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Quantitative EEG Significantly and Clinically Differentiates Acute Mild TBI Patients From Matched Neurotypical Controls: Power Spectral and Connectivity Analyses

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Abstract

Concussive head injuries result in not only coup–contrecoup trauma to neurological tissue at injury sites but also a mechanical shearing of neurological pathways throughout the brain. Unfortunately, however, the diagnosis of concussion has long been based largely on self-reports of overt symptoms and virtually never includes an assessment of involved neurological tissues and pathways. This deficiency then leads to premature return to play or duty, to the risk of subsequent neurological reinjury and, in worse cases, to chronic traumatic encephalopathy. We offer here a test of quantitative EEG (qEEG) as a convenient, low-cost remedy to this problem in the evaluation of acute head injury in 19 diagnosed concussion patients matched to neurotypical controls. Results of qEEG indicate numerous Brodmann area functional clusters of highly significant and very large effect sizes in the differentiation of these two groups in EEG connectivity measures of coherence and phase difference. These findings indicate that qEEG can be used as a "hard" neurological measure of traumatic brain injury that directly assesses this neuronal shearing process as well as direct tissue injury and may offer an essential biomarker of readiness to return to play or duty and the avoidance of subsequent retraumatization of the brain.

Keywords: qEEG; power spectral; connectivity; coherence; phase difference; concussion

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Introduction

Quantitative Electroencephalography

Quantitative electroencephalography (qEEG) is a methodology for transforming analog raw signals from the standard clinical EEG into digital information that can be further entered into mathematical algorithms that represent a number of important characteristics of brain electrical activity. Two general categories of these characteristics are EEG spectral power, or the relative amount of energy contained in frequency components of the signal, and neurological connectivity, or the integrity of connections among neural pathways throughout the brain. Once digitized, these qEEG values for the individual patient can be compared with similar characteristics from selected normal control individuals or with established normative databases of typical, or "neurotypical," individuals. The latter have been challenged as perhaps not representative of the population from which the targeted individuals have been derived, although such criticisms have

been disputed (Tenney et al., 2021; Thatcher, 2016; Thatcher & Lubar, 2009).

Over the past century, outcome measures from the EEG and qEEG have been related to a broad variety of neurological functions as well as to neuropathologies. One of the earliest applications of the clinical EEG was to identify differences in the amplitudes of certain frequencies, both within and across homologous brain regions. For example, it has been well documented that neurological pathologies are frequently associated with increased slow-wave (delta, 0–4 Hz; theta, 4–8 Hz) amplitudes (Alexander et al., 2006; Ianof & Anghinah, 2017; Jelic, et al., 2000; Moretti, 2015; Pourmand, 1994; Thatcher, 2009; Thatcher et al., 2001; Wallace et al., 2001) and reduced faster wave (alpha, 8–12 Hz; beta, 12–30 Hz; and gamma, 30–100 Hz) amplitudes (Thatcher, 2009). Additionally, amplitude differences within a frequency and across homologous cortical regions have long been observed. Such amplitude asymmetries, most frequently and easily noticed in the alpha frequency, were thought to be indicative of neurological dysfunction (e.g., from documented cortical lesions) in early clinical reports, although nonpathological asymmetries were frequently found in neurotypical participants as well (Pourmand, 1994; Strobos, 1960). Focal amplitude asymmetries have been statistically associated with epileptiform activity, early infantile autism, lower intelligence, and individual differences in affective and motivational dispositions and are generally recognized as indicative of neuropathology when other supportive factors are present (e.g., neurotrauma; Dawson et al., 1982; Hagemann, 2004; Seneviratne et al., 2016; Thatcher et al., 2005).

More recently in the history of qEEG has been the discovery and assessment of connectivity measures among neurological networks. Such measures are rather commonsensical in the understanding of neurological trauma from blunt-force injuries to the brain, given the coup–contrecoup damage that results from viscous neurological tissue coursing back and forth from the site of injury to contralateral bony structures. The shearing of neurological tissue from such injuries results in serious structural and biochemical disturbances from diffuse axonal stretching and tearing in neurological networks across the brain (Bigler, 2013; Giza & Hovda, 2014; Mustafi et al., 2018; Seifert & Shipman, 2015; Thatcher et al., 1991). Millisecond electrical quantification of connectivity disturbances has only been obtainable with the development of qEEG algorithms. These measures include *coherence* and *phase differences* between related waveforms.

Coherence is an important statistical measure of the degree of linkage or coupling of two distinct areas of the brain, primarily in the cortex, and is often used as a measure of the functional association of different neural networks (Lubar, 1997; Thatcher, 2012). Coherence reflects the temporal stability of EEG waveform phase angle differences between two sites on the cortex, or phase locking. In the multichannel EEG, coherence is typically computed across all pairs of electrodes and frequencies. Although conceptually it is scored like a simple zero-order correlation coefficient between 0–1 and historically was computed as the simple correlation of amplitude, or power, over time, the more contemporary computation of coherence is much more complex. It involves phase and power relationships, is designed to be free of volume conduction properties of the brain, and is independent of amplitude alone (Hindriks, 2021; Thatcher, 2009; Thatcher et al., 1986). Coherence output is best interpreted as taking an inverted U-shape form, with low coherence (hypocoherence) reflecting either regional differentiation and specialization of functions or, in the case of documented neuropathology, impaired connections among neural networks, and high coherence (hypercoherence) suggesting a compensatory lack of differentiation or increased redundancy in cortical functioning. Both extremes are often seen in the reduced information processing efficiency with certain neuropathologies (Jelic et al., 1996; Thatcher, 2016; Wallace et al., 2001). Neurologically, a perfect coherence of 1 indicates a constant phase difference over time between signals and suggests some functional connectivity, and a coherence of 0 indicates random phase differences and less organized functionality. Thatcher (2016) has proposed a two-compartment model for coherence, with this measure reflecting phase synchrony among (a) long-axon pyramidal thalamo-cortical cells and (b) short-axon stellate and Martinotti cortico-cortical cells, and with the latter cells contributing the most to coherence measures among more proximal electrodes.

Phase differences reflect the cyclical differences between waveforms that one is interested in comparing. These differences occur quite commonly in the EEG when the wave patterns across any two channels do not coincide; overlapping waves having the same cycle are in-phase waves and those with different cycles are out of phase. Very simply, one can measure the phase difference between waves

having the same frequency by comparing analogous points on each wave in degrees of phase difference (e.g., 15 degrees out of phase). Obviously, with very complex and rapidly changing waveforms across multiple electrode sites such as seen in the EEG, the algorithms for calculating these phase differences are quite mathematically sophisticated (see Thatcher et al., 2009, for a guide in calculating EEG phase differences). In short, phase difference metrics reflect the degree of entrainment and synchronization, or locking, of EEG oscillations within a specified frequency band and represent a somewhat purer and more immediate measure of EEG connectivity than the time-averaged coherence measure (Chaturvedi et al., 2019; Thatcher et al., 2009; Thatcher et al., 2005). As with coherence, diminished or excessive phase synchronization can be suggestive of cognitive dysfunction. Thus, phase desynchronization has been reported for mild cognitive impairment, with excessive phase synchronization indicated for some stages of Alzheimer's disease (Alexander et al., 2006; Moretti, 2015). A related connectivity measure *phase lag index* which also quantifies phase synchronization, can suggest chaotic signal relationships across cortical networks for low values and synchronized or perfect phase locking and connectivity for high values (Stam et al., 2007; Thatcher et al., 2008). Phase measures are also free of volume conduction and amplitude characteristics of the EEG signal and serve as a measure of directional flow of information among electrode sites (Kuang et al., 2022; Stam et al., 2007; Thatcher, 2012).

Brodmann areas represent the most widely known and frequently cited mapping system of the primate brain, commonly utilized in MRI, qEEG, and other imaging programs. In the early 1900s, Korbinian Brodmann undertook an exhaustive cytoarchitectural study of the primate cerebral cortex, including humans, utilizing Nissl cell staining procedures to examine the histological structure and organization of brain cells (Brodmann, 1909; Garey, 2010). Using this process, Brodmann identified 52 regions that differed in cell structure and, over the decades since, these Brodmann areas have been closely associated with various functions. Contemporary neuroimaging software can target specific cortical regions and associate those regions with Brodmann areas having defined functions. For example, Broca's speech and language areas have been consistently localized to Brodmann areas 44 and 45 in the human brain. Comprehensive Brodmann maps have been prepared and may be utilized to identify brain regions corresponding to normal and pathological functioning, as in traumatic brain injury (TBI; Trans Cranial Technologies, 2012).

