

QEEG and Traumatic Brain Injury: Present and Future

Robert W. Thatcher, PhD

Introduction

The human brain is a highly energetic three-pound mass of soft tissue that sits in a hard bony vault. This small but vital organ is particularly vulnerable to rapid acceleration/deceleration by virtue of its relationship to the skull as well as its geometry and relative density of different brain regions. Although the brain only constitutes approximately 2% of total body weight, it consumes approximately 20% of oxygen intake with each breath, as much as our muscles consume in active contraction. One must ask: how is this disproportionate amount of metabolic energy utilized? The answer is that most of the brain's metabolic energy is transformed into electrical and magnetic energy by which the essential perceptual, cognitive, emotive, regulatory and motoric functions are carried out at each moment of time.

The electroencephalogram (EEG) is typically recorded at the scalp surface with reference to the ear and represents the moment-to-moment electrical activity of the brain. The EEG is produced by the summation of synaptic currents that arise on the dendrites and cell bodies of billions of cortical pyramidal cells that are located primarily a few centimeters below the scalp surface. The quantitative measurement of the electrical activity of the brain through the use of high-speed computers is referred to as quantitative EEG (QEEG) (Niedermeyer & Da Silva, 1995).

Since 1929, when the human EEG was first measured (Berger, 1929), modern science has learned an enormous amount about the current sources of the EEG and the manner in which ensembles of synaptic generators are synchronously organized. It is known that short distance local generators are connected by white matter axons to other local generators that can be many centimeters distant. The interplay and coordination of short distance local generators with the longer distant white matter connections has been mathematically modeled and shown to be essential for our understanding of the genesis of the EEG (Nunez, 1981; Nunez, 1995; Thatcher & John, 1977; Thatcher et al., 1986). The relevance of QEEG to the diagnosis and prognosis of traumatic brain injury (TBI) stems directly from the QEEG's ability to measure the consequences of rapid acceleration/deceleration to both the short and long distance compartments of the brain.

This article will review briefly the present state of knowledge about the diagnostic and prognostic value of QEEG in TBI and then speculate about some of the future roles of QEEG in TBI, with special emphasis on the integration of QEEG with MRI and other imaging technologies. Criticisms of the use of QEEG and TBI have been discussed and rebutted elsewhere (Thatcher et al., 1999).

Test-Retest Reliability of QEEG

The clinical sensitivity and specificity of QEEG is directly related to the stability and reliability of QEEG upon repetition shows that QEEG is highly reliable at 1996; Burgess & Gruzelier, 1993; Corsi-1994; Gasser et al., 1985; Hamilton-Bruce

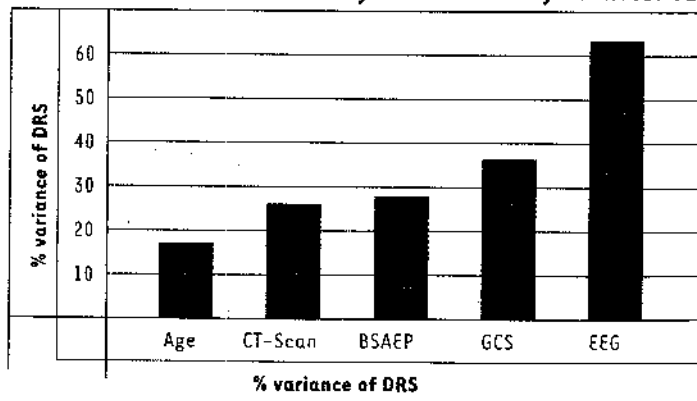
1993; Hughes & John, 1999; Lund et al., 1995; Pollock et al., 1991; Salinsky et al., 1991). The inherent stability and reliability of QEEG can be demonstrated with quite small sample sizes. For example, Salinsky et al. (1991) reported that repeated 20-second samples of EEG were about 82% reliable, at 40 seconds the samples were about 90% reliable and at 60 seconds they were approximately 92% reliable. Gasser et al. (1985) concluded that 20 seconds of activity are sufficient to reduce adequately the variability inherent in the EEG and Hamilton-Bruce et al. (1991) found statistically high reliability when three different individuals independently analyzed the same EEG. Although the QEEG is highly reliable even with relatively short sample sizes, it is the recommendation of most QEEG experts that larger sample sizes be used, for example, at least 60 seconds of artifact free EEG, and preferably two to five minutes, should be used in a clinical evaluation (Duffy et al., 1994; Hughes and John, 1999).

