Plan: Aetna Better Health  
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**Type of Submission – Check all that apply:**
- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

**CPB 0221 Quantitative EEG (Brain Mapping)**

This CPB has been revised to state that the following are considered experimental and investigational: (i) quantitative EEG for screening for depressed mood after stroke; and (ii) the BrainScope One system (Ahead 300) for evaluation of concussion / traumatic brain injury.

**Name of Authorized Individual (Please type or print):**

Dr. Bernard Lewin, M.D.

**Signature of Authorized Individual:**

[Signature]
Quantitative EEG (Brain Mapping)

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

1. Aetna considers the use of quantitative EEG (brain mapping), also known as BEAM (Brain Electrical Activity Mapping), medically necessary only as an adjunct to traditional EEG for any of the following:
   1. For ambulatory recording of EEG to facilitate subsequent expert visual EEG interpretation; or
   2. For continuous EEG monitoring by frequency-trending to detect early, acute intracranial complications in the operating room or intensive care unit (ICU); or
   3. For evaluation of certain members with symptoms of cerebrovascular disease whose neuroimaging and routine EEG studies are not conclusive; or
   4. For evaluation of dementia and encephalopathy when the diagnosis remains unresolved after initial clinical evaluation; or
   5. For screening for possible epileptic seizures in high-risk ICU members; or
   6. For screening for possible epileptic spikes or seizures in long-term EEG monitoring; or
   7. For topographic voltage and dipole analysis in pre-surgical evaluations for intractable epilepsy.

Definitions

Additional Information
II. In accordance with the American Academy of Neurology/American Clinical Neurophysiology Society's assessment and available evidence, Aetna considers the use of quantitative EEG experimental and investigational for all other indications, including any of the following diagnoses because there is inadequate scientific evidence to prove its clinical usefulness for these indications:

- Alcoholism
- Asperger syndrome and other autism spectrum disorders
- Attention disorders
- Bipolar disorder
- Chronic pain (diagnosis and guide to strategies for pain control)
- Depressed mood after stroke (screening)
- Depression
- Drug abuse
- Fibromyalgia
- Hypoxic ischemic encephalopathy
- Insomnia
- Learning disability
- Mild or moderate head injury
- Minimally conscious state/persistent vegetative state
- Panic disorder
- Parkinson's disease
- Post-concussion syndrome
- Predicting response to psychotropic medication
- Prion diseases
- Schizophrenia
- Sepsis-associated encephalopathy prognosis
- Sports concussion (diagnosis and assessment of recovery)
- Tinnitus.

Aetna considers the BrainScope One system (Ahead 300) for evaluation of concussion / traumatic brain injury experimental and investigational because of insufficient evidence.

See also CPB 0480 - Tourette’s Syndrome (../400_499/0480.html).
Background

Quantitative EEG (qEEG) is a method of analyzing the electrical activity of the brain to derive quantitative patterns that may correspond to diagnostic information and/or cognitive deficits.

Quantitative EEG, a technique for topographic display and analysis of brain electrophysiological data, has been proposed for use in the diagnosis of various psychiatric disorders. Clinical studies have demonstrated distinctive forms of brain electrical activity in psychiatric conditions including attention deficit disorder, schizophrenia, major depression, and obsessive-compulsive disorder. However, the clinical significance of these distinctive patterns of brain wave activity is unknown. Thus the role of quantitative EEG in diagnosis, evaluation of disease progression, and treatment of these conditions has yet to be elucidated. A report from the American Academy of Neurology and the American Clinical Neurophysiology Society concluded that quantitative EEG remains investigational for clinical use in post-concussion syndrome, mild-to-moderate head injury, learning disability, attention disorders, schizophrenia, depression, alcoholism, and drug abuse.

Clinical studies have demonstrated distinctive forms of brain electrical activity in neurologic and psychiatric conditions including learning disabilities, autism, traumatic brain injury, coma, schizophrenia, major depression, and obsessive-compulsive disorder. However, the clinical significance of these distinctive patterns of brain wave activity is unknown. Thus the role of quantitative EEG in diagnosis, evaluation of disease progression, and treatment of these conditions has yet to be elucidated.