Concussion/Traumatic Brain Injury

One of the most common sources of neurological trauma is TBI. A review of the reported incidence of concussive head injuries over the past 3 decades indicates that TBI has reached epidemic proportions in the United States. Head injuries occur across the lifespan and from multiple sources, including recreational activities, sports, accidents, and military operations. Military and sport-related injuries share common characteristics in the diagnosis, treatment, and prognosis of TBI (Lew et al., 2007). For example, from 2000 to 2016, 352,612 military personnel were diagnosed with TBI, approximately 20% of U.S. combatants in the Iraq and Afghanistan theaters of war, with 82% of those suffering mild TBI (mTBI; Logan et al., 2013; Swanson et al., 2017). Indeed, TBI has been considered the "signature wound" of U.S. combatants (Connelly et al., 2017; Swanson et al., 2017). Additionally, as many as 3.8 million concussions from competitive sports occur yearly in the United States, with approximately 25% of all patients presenting to hospital emergency departments (ED) for sports and recreational head injuries (Daneshvar et al., 2011; Harmon et al., 2013; Kelly et al., 2001). The Centers for Disease Control (CDC) has reported increasing rates of mTBI-related ED visits between 2001 and 2010, with an 800% increase relative to all ED visits between 2006 and 2010 (Wright et al., 2013; Zhang et al., 2016). These statistics spotlight sport-related concussions as the leading cause of mTBI ED admissions among children and teens—with rugby, hockey, and American football having the highest frequency of concussion and with the NCAA reporting a doubling of concussion incidence in 2010 (Pfister et al., 2016; Zuckerman et al., 2015). Unfortunately, due to poor, uncertain, and avoidant diagnoses, as many as 50% of sport-related concussions go unreported and untreated, with evidence of cumulative effects following repeated injury (Harmon et al., 2013; Langlois et al., 2006; Pfister et al., 2016).

Strategies for the diagnosis of concussion/TBI (C/TBI) are variable and are heavily influenced by patient self-report. Although exams vary considerably in comprehensiveness, the current "gold standard" of concussion diagnosis is the medical examination, including a neurological evaluation of hearing, vision, reflex, balance, coordination, strength, sensation, memory, and attention span. Physicians sometimes follow up with referral for a formal cognitive test, such as the

ImPACT, and, if symptoms warrant, an imaging test (e.g., CAT scan). However, in lieu of rare formal neuroimaging, the diagnosis and recovery of mTBI are almost exclusively based on the self-report of the patient and testing for "soft," more peripheral, neurological signs. Even the medical neurological exam tests peripheral nerve and motor function rather than directly observing brain physiology. This omission is critical for judgements of return to play or duty, which involve the risk of repetitive injury.

It is well documented that athletes commonly hide and underreport symptoms and that a commanding officer will often waive the postconcussion recovery period if the injured military combatant is deemed critical to the mission and to the survival of fellow soldiers (Marshall et al., 2012; Teel et al., 2014). A recent review of return-to-play or -duty decisions found that most relied on symptom reports to determine recovery (Haider et al., 2017). The risks of neurological retraumatization based on self-reports of questionable validity—added to the diagnosis of concussion also based in large part on self-reports and visual observation of symptoms—have led the 2017 International Concussion in Sport Group (CISG) and the CDC to recommend the development of improved neurological measures of C/TBI (McCrory et al., 2017; Centers for Disease Control and Prevention [CDC], 2018). The most recent CDC clinical guidelines on mTBI point to weak diagnostic consistency; primary use of subjective judgments in identification, treatment, and return to play; and the critical need for objective evidence-based diagnostic and intervention strategies (CDC, 2018). These guidelines also encourage the use of computerized assessments for the multifactorial evaluation of mTBI and call for research-based evidence to improve diagnostics and treatment (CDC, 2018).

Given the unique and very specialized power and connectivity measures of "hard," more direct and centralized, neurological functioning available in the computer-administered qEEG, this technology is certainly poised to be a critical diagnostic and prognostic assessment tool for TBI. Indeed, over the past decades, qEEG has developed into a targeted TBI assessment instrument. The application of normative databases to plot departures from normality can be used to quantify and to localize brain trauma and to track return to normality during recovery, more confidently and accurately deciding recovery and return to play or duty without premature retraumatization (Slobounov et al., 2012; Thatcher, 2009). One normative database includes an empirically validated TBI Severity Index which reports the patient's severity and likelihood of TBI with confidence intervals across mild, moderate, and severe levels. Research on the Severity Index has reported a classification accuracy of 96.39%, a sensitivity index (true TBI positive) of 95.45%, and a specificity index (true TBI negative) of 97.44% (Thatcher et al., 2001; Thatcher et al., 1989). qEEG has been used to document concussions in sports-related injuries (Donaldson et al., 2018; Fickling et al., 2019; Thompson et al., 2005), civilian accidents (Thatcher et al., 1989), and in combat veterans (Lewine et al., 2019; Trudeau et al., 1998).

In a sample of 608 civilian chronic mTBI patients compared with 108 neurotypical controls, Thatcher et al. (1989) found three classes of neurophysiological injuries: (a) increased coherence and decreased phase in frontotemporal regions, (b) decreased anterior-posterior power differences, and (c) reduced posterior alpha EEG power. Similarly, in a well-controlled EEG study of 71 active duty and veteran personnel with chronic mTBI compared with 82 neurotypical control participants, Lewine et al. (2019) found significantly (a) increased relative theta power, (b) decreased relative alpha power, and (c) decreased interhemispheric beta coherence in mTBI patients relative to controls. These findings have been supported by MRI Diffusion Tensor Imaging (DTI) outcomes (Mustafi et al., 2018). In addition to these legacy, normative, localization, diagnostic, and quantitative advantages of the qEEG, it is important to note that EEGs are much less expensive (~1/10th the cost) and far more portable (e.g., can be taken to the locker room of a sporting event or to a military field hospital) than MRIs and other imaging techniques. McLoughlin et al. (2014) have noted that EEG is the most portable and noninvasive among neuroimaging methodologies and holds remarkable promise for the identification of neuropathology biomarkers.

Recovery from mTBI is conventionally split into three phases: acute, subacute, and chronic. In general, the acute phase occurs within the first 24–48 hr postinjury; the subacute phase is from 2 days up to 3 weeks postinjury; and the chronic phase extends from 3 weeks and beyond (Liu et al., 2008; Svetlov et al., 2015; Toshkezi et al., 2018; Tshibanda et al., 2009; Weiss et al., 2007). An informal review of 30 EEG controlled-research investigations published over the past 2 decades reveals only five studies that examined the truly acute effects of diagnosed concussion on the EEG, and these studies utilized a reduced montage of frontal electrode measurements and a proprietary machine learning algorithm (Bazarian et al., 2021; Hanley et al., 2018; Hanley et

al., 2017; Jacquin et al., 2018; Wilde et al., 2020). The vast majority of studies of qEEG effects of concussion have been chronic investigations. It has been well documented that most mTBI patients either recover symptomatically after approximately 10 days and return to play or duty, risking further neurological injuries which obfuscate subsequent neurological measures, or they seek alternative medical or other therapy treatments for their injuries if their symptoms continue, treatments which can have an impact on subacute and chronic phase EEG testing (Marshall et al., 2012; Slobounov et al., 2012; Swanson et al., 2017; Wallace et al., 2001). It is the purpose of this research project to examine the more immediate and purer acute effects of diagnosed concussion on comprehensive 19-channel qEEG assessment measures.

Methods

Participants

As noted above, studies of concussion/mTBI patients during the acute phase of injury have been uncommon in the qEEG literature. No doubt this is a result of the difficulty in accessing patients at the time of injury and of administering a complex, computer-based, multichannel scan of their brain activity. Certainly, in the military combat situation, immediate access to injured combatants is nearly impossible and must await movement and care of the injured to a field medical facility. As well, on the professional or recreation sports field, access to an injured player must wait for their transport to an off-field waiting area, locker room, or field medical facility. Most frequently, patients are not accessible for a formal EEG study for days or even weeks to months postinjury. Even though EEG technology has become quite miniaturized, with multichannel units now book-sized and either self-contained or operating from a computer laptop, acute patient access for research purposes remains a difficulty.

