Electrophysiologic Techniques

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INTRODUCTION
Assessing the extent and functional impact of a traumatic brain injury (TBI), obtaining reliable prognostic indicators, gauging the best therapeutic interventions, and following the course of disease with reliable and objective markers is challenging. Electrophysiological techniques are relatively inexpensive, broadly deployable, repeatable, and safe methods that hold the promise of addressing some of these major clinical needs. Electrophysiological techniques can not only provide continuous and objective monitoring but can also pick up specific functional deficits and pathologies, provide a quantitative scale of severity, and be of great help in guiding rehabilitation and treatment interventions.

Electrophysiological techniques can be used to characterize the brain and central nervous system, as well as various aspects of the peripheral and autonomic nervous system. Evaluation of the peripheral and autonomic systems can be extremely important in patients after TBI because they may reflect consequences of brain injury and offer important prognostic insights. However, the focus of this chapter will be on the role of electrophysiological techniques to assess brain function with the use of electroencephalography (EEG), evoked potentials (EPs), and transcranial magnetic stimulation (TMS) in aiding the diagnosis, prognosis, and therapy of TBI.

ELECTROENCEPHALOGRAPHY
EEG measures electrical activity of the cerebral cortex through surface electrodes placed on the scalp adhering to standardized placement methods (e.g., the 10–20 International System of Electrode Placement; Figure 17-1A and 17-1B). Typical wave frequencies detected include delta (up to 4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz) and gamma (above 30 Hz). Within each frequency band, different rhythms have been indentified and ascribed to different brain/cognitive states (1). The alpha rhythm is a common starting point in the conventional analysis of a clinical EEG, is the dominant rhythm over posterior brain regions, and is attenuated with eye opening. Generally, alpha activity is thought to be related to inhibitory cortical tone and linked to thalamocortical patterns of activation. Mu rhythms are centrally located rhythms in the alpha frequency band that are attenuated with contralateral movement of an extremity. Beta rhythms are normally activated with mental, lingual, or cognitive efforts, mostly over the frontal areas. Furthermore, many pharmacologic agents increase power in the alpha band activity, notably benzodiazepines, for example. The rhythms can be recorded intermittently over the frontoparietal head regions during awake resting or while performing moderately difficult mental tasks; these are enhanced by drowsiness. Delta rhythms are considered a normal finding in the awake state in the very young and in the elderly, they are also considered normal across all ages during slow-sleep (1). Finally, gamma rhythms are associated with higher cognitive functions involving perception, attention, learning, and memory. These may also serve to assess the temporal dynamics of cortical networks and their interactions (Table 17-1).

Abnormalities detected in EEG recordings can indicate primary cortical pathology or be the result of deeper structures modulating cortical regions erratically. In patients with TBI, EEG is one of the electrophysiological techniques used to assess severity of brain injury and predict prognosis and outcomes (3–4). EEG analysis can be divided into conventional and quantitative methods.

Conventional EEG
Conventional EEG is the standard method for recording cortical electrical waveforms as mentioned earlier (Figure 1C). Although conventional EEG might have some value when assessing injury severity and depth of coma in patients with TBI (5–6), it remains a qualitative tool. Therefore, it does not provide great resolution and cannot quantify waveform spectrum frequencies. This makes it impractical for long-term monitoring of patients with TBI and predicting prognosis (6). Nevertheless, it is often used in neurocritical care for assessment and monitoring of patients with moderate-to-severe TBI (7). Conventional EEG can certainly help in the detection of epileptic activity, a common consequence of more severe TBI. However, use of conventional EEG in the evaluation of patients with mild TBI is rather limited.

Mild TBI
There are no clear EEG features unique to TBI of mild severity (8), and conventional EEG is not reliable in differentiating
between mild and moderate TBI either (4,9). There are studies that note an absence of any early EEG abnormalities, (10) even when a structural abnormality is present on magnetic resonance imaging (MRI) (11) or the patient clinically exhibits symptoms of TBI (12–14). However, not all studies report normal conventional EEG following mild TBI or concussion. One study, conducted in 1944 (15), involved the EEG recording of patients with industrial injuries acquired in a shipyard. Most patients, in whom EEG was measured within 15 minutes postinjury, showed little or no apparent alteration in the recording. However, certain patients who experienced the least delay between trauma and EEG recording showed diffuse slowing of EEG activity. This generally resolved within 15 minutes but for some lasted up to an hour. Within the first several hours after mild trauma, attenuated posterior alpha waves (decreased alpha frequency) as well as generalized or focal slow wave activity with a preponderance of theta waves are sometimes observed (3,8,16–18). The presence of these signs may be dependent on the length of loss of consciousness (19). Further, when associated with other signs of complicated injury, these abnormalities predict a poorer prognosis (20). However, the changes are often subtle and sometimes within the range of normal findings in the general population. Even if a longer lasting abnormality is present, it often resolves completely within months after a mild TBI. Correspondence between clinical and EEG findings is relatively poor (8), and any abnormalities discovered tend to resolve during the first several months postinjury (21). In the late period postinjury, approximately 10% of the individuals tend to show mild EEG abnormalities (10). However, the etiology of these is not always clear, and they may not be indicative of brain
TABLE 17-1 Electroencephalography Rhythms and Their Significance in Healthy and TBI Populations

<table>
<thead>
<tr>
<th>RHYTHMS</th>
<th>FREQUENCY</th>
<th>MAIN DISTRIBUTION</th>
<th>RECORDED IN HEALTHY</th>
<th>STANDARD EEG FINDINGS IN PATIENTS WITH TBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>&lt; 4 Hz</td>
<td></td>
<td>Awake state in the very young and in the elderly. Across all ages during slow-wave sleep.</td>
<td>Increased slow waves in the delta frequency band in severe TBI</td>
</tr>
<tr>
<td>Theta</td>
<td>4–8 Hz</td>
<td>Frontocentral</td>
<td>Resting or while performing moderately difficult mental tasks; enhanced by drowsiness.</td>
<td>Rise in slow focal or diffuse theta activity.</td>
</tr>
<tr>
<td>Alpha</td>
<td>8–13 Hz</td>
<td>Posterior</td>
<td>Attenuated with eye opening.</td>
<td>Immediate decrease in the power frequency of alpha waves.</td>
</tr>
<tr>
<td>Mu</td>
<td>8–13 Hz</td>
<td>Central</td>
<td>Attenuated with contralateral movement of an extremity.</td>
<td></td>
</tr>
<tr>
<td>Beta</td>
<td>13–30 Hz</td>
<td>Frontal</td>
<td>Mental, lingual, or cognitive efforts</td>
<td></td>
</tr>
<tr>
<td>Gamma</td>
<td>&gt; 30 Hz</td>
<td>Diffuse, central</td>
<td>Higher cognitive functions involving perception, attention, learning, and memory. Assess the temporal dynamics of cortical networks and their interactions</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: EEG, electroencephalography; TBI, traumatic brain injury.

damage. For example, a low-voltage alpha EEG pattern, months to years after a mild TBI or concussion, is indicative of more anxiety than brain injury (16).

