Traumatic Brain Injury and Electroencephalogram Findings

8

Renato Anghinah and Jéssica Natuline Ianof

History

The discovery of electroencephalography (EEG) in 1929 by the German psychiatrist Hans Berger was a historical advancement that provided a new neurological and psychiatric diagnostic tool at the time, mainly considering the lack of all the exams that are available in daily practice today, such as computed tomography (CT) and magnetic resonance *imaging* (*MRI*), without which the preparation of neurological diagnoses and the planning of neurosurgical operating procedures would not be acceptable [1]. Based on the discovery of Caton and Beck, Danilevsky, Prawdicz-Neminsky, and others that there was a spontaneous (intrinsic) brain electrical current that could be recorded, Berger made the first EEG recording (electrocorticogram) on July 6, 1924, during a neurosurgical operation on a 17-year-old boy. He reported this in 1929, being the first to use the terms alpha and beta [1]. The discovery of electroencephalography was a landmark for the advancement of neuroscience neurological and neurosurgical practice every day, especially for patients with seizures. At a time when lumbar puncture, pneumoencephalography, and ventriculography were the only diagnostic tools to detect and locate "sick sites" in the brain, the EEG revolutionized daily neurological and neurosurgical procedures and exceeded a period of approximately 40 years (1930–1970) until the advent of computed tomography [2]. Its importance, currently, may not be as great as it was before, but it still has its place in the diagnosis of seizures, brain tumors, degenerative brain disorders, and other diseases.

R. Anghinah (✉)
Department of Neurology – Cognitive Rehabilitation after TBI, Clinics Hospital – School of Medicine – University of São Paulo, São Paulo, Brazil

Center of Excellence in Neurology – Americas Serviços Médicos, São Paulo, Brazil

J. N. Ianof
Department of Neurology – Cognitive Rehabilitation after TBI, Clinics Hospital – School of Medicine – University of São Paulo, São Paulo, Brazil

Introduction

In traumatic brain injury (TBI) patients, diagnosis and treatment are essential for acute patient care and long-term rehabilitation. Cognitive dysfunction (memory impairment, attention, and information processing skill) [3], somatic problems (headache, fatigue, sexual dysfunction, and sleep disorders), mood swings (depression, aggression, emotional liability, and anxiety), and post-traumatic personality changes (self-centered behavior, reduced social awareness, and disinhibited behavior) are some of the several consequences that may occur after TBI.

Electroencephalography (EEG) is important for clinical assessment of consciousness to support diagnosis and prognosis [4, 5]. The electrical activity of brain tissue may have good prognostic value after brain injury. EEG can provide an objective and quantitative measure of the severity of brain injury [6], when performed from 15 days to 4 years after TBI. In addition, EEG can detect early seizure activity and give information about sleep patterns during polysomnography, since sleep disturbances (insomnia, hypersomnia, and altered sleep-wake cycles [7–9]) are common after TBI. The neural mechanisms that contribute to sleep disturbances are multiple – the degree of damage to sleep-wake regulation centers, such as ascending reticular formation and associated pathways or neurotransmitter systems – and may affect sleep [10, 11]. Also, anxiety and depression often occur after TBI, and increased depression is associated with poor sleep quality [12, 13].

Most cognitive disorders have a primary diagnosis that is clinically based, but the EEG plays a role in evaluation, classification, and follow-up of some of these disorders. The EEG is a widely accepted method for evaluating cortical information processing and neurophysiologic changes that occur during unconsciousness and the different states of conscious awareness [14]. In addition, it is now possible to increase EEG sensitivity through the use of digital EEG (dEEG) and the mathematical procedures implemented in quantitative EEG (qEEG).

R. Anghinah et al. (eds.), *Topics in Cognitive Rehabilitation in the TBI Post-Hospital Phase*,
https://doi.org/10.1007/978-3-319-95376-2_8

Clinical electrophysiologic techniques are frequently used in the evaluation of cerebral function following TBI [15]. These tools enables noninvasive recording of the electrical or magnetic activity of the brain. Conventional EEG is the prototypic clinical electrophysiological assessment and was the first neurodiagnostic tool to allow characterization of disturbances in cerebral physiology produced by TBI [16, 17]. The digital recording of cerebral function is acquired from 21 electrodes arranged on the scalp, according to the International 10–20 System, and generates waveform tracings suitable for visual inspection by a qualified electroencephalographer [18, 19].