At Northern Arizona University (NAU), we found ourselves in a somewhat fortuitous situation for the implementation of an acute concussion study of this nature. Flagstaff, Arizona, is a relatively small town located at the base of a dormant volcano, within close proximity to the Grand Canyon and to many other major hiking, cross-country and downhill skiing, snowboarding, mountain-biking, and rock-climbing venues, and known for its outdoors lifestyle. Additionally, Flagstaff is home of a large, young, residential, and quite active university community characterized by students who ride motorized and self-propelled skateboards around campus, often at high speeds, and must often walk to classes on icy and snow-packed streets and sidewalks. Additionally, as for most any university, there are many collegiate and intramural sports activities occurring throughout the year. As a result of these many rather high-risk activities, the NAU Campus Health Services (CHS) reports between 50–70 cases of diagnosed concussion/mTBI per academic year. And, while the ages of our university students are very similar to those of young military combatants who suffer head injuries, most of the concussions reported to CHS occur during the performance of enjoyable recreational activities, lessening the conflation of mTBI with PTSD diagnoses more common in combat and other traumatic injuries. Furthermore, potential concussion participants need only walk across the street from CHS or a short distance from their dormitory to our laboratories to participate in a research study to be accessed rather soon after injury. We still must schedule participant runs around their busy academic and work schedules, producing some delays, but we have found that we can generally access concussion patients within 3 days postinjury, most often sooner.

Consequently, we recruited a cohort of 24 acute concussion patients from CHS for participation in a larger investigation of the enhanced diagnostics, prognostics, and treatment of concussion/mTBI utilizing combined computer-brain interface and standard protocols. Recently concussed patients, each formally diagnosed by a CHS physician, were given a flyer for the study with contact information. Those interested in participating signed an internal HIPAA release form giving their physician permission to share their medical information with the PIs of the study. The CHS physician administered the routine Acute Concussion Evaluation (ACE) concussion assessment (Gioia et al., 2008) and a standard neurological examination and rendered an ICD-10 diagnosis. Concussed patients then contacted the primary PI and were interviewed via phone regarding the participation criteria. Inclusion criteria were (a) age 18–40 years, (b) physician-diagnosed concussion/mTBI within 24–48 hr of injury, (c) no other history of concussion/TBI within 1 year, (d) not currently taking any psychoactive medications or drugs or able to undergo a 24-hr washout, and (e) no diagnosed neurological disorder within 5 years of the study. A matched control cohort of 20 neurotypical participants was also recruited from a local online research participation recruitment website. Controls were individually matched to concussed patients by age range, biological gender, handedness, student status, and quality of the EEG recording and met

identical inclusion criteria with the exception of a recent concussion.

Procedures

All concussion patients were scheduled for their initial assessments within a target date of 24–48 hr postinjury. Due to scheduling conflicts, some of the patients had to be scheduled outside of this window but they were required to still be experiencing the same level of symptoms as immediately after injury. Control participants were scheduled within the same academic semesters as the concussion patients. All participants were invited to the laboratories for a 2.5-hr assessment session and initially completed informed consent, demographic, and contact forms. Additionally, all participants completed the Post-Concussion Symptom Scale (PCSS), a 22-item self-report Likert rating checklist of concussion symptoms (McLeod & Leach, 2012); the Brief Symptom Inventory (BSI), a 53-item self-report Likert rating inventory of psychopathology and psychological distress including measures of somatization, obsessive-compulsivity, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and general psychological distress (Derogatis & Melisaratos, 1983), the latter instrument included as an overall measure of psychological distress and to assess psychopathology which could potentially influence the EEG (Tenney et al., 2021); and a battery of standard concussion assessment instruments not analyzed in this report of acute outcomes.

Each participant also received a 19-channel qEEG comprised of, in this order, 10 min eyes closed, 10 min eyes open, and 22 min of a cognitive/attentional challenge (Test of Variables of Attention [TOVA]), with each EEG recorded continuously and stored in separate data files. The TOVA is a computerized continuous performance, go/no-go task that assesses attentional abilities across five dimensions: response time, response time variability, inattention (errors of omission), impulse control (errors of commission), and *d* prime (ratio of hits to false alarms, or the ability to discriminate target from nontarget events in one's environment; The TOVA Company, 2024). In addition to allowing the recording of cortical electrical activity during a rather demanding cognitive/attentional challenge for both concussed and neurotypical participants, the TOVA results allowed a further comparison of both cohorts on each of these attentional measures. The qEEGs were recorded with a Mitsar 201 24-channel amplifier, utilizing WinEEG recording and processing software (Mitsar Co. Ltd, St. Petersburg, Russia), further processed with ANI NeuroGuide neuroanalysis software (Applied Neuroscience, Inc., St. Petersburg, Florida), and a 24-channel International 10-20 electrocap system (Electro-Cap International, Eaton, Ohio) with impedances adjusted to < 5 kΩ. EEG data were sampled at 250 Hz, referenced to linked earlobes, and bandpassed at 0.3–50 Hz with notch filter set at 55–65 Hz. All data were carefully and individually artifacted utilizing ANI NeuroGuide Automatic Editing software with automated rejection of drowsiness, eye movement, and muscle artifact exceeding a *Z*-score threshold of 2.00. All files were additionally visually and blindly inspected by the PI for any remaining artifacts, including evidence of sleep onset, with offending epochs removed, and split-half and test–retest reliabilities held at > .90. Absolute EEG amplitude was computed from the 19 scalp electrodes for delta, theta, alpha, and beta frequency bands. EEG coherence and phase differences were computed for all electrode pairs utilizing automated computations of algorithms described in Thatcher et al. (2001, 2009).

Participants were debriefed at the conclusion of the study, and each participant was compensated for their participation. As the concussed participants were active medical patients, any worsening of symptoms at any point in the study was noted and such patients were referred back to their health care professional at CHS for further care. Each patient had improved by conclusion of the study and had returned to normal activities. All procedures were previously approved by the NAU Institutional Review Board for the protection of human subjects.

Design and Analysis

Our hypotheses were that acute concussion and neurotypical groups would significantly differ in low frequency, delta and theta, power with the concussed groups scoring with higher power in these frequencies, and would significantly differ in hyper- or hypocoherence and phase differences at selected frequencies. We predicted that these effects would be seen in all three assessment conditions, with most remarkable differences seen in the eyes-closed and TOVA conditions. We also predicted that the concussion group would score in a more impaired direction on the PCSS and on all five TOVA measures compared with the neurotypical group. The outcomes reported here represent a 2 (groups) x 3 (conditions) between dependent (matched) groups design, with concussed and neurotypical groups individually matched by biological gender, age range (within 1–3 years over 18–24 years of age), handedness, student status,

and quality of the EEG recording and examined across three conditions (eyes closed, eyes open, and cognitive/attentional challenge). Dependent variables were EEG absolute power and amplitude asymmetry across four frequencies (delta, theta, alpha, and beta) and two connectivity measures (coherence and phase difference) across the same four frequencies. All EEG statistical and neuroimaging analyses were conducted utilizing ANI NeuroGuide NeuroStat and NaviStat statistical computational software available within the ANI NeuroGuide EEG analysis platform. The software utilized for our neuroimaging targets the center voxel of each Brodmann area in order to estimate the current source density of the respective area and to plot connectivity patterns. Demographic and questionnaire analyses were conducted utilizing SPSS statistical software (Version 29.0.0.0, 2022, IBM Corp., Armonk, NY). For all analyses, assessment conditions, power and connectivity functions, EEG frequencies, and Brodmann areas were treated by convention as orthogonal measures, and hypothesized effects were evaluated as planned comparisons with no corrections for potential inflation of Type I error. However, all comparisons were further subjected to Bonferroni corrections conducted within conditions, functions, frequencies, and Brodmann areas to reduce the potential false discovery rate (Lewine et al., 2019; Pagano, 2010).

A statistical power analysis was conducted to determine if our planned cohort numbers were sufficient to generate satisfactory power. For a moderate effect size of 0.5 and alpha = 0.05, a total dependent groups *t*-test sample size of 36 would be sufficient to produce a power of 0.90 for each analysis. Thus, our total paired sample size of 38 was adequate to test for potential significant effects.