**Severe TBI**

The use of EEG in severe TBI is higher than in mild TBI. EEG recordings after severe brain injury correlate well with the depth of post-traumatic coma (22–25). During initial stages of a TBI-induced coma, EEG variables such as the amplitude, frequency, and shape of wave potentials are not stable (6). Initial recordings taken within 24 hours postinjury are of less prognostic significance, however, than those from the 24- to 48-hour period (23,26). This could be caused by an interplay between both irreversible brain lesions and reversible functional disturbances. The degree of unconsciousness in patients can rapidly change, and thus continuous monitoring has been used for detecting possible signs of clinical deterioration during the first few weeks postinjury (27). Findings, during a post-traumatic coma, range from increased slow activity to amplitude suppression (28). Features typical of sleep, various sharply contoured discharges, epileptic spikes, periodic lateralized epileptiform discharges (PLEDs), and triphasic waves can also be found. However, reactivity and the typical sleep features mentioned earlier are more common among patients who show a good recovery (29).

In the late postinjury period of severe brain injuries, EEGs may show a wide variety of dysrhythmias, focal or generalized suppression, focal slowing, frontal alpha waves, and epileptiform discharges (30–31).

In summary, the use of conventional EEG in mild TBI is limited. Although there are abnormalities sometimes discovered in the EEG of patients with mild TBI, sensitivity is low, and the clinical and functional significance are uncertain. Further, any detected abnormalities may be similar to those present in the general population. Even in the late post-injury period, there is a lot of skepticism toward the significance of epileptiform EEG findings. In severe cases of TBI, however, the EEG can be more helpful and may even aid a hand in determining a prognosis for the patient.

**Post-Traumatic Epilepsy**

Post-traumatic epilepsy (PTE) will be covered in depth in Chapter 39 [Post-traumatic Seizures and Epilepsy] of this book. PTE is a recurrent seizure disorder that results from a traumatic brain injury (TBI). PTE is estimated to constitute more than 20% of cases of symptomatic epilepsy and about 5% of all cases of epilepsy. PTE must be differentiated from post-traumatic seizures (PTS), which refers to isolated seizures that occur as a sequel to brain injury either within 24 hours (immediate PTS), within 1 week (early PTS), or more than 1 week after injury (late PTS). About 20% of people who have late PTS never have any further seizures and should not be labeled as having PTE.

How to predict who will develop epilepsy after TBI is not easy. The onset of PTE can occur within a short time of the TBI but also months or even years later, and compared with the general population, people with TBI remain at a higher risk for epilepsy even decades after the injury. Serial EEGs may, thus, be helpful in following a patient after TBI and assessing the risk of PTE. However, this practice is not free of challenges.

The severity and type of injury certainly contribute to the risk of developing PTE, for example, penetrating injuries and those causing intracerebral hemorrhages confer higher risk. On the other hand, development of PTE is a relatively uncommon consequence of mild TBI (32). Nonetheless, a recent study showed that epileptiform abnormalities assessed with magnetoencephalography (MEG) were present in 19% of cases long after an episode of mild TBI (33). However, the statistic may not differ much from the prevalence of abnormalities in the general population. Indeed, a recent study (14) reported that 6 months after a mild TBI, a number of patients with epileptiform EEG abnormalities equal to those who had sustained only a whiplash injury. However, the authors did notice that post-traumatic epileptiform abnormalities increased as time passed.
EEG abnormalities did not. It should be noted that epileptiform activity could also be observed in healthy subjects with no history of seizures. In addition to various epileptiform paroxysmal patterns that are nonepileptic in nature, interictal epileptiform discharges (IED) can be recorded in healthy volunteers (35). Overall, spontaneous IEDs appear to be higher in patients who are nonepileptic with TBI than in healthy adults (2%-12% vs 0%-6.6%), and rates for seizure after IED detection are also higher in patients than in healthy adults (up to 14% in patients vs 2% in healthy adults).

It is thus difficult to predict the occurrence of PTE when based only on the recording of spontaneous IEDs, particularly after mild TBI. It is usually considered that sleep deprivation is an enhancer of epileptiform discharges and seizure frequency. However, this could also be because sleep deprivation often occurs in association with physical or emotional stress and arousal. When controlling for these factors, sleep deprivation facilitates IEDs but does not seem to affect seizure frequency (36). However, EEGs after sleep deprivation might be a useful indicator of brain damage after TBI and follow-up imaging studies (computer tomography [CT] or MRI) seem warranted and frequently reveal abnormalities (37).

In case of greater clinical suspicion, admission to an epilepsy monitoring unit (EMU) for prolonged video-EEG monitoring is the best way to confirm and clarify a diagnosis of epilepsy. In patients with suspected diagnosis of PTE, video-EEG monitoring can provide further diagnostic clarification and certainty in about 80% of the cases. Importantly, about 20% will be diagnosed as having psychogenic nonepileptic seizures (38). Finally, deep brain recordlings might be necessary to precisely localize the epileptic focus before surgery at case of intractable epilepsy.

In summary, the development of PTE is rare after mild TBI, although higher following other more severe TBIs (particularly penetrating wounds and those with intracerebral bleeds). Symptoms can develop long time after the TBI and while EEGs can be helpful in serially assessing the relative risk, presence of epileptiform activity in the EEG does not necessarily predict the occurrence of future seizures. However, it might indicate the existence of more significant brain damage.

