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CHAPTER IN: Foundations of Sport-Related Brain Injuries. Semyon Slobounov (Ed.), 2006.

ELECTROENCEPHALGRAPHY AND MILD TRAUMATIC BRAIN INJURY

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Abstract: This chapter is a review and analysis of quantitative EEG (qEEG) for the evaluation of the locations and extent of injury to the brain following rapid acceleration/deceleration trauma, especially in mild traumatic brain injury (TBI). The earliest use of qEEG was by Hans Berger in 1932 and since this time over 1,600 peer reviewed journal articles have been published in which qEEG was used to evaluate traumatic brain injury. Quantitative EEG is a direct measure of the electrical energies of the brain and network dynamics which are disturbed following a traumatic brain injury. The most consistent findings are: 1- reduced power in the higher frequency bands (8 to 40 Hz) which is linearly related to the magnitude of injury to cortical gray matter, 2- increased slow waves in the delta frequency band (1 to 4 Hz) in the more severe cases of TBI which is linearly related to the magnitude of cerebral white matter injury and, 3- changes in EEG coherence and EEG phase delays which are linearly related to the magnitude of injury to both the gray matter and the white matter, especially in frontal and temporal lobes. A review of qEEG reliability and clinical validation studies showed high predictive and content validity as determined by correlations between qEEG and clinical measures such as neuropsychological test performance, Glasgow Coma Scores, length of coma and MRI biophysical measures. Inexpensive and high speed qEEG NeuroImaging methods were also discussed in which the locations of maximal deviations from normal in 3-dimensions were revealed. Evaluation of the sensitivity and specificity of qEEG with a reduced number of EEG channels offers the feasibility of real-time monitoring of the EEG using Blue Tooth technology inside of a football helmet so that immediate evaluation of the severity and extent of brain injury in athletes can be accomplished. Finally, qEEG biofeedback treatment for the amelioration of complaints and symptoms following TBI is discussed

Keywords: qEEG; traumatic brain injury (TBI); LORETA, EEG biofeedback.

1. INTRODUCTION

When evaluating neuroimaging techniques to measure the effects of traumatic brain injury an important fact to keep in mind is that the brain, while only constituting approximately 2% of our body weight, consumes approximately 60% of total blood glucose (Tryer, 1988). For example, the approximately two and 1/2 pound brain consumes approximately 20% of the total energy of the body, as much as muscles in active contraction at every moment of time (Tryer, 1988). A pertinent question is how is this disproportionate amount of energy utilized? The answer is that most of the brain's metabolic energy is transformed into electricity by which the essential perceptual, cognitive, emotive, regulatory and motoric functions are carried out at each moment of time.

The human brain is vulnerable to traumatic injury by the fact that it sits on a hard bony vault. Rapid acceleration/deceleration forces often result in contusions or bruising of the frontal and temporal lobes which are located at the interface between the soft tissues of the brain and the hard bone of the skull. For example, because of physics even blunt impacts to the occipital bone result in frontal and temporal brain injuries (Ommaya, 1986; 1994; Sano et al, 1967). In addition to linear percussion forces, rapid acceleration/deceleration often produces shear forces in which different regions of the brain move at different rates resulting in stretching of axons with effects on the myelin and on conduction velocities. Similarly, rotational forces can also be imparted to the brain and both the shear and rotational forces can damage the cerebral white matter as well as brain stem structures even in whiplash injuries (McLean, 1995; Ommaya and Hirsch, 1971). The duration of reduced brain function following traumatic brain injury can be many years even in the case of mild head injuries in which there is no loss of consciousness (Ommaya, 1995, Barth et al, 1983; Rimel et al, 1981).

2. ELECTROCHEMISTRY AND THE EEG

The electroencephalogram or 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 electroencephalogram or 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 primarily located a few centimeters below the scalp surface. The synaptic currents involve neurotransmitter storage and release which are dependent on the integrity of the sodium/potassium and calcium ionic pumps located in the membranes of each neuron. Metabolic activity is the link between

EEG/MEG and PET, SPECT and fMRI which are measures of blood flow dynamics. Glucose regulation and restoration of ionic concentrations occurs many milliseconds and seconds and minutes after electrical impulses and synaptic activity and therefore, blood flow changes are secondary to the nearly instantaneous electrical activity and metabolic activities that give rise to the EEG at each moment of time (Thatcher and John, 1977).

The effects of traumatic injury on the electrical activity of the brain due to injury to the number and integrity of ionic channels and electrical generators and on the network dynamics involved in the distribution and coordination of the electrical energy is easily measured with the EEG using high speed modern and inexpensive computers. As would be expected EEG measurements are sensitive and accurate in the detection and evaluation of the effects of rapid acceleration/deceleration on brain electrical activity. This fact is supported in the sections that follow with citations to a vast scientific literature of EEG studies showing similar affects of traumatic brain injury, as would be expected when a small and energetic mass of tissue is suddenly accelerated and banged against a hard bony vault.

2.1. American Academy of Neurology and Quantitative EEG

In 1997 the American Academy of Neurology officially acknowledged and supported the widespread use of "Digital EEG" and in support of visual examination of EEG traces by a Neurologist. In the same AAN position paper qEEG was arbitrarily restricted or limited and assigned to the less worthy category "Experimental" as distinct from "Clinically Acceptable". This is important because the outdated, flawed and politically motivated 1997 ANN position opposing qEEG still holds sway in 2006 and it still influences insurance companies and it still restricts the availability of 21st century technology to people with serious clinical problems including brain injury in athletes.