The electroencephalogram (EEG) records the electrical potential difference between brain electrical activities recorded between two electrodes [20]. EEG records the average membrane potential of apical dendrites of cortical pyramidal neurons, which tends to oscillate. It detects the synchronous occurrence of dendritic synaptic potentials – excitatory and inhibitory postsynaptic [21].

The physiological basis of these oscillations is a manifestation of both intrinsic properties of neurons (ionic conductances) and network interactions (connectivity). Different frequency oscillations are guided principally by corticocortical connections and thalamocortical connections to varying degrees depending on the specific oscillation. EEG oscillations exist in a broad range of frequencies from below 1 Hz to several hundred hertz. The physiology is best understood for several "classic" frequency bands including delta (0.5–4 Hz), theta (4–7 Hz), alpha (8–13 Hz), beta (14–30 Hz), and gamma (30–100 Hz). These frequency ranges [22] represent different oscillatory phenomena with unique underlying physiological mechanisms, cortical topographies, and functions. Different combinations of frequency bands in different quantities represent different states of the brain – attentive wakefulness, drowsiness, and stages of sleep.

EEG clinical assessment usually involves a visual inspection of the electrical activity of the brain in a variety of brain states and the evaluation of the topography and amount of appropriate oscillatory activity of the state, as well as examination for the presence of pathological potentials. For the detection of epileptiform activity, the human eye actually exceeds computerized waveform analysis despite decades of attempts to automate EEG interpretation [23]. But when it comes to the evaluation of topography and the amount of oscillating activity and what constitutes a normal or abnormal distribution of this activity, visual inspection fails considerably, and the use of computerized algorithms is needed.

For example, to obtain a quantitative evaluation of the amount of oscillatory activity at any and all frequencies in a specific region of the brain, the qEEG frequency analysis transforms the original EEG data over a period of time into a representation of its frequency content, generating a continuous EEG "force spectrum."

Utility of EEG

EEGs enhance conventional medical approaches to imaging the structure and function of the brain. EEG as a neuroimaging modality holds several advantages over more conventional medical approaches. Nowadays, computed tomography (CT) and MRI are the current "gold standards" for imaging assessment of neurophysiological trauma. They have an excellent spatial resolution for easily identifying lesions; but both approaches require very large and expensive equipment, special facilities for their use, and dedicated technicians for operation and are not available everywhere. CT uses small doses of radiation, which can carry potential risks for long-term side effects if patients are scanned frequently and MRI uses an extremely strong magnetic field, and needs a careful operating room. Also, it has a lot of limitations – its use has contraindication of medical devices, implants, and any foreign ferrous metal objects in the patient's body. Equipment used for EEG is more portable and cheaper and requires no special facilities. These characteristics lead to field ability and a broader operational effectiveness [24].

The data derived from EEG are also essentially distinct as compared to CT and MRI data. In particular, while CT and MRI have excellent spatial resolution, the resulting images (which may take several minutes to acquire) are temporally static and thus provide no direct measurement of functional, ongoing brain activity. Even the best current methods of "functional MRI" are limited to multiple seconds for the acquisition of whole-brain images. In contrast, EEG is extremely high-resolution in the time domain (EEG can be sub-millisecond) and, as described above, is a direct measurement of neuronal activity. This enables a great number of analyses, which capitalize on direct responses to stimuli, cognitive responses, interrelatedness of continuous signals, and the oscillation of both discrete and cross-regional networks of brain areas [20].

EEG in TBI

Electrical activity is a relatively sensitive index of the pathophysiological response of the brain to the immediate and secondary damage of the TBI, and that is why it is intimately related to the outcome of the patient's situation [25].

Glasgow Coma Scale, duration of loss of consciousness, and duration of post-traumatic amnesia (PTA) are considered important clinical predictors of the severity and long-term prognosis of brain damage. However, these assessments are often unknown or unregistered. Therefore, there is a need to develop an objective and quantitative measure of the severity of brain injury using the EEG tests [26].

Immediately after TBI, EEG initially shows epileptiform activity [27], followed by suppressed cortical activity – which can last from seconds to about 1 min [28]. Many patients return to normal within 1 h, while others continue to have focal or generalized EEG slowing – that can last from weeks to months. The posterior alpha frequency is on average 0.7 Hz lower and gradually returns to baseline frequency over a period of time ranging from weeks to a few months [29]. The theta/alpha ratio increases after mild TBI and tends to return to normal within weeks to months [30].