Results

Sample Characteristics

Demographic and questionnaire data for each of our 24 concussed and 20 neurotypical control participants are presented here in text and in Table 1. As noted above, each of our participants reported no head injuries nor unconsciousness within 1 year nor diagnosed neurological disease within the previous 5 years of the study. Although participants were matched by age range, biological gender, handedness, and student status, mean age did not significantly differ between groups (concussed, 20.33; neurotypicals, 19.70, $t(42) = .93$, $p = .36$). Our sample was primarily female (66%), with 10 and 5 males in the concussed and neurotypical groups, respectively, necessitating omitting 5 males from the dependent groups comparisons (5 males with excessively noisy EEGs or who prematurely dropped from the full study were omitted from the paired-subjects' comparisons). There were two matched left-handed participants in each group, and all participants were enrolled students. Additionally, both groups did not significantly differ in cultural identity (concussed/neurotypical: White American, 19/14; Hispanic American, 4/5; African American, 0/1; Unidentified, 1/0; $\chi^2 = 2.53$, $p = .47$), current pregnancy (0/0), prior epilepsy (0/0), current chronic pain (4/1, Fisher's Exact $p = .36$), current peripheral neuropathy or nerve damage (0/0), current antianxiety medication use (4/0, Fisher's Exact $p = .11$), current asthma medication use (0/0), current birth control use (5/4, Fisher's Exact $p = 1.00$), current blood pressure medication use (0/0), current diabetic medication use (0/0), current heart medication use (0/0), current prescription pain medication use (0/0), current unspecified other medications (5/1, Fisher's Exact $p = .20$), or in current use of the following recreational drugs more than 1 time per week: amphetamines (0/0), cocaine (0/0), pain killers (4/0, Fisher's Exact $p = .11$), downers (0/0), uppers (0/0), ecstasy (2/1, Fisher's Exact $p = 1.00$), and other unspecified recreational drugs (2/0, Fisher's Exact $p = .49$). Our sample of participants did show trends toward between-group differences in current antidepressant medication use (5/0, Fisher's Exact $p = .05$) and in marijuana use more than once per week (7/1, Fisher's Exact $p = .05$), and significantly greater alcohol use more than once per week for the concussion group (11/0, Fisher's Exact $p < .001$). Thus, our participants also matched quite well culturally and in most medications and recreational drug usages, with the exception of more frequent alcohol use and somewhat greater antidepressant medication and marijuana use in our concussion patients. All participants using medications or drugs abstained from use within 24 hr of testing.

Each concussion participant entered the study with a formal ICD-10 diagnosis of concussion rendered by a medical doctor and a completed ACE concussion assessment. On some occasions, ACE scores had to be completed by the PI based on PCSS scores at point of entry. As ACE scores are based on a patient self-report checklist in the ACE questionnaire which is identical to the patient-completed checklist on the PCSS, minus one item, unavailable ACE scores could easily and accurately be generated for the few patients with missing physician ACE scores. Similarly, ACE scores were completed by the PI for each neurotypical participant on the basis of their PCSS self-report of symptoms. Each participant also

completed a PCSS concussion symptom checklist and a BSI assessment of psychological distress at the initial assessment, and during their qEEG each participant completed the TOVA test. Only the BSI/GSI average total score is reported here, as BSI psychopathology sub-scores were not a critical part of this analysis. ACE, PCSS, and BSI questionnaires were blindly scored by the researchers and are here reported as raw scores. The TOVA test is automatically and blindly scored and reported by the TOVA software. As noted above, the TOVA scoring generates multiple measures of cognitive/attentional abilities, including errors of omission (inattentiveness), errors of commission (impulsivity), response time (reaction time), response time variability (variability in reaction time), and an overall attentional measure called *d* prime. Additionally, two experimental indices were considered in our analyses, an Impulsivity Index and an Attention Comparison Score, the latter comparing the score with those from independently diagnosed ADHD individuals. These raw score measures are standardized and are then compared with the current, relevant TOVA normative database for departures from normality. For ease of explication, these standardized scores may then be converted into *Z*-scores having a mean of 0 and a standard deviation of 1. Each *Z*-score thus represents the number of standard deviation units the individual score differs from the mean of the normative group. The greater the departure from 0, the more different from the norm the score is, and, in general, the more negative the score, the poorer the performance. Group means, standard deviations, and significance statistics for each of these instruments are presented in Table 1.

Review of Table 1 indicates that on average our concussion participants endorsed over 14 of the 22 symptoms of concussion on the ACE instrument, significantly higher than the 1.65 symptoms identified by our neurotypical controls. Rating the severity of these symptoms on the PCSS revealed a similar significant difference between the two groups, with the mean of 43.33 placing the concussed patients at the top end of the *very high* (just below *extremely high* and near the 98th percentile) concussion symptom score classification range relative to healthy young women in the Lovell et al. (2006) normative study.

BSI Global Severity Index (GSI) scores were used as a measure of psychological distress for this study. BSI/GSI scores were likewise significantly different between groups, with our concussion sample scoring significantly higher on psychological distress than our neurotypical controls. However, GSI average scores for our concussed patients (.85) were only somewhat higher (+.33 *SD* units), and means for our neurotypical participants (.17) were much lower (−1.29 *SD* units) than those values

Table 1

Assessment Variable Statistics by Group

Variable	Concussion Group		Neurotypical Group		*t*	*p*
	n	*M* (*SD*)	*n*	*M* (*SD*)		
ACE	24	14.46 (3.54)	20	1.65 (2.60)	13.43	< *.001*
PCSS	24	43.33 (14.74)	20	3.70 (5.29)	12.26	< *.001*
BSI/GSI	20	0.85 (0.46)	20	0.17 (0.16)	6.32	< *.001*
TOVA Omission Errors	24	−4.36 (8.50)	20	−0.95 (3.70)	−1.77	*.043*
TOVA Commission Errors	24	−1.30 (2.38)	20	−0.72 (1.30)	−0.97	.17
TOVA Response Time	24	0.29 (1.34)	20	1.25 (0.89)	−2.85	*.003*
TOVA Response Variability	24	−2.10 (3.22)	20	−0.79 (2.19)	−1.55	.06
TOVA *d* Prime	24	−1.37 (1.29)	20	-0.82 (1.05)	−1.55	.07
TOVA Impulsivity Index	24	1.35 (1.24)	20	1.45 (0.67)	−0.33	.37
TOVA Attention Comparison	24	−1.44 (4.30)	20	1.70 (3.30)	−2.67	*.005*

Note. ACE = Acute Concussion Evaluation; PCSS = Post-Concussion Symptom Scale; BSI/GSI = Brief Symptom Inventory Global Severity Index Average Scores; TOVA = Test of Variables of Attention. ACE, PCSS, and BSI scores are raw scores. TOVA scores are standardized *z*-scores having a mean of 0 and a standard deviation of 1. All *t*-tests are 1-tailed as per *a priori* predictions.

reported for normal college females (.71) in an earlier study by Cochran and Hale (1985). These results suggest that while our sample of concussion patients reported significantly more psychological distress following their injury than our neurotypical controls, our concussed patients were not significantly more distressed than a normative sample of college females.

TOVA testing during the qEEG also revealed, as predicted, significant differences between groups. Relative to neurotypicals, concussion participants showed significantly more errors of omission, $t(32.6) = -1.77$, $p = .04$, and slowed response time $t(40.11) = -2.85$, $p = .003$, with trends toward increased response time variability, $t(42) = -1.55$, $p = .06$, and increased d prime, $t(42) = -1.55$, $p = .07$. Additionally, TOVA concussed patients' overall responses during qEEG were much more similar to responses of attention-deficit/hyperactivity disorder (ADHD) patients than were those of our neurotypical group, $t(42) = -2.67$, $p = .005$. These results indicate that our head injury patients were having attentional, reaction time, and stimulus discrimination difficulties (problems differentiating relevant from nonrelevant events in one's environment) and were responding more like ADHD individuals.

Quantitative EEG Results

Eyes-Closed Assessment. The qEEG paired comparisons between conditions (concussed minus neurotypicals, $N = 19$ matched pairs) outcomes for the eyes-closed assessment condition are presented in Table 2 for FFT absolute power, amplitude asymmetries across homologous sites, coherence, and phase differences across each frequency (delta, theta, alpha, beta). Significance values and effect sizes are presented for Brodmann area hubs (concentrated regions of neural interconnectivity within a Brodmann area) and not for electrodes or electrode pairs as the former are more meaningful and relevant to concussion symptom manifestation.