One is struck by the fact that the less worthy categories according to the AAN 1997 paper include many serious neurological and psychological conditions such as traumatic brain injury, learning disabilities, language disorders, schizophrenia, depression, addiction disorders, obsessive compulsive disorders, autism, bipolar disorders, etc. (Nuwer, 1997). One is also struck by the fact that AAN has not revised its 1997 position to more accurately represent the scientific literature and given scholarly rebuttal publications (Hughes and John, 1999; Hoffman et al, 1999 and Thatcher et al, 1999). Another remarkable fact is that the 1997 AAN assignment to the "unworthy" category occurred without a proper review of the scientific literature and without any citations that rebutted the last 20 years of quantitative EEG studies. It is also remarkable that the AAN position paper

supported visual examination of the EEG tracings as the "Gold Standard" for acceptance in Courts and for third party reimbursement when it is well known that subjective visual examination of EEG traces is unreliable and inferior to quantitative analyses (Cooper et al, 1974; Woody, 1966; 1968; Majkowski et al, 1971; Volavka et al, 1971; Niedermeyer and Lopez Da Silva, 1995).

The subjectivity and the lack of inter-rater and intra-rater reliability in the visual analysis of EEG tracings is explained in the primary textbook that Neurologists study before taking an EEG examination:

> "There is simply no firm rule concerning the manner in which the reader's eyes and brain have to operate in this process. Every experienced electroencephalographer has his or her personal approach to EEG interpretation. This is also true for the manner in which the EEG report is written. Although standardization is an important goal in many areas of EEG technology, experienced electroencephalographers should not abandon a certain individualistic spirit…." (Niedermeyer and Lopes Da Silva, 1995, p., 185-186).

As mentioned previously, in response to the AAN 1997 position paper, Hughes and John (1999) wrote a rebuttal that included 248 publications and systematically categorized and analyzed the consistency and high sensitivity of quantitative EEG studies in all of the areas that the AAN labeled as "experimental" and they also showed that the sensitivity and specificity of the AAN's alleged "clinically valid" categories often had lower sensitivity and specificity than the category that the AAN labeled as "experimental". The Hughes and John (1999) rebuttal was the first paper to show that the AAN 1997 position paper was a sham and Hughes and John's rebuttal was followed by two additional rebuttals that cited the scientific literature and pointed out misrepresentations and omissions in the 1997 AAN position paper (Hoffman et al, 1999; Thatcher et al, 1999). Nevertheless, the 1997 AAN position paper still holds sway in the minds of many Neurologists and insurance companies in the year 2006 to the disadvantage of millions of people, including athletes who may have suffered a brain injury or those who had the misfortune of having a traumatic brain injury of any type.

The arbitrary and subjective opinion of the AAN is also contradicted by the fact that the National Library of Medicine database lists over 70,000 qEEG studies published since 1970 proving that there is a very widespread use and acceptance of this technology. The disconnect between the AAN opinion paper is further contradicted by a search of the National Library of Medicine database using the search words "EEG and Traumatic Brain Injury" which resulted in 1,672 citations and the majority of these articles involve quantitative EEG and not visual examination of EEG tracings drawn

by ink pens or on a computer display. A similar search of the National Library of Medicine database for each of the restricted or alleged experimental uses of qEEG also yields a larger number of clinical publications.

Below is a partial list of organizations, in contrast to the AAN, that do support or certify by examination Ph.D. and M.D. properly trained and experienced in EEG and qEEG including the use of qEEG for the evaluation of mild to severe traumatic brain injury. The list below helps demonstrate that the AAN is not the relevant community of users of qEEG.

1- American Medical EEG Society
2- American Board of EEG and Clinical Neurophysiology
3- American Psychological Association
4- EEG and Clinical Neuroscience Society
5- International Society for NeuroImaging in Psychiatry
6- International Society for Brain Electrical Activity
7- American Board of Certification in Quantitative Electroencephalography
8- Biofeedback Certification Institute of America
9- Association for Applied Psychophysiology and Biofeedback
10- International Society for Neuronal Regulation
11- Society for Applied Neuroscience

The large list and numbers of Ph.D. and M.D. qualified individuals and professional organizations that support the use of qEEG for the evaluation of TBI shows that the AAN "does not represent the relevant community" in a court of law. The definition of the "relevant community" is critical in medical-legal issues for the admission of evidence in a court of law under Frye criteria which are: 1- acceptance by the relevant community of users of the methodology and, 2- reliability. Neurologists are in the minority of those using qEEG technology, and therefore, the first prong of Frye is not met because Neurologists do not represent the relevant community of users of qEEG. The second prong of Frye is easily met by the facts because the reliability of qEEG is usually 90% to 98% (Thatcher et al, 1999; 2003).

2.2. Definitions of Digital EEG and Quantitative EEG

The AAN defined digital EEG as "the paperless acquisition and recording of the EEG via computer-based instrumentation, with waveform storage in a digital format on electronic media, and waveform display on an electronic monitor or other computer output device." The primary purposes of digital EEG is for efficiency of storage, the saving of paper and for the purposes of visual examination of the EEG tracings. The 1997 AAN position paper concludes that "Digital EEG is an excellent technical advance

and should be considered an established guideline for clinical EEG." (Nuwer, 1997, pg. 278).

The American Academy of Neurology position paper (Nuwer, 1997) then attempted to create a distinction between digital EEG and quantitative EEG by defining quantitative EEG (qEEG or QEEG) as "the mathematical processing of digitally recorded EEG in order to highlight specific waveform components, transform the EEG into a format or domain that elucidates relevant information, or associate numerical results with the EEG data for subsequent review or comparison." (Nuwer, 1997) (p. 278). The reality is that there is no clear distinction between digital EEG and quantitative EEG because both involve mathematical transformations. For example, the process of analog-to-digital conversion involves transforms by analog and digital filtering as well as amplification and sample and hold of the electrical scalp potentials and re-montaging and reformatting the EEG. Clearly, digital EEG involves mathematical and transformational processing using a computer and therefore the distinction between quantitative EEG and digital EEG is weak and artificial. It would appear that the AAN's artificial distinction between digital EEG and quantitative EEG is aimed to support the practice of visual examination of EEG tracings which is highly unreliable and insensitive (Cooper et al, 1974; Woody, 1966; 1968; Majkowski et al, 1971; Volavka et al, 1971; Niedermeyer and Lopez Da Silva, 1995) while at the same time down playing modern advances in quantitative EEG which is more reliable and more sensitive than visual examination alone and simultaneous qEEG with visual examination of EEG tracings can significantly aid a competent clinician in their assessment of a patient's problems.