In general, high-frequency EEG (beta and gamma) rhythms are produced by cortical generators, whereas lower-frequency rhythms (delta) are the product of corticothalamic synchrony and may be more prominent when the chorothalamic connections are interrupted [31].

EEG abnormalities are more common than clinical symptoms in the early months after mild TBI. Later, after the injury, there is little correspondence between EEG and clinical signs, symptoms, results of images, or psychometric tests [29].

Quantitative EEG (qEEG) also shows immediate reduction in mean alpha frequency and increase in slow theta activity. These changes usually take weeks to months to resolve. Improvement is associated with symptom reduction [29]. Theta/beta ratio is increased. Compared to healthy controls, there are more slow waves in patients with mild TBI [32].

Mild TBI

Electroencephalography (EEG) was the first clinical neurodiagnostic assessment that revealed abnormal brain function following traumatic brain injury [17, 33, 34]. EEG may be more sensitive than clinical neurological examination to detect brain injury. After mild traumatic TBI (mTBI), most patients (86%) with an abnormal neurological examination had an abnormal EEG. But only 23% of abnormal EEGs were accompanied by an abnormal neurological examination [35]. EEG changes are not uniform in all individuals, due to differences in the severity of head injury. Some people have a clinically normal EEG as early as 15 min after concussion [36].

EEG abnormalities are more frequent in patients with durations of unconsciousness lasting more than 2 min (56%) than in patients with briefer periods of unconsciousness (17%) [37].

It is important to emphasize that there are no clear EEG or qEEG features unique to mild traumatic brain injury.

- *Acute EEG changes*
- Immediately after mTBI, there is epileptiform activity (high-amplitude sharp waves or high-frequency discharges), followed by diffuse suppression of cortical activity that usually last for 1–2 min, then there is a diffuse slowing of the EEG, and brain activity returns to the normal baseline within 10 min to 1 h [27, 38, 39]. qEEG often shows immediate reduction in mean alpha frequency [40], with increased theta [41, 42], increased delta [43], or increased theta/alpha ratio [44, 45].
- *Subacute EEG changes*
- Weeks to months after mTBI, there is a 1–2 Hz increase in the frequency of the posterior alpha rhythm – it represents a return to the original baseline from the post-traumatic slowing [29, 35]. The majority of the acute EEG abnormalities resolve by 3 months – 90% resolve within 1 year of the head trauma [29].
- *Chronic EEG changes*
- Lewine et al. (2007) studied a group of 30 patients with persistent psychiatric, somatic, or cognitive complaints (lasting >1 year) that was developed within the first few weeks of mTBI. The magnetoencephalography (MEG) revealed epileptiform abnormalities in 16% and slow-wave abnormalities in 63% [46]. They found a higher power in the delta band (1.5–5 Hz) and a lower power in the alpha band (8.5–12 Hz) in postconcussive syndrome patients compared with matched controls.

Improving EEG Analysis

Digital EEG (dEEG) is not recorded on paper, like the conventional EEG. The collected data is presented in video monitor and its storage is in digital format, which allows flexibility in the analysis. The qEEG represents the mathematical processing of the digital EEG. Often, it is not possible through visual analysis to recognize changes in the electroencephalographic record. In addition, despite the presence of neurological disorders, the visual analysis of the EEG tracing may be normal. The use of the qEEG allows a more in-depth analysis of the base activity, slow or fast focal activities, subtle asymmetries, waves, and spicules [47].

The routine EEG (up to 32 electrodes) has a high temporal resolution (on the order of milliseconds) but poor spatial resolution. This limits the use of conventional EEG in mapping and distributing brain electrical activity spatially [48]. One way to improve spatial resolution is through the use of a larger number of electrodes. The low-resolution brain electromagnetic tomography (LORETA) method helps to solve the inverse EEG problem – problem in calculating the distribution of currents for a given electrical potential – since the electrical activity found in the exam is distributed in a CT scan image that corresponds to an average brain of the population. The functional images of LORETA represent the electrical activity in each voxel as power of the spectral density [49].

LORETA is a mathematical algorithm that estimates the sources of EEG recorded on the scalp [50] and is widely used

in EEG studies. New improved versions of LORETA have been developed – standardized low-resolution brain electromagnetic tomography (sLORETA) and exact low-resolution brain electromagnetic tomography (eLORETA). sLORETA [51] and eLORETA [52] have the same low spatial resolution, with zero localization error, but the eLORETA provides better localization of the signal source in the presence of noise [53].