Quantitative EEG has been proposed for use in a broad array of potential applications. This evidence has focused on the diagnostic accuracy of QEEG. There is, however, a paucity of evidence regarding its clinical utility.

There are no current guidelines from leading medical professional organizations recommending the use of quantitative EEG as a screening test for neurological and psychiatric conditions. In addition, there are no peer-reviewed published prospective studies of the use of quantitative EEG screening for these conditions showing that management is altered such that clinical outcomes are improved.

There are no published clinical studies demonstrating that use of quantitative EEG
reduces the number of imaging studies or other follow-up tests. In addition, there are no current guidelines from leading medical professional organizations recommending the use of quantitative EEG either as a prerequisite to, or as a replacement for, imaging studies.

While there is some evidence that electroencephalograph activity differs between normal control subjects and subjects suffering from tinnitus, additional evidence is needed to evaluate the value of including quantitative EEG in a battery of electrophysiological tests for the clinical identification of a predominantly central type of tinnitus. In addition, there is little evidence to support the use of quantitative EEG to determine the need for change of medications in the treatment of tinnitus.

Some investigators have proposed use of quantitative EEG in psychiatric cases to facilitate selection of medications. However, there is a lack of reliable evidence from prospective studies demonstrating that clinical outcomes are improved by basing selection of psychotropic medications on quantitative EEG results compared to empiric selection. The FDA approved prescribing information for psychotropic medications includes no recommendation for use of quantitative EEG in selection or dosing, and there are no current guidelines from leading medical professional organizations recommending such use of quantitative EEG.

Crumbley and associates (2005) examined the use of quantitative EEG in predicting response to psychotropic medication. The clinical outcomes of 2 groups of patients were compared: (i) those with prescribed medication regimens that were concordant with the quantitative EEG predictors, and (ii) those whose medication regimens were discordant with the quantitative EEG predictors. Participants included 70 adolescent inpatients who were administered quantitative EEG upon admission. The results indicated no significant difference in clinical outcome between the two groups. The failure of this study to find significant differences in patient outcomes questions this particular use of the quantitative EEG (Crumbley et al, 2005).

John and Prichep (2006) noted that as quantitative EEG and pharmaco-EEG have evolved, a vast body of facts has been accumulated, describing changes in the EEG or event-related potentials observed in a variety of brain disorders or after administration of a variety of medications. With some notable exceptions, these studies have tended to be phenomenological rather than analytical. There has not been a systematic attempt to integrate these phenomena to provide better
understanding of how the abnormal behaviors of a particular psychiatric patient might be related to the specific pattern of the deviant electrical activity, nor just how pharmacological reduction of that deviant activity may have resulted in more normal behavior.

There is insufficient evidence to support the use of quantitative EEG in the diagnosis and/or classification of attention-deficit hyperactivity disorder (ADHD) (Krull, 2009). Several studies have demonstrated differences in qEEG between groups of children with ADHD and normal children. However, these studies are limited by non-random assignment, lack of blinding, failure to consider comorbidities, and/or failure to control for pharmacologic therapy. In addition, the specificity of the findings for ADHD has not been demonstrated.

Snyder and Hall (2006) performed a meta-analysis on the use of quantitative EEG in evaluating patients with ADHD. The 9 eligible studies (n = 1,498) observed quantitative EEG traits of a theta power increase and a beta power decrease, summarized in the theta/beta ratio with a pooled effect size of 3.08 (95% confidence interval: 2.90 to 3.26) for ADHD versus controls (normal children, adolescents, and adults). These investigators concluded that this meta-analysis supports that a theta/beta ratio increase is a commonly observed trait in patients with ADHD relative to normal controls. Moreover, they noted that since it is known that the theta/beta ratio trait may arise with other conditions, a prospective study covering differential diagnosis would be needed to determine generalizability to clinical applications. Furthermore, standardization of the quantitative EEG technique is also needed, specifically with control of mental state, drowsiness, and medication.

Although QEEG may prove to be helpful in the diagnosis and/or classification of ADHD in the future, at present, there is insufficient evidence to support its use in clinical populations.