Table 2

Eyes-Closed qEEG Power and Connectivity Group Differences by Frequency Statistical Significance, Effect Size, and Brodmann Areas

Function	Delta *p Value, Effect Size, and Brodmann Area*	Theta *p Value, Effect Size, and Brodmann Area*	Alpha *p Value, Effect Size, and Brodmann Area*	Beta *p Value, Effect Size, and Brodmann Area*
Absolute Power	+*.037*, 1.06, (L)8,9	n.s.	n.s.	n.s.
	+*.045*, 1.02, (R)10	n.s.	n.s.	n.s.
	+*.043*, 1.03, (R)7	n.s.	n.s.	n.s.
Amplitude Asymmetry	n.s.	n.s.	n.s.	n.s.
Coherence	n.s.	−*.047*, 1.01, (L)10-37	n.s	n.s.
	n.s.	−.035, 1.07, (L)8,9-4,3	n.s.	n.s.
	n.s.	−.009, 1.38, (L)8,9-7	−*.005*, 1.51, (L)8,9-7	n.s.
	n.s.	−.046, 1.01, (R)8,9-7	n.s.	n.s.
	n.s.	−.038, 1.06, (L)8,9-18	n.s.	n.s.
	n.s.	−*.002*, 1.70, (L)8,9-37	n.s.	n.s.
	n.s.	−.039, 1.05, (R)8,9-37	n.s.	n.s.
	n.s.	−*.004*, 1.55, (L)4,3-7	−*.006*, 1.47, (L)4,3-7	−*.001*, 1.85, (L)4,3-7
	n.s.	−.028, 1.13, (L)4,3-18	−*.003*, 1.62, (L)4,3-18	n.s.
	n.s.	−*.006*, 1.47, (L)4,3-37	−*.016*, 1.25, (L)4,3-37	−.027, 1.13, (L)4,3-37
	n.s.	−.047, 1.01, (L)7-21	−*.015*, 1.27, (L)7-45	n.s.
	n.s.	−*.008*, 1.41, (L)7-37	n.s.	−.040, 1.04, (L)7-31
	n.s.	−.030, 1.11, (R)7-37	n.s.	−*.016*, 1.25, (R)7-37
	n.s.	−*.025*, 1.15, (L)18-21	n.s.	−.035, 1.07, (L)18-37
	n.s.	−*.006*, 1.47, (L)45-37	n.s.	−.032, 1.10, (R)18-37
	n.s.	−*.010*, 1.36, (L)21-37	n.s.	n.s.
	n.s.	−*.022*, 1.18, (R)21-37	n.s.	n.s.

Table 2 (Cont.)
Eyes-Closed qEEG Power and Connectivity Group Differences by Frequency Statistical Significance, Effect Size, and Brodmann Areas

Function	Delta *p Value, Effect Size, and Brodmann Area*	Theta *p Value, Effect Size, and Brodmann Area*	Alpha *p Value, Effect Size, and Brodmann Area*	Beta *p Value, Effect Size, and Brodmann Area*
Phase Difference	−*.029*, 1.12, (R)10-4,3	−*.038*, 1.06, (R)10-8,9	+.049, 1.00, (L)10-18	n.s.
	n.s.	n.s.	+.040, 1.04, (R)10-47	n.s.
	−.048, 1.00, (R)8,9-4,3	n.s.	+*.011*, 1.34, (L)8,9-18	n.s.
	−*.013*, 1.30, (L)8,9-45	+*.003*, 1.62, (R)8,9-21	−*.003*, 1.62, (L)8,9-45	n.s.
	n.s.	n.s.	+.038, 1.06, (L)8,9-37	n.s.
	−.041, 1.04, (R)4,3-18	+*.016*, 1.25, (L)4,3-37	n.s.	n.s.
	−.026, 1.14, (L)4,3-45	n.s.	n.s.	n.s.
	−*.037*, 1.06, (R)7-18	n.s.	+*.044*, 1.02, (R)7-21	n.s.
	−*.046*, 1.01, (R)18-37	n.s.	+*.021*, 1.19, (L)18-45	n.s.
	n.s.	n.s.	+*.043*, 1.03, (L)45-37	+*.022*, 1.18, (L)45-37

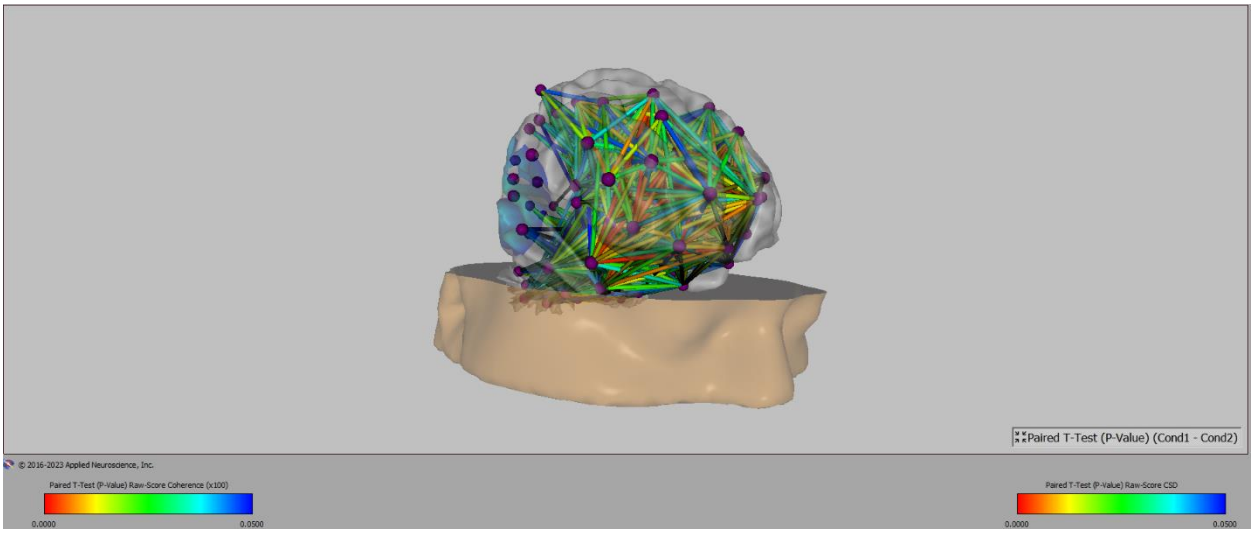
Note. + = concussed group higher; − = concussed group lower; for coherence and phase, a dash (-) between Brodmann areas indicates neural connectivity pathway between the indicated Brodmann areas. Bonferroni adjusted significant *p* values are in italics. Cohen's (1988) effect size ranges: small = .00–.20; medium = .21–.79; large = .80+.

For the eyes-closed condition, absolute power differences between groups were scant and marginally significant for higher delta power in the concussed group, but with large effect sizes observed across four Brodmann areas, 7, 8, 9, and 10. These areas are involved in personal spatial orientation and visual-spatial attention and focus (R7), muscle and executive control and planning, working memory, language processing, verbal fluency, empathy, and emotional processing (L8 and 9), and attention, recognition, and recall and risk benefit analysis (R10; Trans Cranial Technologies, 2012). Increased very slow-wave power in these regions may suggest impaired functioning in these activities. There were no significant amplitude asymmetry differences between groups.

For coherence, there were highly significant and very large effect size differences between groups within the theta band, with fewer effects in the alpha and beta bands, all indicating hypocoherence (impaired communication) across frequencies for the concussed group. Most frequent were theta hypocoherence connectivities between Brodmann areas 8 and 9 (frontal eye fields and dorsolateral-prefrontal cortex [DL-PFC]) on the one hand and areas 3, 4, 7, 18, and 37 (postcentral gyrus, primary motor cortex, somatosensory association cortex, secondary visual cortex, and fusiform gyrus, respectively) on the other, suggesting potential communication difficulties between frontal executive planning and control and working memory processes (8 and 9) and sensorimotor processing, control, and execution (3 and 4), spatial orientation and visuomotor coordination (7), visuomotor organization (18), and visual analysis, recognition, and association (37) processes. Hypocoherence connectivity anomalies were likewise found across the theta, alpha, and beta frequencies between Brodmann areas 3 and 4 on the one hand and 7, 18, and 37 on the other, suggesting potential sensorimotor processing and execution difficulties involved in visuospatial analyses. Similar visuospatial orientation, association, analysis, self-referential, empathic, and related semantic expression deficits are consistent with theta, alpha, and beta hypocoherences between areas 7, 18, 21, 31, 37, and 45. Figure 1 presents swLORETA neuroimages of eyes-closed concussed minus neurotypical significant theta coherence differences.

Phase difference effects were somewhat mixed, with lower phase differences (synchronization) for the concussed group within the delta band and higher phase differences (desynchronization) for the concussed group primarily within the alpha band. Interestingly, these phase difference connectivity anomalies were largely localized to the same Brodmann areas as found for coherence, suggesting desynchronization of these waveforms and the same communication impairments for theta, alpha, and beta. However, in the delta band, waveforms within these same Brodmann areas appeared to be significantly and highly synchronized, which could further interfere with communication during synchronized slow-wave activity in these areas.

Figure 1. *ANI NaviStat swLORETA NeuroImage of Eyes-Closed Concussed Minus Neurotypical Significant Theta Coherences Differences, Right Frontal View*.