Leon-Carrion et al. (2008) performed a study with 16 patients with TBI, among them 7 subjects had minimally conscious state, and 9 had severe neurocognitive disorders. The presence of slow waves was twice as large in the first group. They also found differences in LORETA in relation to the theta frequency in the middle occipital cortex [54].

The study of Tomkins et al. (2011) included 37 patients, of whom 19 suffered from post-traumatic epilepsy. They found, through sLORETA, that TBI patients had slower delta waves than controls, regardless of whether or not they had post-trauma epilepsy [55].

Corradini and Persinger (2013) noted, through the use of sLORETA, a decrease in parahippocampal electrical activity and in regions adjacent to the temporal lobe in individuals with mild TBI [56].

The study of Ledwidge and Molfese (2016) used sLORETA to compare athletes with concussion and control athletes and found that those with concussion had higher electrical current density in the lower parietal gyrus than controls. These findings support the hypothesis that individuals with a past concussion recruited compensatory neural resources to meet the demands of executive functioning [57].

The study of Ianof et al. (2017) compared 19 patients with diffuse axonal injury (DAI) –type of TBI that results from acceleration/deceleration or rotational injuries to the brain – and 17 healthy adults submitted to high-resolution EEG with 128 channels. Cortical sources of EEG rhythms were estimated by exact low-resolution electromagnetic tomography (eLORETA) analysis. The mean alpha frequency peak was 10.23 Hz (±0.90 SE) for the control participants and 9.73 Hz (±1.02 SE) for the DAI group. No statistically significant difference was found between the control and DAI groups (Mann-Whitney U test, $p > 0.125$). In comparison to the control, the DAI group had increased theta activity in the limbic, occipital, sublobar, and temporal areas [58].

Post-traumatic Epilepsy: An Overview

Epilepsy is a disorder of the brain characterized by a predisposition to generate epileptic seizures with neurobiological, cognitive, psychological, and social consequences [59]. It can also be defined as unprovoked recurrent seizures that occur 24 h apart, at least [60].

Seizures are a frequent consequence of TBI, and its incidence is of 15–22% in TBI patients [61]. Post-traumatic epilepsy (PTE) and post-traumatic seizures (PTS) are terms used to describe seizures that occur after head trauma that are believed to be causally related to the trauma itself [62]. PTS are seizures that occur in the first week after TBI and are considered to be provoked by head injury. PTE is defined as one or more unprovoked seizures that occur at least a week after TBI [63].

The occurrence of seizures after head injury is a lifelong complication of TBI and has been demonstrated to worsen functional outcome significantly [64].

Seizures begin, in approximately half of PTE cases, within the first year and in 80%, within the first 2 years. One population-based study estimated that 86% of patients with one seizure, occurring at least 1 week after TBI, had a second seizure within 2 years [65].

There has been significant focus on computed tomography, EEG, and MRI after TBI to evaluate risk of PTE. Angeleri et al. (1999) performed a 12-month prospective study evaluating clinical progress, EEG, and computed tomography at four scheduled intervals. Some of the patients in this study also underwent MRI. Their study showed correlation of PTE with early seizures, frontal or temporal lesions on acute computed tomography, development of an EEG focus 1 month after TBI, and cortical MRI hyperintense areas [66]. It is recommended to obtain neuroimaging and EEG after PTS.

EEG and Sleep

Electrophysiologic changes in sleep may be present in both the acute and chronic stages of TBI and vary according to the severity of the injury. Cognitive dysfunctions may be caused by sleep disturbances and may aggravate impairment in patients with TBI. Sleep disturbances can include hypersomnia, insomnia, altered sleep-wake cycles, periodic limb movements during sleep, disorders of rapid eye movement during sleep, and respiratory disorders of fast sleep in the movement of the eyes, such as obstructive sleep apnea or central apnea. In patients with obstructive sleep apnea, there is a greater impairment of neurocognitive function, mostly memory and sustained attention, than patients who do not present disordered breathing during sleep [67].

After the acute stage of TBI, sleep disorders are common [67]. Mild TBI patients may show longer sleep latency and lower sleep efficiency. Also they have a lower delta power (but higher alpha and beta power) during non-REM (NREM) sleep [68, 69]. This EEG pattern of fast frequencies intruding into deep NREM sleep has been described in insomnia patients and may represent a deficit in turning off arousal [70].