Present Use of QEEG for Diagnosis of TBI

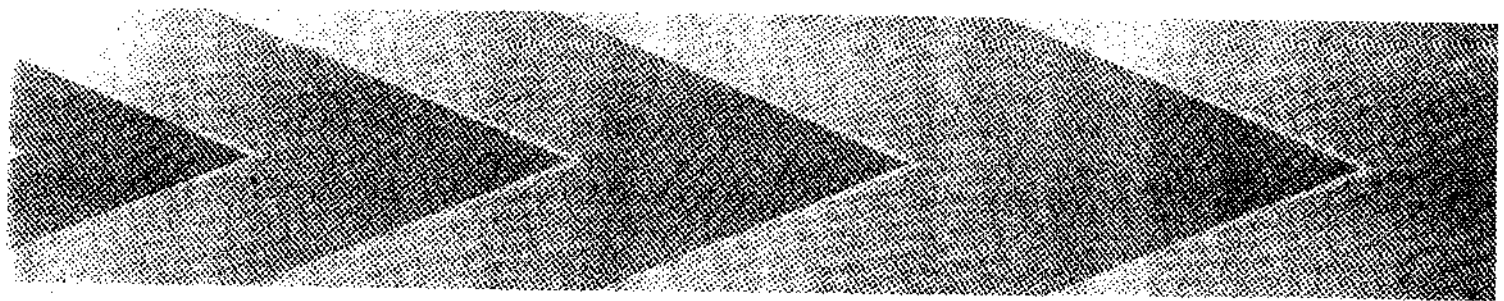
The scientific literature presents a consistent and common QEEG pattern correlated with TBI. Namely, reduced amplitude of the higher frequencies of EEG (Mas et al., 1993; Ruijs et al., 1994; Tebano et al., 1988; Thatcher et al., 1998a; von Bierbrauer et al., 1993) and changes in EEG coherence (Hoffman et al., 1995; Hoffman et al., 1996a; Thatcher et al., 1989; Thatcher et al., 1991; Thatcher, 1996a; Thatcher, 1998b; Trudeau et al., 1998). The reduced amplitude of EEG is believed to be a result from a reduced number of synaptic generators and/or reduced integrity of the protein/lipid membrane structures of neurons (Thatcher et al., 1997; Thatcher et al., 1998a). EEG coherence is a measure of the amount of shared electrical activity at a particular frequency and is analogous to a cross-correlation coefficient. EEG coherence is amplitude independent and reflects the amount of functional connectivity between distant EEG generators (Nunez, 1981).

Of the few QEEG studies of the diagnosis of TBI, quite a high level of sensitivity and specificity has been demonstrated. For example, a

FIGURE 1: Predictive accuracy of outcome 1 year after TBI



the Rappaport Disability Rating Scale (DRS) measured at one year various measures. In this figure, measures from each diagnostic category are regression analysis. BSAEP=Brainstem Auditory Evoked Potential, of EEG test (adapted from Thatcher et al., 1991).



study of 608 individuals with mild TBI and 103 age-matched control subjects demonstrated discriminant sensitivity=96.59%; Specificity=89.15%; Positive Predictive Value (PPV)=93.6% (Average of tables II, III, V) and Negative Predictive Value (NPV)=97.4% (Average of tables III, IV, V) in four independent cross-validations. Trudeau et al. (1998) and Hoffman et al. (1995) published a similar sensitivity and specificity for QEEG diagnosis of TBI. All of these studies met most of the American Academy of Neurology's criteria for diagnostic medical tests:

1. The criteria for test abnormality was defined explicitly and clearly
2. Control groups were different from those originally used to derive the test's normal limits
3. Test-retest reliability was high
4. The test was more sensitive than "routine EEG" or "neuroimaging tests"
5. The study occurred in an essentially "blinded" design (i.e., objectively and without ability to influence or bias the results).

The QEEG/MRI project of the Defense and Veterans Head Injury Program (DVHIP) has replicated and extended the earlier QEEG studies of TBI, thus adding additional validity and reliability to the use of the QEEG in the diagnosis of TBI (Thatcher et al., 1998a; Thatcher et al., 1998b)

Present Use of QEEG for the Prognosis of TBI

An example of the prognostic value of QEEG in predicting outcome one year following TBI is demonstrated in a study by Thatcher et al. (1991). In this study, a total of 162 individuals were diagnosed as having a closed head injury. Of the 162 individuals, 60% sustained motor vehicle-related injuries, another 10% were pedestrians and the remainder of the injuries were incurred in industrial or home incidents or as a result of violent crime. Glasgow Coma Scores were obtained at the time of admission (GCS-A) and at the time of computerized EEG testing (GCS-T). CT scans were obtained within one to seven days after admission. QEEG and evoked potential testing occurred within 1 to 21 days following injury. Outcome scores were obtained at one year post-injury using the Rappaport Disability Rating Scale (DRS) (Rappaport et al., 1982). Multiple regression analyses were performed in which the DRS was the dependent variable and the CT scan, GCS-A, GCS-T, age and computerized EEG and evoked potentials were the independent variables.