Quantitative EEG

With signal processing technology, EEG data can be quantitatively and objectively analyzed (Figure 17-1D). Computer-assisted analyses of EEG data, that is, quantitative EEG (QEEG), offers definite advantages over a trained electroencephalographer’s eye in identifying the electrophysiological features of TBI (3-4). Although some studies raise concerns about the overall validity and accuracy of QEEG findings (8), many discuss the reliability of use in assessing various neurological disorders (9), specifically in diagnosing and classifying the severity of TBI (4,39). Studies have determined QEEG variables known as discriminant variables. Because of their low cost, speed, and objectivity, these can help in predicting functional characteristics and abnormalities in patients with mild TBI from controls and also from patients with more severe TBI. They were able to achieve a discriminant classification accuracy of 95.45% in mild TBI and 108 age-matched controls. In 2001, the sensitivity in discriminating between mild and severe TBI was 95.45%, and specificity was 97.44%. Thatcher et al. went on to propose “big bump theory” stating that pathological residues and/or compensation could be detectable by QEEG even years later after the original trauma. This is analogous to the big bang theory where cosmic radiation is still detected billions of years after the explosion. The study also discovered that the greatest contribution to discriminant function was actually multivariable and consisted of coherence, phase, and amplitude differences. Consensus says that QEEG of TBI cases show an immediate decrease in the mean frequency of alpha waves and a rise in slow focal or diffuse theta activity (8-9). These often later resolve within weeks and months coinciding with clinical improvement (8).

Methods of analysis of continuous EEG recording have been developed to evaluate changes in connectivity between different brain areas after TBI. EEG coherence, that is, correlation between the spectral content of 2 electrodes over time, is believed to reflect the strength of functional interactions between cortical neural networks; EEG phase, that is, the time lag between 2 similar activations at different locations, is believed to be linked to the speed of the connection between the 2 areas. TBI has been characterized by a decreased coherence and increased asymmetry (9). However, these coherence changes can be considered nonspecific findings and can certainly be found in pathologies other than TBI (8). Kumar et al. (42) showed that patients with mild TBI depicted normal connectivity at rest from 1 to 6 months after their concussion. These patients, however, had impaired verbal and visuospatial working memory tasks. This impairment was associated with decreased frontoparietal, frontotemporal, temporoparietal, and orbitofrontal connectivity during working memory performance. Similarly, during an auditory memory activation condition, abnormal frontal connectivity measures within the low and high beta bands (coherence and phase), as well as a shift toward right temporal functioning, have been associated with auditory memory deficits in patients with TBI (43). Thus, abnormalities of functional connectivity, explored during tasks execution, might be more prominent and more sensitive than abnormalities explored during the resting state.

However, impairment in functional connectivity at rest can be revealed with more sophisticated methods. Cao and Sloubovov (44) described a method in which an independent component analysis (ICA) was run to transform multichannel EEG recordings into independent processes. A source reconstruction algorithm followed this transformation. A graph theory analysis was then performed to assess the connectivity between regions of interest (ROIs). This method was applied to athletes, selected for their high risk of concussion, up to 6 months before and 7 days after a sport-related mild TBI. TBI resulted in a decrease in the long-distance connectivity (between frontal areas and other areas of the brain) and significant increase in the short-distance connectivity (within occipital and parietal areas) at rest, which could not be observed when traditional coherence analysis was implemented.

In summary, these studies reveal how the information contained in the EEG signal is rich and can be mathemati-
tioned in regard (among others) to the demonstrated accuracy of visual examination and the large amount of time based on QEEG. Discriminate analysis with QEEG also challenging given the fact that frequently, it is not simply a differentiation between "TBI" vs. "no TBI". Is, patients may have prior mental health issues, post-traumatic stress disorder (PTSD), depression, anxiety, drug abuse, alcohol, medications, and so forth. In addition, there is ongoing controversy regarding the various databases used for QEEG analysis. Thus, QEEG has become fully established in the clinical realm, yet it remains a role in the medicolegal arena, where it can find some resistance in courts and for third-party reimbursement (45). XIX (Medicolegal and Ethical Issues) of this book will go in depth these forensic considerations.

EEG Biofeedback

EEG biofeedback will be covered in depth in chapter (Complementary and Alternative Medicine) of the book. Here, we shall just provide some basic descriptions of principles. EEG biofeedback offers the opportunity for the patient to go from diagnostic and prognostic applications to therapeutic. Biofeedback techniques have been used to improve improvement of cognitive functions. Biofeedback causes measuring certain physiologic parameters from a person and then converting them into a signal that is provided to the patient. The feedback is positive (or negative) when the desired physiological response is obtained, whereas it is negative when the undesired physiological response occurs. Thus, the patient learns to control his or her physiological process (Figure 17.3).

When the physiological signals of interest are extracted from EEG, this technique is called EEG biofeedback, neurofeedback, or neurotherapy. The electrophysiological signals are believed to be related to different functional and mental states. The patient can hear or see an audio or visual feedback whenever the target parameters equal or exceed a threshold setting. The threshold is usually adjusted periodically to ensure the patient can receive the feedback for a fixed duration of time. The patient is instructed to discontinue the mental set or strategy to produce and maintain the desirable feedback; no further instruction is given. The sessions are discontinued when the patient reaches the desired level of brain activity and/or behavioral improvement, when neurophysiologic and/or neuropsychological outcomes are main stable, or after a fixed number of sessions.

Originally, the target electrophysiological signal or biofeedback was the amplitude in a given frequency band and the purpose was to normalize the EEG by increasing abnormally weak frequency bands and/or decreasing excessively dominant frequency bands. However, other physiological parameters can be targeted. Thornton (49) defined 2 distinct categories. In addition to the absolute magnitude in a given frequency band, the activation measures comprised of the relative magnitude (ratio of the magnitude of one band to the total magnitude of all bands), peak amplitude, peak frequency, and symmetry (peak amplitude asymmetry between 2 locations in a particular bandwidth). All of these connection measures are mainly comprised of measure coherence and phase.

On the Use of EEG Versus Quantitative EEG: Clinical and Forensic Considerations

In a report of the American Academy of Neurology and the American Clinical Neurophysiology Society on the assessment of digital EEG, QEEG, and EEG brain mapping published in 1997 (still holding in 2006), it was stated that QEEG remains investigational for clinical use in postconcussion syndrome resulting from mild or moderate head injury (46). This statement was criticized in later publications (e.g., 9,47–48). The superiority of visual examination over QEEG defended by the American Academy of Neurology is ques-
The promise of EEG biofeedback is to promote normalization of abnormal brain activity and thus lead to behavioral and cognitive advantages. This promise is not specific to TBI, and indeed, EEG biofeedback is explored and claimed to be beneficial in a long list of diverse conditions, reaching from anxiety/mood disorders, attention deficit and hyperactivity disorders and autism, to age-related cognitive decline, and dementia. This chapter focuses on the notion that EEG biofeedback might leverage the diagnostic virtues of quantitative EEG in TBI and offer a valuable therapeutic intervention.