Note. Purple spheres represent center voxels of Brodmann areas referred to in text. Colored bars represent the significance of connectivity pathways among Brodmann areas. Colored scales reflect significance levels of differences (red end of color bar → difference p = .0000). Note significant frontal executive processing connectivity anomalies.

Eyes-Open Assessment. Outcomes for the eyes-open resting focus assessments are presented in Table 3 for FFT absolute power, amplitude asymmetries, coherence, and phase differences across the same frequencies of delta, theta, alpha, and beta. Similarly, statistical significance and effect size values are presented for respective Brodmann areas.

Generally, the eyes-open assessment condition revealed involvement of the same Brodmann areas, but with a somewhat different configuration of coherence and phase difference effects. Again, absolute power was only significant for an increase in delta power for the right somatosensory association cortex (Brodmann area 7) suggesting impaired functioning in spatial orientation and visual spatial attention and focus during eyes-open attention. There were no significant amplitude asymmetry effects for this condition.

Theta and beta coherence measures indicated the same hypocoherences in communication pathways involving frontal executive planning, control, and working memory (areas 8 and 9), sensorimotor processing, control, and execution (areas 3 and 4), spatial orientation and visuomotor organization (areas 7 and 18), visual analysis, recognition, and association (area 37), and self-referential, empathic, and semantic processing (areas 21, 31, and 45). Functions involving these areas would correspondingly be expected to be impaired for concussed patients with these observed hypocoherences. Within the delta band, there were significant hypocoherences between the left DL-PFC (area 9) and the frontal eye fields (area 8) executive motor planning areas on the one hand and primary sensorimotor cortices (areas 3 and 4) on the other, between primary sensorimotor areas (3 and 4) and somatosensory association cortex (area 7), and between somatosensory association cortex (area 7) and the fusiform gyrus (area 37), all suggesting visuo-sensorimotor integration difficulties. Interestingly, there were no coherence anomalies for the alpha band.

Table 3

Eyes-Opened qEEG Power and Connectivity Group Differences by Frequency Statistical Significance, Effect Size, and Brodmann Areas

Function	Delta *p Value, Effect Size, and Brodmann Area*	Theta *p Value, Effect Size, and Brodmann Area*	Alpha *p Value, Effect Size, and Brodmann Area*	Beta *p Value, Effect Size, and Brodmann Area*
Absolute Power	+*.027*, 1.13, (R)7	n.s.	n.s.	n.s.
Amplitude Asymmetry	n.s.	n.s.	n.s.	n.s.
Coherence	n.s.	n.s.	n.s	−.026, 1.14, (L)10-18
	n.s.	−*.042*, 1.03, (L)10-37	n.s.	−*.012*, 1.32, (L)10-37
	−*.042*, 1.03, (L)8,9-4,3	−*.002*, 1.70, (L)8,9-4,3	n.s.	n.s.
	n.s.	−*.006*, 1.47, (L)8,9-7	n.s.	n.s.
	n.s.	−.022, 1.18, (R)8,9-7	n.s.	n.s.
	n.s.	−.035, 1.07, (L)8,9-18	n.s.	n.s.
	n.s.	−*.004*, 1.55, (L)8,9-37	n.s.	n.s.
	n.s.	−.033, 1.09, (R)8,9-37	n.s.	n.s.
	−*.032*, 1.10, (L)4,3-7	−.011, 1.34, (L)4,3-7	n.s.	−*.004*, 1.55, (L)4,3-7
	n.s.	−.039, 1.05, (L)4,3-18	n.s.	n.s.
	n.s.	−.036, 1.07, (R)4,3-47	n.s.	−.038, 1.06, (L)4,3-45
	n.s.	−*.010*, 1.36, (L)4,3-37	n.s.	−.015, 1.27, (L)4,3-37
	n.s.	n.s.	n.s.	−.032, 1.10, (R)4,3-37
	n.s.	−*.010*, 1.36, (L)4,3-37	n.s.	−.015, 1.27, (L)4,3-37
	n.s.	−.028, 1.13, (L)7-45	n.s.	−.022, 1.18, (L)7-45
	−*.046*, 1.01, (L)7-37	−*.010*, 1.36, (L)7-37	n.s.	−.047, 1.01, (L)7-37
	n.s.	n.s.	n.s.	−.019, 1.21, (R)7-37
	n.s.	n.s.	n.s.	−*.046*, 1.01, (R)18-37
	n.s.	−*.017*, 1.24, (L)45-37	n.s.	−*.022*, 1.18, (L)45-37
	n.s.	−*.016*, 1.25, (R)47-37	n.s.	n.s.
	n.s.	−*.041*, 1.04, (L)21-37	n.s.	n.s.
Phase Difference	+*.008*, 1.41, (L)10-8,9	n.s.	+*.038*, 1.06, (R)10-4,3	n.s.
	+*.008*, 1.41, (L)10-21	n.s.	n.s.	n.s.
	−*.039*, 1.05, (R)4,3-18	n.s.	n.s.	n.s.
	−*.044*, 1.02, (R)7-18	n.s.	n.s.	+*.046*, 1.01, (L)45-37

Note. + = concussed group higher; − = concussed group lower; for coherence and phase, a dash (-) between Brodmann areas indicates neural connectivity pathway between the indicated Brodmann areas. Bonferroni adjusted significant *p* values are in italics. Cohen's (1988) effect size ranges: small = .00–.20; medium = .21–.79; large = .80+.

Phase differences during the eyes-open condition were again mixed and much less in number than for eyes closed. Desynchronized (+) executive and self-reflective functional connectivity within the delta and alpha bands from the left frontal pole of the DL-PFC (area 10) to proximal executive motor planning (left areas 8 and 9) and more distal semantic processing areas (left area 21) and to sensorimotor areas (3 and 4) suggest impaired functions within these sensorimotor domains. Similarly desynchronized beta phase connectivity between Broca's area (45) and the fusiform gyrus (area 37) would suggest word-finding and verbal expressive difficulties as well. Negative delta phase difference scores between right sensorimotor cortex (areas 3 and 4) and the somatosensory association cortex (area 7) on the one hand and secondary visual cortex (area 18) on the other would indicate slow-wave synchronization of these visual sensorimotor functions.

TOVA Assessment. Given the high cognitive information processing demands required for our college student population, we chose to administer an additional cognitive/attentional assessment challenge to our participants. The TOVA test required sustained attention for 22 min to a repetitive and monotonous go/no-go task necessitating immediate button press to a defined target and inhibition of presses to a nontarget. Table 1 results above demonstrated significant reaction time delays and inattention in our concussed participants, with trends toward increased variability in reaction time and in overall attentional skills, and with significant similarity to diagnosed ADHD patients relative to matched neurotypicals. To determine potential EEG anomalies that might suggest these attentional deficits, we computed the same absolute power, amplitude asymmetries, coherence, and phase differences between our concussed patients and our matched controls during the TOVA challenge. Table 4 shows these results.

As for the eyes-closed and eyes-open conditions, there were minimal to no significant between-groups differences in absolute power or in amplitude asymmetry during the TOVA test. Only a significant increase in alpha and beta asymmetry was found for Brodmann area 7, the somatosensory association cortex. This effect could possibly indicate a significant deterioration in visual-motor coordination, particularly in purposeful skilled movements such as reaching and grasping for an object, or perhaps reaction time in pressing the TOVA switch for our concussed patients.

Table 4

TOVA qEEG Power and Connectivity Group Differences by Frequency Statistical Significance, Effect Size, and Brodmann Areas

