A History and Review of Quantitative Electroencephalography in Traumatic Brain Injury

The electroencephalogram (EEG) is a physiologic measure of cerebral function that has been used by some to assess coma and prognosticate survival and global outcome after traumatic brain injury (TBI). Surface recordings of the brain's electrical activity reveal distinct patterns that indicate injury severity, depth of unconsciousness, and patient survival. The data produced with traditional qualitative studies, however, does not allow resolution and quantification of the wave frequency spectrum present in the brain. As a result, conventional EEG typically has only been used for gross and qualitative analyses and is not practical for use in long-term patient monitoring or as a sophisticated prognostic tool. One area of investigation that is working to address the limitations of conventional EEG has been the development and implementation of Fourier Transform (FT) EEG which resolves and quantifies frequency bands present in the brain. When FT analysis is applied to EEG, it provides concurrent and continuous monitoring, resolution, and quantification of all frequencies emitted. This review discusses the history and significance of conventional EEG and provides a review of how FT-EEG, commonly referred to as Quantitative EEG (QEEG), is being used in the clinical setting. The specific applications and significance of QEEG methods regarding treatment of patients with TBI are discussed in detail. The advantages, disadvantages, and future directions of QEEG in TBI are also discussed. Key words: *traumatic brain injury, quantitative electroencephalography, fourier transform, spectral analysis, dementia, learning disorders*

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INTRODUCTION

The electroencephalogram (EEG) provides valuable insight into cerebral function by recording the electrical activity of the brain and displaying fluctuating electrical field potentials produced in the cortex as a function of time. The resultant EEG patterns provide clinical electroencephalographers with qualitative information regarding normal and abnormal cerebral activity. These distinguishing electrical patterns make the EEG a useful diagnostic tool for coma and many central nervous system disorders including epilepsy and seizures.

The EEG was introduced in 1929 by Hans Berger (1873–1941), who published his observations after performing human scalp recordings. He noticed continuous, rhythmic oscillations that were virtually independent

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of certain stimuli including sound, light, and touch. Berger's discovery initiated numerous investigations attempting to understand the nature and origin of the electrical potentials produced in the brain.[1] Seventy years of EEG research and technological advancements have produced an enhanced understanding of cerebral electrophysiology and pathology.

Electrical activity originates from chemical events that occur on the cellular level when neurons receive and process information transmitted from other nerve cells in the form of electrical impulses or action potentials. Each neuron has a resting membrane potential of −60 to −70 mV that fluctuates when action potentials trigger ionic flow across the cellular membrane resulting in neurotransmitter release at the synaptic cleft.[2,3] Action potentials occurring in axons that terminate with excitatory synapses cause excitatory post-synaptic potentials (EPSPs) in connecting neurons. The ensuing net influx of cations depolarizes the postsynaptic membrane and a potential gradient forms between the intra- and extracellular spaces. Cations then travel down the neuronal membrane through the extracellular space toward the post-synaptic locale. Action potentials occurring in neurons with inhibitory synapses cause an inhibitory post-synaptic potential (IPSP). This hyperpolarizes the cell causing an efflux of cations and an influx of anions. The post-synaptic membrane potential increases compared to the other areas of the cell, and a potential gradient results along the neuronal membrane causing a flow of cations into the extracellular space. The cations then move down the membrane creating collective ion fluxes in the extracellular spaces of neuronal populations that generate electrical field potentials.[4] These neuronal clusters are synchronized when they mutually excite or inhibit one another.

Synchronization also can occur when the cells are led by a pacemaker such as the pulsating discharge of action potentials in the thalamus. Synchronized activity is generally associated with a combination of intercommunication and self-sustaining pacemaker mechanisms, and when these potentials collectively fluctuate in an ordered sequence, they create EEG oscillations. Neuronal populations large enough to produce EEG signals range from approximately 10^4 to 10^7 neurons and may occupy a few square millimeters of cortical surface.[4]

EEG METHODS AND MATERIALS

EEG signals depend on the continuous voltage fluctuations of neuronal populations. Therefore, an electrical connection is made between the scalp and EEG apparatus using an electrolyte gel or paste and metal electrodes. Actual cortical potentials range from 500–1500 mV, but the scalp recordings are much weaker due to the insulating effects of intermediate tissues. Therefore, the EEG instrument includes amplifiers that enhance the weak signals and filter undesired interference such as line noise and other high frequency noise signals.[5] These enhanced signals have traditionally been recorded to paper with pens. However, the use of digital or computerized systems is now commonplace due to their ability to preserve data and display information easily using different parameters.

Early investigators, recording over different scalp areas simultaneously through multiple electrodes and channels, noticed dissimilar activity patterns occurring in different head regions. Various patterns of measuring the electrical activity between any two electrodes, referred to as montages, were developed to analyze and accentuate these particular patterns. Over time the International 10–20 system was introduced as a standard method of relative electrode placement on the head using bony anatomic landmarks to help determine the arrangement of electrodes.[6] Today,

the American Encephalography Society recommends the International 10–20 system for use with 21 electrodes. This system renders acceptable data in patients with a head circumference of 23 cm or more.

EEG WAVEFORMS

Traditional time domain EEG spectra are separated into fundamental bands qualitatively based on shape and range of frequency for clinical applications. These generally occur within the limits of 0.1 to 35 Hz and include alpha, beta, delta, and theta waves. When many of the individual bands occur repeatedly in a specific area of the brain, they produce a complex EEG waveform observed in traditional EEG recording methods.

Normal alpha rhythms are characterized by sinusoidal wave forms occurring between 8 to 13 Hz. Although the specific amplitude varies from one individual to another, it typically ranges from 20 to 60 mV and rarely exceeds 100 mV. They are believed to originate in the posterior region of the brain and are generally observed in the parietal, occipital, and posterior temporal areas. Alpha rhythms are best detected when an individual is mentally inactive, and they are often seen when the subject is awake, relaxed, and in an environment relatively free of stimuli. These rhythms are inhibited by the ascending reticular activating system at the onset of an unanticipated stimulus or when an individual exhibits increased mental and visual activity. The rhythms disappear completely when a person becomes drowsy. This "alpha dropout" is characterized by the eventual replacement of the alpha waves by a low voltage, mixed frequency pattern. Once asleep, patterns known as sleep spindles may appear which resemble alpha rhythms but periodically produce clusters of extremely large spikes in 1 to 2 second intervals.[7] These spindle formations are referred to as spindle coma patterns when observed in comatose patients who have preserved their normal sleep patterns.[8] Despite the somewhat similar appearance to alpha waves, spindle waves are clearly different and originate in the thalamus where they inhibit the synaptic transmission of that structure.[9]

Beta rhythms include all frequencies above 13 Hz with low amplitudes rarely exceeding that of 30 mV. They can exist simultaneously throughout the cortex at various frequencies but are most common to the frontal and central head regions in nearly all healthy adults. Beta rhythms can be extremely fast with an upper limit between 50 and 100 Hz. Enhanced or fast beta activity occurs over isolated bone defects and is also an effect of minor tranquilizers, barbiturates, and some nonbarbiturate sedatives. Remarkably accentuated beta rhythms are usually classified as only slightly abnormal unless they occur in unresponsive individuals, which may be an indication of a severe abnormality.[10] Frontal beta activity may be one of the fastest EEG frequencies and is common in normal sleeping individuals. Posterior beta activity also may be present in some individuals where it mimics the alpha rhythms' blocking and enhancement reactivities to eye opening. In addition, localized bursts of 40 Hz oscillations are characteristic prior to voluntary movement, such as wrist or finger extensions, and beta synchronization appears at approximately 20 Hz after movement.[11,12]

Delta rhythms consist of low-frequency, high-amplitude waveforms recorded between 1 to 4 Hz with amplitude ranges commonly from 20 to 30 mV. Delta waves can be seen in the posterior regions of the head, and/or they can occur on either side of the temporal region. However, they are most often recorded over the left cerebral cortex. These rhythms are produced by thalamocortical neurons and are virtually absent in the EEGs of normal alert individuals. Delta waves are associated with periods of unconsciousness typically

appearing in cerebral monitoring during sleep, coma, or after convulsive seizure. They also are common following traumatic brain injury (TBI) and can occur in conjunction with elevations in intracerebral pressure (ICP) due to an obstruction of the cerebral spinal fluid system or an expanding lesion.[13] In such cases, waveforms of 0.5 to 5 Hz are recorded diffusely over the cranium. Customarily, waveforms below 1 Hz have been classified as delta waves. However, intracellular recordings indicate that these waveforms are derived from different mechanisms than those waves ranging from 1 and 4 Hz. The slower oscillations are generated by corticothalamic and reticular thalamic neurons, and they are significant abnormalities in severe coma patients.[9]