Two main approaches of EEG biofeedback in patients with TBI can be found in the literature. The first one relies on predefined protocols, based on previous studies revealing EEG abnormalities in patients with TBI, aiming to eliminate or supress abnormalities. The second one is based on individual deviations from normal EEG values as defined by a control group of participants or with a previously constructed database. Although most protocols train patients to control their brain activity at rest (eyes opened or eyes closed conditions), rehabilitating the EEG abnormalities while the patient is performing a task involving the target function is also possible and might increase the efficiency of EEG biofeedback.

According to the aim of the protocol, the EEG electrodes of interest can differ. By default, the vertex of the head (electrode position Cz) is generally chosen. However, in TBI, one can choose the electrode closest to the impact site of the head injury (e.g., P50) or electrodes that reveal the largest abnormalities (e.g., Oz). The frequencies considered have been traditionally limited to frequencies lower than 32 Hz. Higher frequencies (high beta or gamma bands), nevertheless, may also have multiple functions in sensory and cognitive processing and are of interest for the rehabilitation of patients with TBI. It should be noted that different definitions of the frequency bands are given across different studies; moreover, methods of calculation of different parameters (e.g., coherence) might vary from one study to another. Thus, generalization of any results in this field requires special care.

The single-case study of Byers (50) offers an example of a protocol aiming to adjust the level of activity in predefined frequency bands. A patient who sustained a TBI 6 years earlier was trained to enhance, over the Cz location, his or her sensory motor rhythm (12–15 Hz) and in a second time his or her beta activity (15–18 Hz) while at the same time suppressing theta activity (4–7 Hz). The expected modifications of frequency were not clearly obtained; nonetheless, many symptoms of this patient were reduced during and following the EEG biofeedback training. The improvement was mainly seen in cognitive flexibility and executive functions.

An example of connectivity training at rest, to normalize coherence values toward values measured in a group of healthy subjects, can be found in the study of Walker et al. (51). Twenty-six patients with TBI with symptoms interfering with daily activities for more than 3 months, including employment, were trained to increase their reduced coherence values and to decrease any elevated coherence values. The initial training involved the use of a pair of electrodes with the most significant abnormalities. After 5 sessions, the training was dedicated to the next pair of electrodes picking up the most significant abnormalities and so on. Using a global improvement scale, based on a reduction of symptoms (e.g., headaches, memory loss or confusion) and the ability to return to work, significant improvements were noted in 88% of the patients.

The studies from Tinious and Tinious (53), Thornton (49), and Thornton and Carmody (52) exemplify EEG biofeedback training while the patient is performing cognitive training
or a task involving the function to be improved. In the study of Tinius and Tinius (53), the treatment decisions for 16 patients with mild TBI followed preestablished rules based on clinical symptoms and a brain map from the Thatcher reference database. For example, if theta activity was high, the treatment aimed to decrease theta activity at Cz; if the primary symptom was pain, the target was to increase sensory motor rhythm at Cz. They postulated that it may be beneficial to use coherence training after unipolar training and that it should start with the rehabilitation of short connections before long connections. Following this methodology, patients reported a decrease in their symptoms, and there was improvement of visual and auditory sustained attention that was trained during the simultaneous cognitive tasks. For the rehabilitation of memory function in patients with TBI, Thornton (49) offered a database for normal EEG reference during 18 different tasks (obtained from subjects without neurological disorder, history of brain injury or learning problems). The EEG variables were correlated with the memory performance of 59 normal right-handed participants to determine the cortically based electrophysiological correlates of effective cognitive functioning. Then, in several multiple single-case studies (49,52), patients with TBI were trained to normalize abnormal connections (coherence and phase values), and this was associated with improvement of general cognitive abilities and memory function.

In summary, EEG biofeedback in patients with TBI is a promising field. However, it needs to be further explored. Thornton and Carmody (54) point out the heterogeneity of parameters chosen and outcomes measured in studies of EEG biofeedback in TBI. It remains to be systematically proven that (a) abnormal EEG parameters and behavioral deficits are correlated, (b) EEG biofeedback is effective in normalizing EEG, (c) EEG biofeedback is effective in improving behavior and cognition, (d) measured improved functions translate into everyday life criteria, and (e) positive changes are long lasting. Ultimately, appropriately powered, randomized, controlled trials are needed.

In this context, a few questions are worth considering. Most prominently, how soon after a TBI the EEG biofeedback should be offered remains an open question. Starting too soon may overload existing resources, whereas waiting for a longer period of time may reduce the potential benefit (50–51). Several studies point toward the absence of a link between the time since the TBI and EEG abnormalities or successful outcomes of EEG biofeedback (51,52,55). These observations contribute to the notion that the brain does not spontaneously repair the damage caused by the TBI but instead allocates different resources to accomplish the task with variable results (49).

**EVOKE POTENTIALS**

Following the presentation of a stimulus or multiple stimuli, an electrophysiological response from the nervous system is known as an EP. The stimuli are most frequently auditory, visual, or somatosensory, and the EPs are frequently recorded from the brain using EEG techniques. These potentials are different from conventional EEG because they are calculated from an averaged response to a presented stimulus. Such averaging allows the response to the stimuli to be isolated from the background EEG activity (Figure 17-4).

**Somatosensory Evoked Potential**

The somatosensory EP (SEP) captures the manner in which the neural system responds to sensory input. SEPs can be elicited through electrical, tactile, vibratory, or painful stimuli applied to different body parts. However, among the different modalities, electrical stimulation is most commonly employed because of its ease of use (56). A peripheral nerve, such as the median, ulnar, or tibial nerve, is stimulated. The EP is picked up over the scalp (Figure 17-5). A SEP is generally characterized by its amplitude and latency. Short-latency SEPs (50 ms from stimulation) are more independent of the level of consciousness than longer latencies and generally reflect higher cognitive processes. For example, the presence of the N20 component of the SEPs, the compression thought to mark the arrival of the thalamic volleys in the cortex, appears to be a reliable indicator of significant subcortical disconnection and suggestive of prognosis. Overall, short-latency SEPs are considered valuable prognostic indicators for TBI (57).
In a consensus for the use of neurophysiologic techniques in TBI (38), short-latency EPs (including auditory and somatosensory) were found to be normal in 50% of severe TBI cases. Further, unilateral normal short-latency EPs predicted a favorable outcome in almost 80% of patients after TBI (59). However, a stronger prognostic indicator (albeit, negative) was in fact the absence of bilateral short-latency EPs (N20), and one study (57) showed a 95% predictive value of not awakening from a coma with such a recording. A systematic review of 25 studies (60) showed that SEP s are the best single predictor of outcome after TBI, superior to CI, EPs, Glasgow Coma Scale (GCS), and pupillary and motor responses. However, when standard clinical tests such as GCS and pupillary and motor responses are combined with SEP recordings, the predictive ability is further enhanced.