Much of the literature submitted focuses on the use of QEEG in the early detection of dementia. Although several markers of early dementia have been reported in the literature, there is a lack of evidence that early detection of dementia alters clinical management such that outcomes are improved, especially given the lack of robust treatments available.
An assessment by the Swedish Office of Health Technology Assessment (SBU, 2008) found insufficient evidence to support the use of quantitative EEG in dementia. The SBU assessment stated: "[t]here is limited evidence that either visually rated EEG or qEEG helps the diagnostic workup differentiate AD (Alzheimer’s Disease) patients from controls or AD from other dementia disorders."

Klassen et al (2011) evaluated qEEG measures as predictive biomarkers for the development of dementia in Parkinson disease (PD). Preliminary work shows that qEEG measures correlate with current PD cognitive state. A reliable predictive qEEG biomarker for PD dementia (PD-D) incidence would be valuable for studying PD-D, including treatment trials aimed at preventing cognitive decline in PD. A cohort of subjects with PD in the authors' brain donation program utilizes annual pre-mortem longitudinal movement and cognitive evaluation. These subjects also undergo biennial EEG recording. EEG from subjects with PD without dementia with follow-up cognitive evaluation was analyzed for qEEG measures of background rhythm frequency and relative power in δ, α, and β bands. The relationship between the time to onset of dementia and qEEG and other possible predictors was assessed by using Cox regression. The hazard of developing dementia was 13 times higher for those with low background rhythm frequency (lower than the grand median of 8.5 Hz) than for those with high background rhythm frequency ($p < 0.001$). Hazard ratios (HRs) were also significant for greater than median bandpower (HR = 3.0; $p = 0.004$) compared to below, and for certain neuropsychological measures. The HRs for δ, α, and β bandpower as well as baseline demographic and clinical characteristics were not significant. The authors concluded that qEEG measures of background rhythm frequency and relative power in the band are potential predictive biomarkers for dementia incidence in PD. These QEEG biomarkers may be useful in complementing neuropsychological testing for studying PD-D incidence.

Marzano and colleagues (2008) stated that in the last 2 decades quantitative EEG analysis has been used to examine the neurophysiological characteristics of insomnia. These studies provided evidence in support of the hypothesis that primary insomnia is associated with hyper-arousal of central nervous system and altered sleep homeostasis. However, these researchers have here underlined that these results have intrinsic methodological problems, mainly related to constraints of standard assessment in clinical research. They have proposed that future studies should be performed on larger samples of drug-free patients, using within-subjects designs and longitudinally recording patients adapted to sleep laboratory.
All these methodological improvements will allow to partial out the contribution of individual differences, pharmacological influences and first-night effects on EEG frequencies. Moreover, they have discussed the potential relevance of recent findings from basic research concerning local changes during physiological sleep, which could be extended to the study of insomnia.

Hargrove and colleagues (2010) stated that there is increasing acceptance that pain in fibromyalgia (FM) is a result of dysfunctional sensory processing in the spinal cord and brain, and a number of recent imaging studies have demonstrated abnormal central mechanisms. These researchers compared quantitative electroencephalogram (qEEG) measures in 85 FM patients with age- and gender-matched controls in a normative database. A statistically significant sample (minimum 60 seconds from each subject) of artifact-free EEG data exhibiting a minimum split-half reliability ratio of 0.95 and test-retest reliability ratio of 0.90 was used as the threshold for acceptable data inclusion. Electroencephalograms of FM subject were compared to EEGs of age- and gender-matched healthy subjects in the Lifespan Normative Database and analyzed using NeuroGuide 2.0 software. Analyses were based on spectral absolute power, relative power and coherence. Clinical evaluations included the Fibromyalgia Impact Questionnaire (FIQ), Beck Depression Inventory and Fischer dolorimetry for pain pressure thresholds. Based on Z-statistic findings, the EEGs from FM subjects differed from matched controls in the normative database in 3 features: (i) reduced EEG spectral absolute power in the frontal International 10-20 EEG measurement sites, particularly in the low-to mid-frequency EEG spectral segments; (ii) elevated spectral relative power of high frequency components in frontal/central EEG measurement sites; and (iii) widespread hypo-coherence, particularly in low- to mid-frequency EEG spectral segments, in the frontal EEG measurement sites. A consistent and significant negative correlation was found between pain severity and the magnitude of the EEG abnormalities. No relationship between EEG findings and medicine use was found. The authors concluded that qEEG analysis reveals significant differences between FM patients compared to age- and gender-matched healthy controls in a normative database, and has the potential to be a clinically useful tool for assessing brain function in FM patients.