Theta waves measure from 4 to 7.5 Hz and have low to moderate amplitudes. They are presumed to originate in the thalamus and are associated with the hippocampus and limbic system. Theta rhythms can be recorded in the frontal, temporal, central, and posterior head regions and are rarely the predominant waveform, frequently mixed with alpha and beta waves. In fact, theta waves are most often seen in conjunction with alpha waves despite their different production mechanisms. Theta rhythms appear in various capacities at different stages of development and maturation. These waveforms also play a vital role in conditions of drowsiness and sleep in all ages and may be linked to the emotional processes in children.[10]

CRANIOCEREBRAL TRAUMA

Traumatic Brain Injury (TBI) affects approximately 1 out of 400 people in the United States each year.[14] More than half a million patients are treated annually for head injuries, 90,000 of whom require extended inpatient rehabilitation services.[15] Injuries range from mild concussions, with no or subtle physical indication of brain damage, to more severe TBIs associated with cerebral contusions, impaired consciousness, and brainstem dysfunction.[16,17] TBI is a common cause of neurological disability and mortality, and this population accounts for 60 percent of all traumatic deaths.[18]

Successful management of an acute TBI depends on accurate diagnostic and prognostic assessment. When evaluating unconscious TBI patients, radiologic methods and clinical neurologic examinations are used to detect the degree of cerebral pathology. Computed tomography (CT) and magnetic resonance imaging (MRI) are utilized to observe the presence of intracranial lesions or damage to the brainstem resulting from focal injuries or diffuse axonal injuries. Clinical neurological examinations and scales such as the Glasgow Coma Scale (GCS) are used to assess the clinical severity of injury. However, none of these methods provide information regarding physiologic brain function after TBI.

The use of positron emission tomography (PET) and functional magnetic resonance imaging (FMRI) following TBI are gaining popularity as measures of cerebral physiology. PET measures the in vivo distribution of positively charged particles emitted by radionucleotides using emission CT to study cerebral blood flow. It allows for quantification of the cerebral metabolic rates of oxygen and glucose consumption. However, it is not often used due to the fact that it uses radioactive materials, is invasive, and is extremely expensive. FMRI is a technique that produces images at a higher resolution than PET and requires no radioactive materials. It obtains functional information from the central nervous system through, sophisticated imaging sequences, by detecting subtle increases in blood flow when various regions of the brain are activated. FMRI is also very expensive and not widely available. In contrast, the EEG is an inexpensive and relatively convenient measure of cerebral neurophysiology that,

although still under investigation, has demonstrated utility as a prognostic tool in TBI.

CONVENTIONAL EEG IN TBI

EEG has some value when assessing injury severity and depth of coma patients with TBI.[17,19] Degree of unconsciousness can quickly change, and continuous EEG monitoring has been used for detecting possible electrophysiological signs of clinical deterioration during the first few weeks after trauma.[20]

During the acute stages of TBI induced coma, the amplitude, frequency, and shape of EEG potentials are not stable. Initial EEG recordings taken within 24 hours of injury are more abnormal and of less prognostic significance than those performed after 24–48 hours.[8,21] The patterns that appear after the initial acute stage in repeated EEG recordings can complement and at times be more sensitive than traditional clinical evaluation. In fact, EEG assessment is more successful than other established neurological investigations in predicting the prognosis for patient survival. Correct assessment of prognosis is essential to the long-term treatment and rehabilitation of the TBI patient.[22] Physicians can use this information to optimize therapeutic interventions and enhance family and patient counseling.

PROGNOSTIC SIGNIFICANCE OF CONVENTIONAL EEG IN COMA

In 1973, Bricolo and Turella used repeated EEG recordings several times daily to determine that EEG evaluation is a practical screening tool for acute TBI coma patients. The investigators classified 500 patients according to neurophysiological patterns emphasizing typical waking and sleep rhythms. They found patients with spindles or sleeplike patterns had more favorable outcomes regardless of their clinical degree of coma. Decerebrate patients with mesencephalic syndrome and sleeplike EEG rhythms had a probability of death around 10%. In contrast, patients with the same clinical condition with monophasic or slow disorganized electric activity patterns, had a 90% probability of death. In general, the monophasic homogeneous EEG rhythms, which are minimally reactive to stimuli, denote a more severe cerebral pathology and an unfavorable prognosis. Bricolo and Turella also concluded that silent or isoelectric EEG patterns signify brain death and have a 100% mortality rate.[21]

Other classification systems using EEG characteristics to predict outcome in comatose patients have been proposed. One significant scale that separates EEG anoxic coma patterns into five different grades has been revised several times since its introduction by Hockaday et al in 1965.[23] It was modified in 1979 when additional descriptors, including sleep-like activities, were added.[13] Ultimately, a number of other common patterns seen in coma were included: spindle coma, alpha pattern coma, and theta pattern coma.[8] The patterns were distributed, in order of increasing abnormality, into 5 grades and 10 subdivisions. When EEG of subjects with posttraumatic and postanoxic encephalopathies were classified by this system, characteristics of the patients' cortical electrical signals clearly demonstrated value in predicting survival.[24]

Synek[24] observed that EEG characteristics of coma considered favorable for survival are usually sensitive to external stimuli. They include relatively normal activity, dominant and rhythmic theta activity, frontal rhythmic delta activity, and spindle coma patterns present where stage two sleep patterns most often appear. Several characteristics were considered prognostically uncertain for survival and involve either mixed activity in the delta and theta frequency ranges or predominant delta activity. Epileptiform discharges with diffuse delta activity and reactive alpha coma patterns

are also considered uncertain for survival. Factors for determining fatal outcome include epileptiform activity and burst suppression patterns with extended periods of isoelectricity and activity bursts in the alpha, delta, and theta frequency ranges. Patients with posttraumatic coma also exhibit burst suppression patterns when cerebral anoxia secondarily results from the injury.

Additional negative prognostic characteristics involve nonreactive alpha pattern coma with alpha range activity predominant in the anterior regions or broadly distributed throughout the cortex. Nonreactive, low-amplitude delta activity with transient one-second interruptions of isoelectricity also have been used to predict a fatal outcome, as well as low amplitude delta waves recorded under concentrations of 5 Hz activity from anteriorly prominent theta pattern coma. The most severe malignant factor for survival is complete isoelectric EEG activity. Although Synek's study clearly demonstrated certain EEG patterns could help to predict survival after TBI, no functional outcomes were evaluated.[24]

Most recently, Gutling et al[25] investigated the prognostic value of EEG reactivity to external auditory and painful stimuli compared to the patient's initial GCS score and the central conduction time (CCT) of somatosensory evoked potentials. The EEG reactivity and CCT were assessed between 48 and 72 hours after trauma in 50 comatose TBI patients whose initial GCS scores ranged from 3–8. Reactivity of the EEG was classified into one of four categories after visual analysis of the paper recordings. Twenty-four percent of the patients had slow wave reactivity, 30% reacted with a flattening of the tracing, 28% had no occurrence of reactivity, and reactivity was considered doubtful in 18% of the patients. The variables were later compared with the patient outcome 1.5 years after trauma. The Glasgow Outcome Scale (GOS) was used to assess global outcome and to classify patients into "good" and "bad" outcome groups for analysis.[26] The good outcome group consisted of patients who fell into the good recovery and moderate disability GOS categories, and the "bad" outcome group included patients in the severe disability, vegetative state, or death categories. Discriminant analysis revealed that EEG reactivity accurately classified 92% of the patients into correct outcome groups. Specifically, 96% of patients with either slow EEG reactivity or flattening of the EEG tracing exhibited a good outcome, whereas 93% of patients with no EEG reactivity had a bad outcome.

In addition, many patients with doubtful EEG reactivity experienced a good outcome. CCT correctly classified patient outcome in 82% of the patients, and both EEG reactivity and CCT combined classified 98% of patients correctly. GCS alone only grouped 72% of patients accurately and its inclusion with either of the electrophysiologic measures did not improve the prognostic accuracy of this scale.[25] The results of this study demonstrate that EEG reactivity is a good prognostic variable for survival and gross global outcome in TBI, and its combination with CCT makes it superior to any other prognostic method for gross outcome classification evaluated in this analysis.