Other EP studies such as brainstem auditory evoked potential (BAEP) are limited to evaluating pharmacological effects of hearing and brainstem dysfunction after brain injury (56, 61); visual evoked potential (VEP) to disturbances in the visual cortex. One study (62) combined the use of SEPs and BAEPs but noticed that it was really only SEPs that accentuated the predictive value of certain clinical parameters over neither of them correlated with cognitive function at 1-year follow-up.

Because EPs provide neurophysiologic monitoring of different neural pathways (SEPs = somatosensory system, VEPs = visual system, BAEPs = auditory pathways, etc.), and because these various pathways show limited overlap, it seems reasonable to assume that multimodal EPs may be of additive diagnostic and prognostic value. A similar argument can be made regarding multimodal EPs within a given domain, where EPs are evoked with a variety of different stimuli (e.g., SEPs can be evoked by touch, pressure, electric stimuli, etc.) because these can tap onto different receptors and be mediated by different fiber pathways. Unfortunately, despite the theoretical appeal of such considerations, the practical use of such approaches is limited. Brain imaging techniques, particularly MRI, appear to offer greater clinical use.

In summary, the use of a SEP test can be of high value when assessing patients with brain injury and can add prognostic information to the clinical assessment. Certain situations need to be considered beforehand though, such as how the use of anesthesia can decrease the amplitude of SEP recordings, to prevent false conclusions.

**Event-Related Potential/P300**

An event-related potential (ERP) is an EP generally influenced by higher cognitive faculties. It is a measured brain response that is the result of either internal (e.g., thoughts) or external stimuli. Similar to EPs, ERPs are typically quantitatively characterized by their amplitude and latency. An ERP is usually referred to by its polarity (positive [P] or negative [N]) and its latency in milliseconds.
A typical ERP protocol involves identifying and discriminating a specific stimulus in a larger series of stimuli (oddball paradigm). The target stimulus is generally presented 20% of the time, whereas the other stimuli (distractors) are presented 80% of the time (63). To accurately judge the brain’s response to these stimuli, the experimenter must record multiple trials and then average the results. ERPs are thought to capture complex coordinated processing of widespread brain networks and appear to be a useful tool in assessing patients following brain injury because of their non-invasiveness and great temporal resolution (56).

One of the important elicited patterns of the ERP is the positive peak elicited 300 ms poststimulus (P300) (63). This response is consistently observed whether the stimulus is visual, auditory, tactile, or even olfactory. It is thought to reflect active attention, working memory, and the ability to discriminate individual stimuli among a group of other similar stimuli (64–67). Following brain injury the absence of P300 does not necessarily predict a negative outcome (68). However, another study (69) emphasized the usefulness of visual ERPs for evaluation of abnormalities following trauma. Doh et al. (69) compared 20 patients with TBI with 32 age-matched controls using a conventional oddball paradigm. They found that the P300 latency was longer in patients than in the controls. In addition, the P300 amplitudes were significantly smaller in patients than in controls but only for certain stimuli. Thus, ERPs may be a potentially useful marker for evaluating cognitive dysfunction in patients after TBI. However, detailed attention to the type of stimulus is important, and the use of ERPs at individual (rather than group) level is insufficiently studied.

Abnormalities in ERP have also been found in asymptomatic patients with TBI. For instance, a 3-tone auditory oddball paradigm revealed subclinical deficits in concussed athletes (e.g., 70–71). This paradigm consists of 3 different stimuli presented in a random order: typically a standard tone presented in 80%, a deviant target tone presented in 10%, and a deviant non-target tone presented in 10% of the trials. Participants are instructed to press a button when they hear the target stimulus while withholding their response to both standard and deviant non-target tones.

A P3a ERP is obtained by averaging brain responses to the rare deviant tone, whereas the P3b ERP is obtained by averaging brain responses to the rare target tone (Figure 17-5). Thus, the P3b component is analogous to the classic P300 described earlier. A P3b amplitude reduction is believed to reflect deficits in memory updating. The P3a component is thought to reflect frontal lobe function; reduced P3a amplitude and latency delays may reflect deficits in shifting of attentional resources to novel stimuli. Although concussed athletes generally show normal behavioral outcomes in the auditory (or the equivalent visual) oddball task, their P3a and/or P3b components frequently show reduced amplitude and/or an increased latency (71–73). Such abnormalities may resolve 2 years after the last multiple concussions (71), but one study showed abnormalities up to 3 decades after the last multiple concussions (70). Further studies along these lines, however, seem warranted. A reliable objective marker of brain function/dysfunction following TBI, such as this one, might provide valuable insights into the neurobiological impact of injury and the compensatory mechanisms that may render the patients asymptomatic but nevertheless render them vulnerable for long-term complications.

In summary, these ERP measures appear to represent a particularly sensitive tool to detect functional abnormalities not noticed on classic neuropsychological tests. ERP-based subclinical findings may explain the vulnerability of patients to subsequent concussions and the reported susceptibility of patients with TBI to develop long-term complications, including a progressive cognitive decline. Longitudinal use of such measures seem to be warranted.

**TRANSCRANIAL MAGNETIC STIMULATION**

TMS is a non-invasive method that uses the principle of electromagnetic induction to induce currents within the brain regions (74,75). These currents can be of sufficient magnitude to depolarize neurons. When applied repetitively, TMS can modulate cortical excitability, decreasing or increasing it, depending on the parameters of stimulation beyond the duration of the train of stimulation.

Following single-pulse TMS, distinct episodes of enhanced and suppressed activity can be observed. Induction of an excitatory postsynaptic potential is followed by a period of suppression of 100–200 ms duration. Furthermore, local and distant reentry mechanisms contribute to the complex and longer lasting suppression-activation dynamics. This results in lasting neuromodulation with a complex pattern of suppression and facilitation of activity, in relation to stimulation of inhibitory and excitatory interneurons, modulatory or metabolic processes, or even vocal responses.

TMS represents a particularly pertinent approach capable of studying the neurophysiologic effects of TBI because it has an unprecedented sensitivity to central excitation/inhibition (E/I) mechanisms (76). TMS can provide additional tools to characterize severity of TBI and evaluate abnormalities in symptomatic and asymptomatic patients. Moreover, it can be used to induce plasticity with TMS and can provide an additional tool to promote recovery.