After severe TBI, EEG patterns in the acute stage may have prognostic implications. A retrospective study of 64

adults with severe TBI admitted to the intensive care unit revealed that sleep features seen on continuous EEG monitoring were associated with significantly better functional outcomes [71].

In patients with TBI, sleep architecture findings are inconsistent and may include no change at all, increase of slow wave, and changes in rapid eye movement (REM) during sleep – decreased REM sleep, increased REM sleep during the second half of the night, no change in the REM sleep, or decreased onset latency of REM sleep. The sleep-wake regulation centers and associated pathways are damaged in the TBI, and these damages are the cause of disturbances of the sleep architecture. Sleep disturbances lead to fatigue that may be associated with mental retardation and slower processing of information [72]. Sleep disorders also contribute to anxiety and depression. Patients with TBI may have disrupted circadian regulation of melatonin synthesis, including lower levels of melatonin production at night [12].

Chronic changes in sleep architecture have also been described after TBI. A review of 105 polysomnograms (PSG) in patients with severe TBI identified lack of deep sleep and increased sleep fragmentation in those more severely affected [73]. PSG 6 months after TBI revealed consolidated NREM sleep and a trend toward a higher amount of delta power compared with controls [74].

Reduced sleep quality induces depression. Early diagnosis is important, and treatment may involve modafinil, melatonin light therapy, lifestyle modifications, and improving alertness and mood [67].

Due to the association between TBI and sleep disturbances, it is important to analyze the qEEG during sleep. There seems to be an interference of sleep disturbances with rehabilitation contributing to long-term disability [75–77].

Conclusion

Quantitative EEG is promising as a diagnostic assessment for TBI and postconcussive symptoms. Further scientific studies are needed to provide a better understanding of the pathophysiology and elucidate how EEG can aid in the care of patients who have sustained a TBI.

Conflict of Interest There is no conflict of interest to declare.