Clearly, conventional EEG has some utility in establishing prognosis for survival, and at least gross functional outcome. However, conventional EEG has a number of limitations. Visual analysis of paper recordings is qualitative, and classification of EEG reactivity depends entirely on the judgement of the reader. The time domain spectrum traditionally used in EEG does not allow resolution and quantification of the frequencies present in the brain, and as a result, this and other studies use EEG only for gross, qualitative analyses. In addition, the conventional EEG is difficult for long-term monitoring due to the large amount of information produced and the need for expert data interpretation.[20,27,28]

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QUANTITATIVE ELECTROENCEPHALOGRAPHY

Quantitative electroencephalography (QEEG), as the name implies, is a means of electrically processing the EEG signal to quantify the relative contributions of each frequency. QEEG really represents a family of related technologies and techniques. However, the common foundation upon which they all are built is spectral analysis.

Spectral analysis is a process by which a given segment of the complex EEG signal is separated into its component frequencies. The process is analogous to when two or more musical notes are played together, resulting in a chord. Each individual note played has a specific frequency, which determines pitch. Each note also has a specific amplitude that is directly correlated to its volume. When the resulting chord is recorded over time through a microphone, one complex waveform is obtained representing all notes present in the chord. The human ear has the ability to resolve and estimate the amplitudes of the notes played in a simple chord, just as the trained eye possesses the capability to resolve and estimate the amplitudes of the frequencies present in a conventional EEG spectrum. As more notes are played and more frequencies are present, it becomes increasingly difficult to analyze the complex waveform. However, through the use of computers, the complex waveform can be digitally sampled and analyzed, regardless of the complexity of the signal. The result is the resolution of each note's frequency and amplitude. Likewise, spectral analysis of the EEG signal reveals the amount of alpha, beta, delta, and theta activity contained in the signal.

The various QEEG technologies are a means of displaying the results of spectral analysis in an understandable format. In a compressed spectral array (CSA), a series of different epochs are measured, usually 30 seconds each, and the signal converted via spectral analysis. The results are then restored sequentially down a printed or video display. This allows for comparison over time of changes in the composition of the EEG signal.

Topographical mapping displays the results of spectral analysis in a readily accessible format. For each frequency range, every electrode in the EEG montage is assigned a specific color, or a shade of gray, which reflects the amount of the frequency underlying the electrode. The color/gray scale is then projected onto a head shaped oval, and colors between electrodes extrapolated from the measured data points. The result is a display that is reminiscent, in appearance, of a PET or SPECT scan. However, in spite of having the appearance of a scan, topographical map must be remembered as being generated from a limited number of data points, and only reflects electrical activity measured at or near the cortical surface.

Lastly, significance probability mapping attempts to further manipulate the topographical map by comparing QEEG to a normative database.[29,30] In these systems, spectral analysis is performed on a number of healthy individuals, producing, in essence, a composite topographical map of a normal population. The subject's map is then compared mathematically to the composite map, and a colored oval generated which highlights the differences, usually two standard deviations, between the subject and the normal population.[29]

In reviewing the literature in this area, it is important to have an understanding of the particular technology and technique used. The choice of electrode montage, length of measured epoch, technique of statistical analysis, and a variety of patient conditions may all significantly affect the results. The interested reader is referred to more comprehensive reviews of these issues.[4,31–35]

FAST FOURIER TRANSFORMATION

The analysis, simplification and ultimate quantification of the EEG signal is made possible by the development of inexpensive, powerful microprocessors, and the application of the mathematical algorithm of Fast Fourier Transformation (FFT). Fourier transformation is a process by which a complex, seemingly irregular waveform is broken down into a series of sinusoidal waves. In a simplified example, if an alpha frequency of 12 Hz and a theta frequency at 6 Hz are the only signals present during data collection, and these two frequencies (Figure 1) are essentially equal in amplitude, the resulting time domain EEG spectrum is the complex waveform shown in Figure 2. When the two frequencies are in phase, the result is an additive effect in the magnitude of the complex waveform. A decrease in magnitude occurs when the two simple waveforms are out of phase. The complex waveform in conventional EEG time domain analysis can be mathematically manipulated through Fourier transform analysis to resolve the individual frequencies and the magnitude of these frequencies that compose the complex waveform (Figure 3).

When applied to EEG, this technology allows for interelectrode comparison measures such as phase and coherence that can not be calculated using conventional EEG methods. Phase examines the arrival time of various frequency components for a tracing at two separate electrodes. Coherence measures the synchronicity of short distance and long distance cortical fibers at different leads.[36] It has been postulated that increased coherence after TBI reflects a lack of differentiation or increased redundancy in cortical processing in the region being studied. Low coherence may reflect either a lack of connection between cortical systems, or conversely, more differentiation of cortical regions due to regional cerebral specialization. This may indicate an increased capacity for processing information. Phase, a function of EEG frequency, interelectrode distance, and conduction velocity, has also been postulated to reflect functional integrity and differentiation between neuronal systems.[35,37–39]

In QEEG, samples of data are collected on the computer from the time domain and are transformed into the frequency domain using Fast Fourier Transformation (FFT). FFT is an algorithm based on the Fourier series allowing for much faster computation and a more efficient use of computer memory. The degree to which the various frequencies in the signal are resolved depends on the digital sampling rate and the total amount of time or data points used in the FFT analysis. The samples are obtained using small blocks of EEG activity referred to as epochs.[36] These epochs contain the information to which the FFT algorithm is applied and typically range from one to 30 seconds in length. However, one-second blocks are so momentary that low frequency components are not easily detected and epochs 30 seconds in length have a higher risk of being contaminated by artifacts. As a general rule, epoch lengths should be as least as long as the wavelength of the lowest frequency component measured. Usually, many individual epochs are acquired and examined for artifacts so that data analysis is based on several minutes or hours of EEG instead of just one single epoch.[36] FFT also requires that at least two data points are collected per cycle for the highest frequency measured before analysis can occur. This is referred to as the Nyquist frequency. For example, a 25 Hz signal must be measured at a minimum data sampling rate of 50 Hz. Typical data collection rates for the EEG signals are usually around 100 to 500 Hz. As the epoch length increases, and thus the number of data points collected increases, the frequency resolution of the spectrum increases (see Figure 3).[40] Choosing the longest epoch length possible with a minimal number