Hathi et al (2010) assessed an EEG-based index, the Cerebral Health Index in babies (CHI/b), for identification of neonates with high Sarnat scores and abnormal EEG as markers of hypoxic ischemic encephalopathy (HIE) after perinatal asphyxia. This was a retrospective study using 30-min EEG data collected from 20
term neonates with HIE and 20 neurologically normal neonates. The HIE diagnosis was made on clinical grounds based on history and examination findings. The maximum-modified clinical Sarnat score was used to grade HIE severity within 72 hrs of life. All neonates underwent 2-channel bedside EEG monitoring. A trained electroencephalographer blinded to clinical data visually classified each EEG as normal, mild or severely abnormal. The CHI/b was trained using data from Channel 1 and tested on Channel 2. The CHI/b distinguished among HIE and controls (p < 0.02) and among the 3 visually interpreted EEG categories (p < 0.0002). It showed a sensitivity of 82.4 % and specificity of 100 % in detecting high grades of neonatal encephalopathy (Sarnat 2 and 3), with an area under the receiver operator characteristic (ROC) curve of 0.912. CHI/b also identified differences between normal versus mildly abnormal (p < 0.005), mild versus severely abnormal (p < 0.01) and normal versus severe (p < 0.002) EEG groups. An ROC curve analysis showed that the optimal ability of CHI/b to discriminate poor outcome was 89.7 % (sensitivity: 87.5 %; specificity: 82.4 %). The authors concluded that the CHI/b identified neonates with high Sarnat scores and abnormal EEG. These results support its potential as an objective indicator of neurological injury in infants with HIE.

Lopes et al (2010) examined and compared the brain cortical activity, as indexed by qEEG power, coherence and asymmetry measures, in panic disorder patients during an induced panic attack with a 35 % CO(2) challenge test and also in a resting condition. A total of 15 subjects with panic disorder were randomly assigned to both 35 % CO(2) mixture and atmospheric compressed air, in a double-blind study design, with EEG being recorded for a 20-min period. During induced panic attacks, a reduced right-sided frontal orbital asymmetry in the beta band, a decreased occipital frontal intra-hemispheric coherence in the delta band at both right and left sides, a left-sided occipital delta inter-hemispheric asymmetry and an increased relative power in the beta wave at T4 were observed. These data showed a disturbed frontal cortical processing, pointing to an imbalance of the frontal and occipital sites, common to both hemispheres, and an increased right posterior activity related to the high arousing panic attack condition. These findings corroborated the neuroanatomical hypothesis of panic disorder.

Velasques et al (2013) examined the relationship between cortical gamma coherence within patients with bipolar disorder and a control group during a prosaccadic attention task. These investigators hypothesized that gamma coherence oscillations act as a main neural mechanism underlying information processing.
which changes in bipolar patients. A total of 32 subjects (12 healthy controls and 20 bipolar patients) were enrolled in this study. Participants performed a pro-saccadic attention task while their brain activity pattern was recorded using qEEG (20 channels). These researchers observed that the maniac group presented lower saccade latency when compared to depression and control groups. The main finding was a greater gamma coherence for control group in the right hemisphere of both frontal and motor cortices caused by the execution of a pro-saccadic attention task. The authors concluded that these findings suggested a disrupted connection of the brain's entire functioning of maniac patients and represented a deregulation in cortical inhibitory mechanism. Thus, these results reinforce the hypothesis that greater gamma coherence in the right and left frontal cortices for the maniac group produces a "noise" during information processing and highlights that gamma coherence might be a biomarker for cognitive dysfunction during the manic state. The authors stated that these findings need to be confirmed in larger samples and in bipolar patients before start the pharmacological treatment.