2.3. Simultaneous EEG and Quantitative EEG

Figure one illustrates some of the features in a typical modern quantitative EEG analysis which can be activated rapidly by a few mouse clicks on a small home computer using free educational software or by using inexpensive FDA registered commercial qEEG software. The EEG traces are viewed and examined at the same time that quantitative analyses are displayed so as to facilitate and extend analytical power.

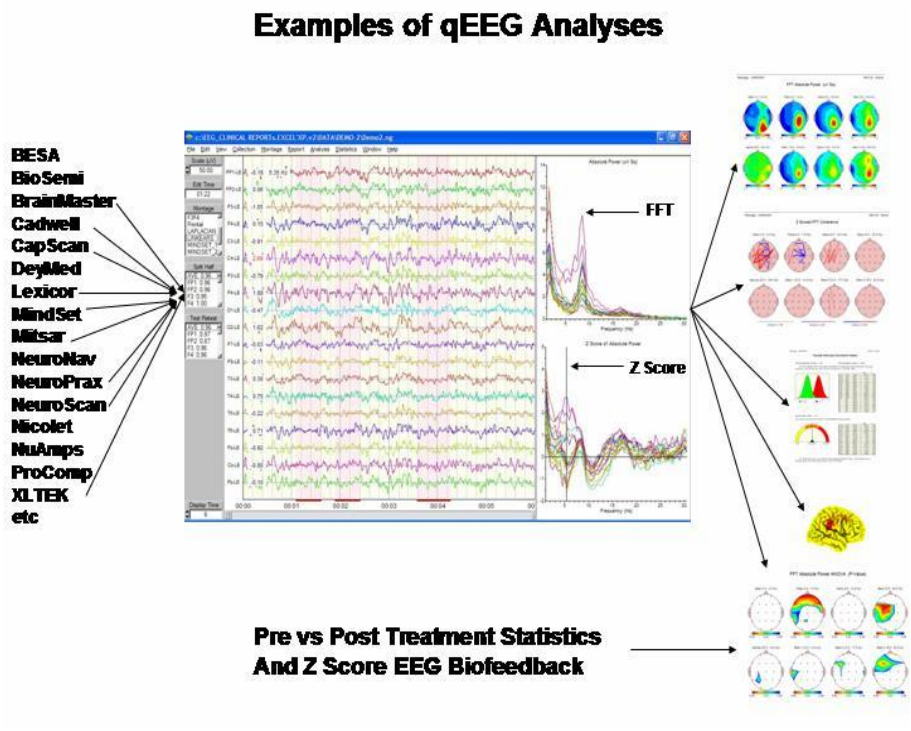

Fig. 1. Example of qEEG analyses in which calibrated EEG digital data is imported, test re-test and split half reliabilities are computed, spectral analyses are performed (FFT) and compared to a normative database (e.g., Z Scores) and discriminant analyses and color topographic maps are produced and 3-dimensional source localization is measured and objective pre-treatment vs. post-treatment or pre-mediation vs. post-medication statistics within a few minutes using the same computer program.

Commonsense dictates that the digital EEG and qEEG when simultaneously available facilitates rapid and accurate and reliable evaluation of the electroencephalograpm. Clearly, the AAN's distinction between digital EEG and quantitative EEG needs to be revisited and a new and more clinically useful position should be adopted by the AAN.

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; 1995; Thatcher and John, 1977; Thatcher et al, 1986).

The first qEEG study was by Hans Berger (1929) when he used the Fourier transform to spectrally analyze the EEG because Dr. Berger recognized the importance of quantification and objectivity in the evaluation of the electroencephalogram (EEG). The relevance of quantitative EEG (qEEG) to the diagnosis and prognosis of traumatic brain injury (TBI) stems directly from the quantitative EEG's ability to measure the consequences of rapid acceleration/deceleration to both the short distance and long distance compartments of the brain as well as to coup counter-coup patterns and focal contusions and neural membrane damage.

In this chapter I will first briefly review the present state of knowledge about the reliability, validity and diagnostic value of qEEG in TBI with special emphasis on the integration of qEEG with MRI and other imaging technologies. As mentioned previously, criticisms of the use of qEEG and TBI have been discussed and rebutted elsewhere (Hughes and John, 1999; Hoffman et al, 1999 and Thatcher et al, 1999).

2.4. Test-Retest Reliability of qEEG

The clinical sensitivity and specificity of qEEG is directly related to the stability and reliability of qEEG upon repeat testing. The scientific literature shows that qEEG is highly reliable and reproducible (Hughes and John, 1999; Aruda et al, 1996; Burgess and Gruzelier, 1993; Corsi-Cabera et al, 1997; Gasser et al, 1985; Hamilton-Bruce et al, 1991; Harmony et al, 1993; Lund et al, 1995; Duffy et al, 1994; Salinsky et al, 1991; Pollock et al, 1991). The inherent stability and reliability of qEEG can even 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 sec. of activity are sufficient to reduce adequately the variability inherent in the EEG" and Hamilton-Bruce et al, (1991) found statistically high reliability when the same EEG was independently analyzed by three different individuals. Although the qEEG is highly reliable even with relatively short sample sizes, it is the recommendation of most qEEG experts that larger samples sizes be used, for example, at least 60 seconds of artifact free EEG, and preferably 2 to 5 minutes, should be used in a clinical evaluation (Duffy et al, 1994; Hughes and John, 1999).