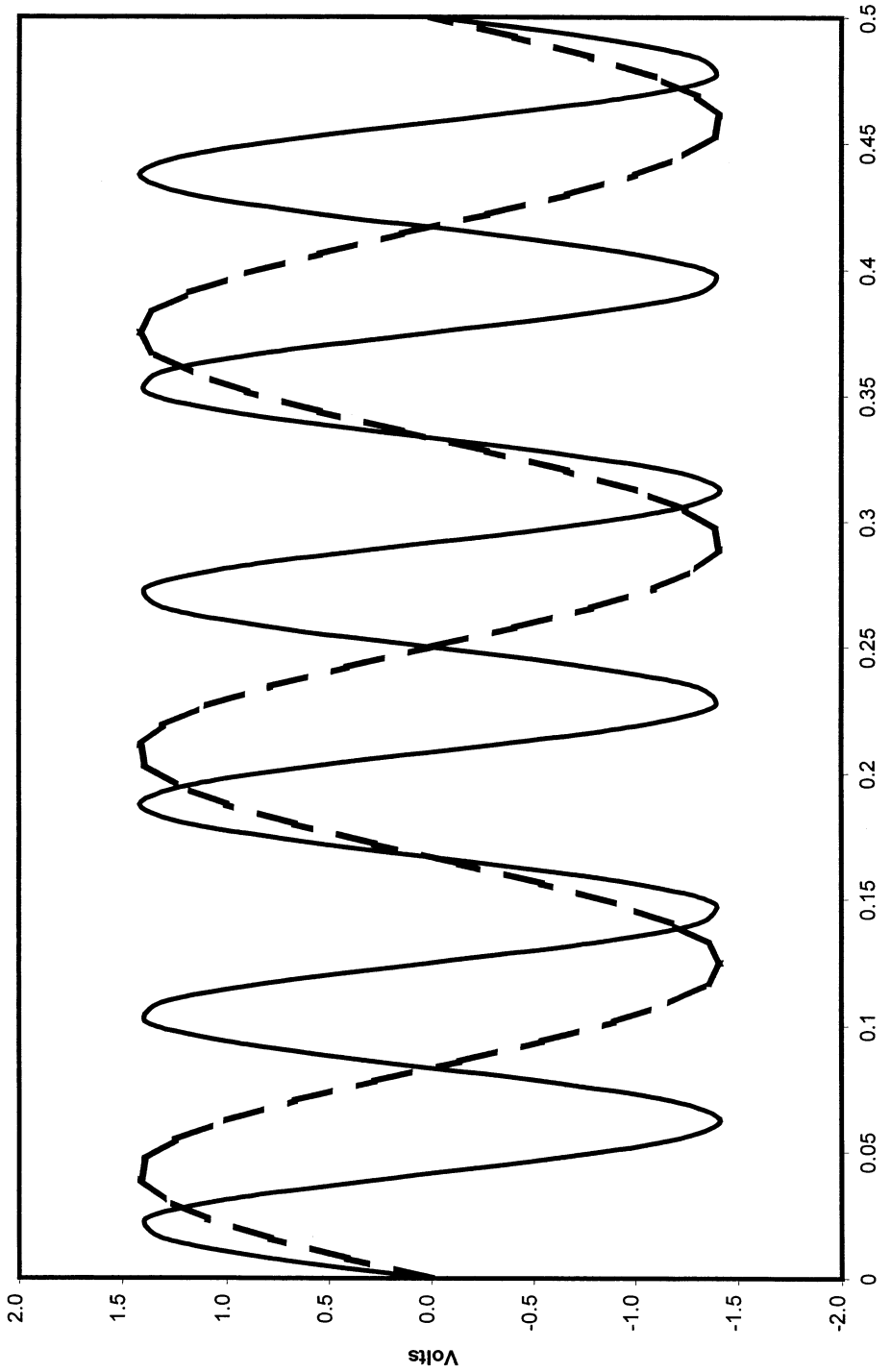

Fig 1. Time domain spectrum of 6 and 12 Hz sinusoidal waveforms produced by a Hewlett-Packard waveform generator.

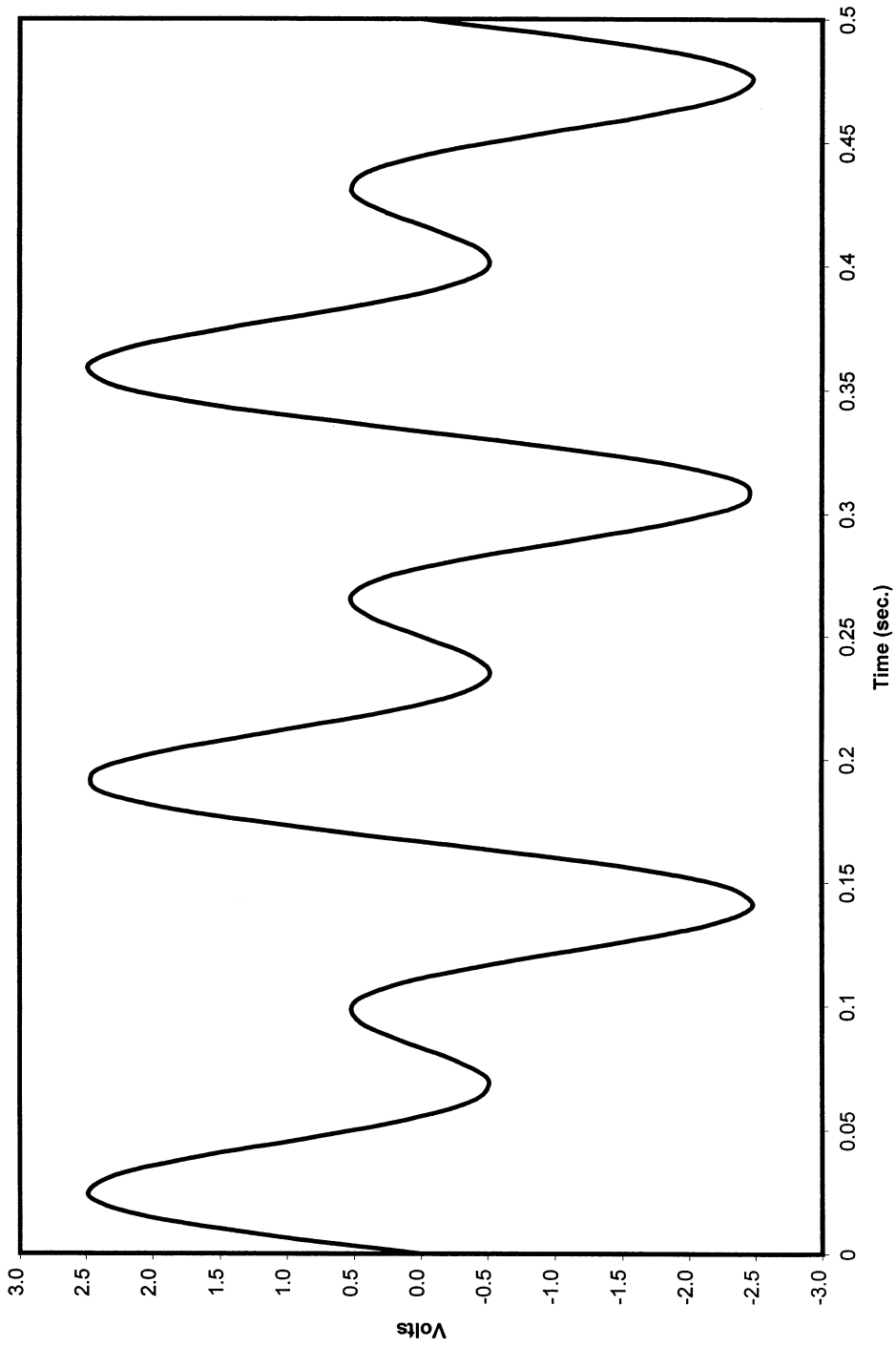

Fig 2. The complex waveform shown here is the result of combining the 6 Hz and 12 Hz sinusoidal waveforms shown in Figure 1. As the epoch length increases, the signal to noise ratio of the time domain spectrum increases. This in turn produces a higher resolution frequency domain spectrum (see Figure 3).