Function	Delta *p Value, Effect Size, and Brodmann Area*	Theta *p Value, Effect Size, and Brodmann Area*	Alpha *p Value, Effect Size, and Brodmann Area*	Beta *p Value, Effect Size, and Brodmann Area*
Absolute Power	n.s.	n.s.	n.s.	n.s.
Amplitude Asymmetry	n.s.	n.s.	+*.009*, 1.38, (R)7	+*.017*, 1.24, (R)7
Coherence	−*.019*, 1.21, (L)8,9-4,3	−*.003*, 1.62, (L)8,9-4,3	−.047, 1.01, (L)8,9-4,3	n.s.
	n.s.	−.048, 1.00, (R)8,9-4,3	n.s.	n.s.
	n.s.	−*.002*, 1.70, (L)8,9-7	n.s.	−*.006*, 1.47, (L)8,9-7
	n.s.	−.030, 1.11, (R)8,9-7	n.s.	n.s.
	n.s.	−.030, 1.11, (L)8,9-18	n.s.	−.026, 1.14, (L)8,9-18
	n.s.	−.015, 1.27, (L)8,9-21	n.s.	n.s.
	n.s.	−*.005*, 1.51, (L)8,9-37	n.s.	−*.005*, 1.51, (L)8,9-37
	n.s.	−.034, 1.08, (R)8,9-37	−.026, 1.14, (R)8,9-37	n.s.
	n.s.	−*.003*, 1.62, (L)4,3-7	n.s.	−*.001*, 1.85, (L)4,3-7
	n.s.	−.041, 1.04, (L)4,3-18	n.s.	n.s.
	n.s.	−.025, 1.15, (R)4,3-47	n.s.	n.s.
	n.s.	−.013, 1.30, (L)4,3-37	n.s.	−.027, 1.13, (L)4,3-37
	n.s.	n.s.	n.s.	−.022, 1.18, (R)4,3-37
	n.s.	−.017, 1.24, (L)7-45	n.s.	−.039, 1.05, (L)7-45
	n.s.	−.029, 1.12, (R)7-47	n.s.	n.s.
	n.s.	-*.008*, 1.41, (L)7-37	n.s.	n.s.
	n.s.	−.034, 1.08, (R)7-37	−*.040*, 1.04, (R)7-37	−*.013*, 1.30, (R)7-37
	−*.023*, 1.17, (L)18-37	−*.011*, 1.34, (L)18-37	n.s.	n.s.
	n.s.	−*.011*, 1.34, (L)45-37	n.s.	−*.035*, 1.07, (L)45-37
	n.s.	−*.045*, 1.02, (R)47-37	n.s.	n.s.
	n.s.	−*.041*, 1.04, (L)21-37	n.s.	n.s.

Table 4 (Cont.)
TOVA qEEG Power and Connectivity Group Differences by Frequency Statistical Significance, Effect Size, and Brodmann Areas

Function	Delta *p Value, Effect Size, and Brodmann Area*	Theta *p Value, Effect Size, and Brodmann Area*	Alpha *p Value, Effect Size, and Brodmann Area*	Beta *p Value, Effect Size, and Brodmann Area*
Phase Difference	−.035, 1.07, (L)10-8,9	n.s.	n.s.	n.s.
	−.018, 1.23, (R)10-8,9	n.s.	n.s.	n.s.
	−*.004*, 1.55, (R)10-4,3	n.s.	n.s.	n.s.
	−.046, 1.01, (L)10-18	n.s.	n.s.	+*.042*, 1.03, (L)10-7
	−.035, 1.07, (L)10-45	n.s.	n.s.	n.s.
	−*.001*, 1.85, (R)10-21	n.s.	n.s.	n.s.
	−.013, 1.30, (R)10-37	n.s.	n.s.	n.s.
	−.040, 1.04, (R)8,9-4,3	n.s.	n.s.	n.s.
	−.034, 1.08, (R)8,9-37	+*.046*, 1.01, (L)8,9-21	n.s.	n.s.
	−*.008*, 1.41, (L)4,3-7	n.s.	n.s.	n.s.
	−.041, 1.04, (L)4,3-18	n.s.	n.s.	n.s.
	−.038, 1.06, (R)4,3-18		+*.035*, 1.07, (L)4,3-37	n.s.
	−*.005*, 1.51, (R)4,3-37	n.s.	n.s.	+*.028*, 1.13, (L)7,21

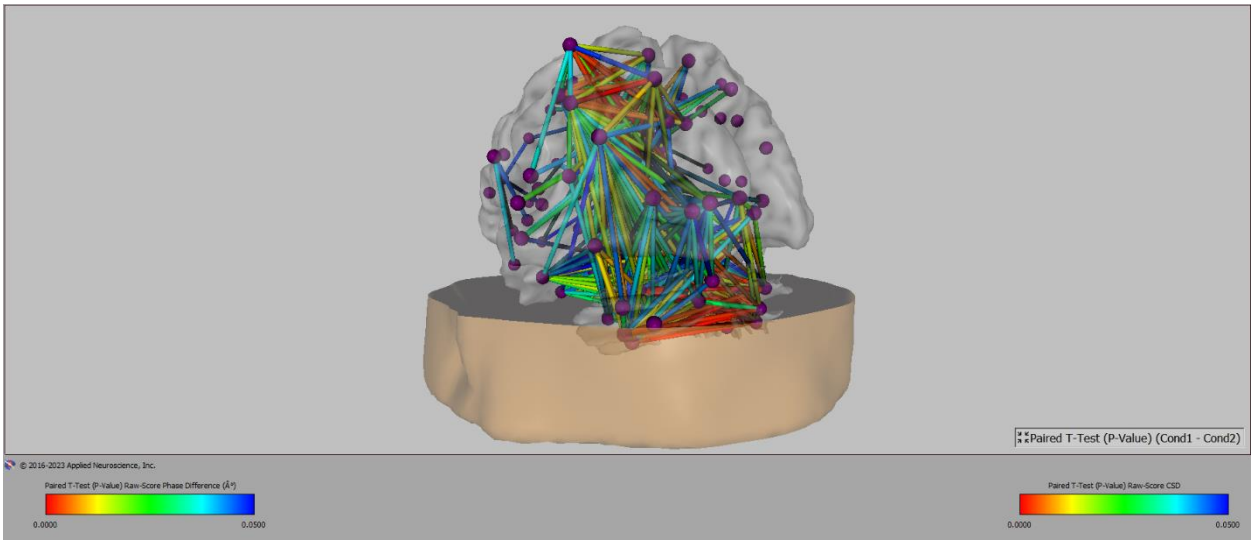
Note. + = concussed group higher; − = concussed group lower; for coherence and phase, a dash (-) between Brodmann areas indicates neural connectivity pathway between the indicated Brodmann areas. Bonferroni adjusted significant *p* values are in italics. Cohen's (1988) effect size ranges: small = .00–.20; medium = .21–.79; large = .80+.

Significant differences between groups were found toward remarkable hypocoherences within the theta and beta frequencies. The same configuration of Brodmann areas was found involved for both of these frequencies for the TOVA condition as for the eyes-closed and eyes-open conditions, but with many more significant theta anomalies than for the eyes-open resting focus condition reported in Table 3. These hypocoherence effects suggest similar difficulties during a cognitive/attentional task in frontal executive planning, control, and working memory (areas 8 and 9), sensorimotor processing, control, and execution (areas 3 and 4), spatial orientation and visuomotor organization (areas 7 and 18), visual analysis, recognition, and association (area 37), and language processing (areas 21, 45, and 47). Somewhat fewer differences were found for the beta frequencies but these were largely within the same Brodmann areas as theta anomalies and for focused eyes open. An important exception for the beta band was an increase in hypocoherences for Brodmann areas 8 and 9 projecting to areas 7, 18, and 37, suggesting impaired information processing during executive functions directed at visuomotor and spatial orientation, recognition, analysis, and association. In the alpha band, areas 7, 8, and 9 experienced significant hypocoherences in connectivity to areas 3, 4, and 37, indicating impaired planning, control, and execution of sensorimotor visuospatial experiences. And, only one hypocoherence was found for the delta band, in the slowed communication of left secondary visual cortex (area 18) with the fusiform gyrus (area 37), suggesting potential word-finding difficulties (e.g., aphasia) in expressing visual experiences.

The most salient differences among the three assessment conditions may be seen in phase differences for the TOVA delta frequency condition. Although remarkably elevated delta *power* was not found across any condition, the synchronization of delta frequencies within the TOVA cognitive/attentional challenge was indeed noteworthy. Across left and right primary somatosensory (area 3), primary motor (area 4), frontal eye fields (area 8), and DL-PFCs (areas 9 and 10), communication among these areas and with somatosensory association cortex (area 7), secondary visual cortex (area 18), middle temporal gyrus (area 21), fusiform gyrus (area 37), and Broca's area 45 were hypersynchronized. Given the very slow frequency characteristics of delta rhythms, these hypersynchronized connectivities would suggest slowed and phase-locked, diminished flexibilities across primary processing, association, and linguistic activities for our concussed patients.

On the other hand, hyposynchronization of theta frequencies from executive processing regions (areas 8 and 9) to linguistic integration regions (area 21), alpha frequencies from sensorimotor reception and expression areas (3 and 4) to fusiform gyrus (area 37) linguistic/semantic regions, and beta frequencies from DL-PFC (area 10) to somatosensory association cortex (area 7), and from somatosensory association cortex (area 7) to middle temporal gyrus (area 21) word-meaning and language processing areas could well indicate complex linguistic difficulties for our concussed patients during the cognitive/attentional challenge. Figure 2 presents an swLORETA neuroimage of the TOVA cognitive challenge for significant concussed minus neurotypical delta phase differences.

