



Clinical Neurophysiology: Evoked Potentials

47

Birger Johnsen

Recommendations

Level I

There are insufficient data to support a Level I recommendation for this topic.

Level II

The presence of event-related potentials (ERPs) (P300 or MMN) in comatose TBI patients predicts a favourable prognosis and justifies continuation of intensive therapy. Bilateral absent somatosensory evoked potentials (SSEPs) indicate only 5% awakening, which may be considered in the decision on continuation of intensive therapy.

Level III

Results from evoked potentials (EPs) should always be interpreted in the actual clinical setting and combined with clinical findings.

B. Johnsen (✉)
Department of Clinical Neurophysiology,
Aarhus University Hospital, Aarhus, Denmark
e-mail: birgjohn@rm.dk

47.1 Overview

Evoked potentials (EPs) are objective, non-invasive tests that may assess brainstem damage and detect cognitive functions in comatose patients; EPs are therefore of predictive value in TBI patients.

EPs are electrical signals recorded from the brain in response to different kinds of sensory stimuli, for example, auditory or somatosensory stimuli. These responses directly track the afferent volleys and appear with latencies less than 25 ms and are therefore also named short-latency EPs. Event-related potentials (ERPs) are EPs with longer latencies (up to 300 ms), and these EPs reflect higher cortical functions (Duncan et al. 2009).

EPs assess functional aspects of brain damage in addition to the clinical examination and in addition to the assessment of structural lesions by imaging techniques.

EPs of different modalities are of prognostic value in TBI patients, with some modalities predictive for a favourable prognosis and others predictive for an unfavourable prognosis. Absence of short-latency EPs predicts an unfavourable outcome (Guérit et al. 2009), while the strongest predictor for a good prognosis is the presence of ERPs (Daltrozzo et al. 2007).

Tips, Tricks, and Pitfalls

- EPs performed too early may show over-optimistic results due to the risk of secondary damage in TBI patients (Guérit et al. 2009).
- Drugs may have a pronounced influence on ERPs (Duncan et al. 2009).
- EPs should be performed by experienced neurophysiology technicians and be interpreted by clinical neurophysiologists.
- The predictive power of EPs should, together with clinical findings and results of imaging techniques, be taken into consideration in the handling of TBI patients.

47.2 Background

The different EP modalities are easily performed, often in less than 15 min in comatose patients. Significant abnormalities of EPs include the absence of responses, increases in latencies, or increases in inter-peak latencies. The absence of responses or the presence of normal responses is the most reliable predictors, although an increase in latencies, an increase in inter-peak latencies, or amplitude changes may also be valuable.

47.2.1 BAEP

Brainstem auditory evoked potentials (BAEPs) are signals generated in the brainstem and recorded by scalp electrodes in response to click stimulation of the ears. Responses from the ear and the neural pathways in the pons are recorded with latencies less than 10 ms. BAEPs are present in about 50% of TBI patients (Guérit 2005). There are some controversies about the prognostic ability of BAEPs, and some of these controversies are probably caused by differences in timing of the examinations and differences in criteria for BAEP abnormalities. There is, however, rather good agreement on the fact that absence of

BAEPs is a bad prognostic sign; for example, in a study of 64 TBI patients, Tsubokawa et al. (1980) found that all 23 cases with absence of the later BAEP waves died or went into a permanent vegetative state. On the other hand, the presence of BAEPs in TBI patients is not a useful predictor for a favourable outcome, as damage to brain regions outside the brainstem will not affect the BAEPs.

47.2.2 SSEP

Somatosensory evoked potentials (SSEPs) are recorded after electrical stimulation of the skin over a peripheral nerve of the limbs. When used as a prognostic tool in comatose patients, the most used technique is to stimulate the median nerve at the wrist while recording responses from the peripheral nerve at the elbow or at Erb's point, over the spine at level C7 and over the primary sensory cortex. A systematic review of 41 articles on SSEP as a prognostic marker for awakening from coma in TBI patients showed only 5% awakening in case of bilateral absent SSEPs, 70% awakening in case of present, but abnormal SSEPs, and 89% awakening in case of normal SSEPs (Robinson et al. 2003). Amantini et al. (2005) found that SSEP showed a good predictive value both for good and bad prognoses. Graded SSEP at day 3 after head trauma was found to correlate with functional and cognitive outcome (Houlden et al. 2010).

47.2.3 VEP

Visual evoked potentials (VEPs) are recorded after visual light stimuli. VEPs are only rarely used as a prognostic tool in comatose patients (Guérit 2005).

47.2.4 ERP

Event-related potentials (ERPs), also called cognitive evoked potentials, reflect higher cortical functions. ERPs are elicited by occasional differ-

ent stimuli within a repetitive standard stimulation, the so-called oddball paradigm. P300 is a positive response with a latency of about 300 ms that can be measured as a response to infrequent, randomly presented stimuli, for example, a different tone in a sequence of frequently presented tones. Some attention or vigilance is required in order to obtain a P300 response, and it cannot be elicited in all normal subjects, which limits its sensitivity in predicting coma outcome. Another kind of ERP, the mismatch negativity (MMN) potential, is the brain's automatic response to change in auditory stimulation, and it has the great advantage of not being dependent on patient attention, as it can be recorded in comatose patients (Näätänen 2000). The MMN response occurs as a negative peak in the ERP 100–250 ms after stimulation change. Kane et al. (1996) reported that the presence of a MMN response in serial studies of TBI patients has a specificity of 100% and a sensitivity of 89.7% for awakening.