An UpToDate review on “Attention deficit hyperactivity disorder in children and adolescents: Clinical features and evaluation” (Krull, 2013) states that “We do not suggest qEEG for the evaluation of children with ADHD. Although the US Food and Drug Administration has licensed the first EEG test for assessment of children (6 to 17 years) for ADHD, and several studies have demonstrated differences in qEEG between children with ADHD and normal children, the studies were limited by non-random assignment, lack of blinding, failure to consider comorbidities, and/or failure to control for pharmacologic therapy. In addition, the EEG patterns differ in boys and girls. A 2013 meta-analysis of nine studies (including 1253 children with ADHD and 517 without ADHD) found significant heterogeneity and concluded that EEG profiles (specifically an increased theta to beta ratio) cannot be used to reliably diagnose ADHD (although they may be helpful for prognosis). Current evidence is insufficient to support the use of qEEG over clinical evaluation of symptoms and functional impairment for the diagnosis of ADHD”.

Kutcher et al (2013) summarized the evidence for the following technologies/strategies related to diagnosing or managing sports-related concussion: quantitative EEG, functional neuroimaging, head impact sensors, telemedicine and mobile devices. Databases used were MEDLINE, PubMed, Cochrane Controlled Trials Registers, SportDiscus, EMBASE, Web of Science and ProQuest databases. Primary search keywords were concussion, sports concussion and mild traumatic brain injury. The keywords used for secondary,
topic specific searches were quantitative electroencephalography, qEEG, functional MRI, magnetoencephalography, near-infrared spectroscopy, positron emission tomography, single photon emission CT, accelerometer, impact sensor, telemetry, remote monitoring, robotic medicine, telemedicine, mobile device, mobile phone, smart phone and tablet computer. The primary search produced 8,567 publications. The secondary searches produced 9 publications that presented original data, included a comparison group in the study design and involved sports-related concussion: 4 studies spoke to the potential of qEEG as a diagnostic or management tool, while 5 studies addressed the potential of fMRI to be used in the same capacity. The authors concluded that emerging technologies and novel approaches that aid in sports concussion diagnosis and management are being introduced at a rapid rate. Moreover, they stated that while some technologies show promise, their clinical utility remains to be established.

Furthermore, the American Medical Society for Sports Medicine’s position statement on “Concussion in sport” (Harmon et al, 2013) did not mention the use of quantitative EEG/brain mapping as a management tool.

Hosokawa et al (2014) noted that several studies have reported the presence of EEG abnormalities or altered evoked potentials (EPs) during sepsis. However, the role of these tests in the diagnosis and prognostic assessment of sepsis-associated encephalopathy remains unclear. These researchers performed a systematic search for studies evaluating EEG and/or EPs in adult patients with sepsis-associated encephalopathy. The following outcomes were extracted: (i) incidence of EEG/EP abnormalities; (ii) diagnosis of sepsis-associated delirium or encephalopathy with EEG/EP; and (iii) outcome. Among 1,976 citations, 17 articles met the inclusion criteria. The incidence of EEG abnormalities during sepsis ranged from 12 % to 100 % for background abnormality and 6 % to 12 % for presence of tri-phasic waves. Two studies found that epileptiform discharges and electrographic seizures were more common in critically ill patients with than without sepsis. In 1 study, EEG background abnormalities were related to the presence and the severity of encephalopathy. Background slowing or suppression and the presence of tri-phasic waves were also associated with higher mortality. A few studies demonstrated that quantitative EEG analysis and EP could show significant differences in patients with sepsis compared to controls; but their association with encephalopathy and outcome was not evaluated. The authors concluded that abnormalities in EEG and EPs are present in the majority of septic patients. They stated that there is some evidence to support EEG use in the detection and
prognostication of sepsis-associated encephalopathy, but further clinical investigation is needed to confirm this suggestion.