The best individual EEG predictor was EEG phase which had a univariate $R^2=44.21\%$, while the least predictive was absolute power with $R^2=19.14\%$. When the most statistically significant univariate EEG variables were entered in the multiple regression analyses then the multiple $R=0.75$ and accounted for 52.56% of the variance of the DRS scores. The QEEG was the single best category of variables for predicting outcome at one year post-injury. **Figure One** shows the comparative strength of the predictability of DRS scores at one year following injury. The best multivariate predictor for each category of variables was the QEEG

($R^2=64.91\%$), the second strongest predictor was GCS-T ($R^2=38.71\%$), the third was the brain stem auditor evoked potential (BSAEP) ($R^2=29.76\%$), the fourth was CT scan ($R^2=28.16\%$) and the weakest was age ($R^2=18.55\%$). The age range of the individuals involved in the study was between 14 and 32.

If these multivariate variable sets then were combined in order to find the best predictor of outcome at one year post-injury using the least number of variables and thus the highest probability of replication, then the combination of QEEG and GCS-T was the best with a $R^2=74.65\%$ of the variance. This combination of variables used only 12 variables (i.e., 11 QEEG variables and 1 GCS-T variable) with an N=129.

Future Uses of QEEG in TBI

This section will be restricted to only three future uses of QEEG:

1. Integration of QEEG and MRI
2. EEG current source localization
3. EEG biofeedback.

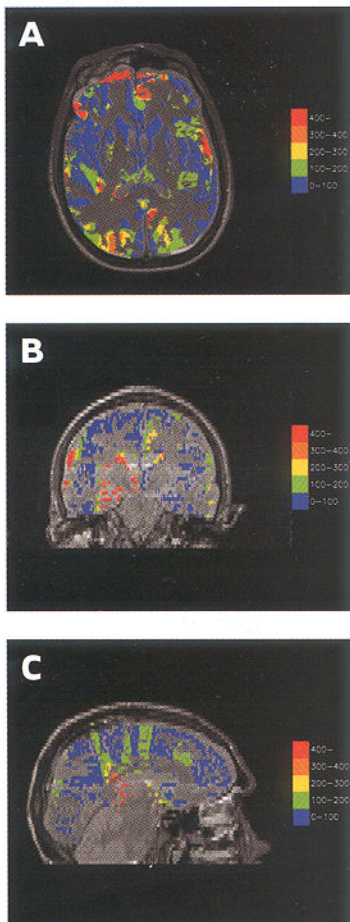
This limited number of possible future uses of QEEG is due to page limitations and already established uses of the QEEG in TBI.

QEEG and MRI Integration and TBI

Magnetic resonance imaging (MRI) provides much more than just a structural picture by which the spatial location of EEG generators can be identified (Thatcher et al., 1994). For example, the spectroscopic dimensions of the MRI can provide information about the biophysics of protein/lipid water exchanges, water diffusion, blood perfusion, cellular density and mitochondrial energetics (Gilles, 1994). The marriage of QEEG with the biophysical and structural aspects of MRI offers the possibility of much more sensitive and specific diagnostic and prognostic evaluations, not to mention the development and evaluation of treatment regimens in TBI. A recent series of DVHIP studies have helped pioneer the integration of QEEG with the biophysical aspects of MRI for the evaluation of TBI (Thatcher et al., 1997; Thatcher et al., 1998a; Thatcher et al., 1998b). These studies have provided MRI quantitative methods to evaluate the consequences of rapid acceleration/deceleration (Thatcher et al., 1997) and to integrate the MRI measures with the electrical and magnetic properties of the QEEG as they are affected by TBI (Thatcher et al., 1998a; Thatcher et al., 1998b). Future studies are expected to further extend our understanding of the molecular consequences of TBI as measured by the QEEG and, hopefully, lead to inexpensive but highly sensitive and specific QEEG measures of TBI.

QEEG Current Source Localization and TBI

Figure Two shows the axial, coronal and sagittal views of the current sources of the QEEG in an individual with TBI. The DVHIP is using current source localization procedures, such as those shown in **Figure Two**, to identify the current density of MRI registered voxels within the interior of the brain. This approach, referred to as Low Resolution Electromotography

FIGURE 2: 3-D EEG Current Source Localization

An example of the current source density that gives rise to the scalp EEG co-registered with the 3-dimensional MRI in a DVHIP TBI patient. The color scale to the right of each view is the EEG current source density in nano-amps/cm². Top (A) is an axial view, middle (B) is a coronal view and bottom (C) is a sagittal view. The current sources of the scalp EEG are derived using this method (LORETA) and then correlated with the MRI derived T2 relaxation times within the interior of the brain.