2.5. Present use of qEEG for the evaluation of TBI

The National Library of Medicine lists 1,672 peer reviewed journal articles on the subject of EEG and traumatic brain injury. The vast majority of these studies involved quantitative analyses and, in general, the scientific

literature presents a consistent and common quantitative EEG pattern correlated with TBI. Namely, reduced amplitude of the alpha and beta and gamma frequency bands of EEG (8–12 Hz and 13–25 Hz and 30- 40Hz) (Mas et al, 1993; von Bierbrauer et al, 1993; Ruijs et al, 1994; Korn et al, 2005; Hellstrom-Westas, 2005; Thompson et al, 2005; Tebano et al, 1988; Thatcher et al, 1998a; 2001a; Roche et al, 2004; Slewa-Younan, 2002; Slobounov et al, 2002) and changes in EEG coherence and phase delays in frontal and temporal relations (Thatcher et al, 1989; 1991; 1998b; 2001b; Hoffman et al, 1995; 1996a; Trudeau et al, 1998; Thornton, 1999; 2003; Thornton and Cormody, 2005). The reduced amplitude of EEG is believed to be due to a reduced number of synaptic generators and/or reduced integrity of the protein/lipid membranes of neurons (Thatcher et al, 1997; 1998a; 2001b). 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; 1994; Thatcher et al, 1986). EEG phase delays between distant regions of the cortex are mediated in part by the conduction velocity of the cerebral white matter which is a likely reason that EEG phase delays are often distorted following a traumatic brain injury (Thatcher et al, 1989; 2001a). In general, the more severe the traumatic brain injury then the more deviant the qEEG measures (Thatcher et al, 2001a; 2001b).

Quantitative EEG studies of the diagnosis of TBI typically show quite high sensitivity and specificity, even for mild head injuries. For example, a study of 608 mild TBI patients 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. A similar sensitivity and specificity for qEEG diagnosis of TBI was published by Trudeau et al (1998) and Thornton (1999) and Thatcher et al (2001b). All of these studies met most of the American Academy of Neurology's criteria for diagnostic medical tests of: 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" and, 5 - the study occurred in an essentially "blinded" design (i.e., objectively and without ability to influence or bias the results).

2.6. Drowsiness and Medication Affects on the qEEG

Artifact removal is important in order to achieve high reliability and validity in the clinical assessment of EEG. Drowsiness is an artifact that is

easy to detect and is rarely a problem in EEG recording, especially, when the first 30 seconds to 2 minutes of a recording session are utilized in the analysis because it is difficult for patients to instantly become drowsy shortly after electrodes are applied and the recording process started. Eyes open EEG analysis is another method to avoid drowsiness. When the EEG recording is excessively long, then careful examination of the EEG to detect and remove drowsiness is necessary. Drowsiness is characterized by reduced amplitude of alpha activity in posterior regions, slow eye movements and with deeper levels of drowsiness, theta rhythms in the frontal lobes. Focal deviations from normal can not be explained by drowsiness, for example, drowsiness does not occur in only a single lead or a localized region of the brain.

Medications of various types can also affect the EEG. However, there is no evidence that a given medication only affects a localized and isolated region of the brain or only one hemisphere and not the other hemisphere because different receptor types that medication acts on are widely distributed and never exclusively present in only one region of the cortex (Wauguier, 2005). Consequently, the use of re-montage procedures such as the Laplacian montage eliminates diffuse and widespread electrical fields produced by medication. For example, the Laplacian sets spatially common fields equal to zero and enhances focally present electrical activity which can then be correlated with the point of impact on to the patient's skull in the case of traumatic brain injury and by Low Resolution Electromagnetic Tomography (LORETA) in order to localize abnormal EEG activity. In addition, it appears that EEG coherence and phase delays are not very sensitive to the affects of medications. This fact was illustrated in a qEEG study of 608 TBI patients in which no difference in an EEG discriminant function were observed when patients on medication were compared to patients with no medication or when different types of medications were compared (Thatcher et al, 1989).

2.7. Predictive Validity of QEEG in the evaluation of TBI – Neuropsychological

Predictive (or criterion) validity has a close relationship to hypothesis testing by subjecting the measure to a discriminant analysis or cluster analysis or to some statistical analysis in order to separate a clinical sub-type. Nunnally (1978) gives a useful definition of predictive validity as: "when the purpose is to use an instrument to estimate some important form of behavior that is external to the measuring instrument itself, the latter being referred to as criterion [predictive] validity." For example, science "validates" the clinical usefulness of a measure by its false positive and false negative rates and by the extent to which there are statistically significant

correlations to other clinical measures and, especially, to clinical outcomes (Cronback, 1971; Mas et al, 1993; Hughes and John, 1999).

Another example of predictive validity is the ability to discriminant traumatic brain injured patients from age matched normal control subjects at classification accuracies greater than 95% (Thatcher et al, 1989; 2001b; Thornton, (1999). Another example of predictive validity is the ability of qEEG normative values to predict cognitive functioning in TBI patients (Thatcher et al, 1998a; 1998b; 2001a; 2001b). Table I shows correlations between qEEG and a variety of neuropsychological tests and serves as another example of clinical predictive validity and content validity. As seen in Table I relatively strong correlations exist between qEEG measures and performance on neuropsychological tests.

Table I. Correlations between neuropsychological test scores and qEEG discriminant scores in TBI patients (N = 108). (from Thatcher et al, 2001a)

NeuroPsych Tests, N = 108

Pearson Product-Moment Correlation	Correlation	Probability
WAIS TEST-Scaled Scores		
Vocabulary	-0.416	0.05
Similarities	-0.640	0.001
Picture Arrangement	-0.576	0.01
Performance	-0.504	0.01
Digit Symbol	-0.524	0.01
BOSTON NAMING TEST		
# of Spontaneous Correct Responses	-0.482	0.05
WORD FLUENCY TEST-Total Correct Words		
COWA	-0.568	0.01
Animals	-0.630	0.001
Supermarket	-0.709	0.001
ATTENTION TEST-Raw Scores		
Trail Making A-Response Time	0.627	0.001
Trail Making B-Response Time	0.627	0.001
Stroop-Word	-0.427	0.05
Stroop-Color	-0.618	0.001
Stroop-Color+Word	-0.385	ns
WISC TEST-Executive Functioning-Raw Scores		
Perseverative Responses	0.408	0.05
% Concept. Level Responses	-0.200	ns
Categories Completed	-0.187	ns
Design Fluency - # Originals	-0.454	0.05
Design Fluency - # Rule Violations	0.304	ns