References

1. Berger H. Über das Elektrenkephalogramm des Menschen. Arch Psychiatr Nervenkr. 1929;87:527–43.
2. Tudor M, Tudor L, Tudor KI. Hans Berger (1873-1941) – the history of electroencephalography. Acta Med Croatica. 2005;59(4):307–13.
3. Schacter DL, Crovitz HF. Memory function after closed head injury: a review of the quantitative research. Cortex. 1977;13:150–76.
4. Thatcher RW, Walker RA, Gerson I, Geisler FH. EEG discriminant analyses of mild head trauma. Electroencephalogr Clin Neurophysiol. 1989;73:94–106.
5. Dockree PM, Robertson IH. Electrophysiological markers of cognitive deficits in traumatic brain injury: a review. Int J Psychophysiol. 2011;82:53–60.
6. Thatcher RW, North DM, Curtin RT, Walker RA, Biver CJ, et al. An EEG severity index of traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2001;13:77–87.
7. Castriotta RJ, Wilde MC, Lai JM, Atanasov S, Masel BE, et al. Prevalence and consequences of sleep disorders in traumatic brain injury. J Clin Sleep Med. 2007;3:349–56.
8. Orff HJ, Ayalon L, Drummond SP. Traumatic brain injury and sleep disturbance: a review of current research. J Head Trauma Rehabil. 2009;24:155–65.
9. Castriotta RJ, Murthy JN. Sleep disorders in patients with traumatic brain injury: a review. CNS Drugs. 2011;25:175–85.
10. Parcell DL, Ponsford JL, Redman JR, Rajaratnam SM. Poor sleep quality and changes in objectively recorded sleep after traumatic brain injury: a preliminary study. Arch Phys Med Rehabil. 2008;89:843–50.
11. Frieboes RM, Müller U, Murck H, von Cramon DY, Holsboer F, et al. Nocturnal hormone secretion and the sleep EEG in patients several months after traumatic brain injury. J Neuropsychiatry Clin Neurosci. 1999;11:354–60.
12. Shekleton JA, Parcell DL, Redman JR, Phipps-Nelson J, Ponsford JL, et al. Sleep disturbance and melatonin levels following traumatic brain injury. Neurology. 2010;74:1732–8.
13. Rao V, Spiro J, Vaishnavi S, Rastogi P, Mielke M, et al. Prevalence and types of sleep disturbances acutely after traumatic brain injury. Brain Inj. 2008;22:381–6.
14. Kotchoubey B, Lang S, Mezger G, et al. Information processing in severe disorders of consciousness: vegetative state and minimally conscious state. Clin Neurophysiol. 2005;116:2441–53.
15. Arciniegas DB. Clinical electrophysiologic assessments and mild traumatic brain injury: state-of-the-science and implications for clinical practice. Int J Psychophysiol. 2011;82:41–52.
16. Glaser MA, Sjaardema H. The value of the electroencephalogram in craniocerebral injuries. West J Surg Obstet Gynecol. 1940;48:684–96.
17. Jasper HH, Kershman J, Elvidge A. Electroencephalographic studies of injury to the head. Arch Neurol Psychiatr. 1940;44:328–48.
18. Nuwer M. Assessment of digital EEG, quantitative EEG, and EEG brain mapping: report of the American Academy of Neurology and the American clinical neurophysiology society. Neurology. 1997;49(1):277–92.
19. Nuwer MR, Comi G, Emerson R, Fuglsang-Frederiksen A, Guérit JM, Hinrichs H, Ikeda A, Luccas FJ, Rappelsberger P. IFCN standards for digital recording of clinical EEG. The International Federation of Clinical Neurophysiology. Electroencephalogr Clin Neurophysiol Suppl. 1999;52:11–4.
20. Rapp PE, Keyser DO, Albano A, Hernandez R, Gibson DB, Zambon RA, Hairston WD, Hughes JD, Krystal A, Nichols AS. Traumatic brain injury detection using electrophysiological methods. Front Hum Neurosci. 2015;9:11.
21. Berridge MJ, Rapp PE. A comparative survey of the function, mechanism and control of cellular oscillators. J Exp Biol. 1979;81:217–79.
22. Penttonen M, Buzsáki G. Natural logarithmic relationship between brain oscillators. Thalamus Relat Syst. 2003;2:145–15210.
23. Harner R. Automatic EEG spike detection. Clin EEG Neurosci. 2009;40(4):262–70.
24. McDowell K, Chin-Teng L, Oie KS, Tzyy-Ping J, Gordon S, Whitaker KW, et al. Real-world neuroimaging technologies. IEEE. 2013;1:131–49.
25. Bricolo A. Electroencephalography in neurotraumatology. Clin Electroencephalogr. 1976;7:184–97.