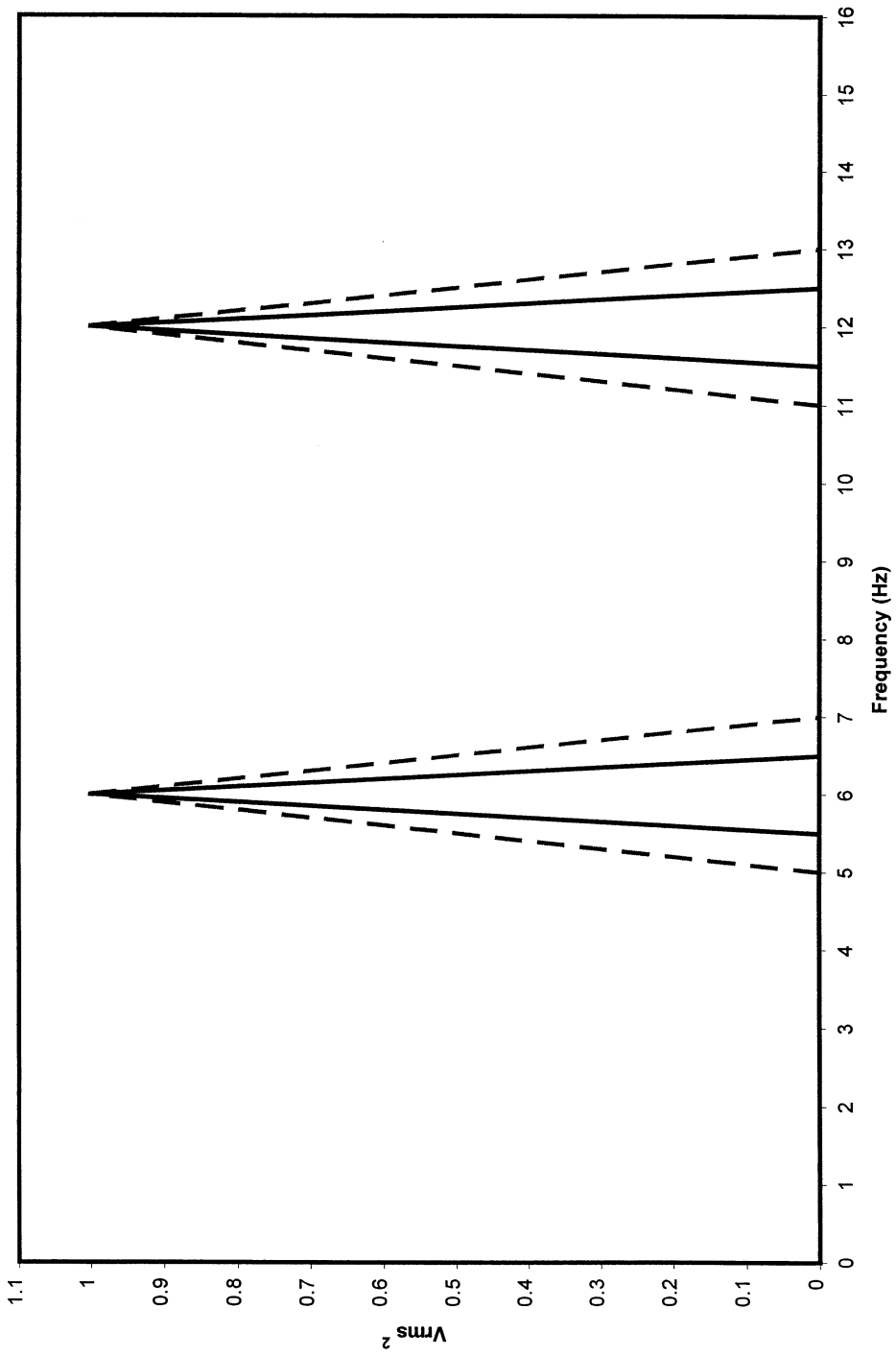

Fig 3. This frequency domain spectrum was constructed from the FFT of the complex waveform shown in Figure 2. The dashed line is the peak width resulting from one second of data collected at 100 Hz. The solid line shows an increase in resolution when the data are collected at the same 100 Hz rate, but for a two-second epoch. *Source:* Author.

of artifacts will result in the highest resolution frequency domain spectrum.

The major advantage of the Fourier Transform technique compared to the standard EEG is that it allows concurrent monitoring, resolution, and analysis of all frequencies emitted from a source.[35] In addition, computer analysis can detect subtle variations in background activity that may not be visible to the traditional electroencephalographer. The simple representations of QEEG data provide a more objective assessment of EEG alterations and can be more easily interpreted by those who are not specifically trained in reading the conventional data.

The continuous frequency information obtained through FFT can be analyzed by combining data into specific bands according to frequency range. Although the traditional EEG frequency bands are acceptable, they are not always used in quantitative EEG techniques. The bands are typically defined in terms of activity occurring within 4-Hz intervals. These include 0–4 Hz (delta), 4–8 Hz (theta), 8–12 Hz (alpha), and 12–30 Hz (beta). The beta band is subdivided into beta-1 (12–16 Hz), beta-2 (16–20 Hz), and beta-3 (20–30 Hz). Alpha bands can also be broken into subcomponents including alpha-1 (8–10 Hz) and alpha-2 (10–12 Hz).[36]

QEEG IN TBI

In 1978, Bricolo et al were the first to study the clinical significance of CSA in the long-term monitoring of comatose patients.[41] Analysis of uninterrupted 48-hour recordings revealed that inter-hemispheric frequency band asymmetries related to cranial defects, location of brain damage, and final outcome. Cranial defects were indicated by a greater spectral amplitude on the damaged side, and slower, less organized spectrograms were associated with the more severely injured hemisphere. Patients who displayed inter-hemispheric asymmetries generally were associated with a fatal outcome. Bricolo also observed that spontaneous variability in the power spectrum was a good prognostic sign and slow monotonous or absent patterns were analogous to a poor outcome.[41]

Later, Cant and Shaw supported these observations and added that a more favorable prognosis was apparent in comatose patients showing a persistence or return of activity within the alpha or theta frequency range. However, their data were derived using only one channel, and each CSA line was comprised of a 10-minute epoch. This is an unusually long amount of time to average frequency components and limited the test's sensitivity and insight into emerging trends and systemic EEG changes. In addition, the investigators use a three-point outcome scale to define prognosis, and the time frame for measurement most predictive of good outcome and return of alpha activity was not discussed.[28]

Steudel and Kruger[19] observed similar findings while studying the prognostic value of continuous, 30-minute, eight-channel QEEG recordings performed every other day throughout the first post-traumatic week in 50 severe TBI patients. Only absolute and relative powers of the standard frequency bands over the occipito-parietal region were calculated because the investigators felt that derivations from the frontal and temporal regions offer no prognostic value. However, no citation or statistical procedure was provided to support this statement. Nonetheless, the best criteria for survival during the first post-traumatic week was concluded to be an increase in amplitude of both the alpha and theta bands, while decreases in amplitudes of the theta and alpha waves were characteristic for the nonsurvivors. The outcome endpoint for this study categorically looks at survival, and its design does not meet criteria for a prospective classification study because the investigators first tested their patients

and then retrospectively determined which analyses were significant. Those individuals receiving barbiturates—who had seizures or alpha or spindle-pattern comas—were eliminated prior to analysis, limiting the scope of the findings. No comments were provided discussing an optimal time to test patients during the first week after coma.[19]

While most early investigators' work described above explored QEEG data for abnormal patterns, Klein et al[42] injected 40 comatose TBI patients with thiopental, an agent known to stimulate the frequency bands of a normal EEG. During this brain "stress test," the authors noted significant EEG pattern changes that preceded deterioration in EEG frequency, brainstem reflexes, and clinical examination. These findings correlated well with eventual patient survival. Patients who showed a distinct increase of power in all frequencies, including a short 3 to 7 minute burst of beta activity, survived 84% of the time. Conversely, the method provided 100% accuracy in predicting a fatal outcome in patients with an absolute power decrease in all frequency bands, even when pain reactions and brainstem reflexes still were apparent.

Investigators also found that cerebral impairment is present when the cortex is unable to produce fast activity after thiopental administration. This lack of EEG stimulation is not reversible and is followed by the eventual loss of the rapid spectral bands exceeding 6 Hz. Patients who died as a result of complete decerebration had a QEEG characterized by a lack of beta or general frequency stimulation, as well as a progressive disappearance of the rapid frequencies. These data support the investigator's original hypothesis that reactivity to thiopental bolus injection can be used as an early prognostic indicator for coma. The population in this study appears to be a mix of patients with various injuries, but Klein et al did not delineate the make-up of their population. Nonetheless, the major strength of this analysis is that it is a classification study based on a hypothesis generated from observations in a normal population. Although the outcome endpoint of survival is not directly beneficial to practitioners in the rehabilitation setting, it is important for the acute trauma evaluation following TBI where patient responses to thiopental could be taken into account with other measures to determine clinical course.[42]

Hakkinen et al compared the prognostic capabilities of CSA to that of GCS in 20 comatose intensive care patients with intracerebral hemorrhage and/or TBI.[20] CSA data was collected using eight-second epochs derived from continuous 48-hour EEG monitoring one to four days after trauma. Throughout this timeframe, GCS was determined at regular intervals to assess patients' level of unconsciousness. CSA data was analyzed and used to categorically rank patients on a 0 to 5 scale according to their frequency content, reactivity, and the amount of EEG isoelectricity. Patients scoring 0 to 2 showed either isoelectric or slow monotonous activity, and patients scoring from 3 to 5 showed intermittent, constant, or reactive EEG patterns. Patients were assessed three months after discharge, and outcome was classified as "well recovered, moderately recovered, poorly recovered, or dead." The patients grouped as "well-recovered" could manage without assistance and had no or only minor neurological deficits, while the "moderately recovered" patients could walk without assistance but had severe neurological deficits. "Poorly recovered" patients were considered permanently disabled and bedridden. Specific neurological deficits and resultant disabilities were not defined.