WECHSLER MEMORY TEST-Raw Scores		
Logical Memory II	-0.382	ns
Visual Production II	-0.509	0.01
Digit Span (Forward+Backward)	-0.336	ns
Digit Span (Forward)	-0.225	ns
%-tile Rank Forward	-0.300	ns
Digit Span (Backward)	-0.213	ns
CVLT TEST-Raw Scores		
Recall - List A	-0.509	0.01
Recall - List B	-0.554	0.01
List A - Short-Delay Free	-0.518	0.01
Semantic Cluster Ratio	-0.162	ns
Recall Errors - Free Intrusions	0.409	0.05
Recall Errors - Cued Intrusions	0.520	0.01
Recognition Hits	-0.595	0.01
Recognition False Positives	0.280	ns

Also, as the severity of TBI increases then there is a systematic increase in deviation from normal EEG values which correlate to a systematic decrease in neuropsychological test performance (Thatcher et al, 1998a; 1998b; 2001a; 2001b). Such relationships between clinical measures and the EEG demonstrate the predictive validity of EEG in the evaluation of TBI as well as normal brain functioning (Thatcher et al, 2003; 2005).

The reliability and stability of the qEEG discriminant function was evaluated by comparing the discriminant scores at baseline to the discriminant scores obtained upon repeated EEG testing at 6 months and 12 months after the initial baseline EEG test. No statistically significant differences were found between any of the post injury periods up to 4 years post injury, thus demonstrating high reliability even several years after injury (Thatcher et al, 2001a).

The results of a cross-validation analysis of the qEEG and TBI are shown in figure two. In this study, quantitative EEG analyses were conducted on 503 confirmed TBI patients located at four different Veterans Affairs hospitals (Palo Alto, CA; Minneapolis, MN; Richmond, VA; and Tampa, Fl) and three military hospitals (Balboa Naval Medical center, Wilford Hall Air Force Medical Center and Walter Reed Army Medical Center). Figure two shows histograms of the distribution of qEEG TBI discriminant scores in the 503 TBI subjects who were tested 15 days to 4 years post injury. It can be seen that the distribution of the qEEG discriminant scores and thus the severity of the injury varied at the different hospitals. The VA patients exhibited more deviant qEEG scores than the active duty military personnel which was consistent with the clinical evaluations including neuropsychological testing.

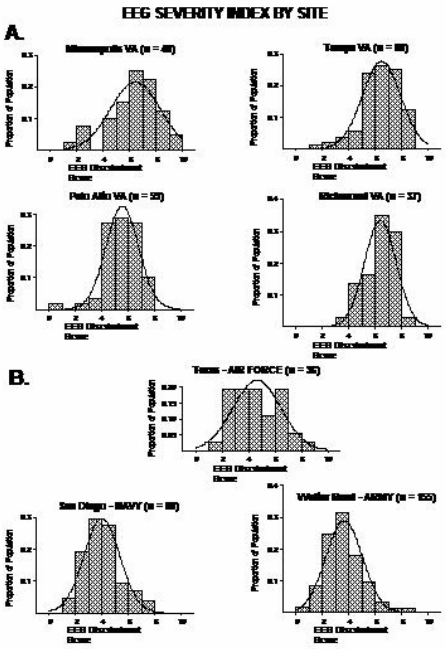

Fig. 2. Histograms showing the qEEG discriminant score distribution from 503 TBI outpatients located at four different Veterans Affairs hospitals (A) and three military hospitals (B). Normal = 0 and most severe TBI = 10. (from Thatcher et al, 2001a).

Table II shows the results of multivariate analysis of variance in which statistically significant differences in neuropsychological performance was predicted by the qEEG discriminant score groupings. The group having lower EEG discriminant scores was associated with higher neuropsychological functioning when compared with the group having higher EEG discriminant scores.

Table 2. Results of multivariate analysis of variance between low and high EEG discriminant score groups in a cross-validation study (Thatcher et al, 2001a).

Group I (0-4) & Group II (6-10) Discriminant Scores		503 Patients
Multivariate Analyses:	F-ratio	Probability
WAIS TEST-Scaled Scores		
Vocabulary	8.7448	0.0038
Similarities	6.3690	0.0130
Picture Arrangement	8.2771	0.0048
Performance	13.2430	0.0004
Digit Symbol	21.0620	0.0001

BOSTON NAMING TEST		
# of Spontaneous Correct Responses	4.8616	0.0290
WORD FLUENCY TEST-Total Correct Words		
COWA	5.2803	0.0230
Animals	14.0170	0.0003
Supermarket	18.8370	0.0001
ATTENTION TEST-Raw Scores		
Trail Making A-Response Time	7.6953	0.0064
Trail Making B-Response Time	4.6882	0.0324
Stroop-Word	16.5080	0.0001
Stroop-Color	9.6067	0.0024
Stroop-Color+Word	4.3879	0.0383
WISC TEST-Executive Functioning-Raw Scores		
Perseverative Responses	ns	ns
% Concept. Level Responses	ns	ns
Categories Completed	ns	ns
Design Fluency - # Originals	ns	ns
Design Fluency - # Rule Violations	ns	ns
WECHSLER MEMORY TEST-Raw Scores		
Logical Memory II	3.9988	0.0484
Visual Production II	7.1378	0.0089
Digit Span (Forward+Backward)	ns	ns
Digit Span (Forward)	ns	ns
%-tile Rank Forward	ns	ns
Digit Span (Backward)	ns	ns
CVLT TEST-Raw Scores		
Recall - List A	ns	ns
Recall - List B	ns	ns
List A - Short-Delay Free	7.0358	0.0089
Semantic Cluster Ratio	ns	ns
Recall Errors - Free Intrusions	ns	ns
Recall Errors - Cued Intrusions	ns	ns
Recognition Hits	ns	ns
Recognition False Positives	ns	ns

2.8. The Use of Fewer Electrodes to Evaluate the Effects of TBI

As the number of recording channels decreases, then the ability of quantitative EEG measures to detect the consequences of rapid acceleration/deceleration forces diminishes. Nonetheless, discriminant

analyses using two channels to five channels still show quite high sensitivity and specificity in discriminanting age matched normals from TBI patients. Fig. 3 shows ROC curves (Receiver Operator Curves) of discriminant accuracy for 2, 3, 4 and 5 channel EEG which range from 74% to 97.3% discriminant accuracy.