**Characterization of Brain Abnormalities After TBI**

**Single- and Paired-Pulse TMS**

EP approaches can be readily adapted along with the use of TMS. TMS is applied as a controlled input to a specific region, and the neurophysiologic nervous system response can be recorded using electromyography (EMG) or EEG. The most commonly used EPs elicited with TMS are motor evoked potentials (MEPs). They are produced by using TMS to target the primary motor cortex (M1) and are recorded using EMG via electrodes placed over specific target areas. MEPs are of great interest to evaluate corticospinal integrity in patients with TBI.

**Central Motor Conduction Time**

Central motor conduction time (CMCT) reflects the latency of the corticospinal tract (77). It is calculated by subtracting the peripheral conduction time (spinal cord to muscle) from the latency of MEPs evoked by TMS. CMCT has been shown...
Symptoms of prolonged severe concussion or TBI may be prolonged in patients with TBI with diffuse and combined brain lesions tested 2 weeks after head trauma (78). However, CMCT was not affected in patients with TBI with minor brain concussions or focal lesions (78). Nonetheless, the absence of CMCT increase does not necessarily demonstrate an absence of impairment at the cortical level.

**Resting Motor Threshold and Motor-Evoked Potentials Amplitude**

Resting motor threshold (RMT) refers to the lowest TMS intensity necessary to evoke MEPs in a target muscle when single-pulse stimuli are applied to the contralateral M1. RMT reflects neuronal membrane excitability, which is highly dependent on ion channel conductivity (79-80). When TMS is applied at suprathreshold intensities, activation of excitatory synapses results in volleys of upper motor neuron activity, which subsequently activate motor neurons in the spinal cord. The summed activity results in an MEP. Latency and peak-to-peak amplitude reflect the integrity of the corticospinal motor pathways. The MEP/M wave amplitude ratio is calculated by dividing the MEP amplitude by the maximal M wave amplitude obtained after supramaximal peripheral electrical stimulation.

RMT did not reveal any abnormality, neither in athletes with 14-7 concussions 9 months after their last concussion (81) nor in athletes with a history of sports concussions more than 30 years prior to testing (70). However, in another study, RMT was significantly increased 2 weeks after mild and moderate head injury (78). This increase was accompanied by a marked reduction in the MEP/M wave amplitude ratio. Similarly, concussed athletes evaluated sequentially between 1 and 10 days postconcussion showed a progressive increase in MEP latency and a reduction in MEP amplitude (82). The loss of the corticospinal neurons, the slowing because of delayed injury or axonal disconnection, and the deafferentation of multiple descending volleys resulting in an ineffective temporal summation of excitatory postsynaptic potentials could explain these observations (78,82). In addition, the reduction of the MEP amplitude may also be indicative of pyramidal tract/brainstem involvement (82).

Finally, increased RMT was also found 3 months after mild to moderate TBI in patients with objective excessive daytime sleepiness (83). A reduced excitability of the corticospinal system during wakefulness, mimicking the hyperpolarization of the thalamocortical system in healthy subjects during sleep, might contribute to the persistent sleepiness observed in patients with TBI.

**Cortical Silent Period**

When TMS is delivered over the motor cortex while the subject maintains a voluntary muscle contraction in the contralateral hand, a pause in ongoing EMG activities follows the MEP (Figure 17-6D). This pause is called the cortical silent period or contralateral silent period (CSP). The initial phase of the CSP might be related to the refractory period of the pyramidal tract neurons, whereas the latter part of the CSP has been attributed to activity of intracortical inhibitory (GABA) receptors.

![Figure 17-6](https://example.com/image.png)

De Beaumont et al. (81) and Tremblay et al. (84) showed that CSP duration was prolonged in athletes who had experienced multiple concussions. Sustaining subsequent concussions exacerbates this deficit and thus provides additional support for the existence of cumulative deficit following multiple concussions; moreover, concussion severity was significantly correlated with CSP lengthening (81). Observed CSP duration lengthening in athletes with multiple concussion seemed to remain unaffected by the time elapsed since the last accident. De Beaumont et al. (70) further showed that former athletes with a history of concussion more than 30 years prior to testing also have an increased CSP duration, despite apparently normal cognitive performance and absence of neuropsychological abnormalities.

However, a previous study (78) showed no alteration of CSP duration in a similar population of patients 2 weeks after a mild TBI; only patients with moderate brain injury showed an increased CSP duration. Such discrepancy could be related to methodological aspects in relation to determination of TMS intensity (78). Alternatively, CSP prolongation could be triggered later after trauma, when acute RMT abnormalities are resolved (81).

**Ipsilateral Silent Period**

When TMS is applied over M1 during an ongoing tonic voluntary contraction of the muscles ipsilateral to the site of stimulation, the activity of these ipsilateral muscles can be temporarily suppressed. This ipsilateral silent period (ISP)
has been attributed to transcallosal inhibition, and this method can evaluate the integrity of the corpus callosum connecting homologous motor cortices. Diffuse axonal injury, in consequence of TBI, might involve disruption of the corpus callosum, which may be uncovered as a reduction of transcallosal inhibition measured with TMS. Takeuchi et al. (85) showed that the amount of transcallosal inhibition was significantly reduced in patients with TBI several months after their concussion compared to healthy controls, and this reduction was significantly correlated with the severity of TBI as evaluated using the GCS.

Transcallosal inhibition can also be assessed by measuring the decrease in amplitude of an MEP evoked by a test pulse applied over the contralateral M1 when this test pulse is preceded by a conditioning pulse applied over the ipsilateral M1 (bi-coil paired-pulse TMS technique). This paired-pulse technique using 2 TMS coils has not yet been used in a TBI population but offers promise to further characterize possible interhemispheric and other corticocortical disconnections.

**Excitatory and Inhibitory Balance**

Chistyakov et al. (78) evaluated the balance between excitatory and inhibitory central mechanisms by calculating the interthreshold difference (ITD) as the difference between the RMT and CSP threshold. Indeed, both RMT and CSP thresholds were significantly increased in patients who sustained mild and moderate head injury, but the increase in CSP threshold was much less pronounced than that of the MEP threshold. This resulted in a significant increase of the ITD. The increase in the ITD, accompanied by reduction of the MEP/M wave amplitude ratio, suggests dissociated impairment of inhibitory and excitatory components of the central motor control.