In a meta-analysis, very high positive predictive values for a favourable outcome were found for P300 (89%) and MMN (93%) when present. However, the sensitivity was not very high (76% for P300 and 34% for MMN) (Daltrozzo et al. 2007). This meta-analysis showed equal predictive power of P300 and MMN, and both techniques are recommended (Daltrozzo et al. 2007). On the other hand, the absence of ERPs has no predictive value for a bad prognosis, as these components are not always present in normal subjects and they are sensitive to other factors, e.g. sedatives.

47.2.5 Combinations of EP Modalities

Some authors combine findings from different EP modality studies in indices for global cortical function and for brainstem conduction, which is of prognostic value (Guérit 2005). Kane et al. (1996) suggest that when short-latency EPs are normal, ERPs may be performed in order to directly check brain function related to cognitive processes.

47.2.6 Influence of Drugs

Drugs interfering with EEG do also interfere with EPs, and drugs may have large influence on EPs, in particular ERPs. Halogenated gases, propofol, and thiopental (membrane interference) may cause latency increase due to interference with subcortical conduction. In contrast, short-latency EPs are very resistant.

47.2.7 Timing of Examinations

EPs performed too early after the trauma may give false optimistic results if secondary brain damage occurs, and some authors suggest serial examinations. Facco et al. (1988) suggest that EPs have the best predictive value when performed 3–6 days post injury.

47.3 Specific Paediatric Concerns

There are only sparse results regarding the use of EPs in children. Robinson et al. (2003) found a higher chance for awakening and less disability in children with absent SSEPs compared with adults. Carter and Butt (2005) found that bilateral absent SSEPs had a specificity of 92% for an unfavourable outcome in 40 children with TBI. In general, there is insufficient evidence of an age limit above which the same interpretation criteria can be used as those used in adults (Guérit et al. 2009), and interpretations should therefore be made more cautiously in children.

References

- Amantini A, Grippo A, Fossi S, Cesaretti C, Piccioli A, Peris A, Ragazzoni A, Pinto F. Prediction of 'awakening' and outcome in prolonged acute coma from severe traumatic brain injury: evidence for validity of short latency SEPs. *Clin Neurophysiol.* 2005;116:229–35.
- Carter BG, Butt W. A prospective study of outcome predictors after severe brain injury in children. *Intensive Care Med.* 2005;31(6):840–5. Epub 2005 Apr 28. PubMed PMID: 15864546.
- Daltrozzo J, Wioland N, Mutschler V, Kotchoubey B. Predicting coma and other low responsive patients

- outcome using event-related brain potentials: a meta-analysis. *Clin Neurophysiol.* 2007;118:606–14.
- Duncan CC, Barry RJ, Connolly JF, Fischer C, Michie PT, Näätänen R, Polich J, Reinvang I, Van Petten C. Event-related potentials in clinical research: guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clin Neurophysiol.* 2009;120:1883–908.
- Facco E, Munari M, Casartelli Liviero M, Caputo P, Martini A, Toffoletto F, Giron G. Serial recordings of auditory brainstem responses in severe head injury: relationship between test timing and prognostic power. *Intensive Care Med.* 1988;14:422–8.
- Guérit JM. Evoked potentials in severe brain injury. *Prog Brain Res.* 2005;150:415–26.
- Guérit JM, Amantini A, Amodio P, Andersen KV, Butler S, de Weerd A, Facco E, Fischer C, Hantson P, Jääntti V, Lamblin MD, Litscher G, Péréon Y. Consensus on the use of neurophysiological tests in the intensive care unit (ICU): electroencephalogram (EEG), evoked potentials (EP), and electro-neuromyography (ENMG). *Neurophysiol Clin.* 2009;39:71–83.
- Houlden DA, Taylor AB, Feinstein A, Midha R, Bethune AJ, Stewart CP, Schwartz ML. Early somatosensory evoked potential grades in comatose traumatic brain injury patients predict cognitive and functional outcome. *Crit Care Med.* 2010;38(1):167–74 . PubMed PMID: 19829103. <https://doi.org/10.1097/CCM.0b013e3181c031b3>.
- Kane NM, Curry SH, Rowlands CA, Manara AR, Lewis T, Moss T, Cummins BH, Butler SR. Event-related potentials—neurophysiological tools for predicting emergence and early outcome from traumatic coma. *Intensive Care Med.* 1996;22:39–46.
- Näätänen R. Mismatch negativity (MMN): perspectives for application. *Int J Psychophysiol.* 2000;37:3–10.
- Robinson LR, Micklesen PJ, Tirschwell DL, Lew HL. Predictive value of somatosensory evoked potentials for awakening from coma. *Crit Care Med.* 2003;31:960–7.
- Tsubokawa T, Nishimoto H, Yamamoto T, Kitamura M, Katayama Y, Moriyasu N. Assessment of brain-stem damage by the auditory brainstem response in acute severe head injury. *J Neurol Neurosurg Psychiatry.* 1980;43:1005–11.