(Malmivuo & Plonsey, 1995).

The integration of QEEG with the MRI biophysical measures of the brain, however, indicate that in the future the capacitive and inductive properties of the brain also will be taken into consideration in the evaluation of TBI. For example, it is expected that future QEEG studies, when integrated with the biophysical measures of the MRI, will provide estimates of the dielectric constants of the electrical generators and the medium in which they are embedded, thus providing for more accurate source localization and a deeper understanding of the consequences of TBI.

EEG Biofeedback

Electroencephalographic (EEG) biofeedback, often referred to as neurofeedback, is an operant conditioning procedure whereby an individual modifies the amplitude, frequency or coherency of the neurophysiological dynamics of his/her own brain (Fox & Rudell, 1968; Rosenfeld et al., 1969; Rosenfeld & Fox, 1971; Rosenfeld, 1990). The exact physiological foundations of this process are not well understood; however, the practical ability of humans and animals to directly modify their scalp recorded EEG through feedback is well established (Fox & Rudell, 1968; Hetzler et al., 1977; Rosenfeld et al., 1969; Serman, 1996).

An emerging and promising treatment approach is the use of quan-

titative EEG technology and EEG biofeedback training for the treatment of mild to moderate TBI. One of the earliest EEG biofeedback studies was by Ayers (1987), who used alpha QEEG training in 250 cases of individuals with brain injury and demonstrated a return to pre-morbid functioning in a significant number of cases. Peniston et al. (1993) reported improved symptomology using EEG biofeedback in Vietnam veterans with combat related post-traumatic disorders. Trudeau et al. (1998) reported high discriminant accuracy of QEEG for the evaluation of combat veterans with a history of blast injury.

More recently Hoffman et al. (1995), in a biofeedback study of 14 individuals with TBI, reported that approximately 60% of individuals with mild TBI showed improvement in self-reported symptoms and/or cognitive performance as measured by the MicroCog assessment test after 40 sessions of QEEG biofeedback. Hoffman et al. (1995) also found statistically significant normalization of the QEEG in those individuals that showed clinical improvement. Subsequent studies by Hoffman et al. (1996a; 1996b) confirmed and extended these findings by showing significant improvement within 5–10 sessions.

A similar finding of QEEG normalization following EEG biofeedback was reported by Tinius and Tinius (1996). Ham and Packard (1996) evaluated EEG biofeedback in 40 individuals with posttraumatic head ache and reported that 53% showed at least moderate improvement in headaches; 80% reported moderate improvement in ability to relax and cope with pain and 93% found biofeedback helpful to some degree.

In summary, EEG biofeedback is a possible future treatment regimen that may help marry the basic science of QEEG and TBI with a cost-effective method of symptom amelioration. Future controlled studies will help determine the clinical efficacy of this methodology.

Dr. Robert W. Thatcher received his bachelor degree in chemistry and his PhD in biopsychology at the University of Oregon. He joined the faculty of New York Medical College as an assistant professor and New York University Medical School as an associate professor and a full professor at the University of Maryland School of Medicine, where he was the director of the Applied Neurosciences Research Institute and the Neurometrics Clinical Service in Shock Trauma. In 1991, he joined the staff at the National Institutes of Health and the National Institutes of Neurological Diseases and Stroke as the project manager for the 128-channel EEG system and the program on functional neuroimaging. Currently, he is a full professor in the Department of Neurology and Radiology at the University of South Florida School of Medicine and Program Manager for EEG and MRI analyses of head injury and quantitative MMRI analyses of aging and dementia at the VA Medical Center in Bay Pines, Florida. Dr. Thatcher has published six books and more than 150 journal articles, book chapters and abstracts. These publications cover the fields of basic neuroscience, neurobiology, developmental psychology, neurometrics, environmental toxicology, clinical medicine and multimodal integration of MRI, EEG and PET scans. He has extensive clinical experience, having performed more than 2,000 clinical evaluations for individuals with a wide variety of clinical disorders (e.g., head trauma, strokes, tumors, epilepsy, attention deficit disorders, Alzheimer's Disease and organic dementias).

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ACKNOWLEDGEMENTS

This paper was supported by contract no. JFC6285006 as part of the Defense and Veterans Head Injury Program (DVHIP).