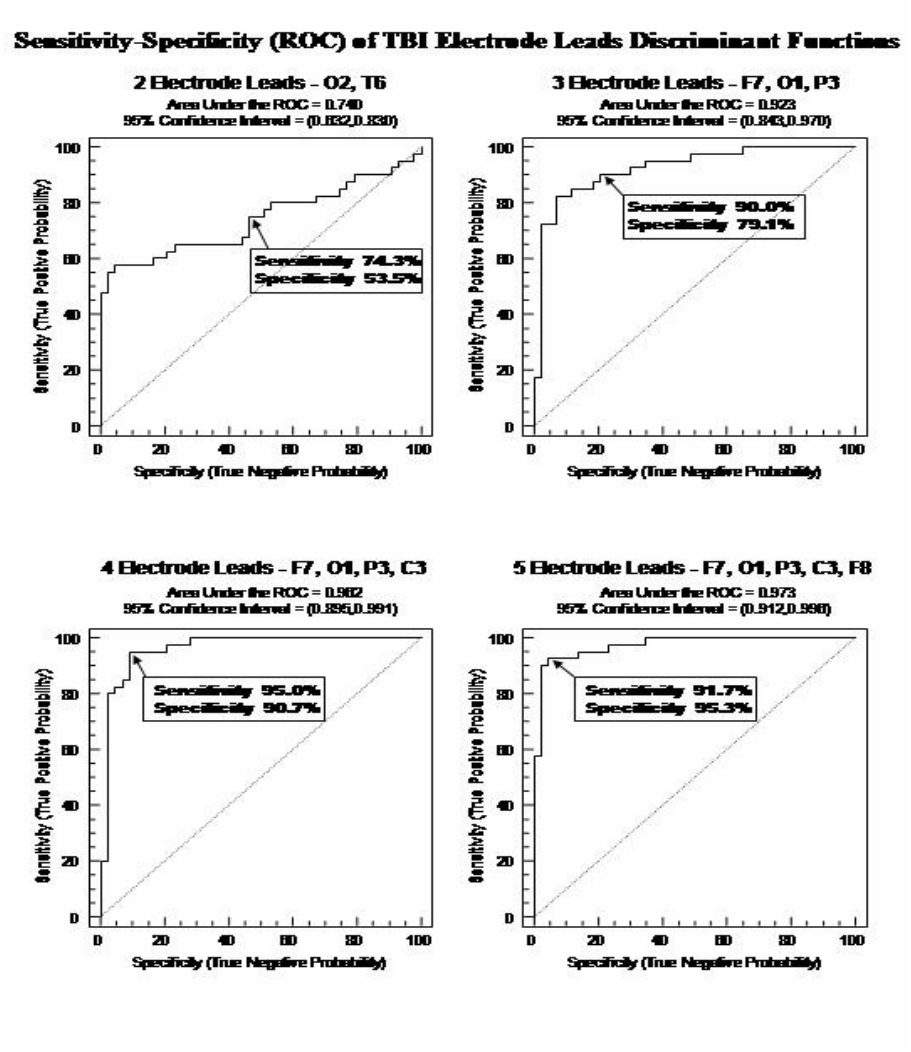

Fig. 3. Receiver operating characteristics curves (ROC) of TBI discriminant functions using different numbers of electrode leads. As the number of leads increases from 2 to 5 leads then the discriminant accuracy correspondingly increases.

Table III shows the correlation of different EEG TBI discriminant functions with neuropsychological test scores in a group of TBI patients (N = 83). As the number of EEG channels increases from two leads to five

leads, then the strength of correlation to neuropsychological test performance increases. This is what is expected if a measure has predictive validity and is cross-validated by correlation with clinical measures, such as a neuropsychological test.

Table 3. Correlations between neuropsychological test scores and qEEG discriminant scores in TBI patients (N = 108) for analyses that used two to five EEG channels (leads)

	Pearson Product-Moment Correlation			
NeuroPsych Tests	**5 - LEADS**	**4- LEADS**	**3- LEADS**	**2- LEADS**
WAIS TEST-Scaled Scores				
Vocabulary	0.285	0.235	0.173	0.094
Similarities	0.475	0.432	0.339	0.253
Picture Arrangement	0.398	0.38	0.243	0.094
Performance	0.249	0.198	0.142	0.29
Digit Symbol	0.454	0.281	0.212	0.188
BOSTON NAMING TEST				
# of Spontaneous Correct Responses	0.360	0.366	0.252	0.132
WORD FLUENCY TEST-Total Correct Words				
COWA	0.496	0.519	0.604	0.457
Animals	0.501	0.501	0.514	0.372
Supermarket	0.599	0,531	0.465	0.495
ATTENTION TEST-Raw Scores				
Trail Making A-Response Time	-0.526	-0.545	0.44	-0.274
Trail Making B-Response Time	-0.469	-0.475	0.376	-0.296
Stroop-Word	0.256	0.229	0.157	0.149
Stroop-Color	0.464	0.416	0.315	0.373
Stroop-Color+Word	0.249	0.199	0.064	0.11
WISC TEST-Executive Functioning-Raw Scores				
Perseverative Responses	-0.404	-0.47	0.369	0.17
% Concept. Level Responses	0.289	0.303	0.293	0.28
Categories Completed	0.265	0.273	0.28	0.273
Design Fluency - # Originals	0.193	0.178	0.18	0.112
Design Fluency - # Rule Violations	-0.166	-0.058	0.043	0.079

Sig. level P < .05 > = or =< 0.246
Sig. level P < .01 > = or =< 0.318
Sig. level P < .001 >= or =< 0.399
Sig. level P < .0002 >= or = < 0.441

The use of a small number of EEG leads is important because a simpler and less expensive analysis is desirable. For example, the use of Blue-Tooth wireless technology with field effect transistors and amplifiers inside of a football helmet is possible and such technology is inexpensive and can be used to immediately evaluate an individual's response to TBI and rapid acceleration/deceleration forces and therefore can lead to more accurate assessments and a more complete understanding of the consequences of a injury.