Hakkinen applied uninterrupted EEG monitoring but only analyzed very small amounts of randomly collected data. No information is provided for the criteria used to isolate the EEG segments used in analysis. An

advantage of uninterrupted QEEG monitoring is that it provides instantaneous information about changes in neurophysiological function which are not apparent when using GCS. However, the brief segments extracted from the continuous data acquired here provide only momentary insight into cerebral function and do not allow for examination of physiologic trends over time. Hakkinen's data suggested that CSA may predict mild cases with greater accuracy, while the GCS was slightly more sensitive in the poorly recovered patients. However, the investigators converted the CSA into a more crude ordinal scale than the GCS, and even then, the predictability of the CSA scores were not significant until the outcome data was collapsed into a dichotomous outcome scale, where "good outcome" included well and moderately recovered patients, and "bad outcome" comprised the poorly recovered and dead patients. The investigators further complicate their study by including patients with TBI and/or intracranial hemorrhage. A larger, more homogenous study population is warranted for more quantifiable results.

Thatcher et al[22] compared the prognostic efficacy of QEEG to that of GCS, brainstem auditory evoked potentials, and CT in 162 TBI coma patients recorded within one to 21 days after injury. Multiple QEEG measurements were obtained, including interelectrode comparisons to measure phase and coherence. Phone interviews with the patients' caregiver or guardian were performed one year after injury to determine functional outcome using Rappaport's Disability Rating Scale (DRS).[43] The diagnostic measures then were compared to patient outcome. Discriminant analyses using the diagnostic measures distinguished patients in one of two categories: complete recovery versus death. Multiple linear regression analyses predicted intermediate scores.

The EEG results combined with patients' GCS score at the time of the electrophysiologic procedure proved to be the best multivariate predictor, accounting for 95.8% discriminant accuracy among good outcome and death and 74.6% of the variance in the analysis of intermediate outcome scores. The greatest single predictor of outcome in both the discriminant and regression analyses was EEG phase measurements that accounted for 44% of the variance in functional outcome. This was followed by coherence, GCS-T, CT-scan, and EEG relative power respectively. The investigators hypothesized that the prognostic power of the changes in EEG phase and coherence measurements may reflect the severity of diffuse axonal injury.

The quantitative EEG capabilities in Thatcher's investigation, like many earlier studies, were limited due to lack of computational efficiency. Because the FFT method could not process QEEG information in a timely manner, the investigators used a second order recursive digital filter analysis to compute the auto and cross-spectral power density for each of the channels. The authors concluded that the data obtained by this method was an effective predictor of ultimate functional prognosis as measured by the DRS. Structured interviews were conducted using the 30-point DRS, and the data was collapsed into three categories including good outcome, intermediate outcome, and death. Variances were reported for the three outcome groups, although a minimum of five categories is typically necessary to perform a statistically appropriate linear regression. Most predictive GCS scores are usually obtained approximately 24 hours after injury; however, the GCS scores analyzed were taken at the time of the EEG procedure (range one to 21 days). Furthermore, the authors determined outcome using telephone interviews, which have never been clinically validated to date for the DRS. The predictability of phase and coherence provides strength to the QEEG analysis and the basis for future

studies to be discussed later in this review. The lack of a validation group, questionable use of regression statistics, and the broad post injury time range for data acquisition limit the applicability of the findings for this study.[22]

Other investigations have compared QEEG and GCS in the assessment of TBI patients.[27,44,45] Karnaze et al determined that alternating CSA patterns in the amplitude of frequency are significantly associated with survival in comatose patients and are equal to the prognostic capabilities of the GCS.[44] Alster showed in a population of 29 comatose patients that changes in spectral EEG recordings were superior to the GCS and brain stem evoked potentials in determining outcome.[45] He also concluded that cyclic changes appearing in the spectral analysis were indicative of an intact diurnal rhythm and brain stem reticular activating system. Moulton compared QEEG to GCS in monitoring the depth of coma in patients with TBI.[27] Changes in the delta band were inversely proportional, and changes in the alpha/beta bands were directly proportional and well-correlated to corresponding changes in GCS scores over time. Further, the delta frequency band appeared to be the best single correlate of the depth of coma and proved to be superior to the GCS in identifying changes in neurologic function. The QEEG also allowed an accurate binary classification of six-month outcome using Glasgow Outcome Scale (GOS) in many patients who had little or no changes in GCS scores during the monitoring period.

Thatcher et al[46] used QEEG to distinguish between 608 adult patients with mild TBI and 108 age-matched controls. These measures included anterior-posterior amplitude gradients, posterior relative power, and the inter-electrode comparison measurements of phase and coherence in the frontal and temporal lobes. Thatcher's initial data analysis using 264 patients and 83 normal subjects proved that the QEEG method was successful in distinguishing the mild TBI group from the control population achieving an overall discriminant classification accuracy of 94.8%. The mild TBI population exhibited three neurophysiological features that were not apparent in the controls. These included increased coherence and decreased phase in frontal and fronto-temporal regions, reduced alpha band amplitudes in the parieto-occipital regions, and decreased power differences between anterior/posterior cortical regions.

Three independent cross validations of the discriminant function were performed to assure the replicability of the initial results. The first cross-validation test yielded a discriminant classification accuracy of 95.4%, while the second and third replications produced discriminant accuracies of 87.5% and 92.8%, respectively. Comparable results were achieved after supplementary examinations were made 17 to 223 days after injury to assess the consistency of the discriminant analysis over time. Thatcher concluded that these distinctive and persistent QEEG patterns may indicate a difference in the neurophysiological organization of the cerebral cortex in mild TBI patients, compared with normal individuals, and suggests a functional reorganization following mild TBI.[46]

A relationship may arise between Thatcher's EEG findings and common post-concussive symptoms, such as dizziness, headache, and attention and memory deficits that may provide a neurophysiological basis for patient complaints. For instance, the localized frontal phase and coherence abnormalities are consistent with axonal injuries and localized contusions to the frontal and temporal regions, injuries associated with attention deficits, problems with planning and sequencing, emotional instability, and short term memory disturbances. The decreased power differences between anterior-posterior

cortical regions may be associated to changes in the long axonal systems, while reduced alpha-band amplitudes in the parieto-occipital regions are consistent with coup-contra coup processes.[39,46] The global effects of such injuries may result in diminished information processing capabilities and may affect the patients' ability to rapidly shift attention and perform concurrent mental tasks.[47,48] Although this exploratory study shows that discriminant QEEG can distinguish between patients with mild TBI and a group of controls, the findings do not yet confirm the clinical acceptance of QEEG as a diagnostic tool for determining or classifying mild brain injury. The authors fail to exclude patients for comorbidities affecting the QEEG, the use of potentially psychoactive medications, or chronic alcohol abuse. Also, these results cannot be extrapolated and applied to the general population until additional prospective blinded studies are conducted that create a clinically useful standard for diagnosing mild TBI and delineating an electrophysiological basis for associated symptoms.

QEEG/MRI

Although QEEG has been shown to detect cerebral dysfunction in mild to severe TBI, it lacks the ability to do so with a high degree of anatomical specificity. In contrast, the conventional visual examination of MRI provides good neuroimaging but often minimizes the true extent of physiologic injury.[49–52] Thatcher integrated the QEEG techniques developed in his previous studies with conventional MRI to study relationships between electrophysiology and anatomy in TBI. Nuclear magnetic resonance (NMR) of brain water proton (^{1}H) T2 relaxation times, determined by the proton density within various tissue compartments, and absolute amplitude measures of QEEG were obtained from 19 patients in the post-acute to chronic period following TBI. The investigators found that lengthened T2 relaxation times in either gray matter or white matter indicate lesions to the respective tissue. Furthermore, Thatcher confirmed that gray matter lesions were related to decreased QEEG alpha and beta frequency amplitudes, while white matter lesions were associated with increased QEEG delta amplitudes. Cognitive deficits also were correlated with an increase in the delta amplitude and a decrease in alpha and beta EEG amplitudes.

Thatcher notes that this study uses a small sample size, and, therefore, is a pilot study warranting further research. The results preliminarily support his hypothesis that either a disruption in the integrity of the protein-lipid membranes of neurons or neuronal death results in lengthened T2 relaxation times and reduced EEG amplitude. Membrane disruption may cause an increase in the neuron's permeability to water resulting in a shift in the relative concentration of water between the intracellular and the extracellular compartments. This may occur independent of actual cell loss and result in a reduction in the efficacy of ionic membrane transport of neurons and a reduced amplitude of EEG. As neurons die, the relative action of intracellular water protons decreases and the relative fraction of water in the extracellular space increases, theoretically resulting in lengthened T2 relaxation times and reduced EEG amplitude.[53]

Thatcher expanded this area of study by investigating the association between EEG coherence and NMR of ^{1}H T2 relaxation times of the cortical white and gray matter in two separate TBI populations. Coherence was calculated from the QEEG results of 19 patients and evaluated in conjunction with the MRI observations. The investigators compared these results to a control population and found that increased gray and white matter ^{1}H T2 relaxation times in the TBI population correlated significantly to coherence variations in EEG delta and theta frequencies in the gray matter.