Figure 2. *ANI NaviStat swLORETA NeuroImage of TOVA Cognitive Challenge Concussed Minus Neurotypical Significant Delta Phase Differences, Posterior Head View*.



Note. Purple spheres represent center voxels of Brodmann areas referred to in text. Colored bars represent the significance of connectivity pathways among Brodmann areas. Colored scales reflect significance levels of differences (red end of color bar → difference p = .0000). Note the significance of left somatosensory and motor areas and corresponding bilateral cerebellar regions in the processing and activation of this cognitive and motor challenge.

Discussion

Because of the relative availability of patients having chronic head injuries, most qEEG studies to date, indeed most studies in general, of TBI have involved chronic TBI patients. It is well documented that chronic TBI symptomatology is contaminated by multiple comorbidities (particularly chronic PTSD), a history of pharmaceutical and other treatments, and sociocultural lifestyle adaptations (Logan et al., 2013; Marshall et al., 2012; Merritt, 2023; Slobounov et al., 2012; Swanson et al., 2017; Thatcher et al., 2001; Thatcher et al., 1989). As noted earlier, very few studies over the past 2 decades have examined the acute (within 48 hr) head injury population, and even fewer of these investigations utilized full International 10-20 recordings of cortical power and connectivity. Indeed, compromises in diffuse cortical connectivity require a more complete assessment of electrical activity in the brain. Additionally, acute concussion patients are more likely to be free of comorbidities and other medications and treatments which could directly impact brain functioning. Consequently, this study is one of the first comprehensive qEEG investigations to examine concussion/mTBI in its purer, nascent state.

The outcomes of this study in some ways contradicted the established lore of TBI neurocognitive effects. Early EEG studies have suggested predominant elevated slow-wave power and increased amplitude asymmetries. It is important to note that our study did not support salient acute effects in these indices. Our outcomes, on the contrary, indicated scant anomalies in these power measures and remarkable and significant impairments in neurological connectivity measures, consistent with salient effects of neuronal shearing

in white and gray-matter conduction pathways across the cortex. Indeed, our consistent, particularly theta, hypocoherence anomalies across eyes-closed, *d* prime, and neurocognitive/attentional challenge conditions were quite extensive across frontotemporal, central, parietal, and even reaching into occipital regions of the cortex. Phase angle differences likewise revealed diffuse hyperconnectivity in slow-wave delta frequencies, particularly in the more cognitively demanding TOVA challenge, while showing some scattered largely hypoconnectivity in faster theta and alpha bands, the latter particularly in the eyes-closed condition. These connectivity anomalies for our acute concussion patients are largely consistent with connectivity anomalies found with more long-term TBI effects for chronic head injury patients, supporting the predominant role of neurological connectivity impairments in TBI and highlighting the catastrophic acute effects of neuronal shearing even in mild head injury (Popa et al., 2020; Thatcher et al., 1998; Thatcher et al., 1986; Thatcher et al., 2001; Thatcher et al., 1989).

Corresponding functional effects were seen in Brodmann areas involved in executive decision-making, working memory, and sensorimotor control, spatial and visuomotor coordination, and self-referential, empathic, and semantic processing and expression. These functional connectivity impairments are consistent with the TOVA deficits found in attentional, reaction time, and stimulus discrimination deficits quite similar to those of diagnosed ADHD patients. An inclusion of a cognitive/attentional measure in our study was important to the assessment of lifestyle characteristics of our sample of college students at a major southwestern United States university and endeavored to assess more pervasive deficits that would be problematic to their daily functioning. It was somewhat surprising that our concussion sample did not show more impulsivity problems on the TOVA nor more remarkable attentional problems as assessed by the *d* prime measure. However, our sample of acute concussion patients did show corresponding psychological difficulties in overall emotional distress on the BSI subsequent to their head injury. Additionally, our concussed participants did report significantly more frequent alcohol use and trends toward greater marijuana and antidepressant use than our controls. These differences could reflect greater risk-taking tendencies on the part of young college students who are more prone to accidents in general.

This was one of only two studies that we have found in our concussion literature review that matched acute concussion patients to similar neurotypical controls. Doing so allowed for a relatively small number of participants but with sizeable power to comfortably reject our null hypothesis. An additional advantage of this design has to do with managing an observed limitation of the study discussed below, that being occasional rather noisy concussion EEGs. By matching carefully artifacted but still somewhat noisy concussion EEGs to similarly noisy controls effectively allowed a further subtraction of noise from the data and a cleaner, more artifact-free overall dataset. We recommend a similar matching of concussion participants in future studies where possible.

Another advantage of this design had to do with the assessment of participants across three conditions, eyes closed, eyes open, and relevant challenge conditions. Conducting identical assessments across two conditions, eyes closed and eyes open, allowed for a quasireplication of the study within one setting. And obtaining nearly identical outcomes, with very large effect sizes on both, across these two conditions provides some support for the validity of these outcomes.

An important implication of this study is that with qEEG we have quantified a serious, potentially severely debilitating, and critical prognostic consequence of traumatic brain injury, that being diffuse axonal injury or axonal shearing, which with repetitive injury could well lead to the tragedy of chronic traumatic encephalopathy. Indeed, the qEEG connectivity metrics of coherence and phase difference could well become important diagnostic, prognostic, and specific localization indicators of “hard” neurological damage from head injuries. We also offer the suggestion that the impacts of co-occurring coup-contrecoup contusions could be reflected in the recorded metrics of elevated low frequency spectral power and amplitude asymmetries. If subsequent studies confirm and extend our findings, then qEEG could offer an added treatment for TBI in targeted neurotherapies to operantly condition damaged neural networks back to normative functioning.

A recent nonstatistical review by the American Clinical Neurophysiology Society (ACNS) of nine selected studies published since 1996 has criticized the current research qEEG literature as not supportive of qEEG in the diagnosis of mTBI, nor in the differentiation of TBI from other neuropsychiatric diagnoses, such as clinical depression, nor from effects of neuropsychiatric medications (Tenney et al., 2021). This ACNS review, while presently

discouraging the diagnostic utility of qEEG, takes pains to offer ways to improve on the research literature and to conduct meaningful and more definitive studies of the effects of this potentially powerful technology in the differential diagnosis of acute C/mTBI. These authors recommend that future research involve (a) use of healthy controls rather than just normative databases, (b) control for other comorbid neuropsychiatric disorders, (c) control for effects of central nervous system medications, (d) control for the effects of drowsiness by recording during an alert and drowsy state, (e) statistical corrections for multiple comparisons, (f) use of standardized and conventional neurophysiological recording technologies and electrode impedance testing, (g) EEG data collection by a qualified EEG technician and review and noise artifacting of raw EEG data by a qualified electroencephalographer, (h) use of accepted, standardized, "gold-standard" criteria for the identification of TBI samples, (i) clear, accepted criteria for identification of qEEG abnormality, (j) analysis of multiple qEEG measures reflecting varied neurophysiological states, (k) development of predictive as well as explanatory models, and (l) blinded qEEG interpretation regarding the clinical status of participants. The present investigation meets 11 of these 12 criteria; we hope that with replications with a larger sample, we can develop more predictive as well as explanatory models for the diagnosis of concussion/mTBI utilizing qEEG.

Limitations. Neuroscientists nearly always lament the size of their samples, for their assessment and intervention measures are so often very resource- and response-intensive. Such was the case for this study, as the number of coauthors and the nature of the assessment devices suggests. As noted above, the matching of participants helped increase our statistical power. But a larger sample could well have allowed us to conduct the desired regression and discriminant analyses to develop further predictive models for the diagnosis and prognosis of concussion/mTBI.

A problem that emerged early on in the conduct of this study was that acute concussion patients, sometimes within hours of their injury, entered the recording session quite physically and cognitively compromised, nearly always with head pain and significant muscle tension, often confused, sometimes aphasic, and generally irritable. This participant status rendered the recording of artifact-free EEGs quite challenging at times and required some clinical skills to reduce head muscle tension. Our careful and painstaking artifacting procedures improved on this condition considerably, but still some records had to be accepted with some artifacts. The matching of concussed EEGs with neurotypical EEGs by quality of recording allowed for a further reduction of these artifacts. Despite this unavoidable handicap, we feel that our analyzed EEG traces were quite free of noise artifacts and reflect valid EEG data.

The homogeneity of our patient and control samples represented both an advantage, as discussed above, but also a disadvantage. While the age, gender, and other characteristics of our sample are quite similar to those of young military personnel and may well generalize to that population, that homogeneity likewise limits the generalization of our outcomes to other more disparate populations. Of course, replication of this study with other populations will improve the predictive capabilities of our outcomes.

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