 1992, **69:**75-80.
5. Nuwer M: **Assessment of digital EEG, quantitative EEG and brain EEG mapping.** *Neurology* 1997, **19:**277-292.
6. John ER: **Invariant reversible QEEG effects of anesthetics.** *Conscious Cogn* 2001, **10:**165-183.
7. Ropcke H, Schwilden H: **Interaction of isoflurane and nitrous oxide combination similar for median electroencephalographic frequency and clinical anesthesia.** *Anesthesiology* 1996, **84:**782-788.
8. Thomsen CE, Prior PF: **Quantitative EEG in assessment of anaesthetic depth: comparative study of methodology.** *Br J Anaesth* 1996, **77:**172-178.
9. Horn B, Schneider G, Ningler M, Stockmanns G, Kochs E: **Identification of EEG parameters that can be used to monitor the full range of anesthesia [abstract].** *Anesthesiology* 2004, **101:**A-329.
10. Schneider G, Ningler M, Stockmanns G, Nebl C, Kochs E: **EEG parameters separate awareness from unconsciousness at loss and return of consciousness [abstract].** *Anesthesiology* 2004, **101:**A-332.
11. Vespa P, Nuwer M, Juhasz C, Alexander M, Nenov V, Martin N, Becker D: **Early detection of vasospasm after acute subarachnoid hemorrhage using continuous EEG ICU monitoring.** *Electroencephalogr Clin Neurophysiol* 1997, **103:**607-615.
12. Vespa P, Nuwer M, Nenov V, Ronne-Engstrom E, Hovda DA, Bergsneider M, Kelly D, Martin N, Becker D: **Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring.** *J Neurosurg* 1999, **91:**750-760.
13. Näätänen R, Picton T: **The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure.** *Psychophysiology* 1987, **24:**375-425.
14. Näätänen R: **the mismatch negativity: a powerful tool for cognitive neuroscience.** *Ear Hearing* 1995, **16:**6-18.
15. Fischer C, Morlet D, Bouchet P, Luaute J, Jourdan C, Salford F: **Mismatch negativity and late auditory evoked potentials in comatose patients.** *Clin Neurophysiol* 1999, **110:**1601-1610.