26. Urakami Y. Relationship between, sleep spindles and clinical recovery in patients with traumatic brain injury: a simultaneous EEG and MEG study. Clin EEG Neurosci. 2012;43:39–47.
27. Walker AE, Kollros JJ, Case TJ. The physiological basis of concussion. J Neurosurg. 1944;1:103–16.
28. Shaw NA. The neurophysiology of concussion. Prog Neurobiol. 2002;67:281–344.
29. Nuwer MR, Hovda DA, Schrader LM, Vespa PM. Routine and quantitative EEG in mild traumatic brain injury. Clin Neurophysiol. 2005;116:2001–25.
30. McCrea M, Prichep L, Powell MR, Chabot R, Barr WB. Acute effects and recovery after sport-related concussion: a neurocognitive and quantitative brain electrical activity study. J Head Trauma Rehabil. 2010;25:283–92.
31. Olejniczak P. Neurophysiologic basis of EEG. J Clin Neurophysiol. 2006;23(3):186–9.
32. Modarres M, Kuzma NN, Kretzmer T, Pack AI, Lim MM. EEG slow waves in traumatic brain injury: convergent findings in mouse and man. Neurobiol Sleep Circadian Rhythms. 2016;1:1.
33. Glaser MA, Sjaardema H. The value of the electroencephalograph in craniocerebral injuries. West J Surg. 1940;48:689–96.
34. Williams D. The electro-encephalogram in acute head injuries. J Neurol Psychiatry. 1941;4:107–30.
35. Koufen H, Dichgans J. Frequency and course of posttraumatic EEG-abnormalities and their correlations with clinical symptoms a systematic follow up study in 344 adults. Fortschr Neurol Psychiatr Grenzgeb. 1978;46:165–77.
36. Dow RS, Ulett G, Raaf J. Electroencephalographic studies immediately following head injury. Am J Psychiatry. 1944;101:174–83.
37. Geets W, Louette N. Early EEG in 300 cerebral concussions.(Fre). Rev Electroencephalogr Neurophysiol Clin. 1985;14:333–8.
38. Meyer JS, Denny-Brown D. Studies of cerebral circulation in brain injury II Cerebral concussion. Electroencephalogr Clin Neurophysiol. 1955;7:529–44.
39. Hayes RL, Katayama Y, Young HF, Dunbar JG. Coma associated with flaccidity produced by fluid-percussion concussion in the cat I: is it due to depression of activity within the brainstem reticular formation? Brain Inj. 1988;2:31–49.
40. Tebano MT, Cameroni M, Gallozzi G, Loizzo A, Palazzino G, Pezzini G, Ricci GF. EEG spectral analysis after minor head injury in man. Electroencephalogr Clin Neurophysiol. 1988;70:185–9.
41. McClelland RJ, Fenton GW, Rutherford W. The postconcussional syndrome revisited. J R Soc Med. 1994;87:508–10.
42. Fenton G. The postconcussional syndrome reappraised. Clin Electroencephalogr. 1996;27:174–82.
43. Gosselin N, Lassonde M, Petit D, Leclerc S, Mongrain V, Collie A, Montplaisir J. Sleep following sport-related concussions. Sleep Med. 2009;10:35–46.
44. Watson MR, Fenton GW, McClelland RJ, Lumsden J, Headley M, Rutherford WH. The post-concussional state neurophysiological aspects. Br J Psychiatry. 1995;167:514–21.
45. Chen XP, Tao LY, Chen AC. Electroencephalogram and evoked potential parameters examined in Chinese mild head injury patients for forensic medicine. Neurosci Bull. 2006;22:165–70.
46. Lewine JD, Davis JT, Bigler ED, Thoma R, Hill D, Funke M. Objective documentation of traumatic brain injury subsequent to mild head trauma multimodal brain imaging with MEG, SPECT, and MRI. J Head Trauma Rehabil. 2007;22:141–55.
47. Kanda PAM, Anghinah R, Schmidt MT, Jorge MS. The clinical use of quantitative EEG in cognitive disorders. Dement Neuropsychol. 2009;3(3):195–203.
48. Zhang X, van Drongelen W, Hecox K, Towle V, Frim D, McGee A, et al. High-resolution EEG: cortical potential imaging of interictal spikes. Clin Neurophysiol. 2003;114:1963–73.
49. Pascual-Marqui RD, Michel CM, Lehmann D. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. Int J Psychophysiol. 1994;18:49965.
50. Babiloni C, Frisoni G, Pievani M, Vecchio F, Lizio R, Buttiglione M, et al. Hippocampal volume and cortical sources of EEG alpha rhythms in mild cognitive impairment and Alzheimer disease. NeuroImage. 2009;44(1):123–35.
51. Pascual-Marqui RD. Standardized low-resolution brain electromagnetic tomography (sloreta): technical details. Methods Find Exp Clin Pharmacol. 2002;24.(Suppl D:5–12.
52. Pascual-Marqui R. Discrete, 3D distributed, linear imaging methods of electric neuronal activity. Part 1: exact, zero error localization. 2007.
53. Canuet L, Tellado I, Couceiro V, Fraile C, Fernandez-Novoa L, Ishii R, et al. Resting-state network disruption and APOE genotype in Alzheimer's disease: a lagged functional connectivity study. PLoS One. 2012;7:e46289.
54. Leon-Carrion J, Martin-Rodriguez JF, Damas-Lopez J. Barroso y Martin JM, Dominguez-Morales MR. brain function in the minimally conscious state: a quantitative neurophysiological study. Clin Neurophysiol. 2008;119(7):1506–14.
55. Tomkins O, Feintuch A, Benifla M, Cohen A, Friedman A, Shelef I. Blood-brain barrier breakdown following traumatic brain injury: a possible role in posttraumatic epilepsy. Cardiovasc Psychiatry Neurol. 2011;2011:765923.
56. Corradini PL, Persinger MA. Standardized low resolution electromagnetic tomography (sLORETA) is a sensitive Indicator of protracted neuropsychological impairments following “mild” (concussive) traumatic brain injury. J Neurol Neurophysiol. 2013;4:176.
57. Ledwidge PS, Molfese DL. Long-term effects of concussion on electrophysiological indices of attention in varsity college athletes: an event-related potential and standardized low-resolution brain electromagnetic tomography approach. J Neurotrauma. 2016;33(23):2081–90.
58. Ianof JN, Fraga FJ, Ferreira LA, et al. Comparative analysis of the electroencephalogram in patients with Alzheimer’s disease, diffuse axonal injury patients and healthy controls using LORETA analysis. Dement Neuropsychol. 2017;11(2):176–85.
59. Fisher RS, van Emde BW, Blume W, et al. Epileptic seizures and epilepsy: definitions proposed by the international league against epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia. 2005;46:470–2.
60. Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota: 1940–1980. Epilepsia. 1991;32:429–45.
61. Friedman D, Claassen J, Hirsch LJ. Continuous electroencephalogram monitoring in the intensive care unit. Anesth Analg. 2009;109(2):506–23.
62. Frey LC. Epidemiology of posttraumatic epilepsy: a critical review. Epilepsia. 2003;44(Suppl 10):11–7. Thorough epidemiological review of post-traumatic epilepsy (PTE) that provides important information on incidence and risk factors for developing PTE in both civilian and military populations, as well as the working definitions involved in PTE
63. Jennett B. Early traumatic epilepsy. Incidence and significance after nonmissile head injuries. Arch Neurol. 1974;30(5):394–8.
64. Asikainen I, Kaste M, Sarna S. Early and late posttraumatic seizures in traumatic brain injury rehabilitation patients: brain injury factors causing late seizures and influence of seizures on long-term outcome. Epilepsia. 1998;40:584–9.
65. Haltiner AM, Temkin NR, Dikmen SS. Risk of seizure recurrence after the first late posttraumatic seizure. Arch Phys Med Rehabil. 1997;78:835–40.
66. Angeleri F, Majkowski J, Cacchio G, et al. Posttraumatic epilepsy risk factors: one-year prospective study after head injury. Epilepsia. 1999;40:1222–30.