Increased T2 relaxation times were also related to increased EEG coherence between long interelectrode distances (e.g., 28 cm), and reduced EEG coherence between short interelectrode distances (e.g., 7 cm). Furthermore, reductions in short-distance EEG coherence and lengthened T2 relaxation times were related to decreased cognitive function. These findings were later replicated using an independent sample of 21 TBI patients similar to the initial test population. The researchers related their findings to the decreased integrity of protein/lipid neural membranes and the differences in short- and long-distance neural synchronization after TBI.[37]

Previous studies have indicated that imagined movement alone or the mental simulation of movement combined with actual exercise has facilitated recovery in post-stroke rehabilitation. Green et al[54] hypothesized that imagined movement in paralyzed individuals may enhance the cerebral reorganization process after TBI or spinal cord injury. He suggests this mental technique may be helpful in these areas of rehabilitation, especially when physical activity is difficult or impossible. Further, he reports that no studies have correlated QEEG findings seen with imagined movement with functional imaging findings during imagined movements. High resolution QEEG was applied to map the cortical potentials and determine the generator sources associated with actual and imagined movements of fingers and toes. Ten normal adult volunteers were fitted with a cap containing 120 scalp electrodes and were cued to rapidly flex and extend their middle finger while continuous EEG data was collected at 500 Hz.

In a separate trial following this exercise, each subject performed mental simulations of the same movement. The EEG data for each trial were co-registered with an MRI in order to map the cortical topography of the motor potentials associated with the actual or imagined movements. Paired t-tests and dipole source analyses were performed to distinguish between such movements, and the motor networks essential for the generation of actual and imagined movements were found to be different. Motor potentials for the actual movements revealed stronger signals and shorter latency, and their dipole generators were located in the contralateral frontal area. Imagined movements were associated most frequently with ipsilateral or midline dipoles and their motor potentials mapped anteromedially. While only 10 subjects were analyzed, the results of this combined high resolution QEEG/MRI study are consistent with findings from other PET and FMRI investigations.[55–57] The data confirmed that brain activation during imagined movement is generated in or near midline structures such as the supplementary motor area and does not involve the activation of primary motor cortex. Green suggests that the efficacy of imagined movements in rehabilitation may be derived from the stimulation of the premotor and/or the supplementary motor areas, and his work provides a point for future study of QEEG as a therapeutic intervention in the treatment of motor deficits after TBI.[54]

QEEG AND BIOFEEDBACK IN TBI

The use of QEEG technology in EEG biofeedback training offers a promising new treatment approach for the rehabilitation of patients with mild to moderate TBI. EEG biofeedback, also known as neurofeedback, is an operant conditioning procedure where an individual attempts to modify his/her physiologic response based on the recorded EEG during therapy. The therapeutic application of EEG biofeedback is often referred to as neurotherapy and is purportedly useful in a wide range of psychological and neurological disorders. In applying this technique to patients with TBI, the QEEG is used to assess their neurological status and determine

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the neurological basis for the patients' complaints. QEEG is also used to evaluate the organizational and electrophysiological status of the patient's brain in order to design an effective neurotherapy regimen. The effectiveness of the neurotherapy is then evaluated by comparing each patient's pretreatment and posttreatment QEEG.[58]

EEG biofeedback investigators have reported improved symptoms and reduced patient complaints with respect to the evaluation and treatment of individuals with TBI.[59–65] Ayers applied QEEG biofeedback training to 250 TBI patients and reported a return to pre-morbid functioning in a significant number of cases.[59] Ham and Packard investigated 40 patients with posttraumatic headache and found that after biofeedback, 53% of the patients reported improvement in their symptoms.[60] The researchers also noted that 80% of the patients reported an improvement in the ability to relax and cope with pain, and 93% of the patients stated that neurotherapy was helpful in some way. Peniston and Trudeau also reported improved symptomology after neurotherapy and the high discriminant accuracy of QEEG in diagnosing in veterans with blast concussion.[61,62]

Hoffman et al reported that approximately 60% of mild TBI patients examined in a biofeedback study showed improvements in cognitive performance and/or self reported symptoms, and their EEGs showed significant normalization after 40 biofeedback sessions.[63] Hoffman later confirmed and expanded these results by showing significant improvements and EEG normalization in TBI patients after only 5–10 sessions.[64,65] These studies seem to show a correlation between electrophysiologic changes and improved symptomatology. Despite these reports, the literature concerning QEEG biofeedback as a treatment following TBI is still sparse. The clinical efficacy of this method of treating mild to moderate TBI needs further validation with standardized application procedures prior to widespread initiation of this treatment tool in the clinical setting. Future controlled studies are warranted to help determine the clinical effectiveness of this rehabilitation technique in the treatment of TBI.[58]

CONCLUSIONS REGARDING USE OF QEEG

The use of QEEG techniques in TBI is an exciting area of study that is still in a relatively early stage of development both as a research tool and as a useful diagnostic aid for the clinician. The majority of the research to date has not taken full advantage of the quantitative power of this tool. Many studies, particularly the work done by early investigators, have qualitatively categorized portions of the power spectrum and used this categorization scheme to determine survival, or at best gross global outcome. These studies do little more than to confirm qualitative EEG findings associated with coma and severe TBI.

Later work has attempted to more fully utilize the capabilities of QEEG and have determined in some populations the ability of QEEG, particularly in conjunction with other neurophysiologic and clinical indicators, to predict gross outcome. Others have shown that QEEG is better at predicting survival than other clinical tools such as GCS, and that QEEG has some predictive ability to correctly differentiate between controls and those with a history and clinical symptoms consistent with mild TBI.[27] Klein's findings regarding brain reactivity after thiopental bolus are particularly significant since patient outcome was prospectively classified based on a hypothesis derived from observations in the normal population.[42] Most recently, work has expanded to use MRI and QEEG as complementary tools in order to relate anatomy, physiology, and possibilities for therapeutic intervention.[37,53,57,64]

Many issues still need to be resolved for QEEG research to continue to move forward and to allow its widespread use as a reliable diagnostic tool. Although most laboratories utilize the standard International 10/20 system for electrode placement, little standardization exists between labs regarding number of electrodes used during data collection, the montages chosen for evaluation and statistics used for analysis. Depending on the epoch length, sampling rate, and other data acquisition parameters, FT analysis of the EEG could potentially filter out brief episodic electrical activity that may be of clinical importance. Although some work has been done to establish normative data and test retest reliability of the spectral parameters of QEEG, much work still needs to be done to establish universally accepted methods of comparing and contrasting data generated among laboratories.[66] Until then, using one study as a comparison or a building block for another will be difficult.

Another ongoing controversy surrounding the QEEG literature revolves around how the data collected are manipulated and statistically analyzed. At the center of this issue are the respective merits of exploratory and confirmatory research.[32] As with all areas of scientific research, one must first make an observation in order to then formulate and test a hypothesis. Critics of QEEG technology have minimized the significance of findings in the literature to date based on the argument that many studies analyze excessively large amounts of data points over several electrodes.[67] The argument is that with many pieces of data to evaluate, some associations are destined to be statistically significant. This issue must be examined carefully and the argument made cautiously. It is true for some exploratory analysis that an overabundance of electrode-to-electrode comparisons may yield statistically significant but questionably meaningful differences. However, these initial comparisons may direct future confirmatory studies that provide clinically meaningful results. Also, when manipulating the data for other analyses (e.g., to include specific frequencies from all electrodes over time), utilizing more data actually increases resolution of the spectral output. Furthermore, appropriate use of regression modeling techniques allows a researcher exploring variations in the spectral analysis to take those associations significant on exploratory analysis and construct hypotheses or models to test in future studies (confirmatory analysis).

Some of the recent QEEG literature has begun to focus on the importance of differentiating between exploratory and confirmatory analysis by including comparison groups' validation populations to test the accuracy and classification power of the constructed model.[46] However, more needs to be done to validate findings using uniform normative data and data collection techniques to prove the efficacy and generalizability of this technology for diagnosis, characterization, and prognostication for patients after TBI.