Alternative ways to assess excitatory and inhibitory central mechanisms is using paired-pulse TMS (ppTMS) paradigms. The ppTMS involves the application of 2 TMS stimuli of independently controllable intensity and with a variable interstimulus interval to the same cortical region. The first stimulus, thus, serves as a conditioning stimulus to the effect of the second test stimulus. Several paired-pulse paradigms have been designed to assess the short-interval intracortical inhibition (SICI; Figure 17-6B), hypothetically GABA\(_A\) mediated, the long-interval intracortical inhibition (LICI), hypothetically GABA\(_A\)-mediated, and intracortical facilitation (ICF; Figure 17-6C), hypothetically mediated by synaptic glutamatergic transmission (80,86–88).

The studies from De Beaumont and collaborators previously cited (70,81,84) did not reveal any abnormalities in SICI or ICF in athletes with 1 or several sport concussions from 9 months to 30 years prior to testing. However, increased SICI has been found 3 months after mild-to-moderate TBI in patients with objective excessive daytime sleepiness (83). These patients also had an increased RMT. Both RMT and SICI correlated with objective measures of sleepiness. It has been suggested that the persistent sleepiness in some patients with TBI is caused by a combination of reduced excitability because of reduced hypocretin signaling (hypothalamic injury) and also injury to other sleep-wake regulating systems.

Finally, LICI was enhanced in asymptomatic concussed athletes with multiple concussions that occurred more than 12 months prior to testing (84). Together with the increase in CSP duration, this result points toward the presence of specific and stable alterations of GABA\(_A\) receptor activity in the M1 (84).

In summary, TMS methodology can provide tools to assess brain abnormalities in the acute and subacute phases of TBI of various severities. Acutely after mild concussion, several measures point toward the loss of corticospinal neurons, the slowing and the desynchronization of multiple descending volleys, and both excitatory and inhibitory circuits seem to be affected. This could be related to cholinergic abnormalities and excessive glutamate accumulation leading to N-methyl-D-aspartate (NMDA)-mediated excitotoxicity. Whether these deficits are also present in asymptomatic patients with mild TBI, shortly after the concussion, remains to be explored. In the long term, months and up to 30 years after the concussion, both glutamatergic excitotoxicity of asymptomatic patients with mild TBI seems to be resolved (normal excitability and ICI), and there is likely no deficit in GABA\(_A\)-mediated inhibition (normal SICI). However, an increase in CSP duration and an abnormal LICI point toward increased GABA\(_A\) transmission. It has been suggested that this increase may cause preliminary excitotoxicity and prevent damage. However, it might be excessive and finally maladaptive (84). While similar mechanisms occur in the sustained phase of pain with more severe TBI remain to be explored.

TMS studies are of particular importance to further characterize the severity of TBI and evaluate subconscious effects. They can also provide insight into the mechanisms of symptoms associated with TBI, such as sleepiness and help to identify patients who would be suitable for treatment (83). If further developed, TMS tools could be useful in the return-to-normal-life criteria. They might turn out to be useful in the prognostic concerning recovery and the prognosis of a second TBI or the development of mild cognitive impairment or Alzheimer disease (84).

**TMS Combined with EEG**

The combination of brain stimulation by TMS with simultaneous EEG recording has become feasible due to the development of novel engineering solutions (89–92). The TMS-EEG integration provides real-time information on both neural activity and connectivity. A noninvasive input of known spatial and temporal characteristics can be used to study local reactivity of the brain and interactions between different brain regions with directional and precise geometric information (Figure 17-7). TMS-EEG combination appears to be of particular interest to explore excitable areas outside the motor cortex that are primarily affected in TBI. In addition, this methodology will allow one to investigate the integrity of entire cortical circuits. Being able to interact directly and across the lifespan is critical to bring findings from animal studies and thus identify potential markers for disease and promote therapeutic monitoring. Systematic exploration of TMS-EEG methods seems warranted and will allow the study of prefrontal, temporal, and other brain regions and distributed...
Repetitive TMS

Trains of repeated TMS (rTMS) pulses can induce a lasting modification of activity in the targeted brain region, which can outlast the effects of the stimulation itself. Depending on the frequency, intensity, and the pattern of stimulation, the induced effects promote inhibition or excitation of the stimulated area. Repetitive TMS paradigms might be used to test the plasticity resources of patients at several time points after TBI of varying severities. Indeed, after a TBI, the nervous system reorganizes in response to injury. Such reorganization is restricted by existing patterns of anatomical and functional brain connectivity. The behavioral impact of such plastic reorganization is not necessarily adaptive and may prove to represent dead-end strategies that ultimately limit functional recovery and promote lasting disability. Assessment of plasticity resources at different time points after TBI might be necessary to develop differential mechanistic interventions and promote functional recovery.

In addition, rTMS can be directly used to facilitate recovery. Such rTMS approaches thus offer, similar to EEG biofeedback, the opportunity to use neurophysiologic techniques in therapeutic rather than diagnostic and prognostic applications. Pascual-Leone et al. (93) performed 30 sessions (6 weeks) of an rTMS protocol in a patient with severe TBI who remained in a vegetative state for longer than 9 months. The rTMS intervention (a repetitive paired-pulse stimulation of the right dorsolateral prefrontal cortex) was designed to use potentially excitatory stimulation parameters while maximizing safety. This methodology proved to be safe, and the patient progressed clinically from a vegetative state to the 15th session. The patient demonstrated incremental neurological improvements simultaneously occurring with the provision of rTMS up to the 25th session. Although a mild decrease of performance occurred during the final 5 sessions, most of the neurobehavioral improvement sustained 6 weeks after rTMS withdrawal and, according to his family, up to 1 year after completion of the study. Obviously, this is a single-case study that requires cautious follow-up and demands confirmation prior to clinical adoption. Whether rTMS might promote adaptive plasticity in other patients, including patients with less severe TBI, remains to be explored. Such studies should be done with care because rTMS can induce significant side effects and complications, particularly in certain predisposed populations (94). Therefore, appropriately controlled studies are needed prior to considering the use of rTMS in clinical practice.