**Minimally Conscious State/Persistent Vegetative State**

In a systematic review and meta-analysis, Bender et al (2015) examined the sensitivity and specificity of new diagnostic methods for the minimally conscious state (MCS). These researchers identified and evaluated 20 clinical studies involving a total of 906 patients with either persistent vegetative state (PVS) or MCS. The reported sensitivities and specificities of the various techniques used to diagnose MCS vary widely. The sensitivity and specificity of functional MRI-based techniques were 44% and 67%, respectively (with corresponding 95% confidence intervals [CI]: 19% to 72% and 55% to 77%); those of quantitative EEG were 90% and 80%, respectively (95% CI: 69% to 97% and 66% to 90%); EEG, event-related potentials, and imaging studies could also aid in prognostication. Contrary to prior assumptions, 10% to 24% of patients in PVS could regain consciousness, sometimes years after the event, but only with marked functional impairment. The authors concluded that the basic diagnostic evaluation for differentiating PVS from MCS consists of a standardized clinical examination. They stated that in the future, modern diagnostic techniques may help identify patients who are in a subclinical MCS.

Furthermore, an UpToDate review on “Hypoxic-ischemic brain injury: Evaluation and prognosis” (Weinhouse and Young, 2016) states that “The clinical value of the electroencephalogram (EEG) is unclear in the assessment of prognosis of anoxic brain injury because investigators have used different classification systems and variable intervals of recordings after resuscitation. Furthermore, the EEG is susceptible to subjective interpretation, the effects of sedative drugs, metabolic disturbances, and sepsis, which can invalidate the results”.

**Attention Deficit Hyperactivity Disorder (ADHD)**

The American Academy of Neurology (AAN)’s practice advisory on “The utility of EEG theta/beta power ratio in ADHD diagnosis” (Gloss et al, 2016) evaluated the evidence for EEG theta/beta power ratio for diagnosing, or helping to diagnose ADHD. The authors identified relevant studies and classified them using AAN criteria. Two Class I studies assessing the ability of EEG theta/beta power ratio and EEG frontal beta power to identify patients with ADHD correctly identified 166
of 185 participants. Both studies evaluated theta/beta power ratio and frontal beta power in suspected ADHD or in syndromes typically included in an ADHD differential diagnosis. A bivariate model combining the diagnostic studies showed that the combination of EEG frontal beta power and theta/beta power ratio has relatively high sensitivity and specificity but is insufficiently accurate. The authors concluded that it is unknown whether a combination of standard clinical examination and EEG theta/beta power ratio increases diagnostic certainty of ADHD compared with clinical examination alone. The AAN provided the following recommendations:

Clinicians should inform patients with suspected ADHD and their families that the combination of EEG theta/beta power ratio and frontal beta power should not replace a standard clinical evaluation. There is a risk for significant harm to patients from ADHD misdiagnosis because of the unacceptably high false-positive diagnostic rate of EEG theta/beta power ratio and frontal beta power. Level B (Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population)

Clinicians should inform patients with suspected ADHD and their families that the EEG theta/beta power ratio should not be used to confirm an ADHD diagnosis or to support further testing after a clinical evaluation, unless such diagnostic assessments occur in a research setting. Level R (Level R recommendations are ones that “the guideline authors assert should be applied only in research settings)

Chronic Pain

Pinheiro and colleagues (2016) reviewed recent findings on EEG patterns in individuals with chronic pain. These researchers also discussed recent advances in the use of qEEG for the assessment of pathophysiology and biopsychosocial factors involved in its maintenance over time. Data collection took place from February 2014 to July 2015 in PubMed, SciELO and PEDro databases. Data from cross-sectional studies and longitudinal studies, as well as clinical trials involving chronic pain participants were incorporated into the final analysis. Primary findings related to chronic pain were an increase of theta and alpha EEG power at rest, and a decrease in the amplitude of evoked potentials after sensory stimulation and cognitive tasks. The authors concluded that increased alpha and theta power at spontaneous EEG and low amplitudes of ERP during various stimuli appeared to be clinical characteristics of individuals with chronic pain; qEEG can be a simple
and objective tool for studying the mechanisms involved in chronic pain, identifying specific characteristics of chronic pain conditions and providing insights about appropriate therapeutic approaches. Nevertheless, more studies are needed before drawing any conclusion on the utility of qEEG on chronic pain. Further clinical studies should be conducted to establish the clinical applicability of this instrument as an effective marker for diagnosis and guide to strategies for pain control. Systematic reviews with samples of individuals who have similar characteristics and type of pain can help determine a specific EEG pattern for each type of chronic pain.