67. Urakami Y. Electrophysiologic evaluation of diffuse axonal injury after traumatic brain injury. J Neurol Neurophysiol. 2013;4:157.
68. Rao V, Bergey A, Hill H, et al. Sleep disturbance after mild traumatic brain injury: indicator of injury? J Neuropsychiatry Clin Neurosci. 2011;23:201.
69. Khoury S, Chouchou F, Amzica F, et al. Rapid EEG activity during sleep dominates in mild traumatic brain injury patients with acute pain. J Neurotrauma. 2013;30:633.
70. Feige B, Baglioni C, Spiegelhalder K, et al. The microstructure of sleep in primary insomnia: an overview and extension. Int J Psychophysiol. 2013;89:171.
71. Sandsmark DK, Kumar MA, Woodward CS, et al. Sleep features on continuous electroencephalography predict rehabilitation outcomes after severe traumatic brain injury. J Head Trauma Rehabil. 2016;31:101.
72. Ponsford JL, Ziino C, Parcell DL, Shekleton JA, Roper M, et al. Fatigue and sleep disturbance following traumatic brain injury--their nature, causes, and potential treatments. J Head Trauma Rehabil. 2012;27:224–33.
73. Harada M, Minami R, Hattori E, et al. Sleep in brain-damaged patients. An all night sleep study of 105 cases. Kumamoto Med J. 1976;29:110.
74. Imbach LL, Valko PO, Li T, Maric A, Symeonidou ER, Stover JF, Bassetti CL, Mica L, Werth E, Baumann CR. Increased sleep need and daytime sleepiness 6 months after traumatic brain injury: a prospective controlled clinical trial. Brain. 2015;138(Pt 3):726–35.
75. Nakase-Richardson R, Yablon SA, Sherer M. Prospective comparison of acute confusion severity with duration of post-traumatic amnesia in predicting employment outcome after traumatic brain injury. J Neurol Neurosurg Psychiatry. 2007;78(8):872–6.
76. Nakase-Richardson R, Sherer M, Barnett SD, Yablon SA, Evans CC, Kretzmer T, Schwartz DJ, Modarres M. Prospective evaluation of the nature, course, and impact of acute sleep abnormality after traumatic brain injury. Arch Phys Med Rehabil. 2013;94(5):875–82.
77. Sherer M, Yablon SA, Nakase-Richardson R, Nick TG. Effect of severity of post-traumatic confusion and its constituent symptoms on outcome after traumatic brain injury. Arch Phys Med Rehabil. 2008;89(1):42–7.