OTHER METHODS OF POTENTIAL INTEREST

Transcranial direct current stimulation (tDCS) is a noninvasive technique of neuromodulation, which passes low amplitude direct current (1–2 mA) through pad electrodes placed on the scalp to alter neuronal firing. Although anodal tDCS elicits prolonged increases in the cortical excitability of the underlying brain area, cathodal stimulation shows opposite effects (95–96). As with rTMS, the duration of the effects outlast the period of stimulation. The mechanisms are believed to be nonsynaptic and result from change in resting polarization of neurons. Although investigation of tDCS in patients with TBI is only starting, this technique is promising because it shows excellent safety record and has proven to be able to improve several brain functions in healthy subjects and in patient populations (for a review, see 97). Several studies conducted on the safety of tDCS have concluded that it is a painless technique for electrically stimulating the brain with almost no risk of harm. The most frequent adverse effects that have been reported include moderate fatigue (35%), mild headache (11.8%), nausea (2.9%) and temporary mild tingling sensation, itchiness, and/or redness in the area
of stimulation. Overall, tDCS features a highly portable, safe, noninvasive means to modulate cortical excitability with reasonable topographic resolution and reliable experimental blinding. It can focally suppress or enhance neuronal firing following TBI and thus may offer a promising method to minimize the damage and promote functional recovery. Cathodal tDCS may be employed to suppress the acute glutamatergic hyperexcitability following TBI. In the subacute stage, when GABAergic activity is excessive and conditions the neurologic, cognitive, and functional disability, anodal tDCS may increase excitability to counter these aberrant GABAergic effects. In the chronic stage, brain stimulation coupled to rehabilitation can enhance behavioral recovery, learning of new skills, and cortical plasticity. Furthermore, tDCS can be combined, with relative ease, with other interventions with the aim of enhancing their effect. For example, tDCS can be applied during cognitive training, robot-supported arm or gait training, physical or occupational therapy, imagery, and so forth. As such, tDCS might prove to be a valuable neuromodulatory tool to promote rehabilitation and functional recovery after TBI.

Cranial electrotherapy/electrical stimulation (CES) is a technique that provides small pulses of electric current (0–4 mA) across the head, using pregelled electrodes, conductive rubber ear clips, or moistened sponges placed on the head either below or directly on the ears. This technique has primarily been investigated for the treatment of anxiety, depression, and insomnia. It is hypothesized that the outcomes of CES would be mediated by neurotransmitters. Some studies have shown effects onto QEEG. However, the mechanisms of action remain uncertain, and, overall, the experimental evidence regarding clinical use is limited. In the treatment of postconcussion symptoms, CES has been shown to be useful in improving several mood measures (98), but further studies with better controlled trial designs are needed to assess its efficacy.

Transcranial pulsed ultrasound stimulation (TCPUS) is another recently developed method of potential interest for noninvasive brain stimulation (99–100). Ultrasound is a mechanical pressure wave with a frequency above the range of human hearing (> 20 kHz), capable of being transmitted over long distances through solid structures. Ultrasound can influence physiological activity through thermal and/or mechanical mechanisms. Tufail et al. (99) used a series of low-frequency ultrasound pulses (typically below 100 cycles per pulse at a frequency within one-tenth of a MHz range) repeated over time (typically hundreds of times at a frequency in the order of 1 kHz) at a low intensity (< 300 mW/cm²) to safely stimulate neural activity in the intact mouse brain. With a negligible increase of temperature, ultrasound stimulation of the motor cortex produced short bursts of activity and peripheral muscle contraction, whereas stimulation of the hippocampus triggered rhythmic bursting lasting about 3 seconds. It was suggested that the fluid-mechanical effects (a) modulate the resting membrane potentials of neurons, (b) directly modulate the kinetics of mechanically sensitive ion channels, and/or (c) produce ephaptic effects by altering the distribution of electric fields. The advantage of this technique over other noninvasive techniques of brain stimulation would be its spatial resolution, estimated to be of approximately 2 mm. Although this technique appears safe in mice, it remains to be proven as to whether it can be safely applied in other species.

Transcranial Doppler sonography (TCD) can be used in the acute assessment of cerebral ischemia following TBI and may offer appealing noninvasive methods in patients in the intensive care setting. A study in patients with mild-to-moderate TBI (102) showed that TCD measures of brain perfusion at time of hospitalization were good predictors of overall neurologic outcome. TCD might be a powerful prognostic tool in TBI. More advances in our understanding of TCD have led to possible therapeutic roles in TBI where clot formation is the result from primary injury. One application is sonography, a technique of focal TCD applied at diagnostic facilities alone or in combination with standard thrombolytic therapy (TPA) (103). TCD may also have the potential to promote neuroprotection during acute TBI by increasing local bioavailability of neuroprotective agents. TCD would be shown to transiently (i.e., hours) enhance blood-brain barrier (BBB) permeability without adverse cellular effects. The mechanism is believed to be a process of stable cavitation, which low acoustic energy causes administered macromolecules to oscillate and expand creating small eddy currents surrounding plasma. These currents provide energy to cells and large molecules to improve BBB transport and paracellular transport (104). Thus, TCD may improve the applicability of novel neuroprotective agents by improving pharmacokinetic optimization. Finally, some studies have alluded to the potential of TCD as a direct neuroprotection (105). In the setting of TBI, these studies of TCD may allow for suppression of neuronal activity, acute energy deficient phase and facilitation in the ischemic phase of active recovery, strengthening our therapeutic capacity against TBI.

Low-level laser therapy (LLLT), or photobiomodulation, is a novel method of noninvasive neural stimulation that, at specific wavelengths, can safely penetrate into the brain. LLLT is thought to promote cellular survival in conditions of reduced energy substrate through interactions with the chromophore cytochrome c oxidase to enhance oxidative phosphorylation, improve mitochondrial function, and increases adenosine triphosphate (ATP) (106,107). LLLT has been shown to generate wound healing, reduce neurological deficit following stroke, and improve outcome in spinal cord injury (108). In LLLT was used for the first time in a rodent TBI model, LLLT-treated rats showed significantly reduced functional impairment and reduced lesion volume (109). Preclinical findings, the promising results in human research (109–111), and the unique properties of LLLT make the therapeutic application in TBI seems worth exploring.

SOME LIMITATIONS OF ELECTROPHYSIOLOGICAL TECHNIQUES

Although all these techniques have proven to be helpful in TBI diagnosis, prognosis, exploration of the mechanisms, and/or rehabilitation, several concerns still need to be addressed. The reliability of most of these measures is paramount.
CONCLUSION

Electrophysiological techniques are essential in the TBI care practice. They are useful for diagnosis, prognosis and monitoring for exploration and characterization of brain deficits, and for detection of subclinical abnormalities that may increase vulnerability to subsequent concussions or susceptibility to long-term complications. In addition, some of these tools can be used to guide functional recovery (e.g., EEG biofeedback brain stimulation). Certainly, these techniques still need to be developed and improved, and for all, studies need to be done to further clarify findings and to assess the validity and safety of these methods when confounding and complicating factors intervene.

KEY REFERENCES


References


17. ELECTROPHYSIOLOGIC TECHNIQUES