One concept absent in the literature is the evaluation of QEEG as it relates to functional outcome. To date, no studies have adequately related neuropathophysiology measured through QEEG with a functional definition of impairment, disability, or handicap. The biofeedback literature begins to incorporate a rehabilitation paradigm with its use as a therapeutic treatment modality in mild and moderate TBI. Recent work by Thatcher indicates promising links between neurophysiologic and anatomic imaging techniques that allow discussions about how neural disruption at a microanatomic level may affect functional reorganization after TBI. Technological improvements with real time, continuous sampling, and automated artifact filtration techniques—along with continued integration of multiple measures of neurophysiologic and anatomic function—may allow future research to link specific

neuropathophysiology to clinically meaningful functional outcome.

QEEG IN THE DIAGNOSIS AND TREATMENT OF DEMENTIAS

QEEG has not only been used in TBI but also in the characterization, diagnosis, and treatment of dementias, particularly Alzheimer's Dementia (AD). Multiple researchers have shown a characteristic QEEG pattern in AD patients, with significant alterations noted in the alpha, theta, and delta frequency band powers, particularly in the temporoparietal region.[68–72] Specifically, alpha amplitudes are markedly decreased, and delta/theta amplitudes are increased.[73] Further, other studies using QEEG have been able to differentiate between AD, frontotemporal dementia (FTD), and healthy age matched controls.[74]

Yener[74] was able to prospectively distinguish between FTD, AD, and healthy controls via QEEG based on hypotheses derived from known histopathologic changes seen with each entity. Findings from 32 seconds of artifact free data showed a relative preservation of right sided alpha activity and less left sided temporal slowing in normals and those with FTD compared to AD. Mini Mental Status Examination Scores (MMSE) also significantly correlated with spectral abnormalities seen in AD. Jackknife classification employed to distinguish between controls and FTD showed a correct classification rate of 100% and 76.9% respectively, and validation tests distinguishing between controls and AD showed a correct classification rate of 81.5% and 73.1%. Rodriguez et al[75] showed a significant correlation between MMSE, low and high frequency amplitudes, and regional blood flow for 42 patients with probable AD compared to 18 elderly healthy controls. Specifically, lower MMSE scores were seen with less regional blood flow, higher low frequency band amplitudes, and lower high frequency band amplitudes, particularly in the left hemisphere. Multivariate regression analysis revealed a combined predictive value of regional blood flow studies and QEEG on MMSE, and post-hoc discriminate classification revealed a combined diagnostic sensitivity of 88%, a specificity of 89%, and an overall correct classification rate of 88.3%.[75] Primavera, Jelic, and Chiaramonti had similar findings in their studies using QEEG to differentiate between AD and elderly controls, with MMSE scores and slow wave activity negatively correlated, and fast wave activity positively correlated with MMSE.[76–78] Jelic found that these characteristic changes in the frequency powers were correlated to MMSE and other neuropsychologic test scores, and alpha coherence in addition to amplitude was also positively correlated with MMSE.[77] Chiaramonti concluded that QEEG power maps might help identify potential neurophysiologic parameters for staging and monitoring this disease.[78]

QEEG has also been used in the Alzheimer's literature as a method to evaluate the neurophysiologic effects of pharmacologic agents and compare these effects to changes in the clinical disease course. Perryman noted trends toward improved dominant parietal rhythm with increased fast activity, and decreased slow wave activity for a small set of patients when using tetrahydroaminoacridine (THA), an approved drug for treatment of AD in the United States.[69] Turan later compared THA to Ginkgo Biloba, an approved treatment for AD in Germany, in a group of patients with mild to moderate AD and found neurophysiologic activation occurs with both drugs.[79] Increased alpha band amplitudes and decrease slow frequency amplitudes were seen with both drugs one to three hours after administration. Ginkgo Biloba was noted to have more of an effect than THA, but the effects of chronic dosing on neurophysiologic parameters and clinical course were not tested. Franco-Maside found similar

neurophysiologic changes with QEEG when administering CDP-choline to patients with AD.[68]

QEEG AND THE DIAGNOSIS AND TREATMENT OF LEARNING DISORDERS

QEEG has also been employed as a diagnostic and therapeutic modality in attention deficit disorders (ADD), memory, and learning disorders. Chabot compared 407 children with ADD to 310 control children via QEEG using the international 10/20 system.[80] In those with ADD, Chabot noted two electrophysiologic profiles, decreased and increased frontal activity, associated with those having ADD. Increased theta to alpha power ratios were noted for both groups. Discriminant analysis resulted in a 94.8% correct classification rate for normal children and a 93.1% correct classification rate for children with ADD but no learning disorder. The authors hypothesize both hypo- and hyperarousal of the cortical and subcortical structures serving the frontal/striatal system as causative for this syndrome, and that findings are due to deviations rather than maturational lag or delay in normal development.

Mann et al performed 16 channel topographic mapping of QEEG in 25 males aged to 12 years and compared findings to normal controls.[81] The authors found increased frontal theta activity and decreased temporal beta activity for those with ADD during reading and drawing activities. Discriminant analysis showed an 80% correct classification rate for the ADD group and a 74% correct classification rate for controls. Suffin evaluated a cohort of patients with either affective or attentional disorders based on DMS-III-R criteria.[82] Relative increases in theta were seen in some, while increases in alpha and increased coherence were seen in others with attentional disorders. Those with increases in alpha amplitudes responded to pharmacological stimulant therapy better than those with increased theta amplitude based on clinical global ratings six months after treatment. While these findings are interesting and may be useful at this point as an adjunctive tool in the clinical diagnosis and treatment of ADD, more work is needed to replicate and validate these findings in other populations before recommending this as a standard technique in the diagnosis of those with ADD.

Other research using QEEG that focuses on learning and learning disabilities shows that there are significant differences between dyslexics and normal controls when tested at rest, during silent reading and during oral reading.[83–87] These investigators have postulated that differences between groups, particularly with theta and alpha amplitudes, suggests that subtle differences may exist in brain organization of recruitment strategies of neural networks during these tasks. Findings in other studies show that increased slow wave representation in the frontal-temporal distribution and differences in anterior/posterior band amplitude gradients are associated with reading and writing disorders. Also QEEG criteria can be used to assess children with reading, writing, and spelling difficulties and to monitor the evolution of their cerebral electrophysiologic dysfunction over time.[88–90]

FUTURE DIRECTIONS FOR THE USE OF QEEG

The literature reviewed using QEEG in TBI and other related areas such as the diagnosis and treatment of dementias and learning disorders lends exciting possibilities and opportunities for expanding future research endeavors. Certainly, work will continue to delineate and integrate measures of anatomic structure with measures of neurophysiologic function such as QEEG. In the future, QEEG combined with regional cerebral blood flow may correlate with neurocognitive deficits

and functional reorganization after TBI. Important links, utilizing this real-time, dynamic measure of cerebral function, hopefully will allow investigators to better relate specific neuropathophysiology with functional outcome, and QEEG may allow, as it has begun to do in the dementia literature, effective neurophysiologic staging of TBI and monitoring of recovery and reorganization of the brain over time. Also, as it has done in the learning disabilities and ADD literature, researchers will be allowed to begin to characterize electrophysiologically specific symptomatology associated with TBI. Further work in relating QEEG characteristics to other functional neuroimaging techniques will be key to fully understanding how structure relates to function after TBI. It is possible that FT-EEG alone—or in combination with other imaging technologies—will provide an accurate diagnostic test for mild TBI.

Future work should focus on delineating and validating QEEG for generally accepted clinical use in diagnosis and monitoring of mild TBI and the prognostication of outcome after TBI. QEEG may hold promise as an objective tool that allows researchers to explore and understand the physiologic effects of neuropharmacologic agents, on cerebral function and reorganization after TBI. QEEG and other techniques also may give researchers the tools to delineate the evolution, treatment, and recovery of specific syndromes, including neglect, aphasias, and apraxias seen with stroke.[91–93] By monitoring cerebral function in real time, QEEG may be helpful in determining the efficacy of controversial treatments such as sensory stimulation rehabilitation programs for low level TBI patients and may provide a noninvasive means of monitoring intracerebral pressure.[94,95] Finally, QEEG may continue to grow as a treatment tool for cognitive and neuromuscular retraining, via biofeedback, in any type of patient with cerebral dysfunction.

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