2.9. Examples of Content Validity of qEEG and TBI Evaluation

Content validity is defined by the extent to which an empirical measurement reflects a specific domain of content. For example, a test in arithmetic operations would not be content valid if the test problems focused only on addition, thus neglecting subtraction, multiplication and division. By the same token, a content-valid measure of cognitive decline following a stroke should include measures of memory capacity, attention and executive function, etc.

There are many examples of the clinical content validity of qEEG in ADD, ADHD, Schizophrenia, Compulsive disorders, Depression, Epilepsy, TBI and a wide number of clinical groupings of patients as reviewed by Hughes and John, (1999). As mentioned previously, there are 258 citations to the scientific literature in the AAN rebuttal review by Hughes and John (1999) and there are approximately 1,672 citations to peer reviewed journal articles in which a quantitative EEG was used to evaluate traumatic brain injury.

Content validity of qEEG is also demonstrated by strong correlations with magnetic resonance imaging (MRI) which provides much more than just a structural picture by which the spatial location of EEG generators can be identified (Thatcher et al, 1994; Thatcher, 1995). 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 mitochrondrial 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 studies have helped pioneer the integration of qEEG with the biophysical aspects of MRI for the evaluation of TBI (Thatcher et al, 1997; 1998a; 1998b; 2001b). These studies have provided MRI quantitative methods to evaluate the consequences of rapid acceleration/deceleration 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; 1998b; 2001b).

Figure 4 shows an example of the relationship between gray matter damage as measured by MRI T2 relaxation time and the EEG in which there is a negative linear relationship between the magnitude of injury and the amplitude of the EEG at higher frequencies (Thatcher et al, 1998a). This same study showed that damage to the cerebral white matter as measured by MRI T2 relationship was positively related to the magnitude of the injury and to the magnitude of delta or low frequency activity of the EEG.

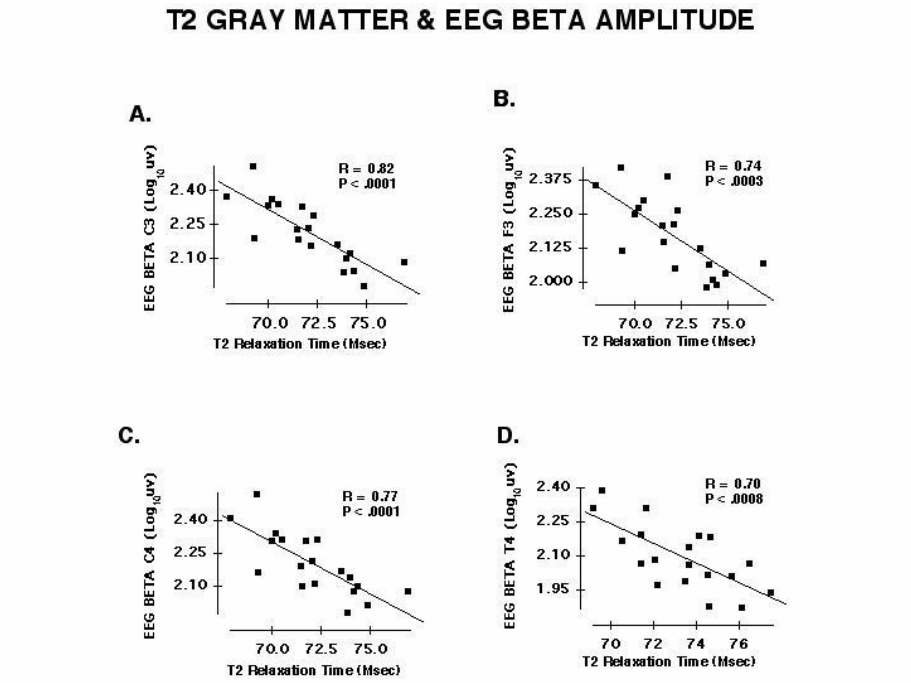

Fig. 4. T2 gray matter and EEG beta (13 – 22 Hz) frequency scattergrams. Representative scattergrams between the $\log_{10}$ EEG amplitude in the beta frequency band on the y-axis and T2 relation time on the x-axis. (A, B, C & D) are scattergrams based on different MRI slices. This is an example of content validity in which there is a strong relationship between EEG and a different clinical measure, in this case the MRI. (from Thatcher et al, 1998a).

In a subsequent study, the inverse relationship between T2 relaxation time and EEG amplitude was demonstrated for the alpha frequency band (Thatcher et al, 2001b). Other examples of qEEG and content validity in the evaluation of TBI is in a recent study by Korn et al (2005) which showed a strong correlation between qEEG and SPECT (content validity). Consistent with other TBI studies, Korn et al (2005) found reduced power in alpha and increased power in the delta frequency band in mild TBI patients which was

evident many months post injury. As mentioned previously, lesions of the white matter as well as MRI T2 relaxation time deviations from normal in the white matter are correlated with increased delta activity in the qEEG (Gloor et al, 1968; 1977; Thatcher et al, 1998a).

3. QEEG CURRENT SOURCE LOCALIZATION AND EEG

Figure five shows the axial, coronal and sagital views of the current sources of the qEEG in a TBI patient. This is just one of many examples in which the qEEG provides an inexpensive and accurate neuroimage of the focal source of abnormal EEG patterns in a patient who was hit by a blunt object in the right parietal region. In figure 5, the focal location of the injury is clearly evident and is validated by the CT-scan results in which a right hemisphere epidural hematoma developed following the injury. The method of source localization called Low Resolution Electromagnetic Tomography (LORETA) developed by Pascual-Margui et al (1994) is a well established and inexpensive (it is free) neuroimaging method based on qEEG which is also helpful in the evaluation of coup contra-coup patterns.

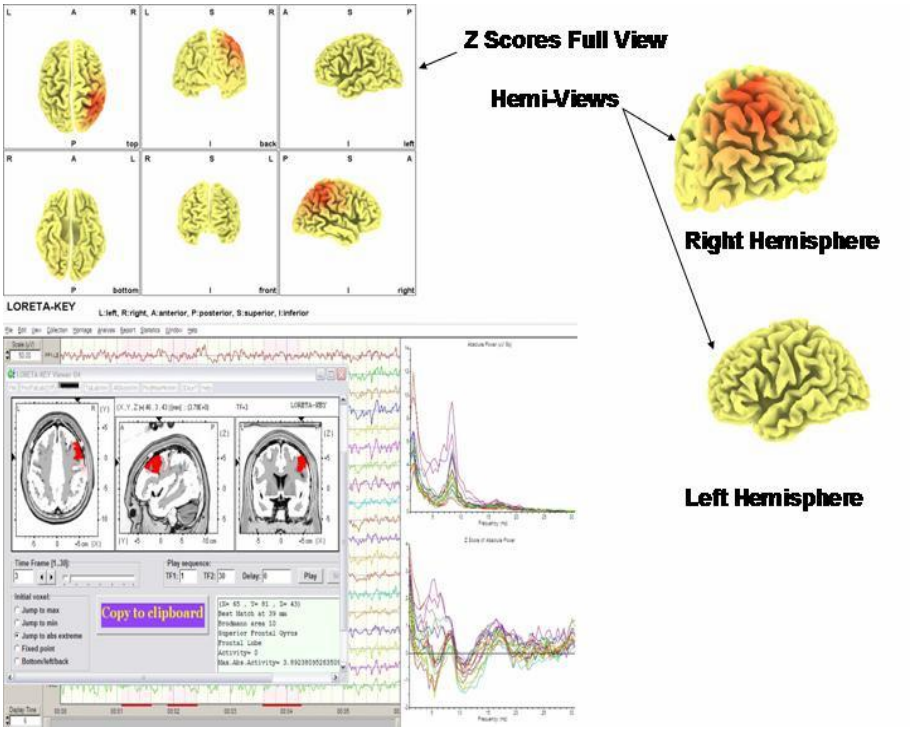

Fig. 5. Example of the use of Low Resolution Electromagnetic Tomography (LORETA) to evaluate the effects of TBI involving a patient hit with a bat on the near the right parietal lobe. The lower left panel is the digital EEG and qEEG that are simultaneously available for the evaluation of the EEG with the Key Institute LORETA control panel superimposed on the EEG. The upper and right panels are examples of the location of Z score deviations from normal which were confined to the right parietal and right central regions and are consistent with the location of impact.

In addition to the LORETA and TBI studies by Thatcher et al (2005) LORETA was a qEEG neuroimaging tool used by by Korn et al (2005) for the evaluation of mild TBI. In the Korn et al (2005) study the generators for abnormal rhythms in the mild TBI patients were closely related to the anatomical locations as measured by SPECT, thus providing additional validation of qEEG and mild TBI.

4. EEG BIOFEEDBACK

Electroencephalograhic (EEG) biofeedback, often referred to as neurofeedback, is an operant conditioning procedure where by an individual modifies the amplitude, frequency or coherency of the neurophysiological dynamics of their own brain (Fox and Rudell, 1968; Rosenfeld et al, 1969; Rosenfeld and 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 and Rudell, 1968; Rosenfeld et al, 1969; Hetzler et al, 1977; Sterman, 1996). EEG biofeedback necessarily uses a computer and is technically quantitative EEG based on the accepted definitions of qEEG (Nuwer, 1997; Niedermeyer and Lopes da Silva, 1995).

An emerging and promising treatment approach is the use of quantitative EEG evaluation 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 quantitative alpha EEG training in 250 head injured cases 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 fourteen TBI patients reported that approximately 60% of mild TBI patients showed improvement in self reported symptoms and/or in 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 patients 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 (2001) and Bounias et al (2001; 2002). Ham and Packard (1996) evaluated EEG biofeedback in 40 patients 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. Thornton and Carmody (2005) reported success in using EEG biofeedback for attention deficit disorders in children with a history of TBI. An excellent review of the qEEG biofeedback literature for the treatment of TBI is in Duff (2004).

CONCLUSION

In conclusion, qEEG is a reliable, objective, clinically sensitive and inexpensive method to evaluate the effects of rapid acceleration/deceleration injuries to the brain. Reduced EEG power in the higher frequencies and frontal and temporal changes in coherence and phase are the most consistently reported changes in the qEEG following traumatic brain injury. Clinical correlations between the qEEG and neuropsychological test performance, length of coma, Glascow Coma score, post-traumatic amnesia and MRI biophysical measures are all convergent and systematic and can be relied upon to help determine the degree of brain injury and likely affects on cognitive functioning. Follow up qEEG measures can help evaluate the rate and extent of recovery from trauma and finally, qEEG biofeedback is a procedure that is increasingly used to ameliorate the effects of brain injury, especially mild TBI.

EEG biofeedback is one treatment regimen that marries the basic science of qEEG and TBI. The fact that the effects of mild TBI can be detected with 2 to 5 electrodes emphasizes the practical and cost efficient aspect of this technology in the evaluation of athletes (see figure 3 and Table II. For example, blue tooth technology and amplifiers inside of a football helmet may potentially instantly evaluate the neurological status of a head injured athlete and thus may be used to ameliorate the effects of brain injury as well as to help understand the long term consequences and rates of recovery from TBI.

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