The drawbacks of this study were: (i) data from the included studies were very heterogeneous, which prevented a meta-analysis. The conclusions were based on a qualitative analysis of the studies. Future studies should try to include similar variables, whenever possible, to allow for greater comparability of findings, and (ii) the exclusion of EEG sleep studies. These researchers attempted to homogenize the sample, understanding that the awake standard EEG can be quite different from the sleep EEG. However, these findings may, in the future, be compared to findings of studies with sleeping participants in order to acquire a more comprehensive understanding of the chronic pain phenomenon. The authors noted that since they did not aim to analyze or discuss the clinical significance of EEG as a tool to detect changes after interventions, their findings and conclusions came from observational studies. Clinical trials are considered the gold standard to provide the highest level of clinical evidence. However, these researchers’ questions are better addressed by the observational design. To control for quality of the evidence presented here, the articles included were assessed by criteria defined by an adapted version of the Newcastle-Ottawa scale. In general, data acquisition, processing and analysis were clearly stated in these studies, which allow reproducibility of their methods.

Prion Diseases

Franko and colleagues (2016) stated that prion diseases are universally fatal and often rapidly progressive neurodegenerative diseases; and EEG has long been used in the diagnosis of sporadic Creutzfeldt-Jakob disease (sCJD). However, the characteristic waveforms do not occur in all types of prion diseases. These researchers re-evaluated the utility of EEG by focusing on the development of biomarkers. They examined if abnormal qEEG parameters can be used to measure disease progression in prion diseases or predict disease onset in healthy...
individuals at risk of disease. In the National Prion Monitoring Cohort study, these investigators performed qEEG on 301 occasions in 29 healthy controls and 67 patients with prion disease. Patients had either inherited prion disease or sCJD. These researchers computed the main background frequency, the $\alpha$ and $\theta$ power and the $\alpha/\theta$ power ratio, then averaged these within 5 electrode groups. These measurements were then compared among participant groups and correlated with functional and cognitive scores cross-sectionally and longitudinally. The authors found lower main background frequency, $\alpha$ power and $\alpha/\theta$ power ratio and higher $\theta$ power in patients compared to control participants. The main background frequency, the power in the $\alpha$ band and the $\alpha/\theta$ power ratio also differed in a consistent way among the patient groups. Moreover, the main background frequency and the $\alpha/\theta$ power ratio correlated significantly with functional and cognitive scores. Longitudinally, change in these parameters also showed significant correlation with the change in clinical and cognitive scores. The authors concluded that these findings supported the use of qEEG to follow the progression of prion disease, with potential to help evaluate the treatment effects in future clinical trials. Priorities for future work should include the use of these technologies in a clinical trial setting as an exploratory biomarker, the continued study of healthy at-risk individuals and consideration of related technologies such as magnetoencephalography.

This study had 2 major drawbacks: (i) studies of a rare disease were limited by sample size in addition to relatively small number of sCJD patients, and (ii) no differences were observed between qEEG parameters in asymptomatic gene mutation carriers compared with healthy controls. Two interpretations were plausible (i) the EEG became abnormal several years before clinical onset, reflecting incipient neurodegeneration, but there were too few patients close to actual clinical onset in the asymptomatic inherited prion disease (aIPD) group to detect this, and (ii) the EEG only became abnormal in IPD at clinical onset. The authors stated that continued follow-up of aIPD patients and retrospective analysis of converting clinical cases may be helpful.

Also, an UpToDate review on “Diseases of the central nervous system caused by prions” (Brown and Lee, 2016) does not mention qEEG as a diagnostic tool.
Wang and colleagues (2017) examined the aberrant EEG oscillation in major depressive subjects with basal ganglia stroke with lesions in different hemispheres. Resting EEG of 16 electrodes in 58 stroke subjects, 26 of whom had post-stroke depression (13 with left-hemisphere lesion and 13 with right) and 32 of whom did not (18 with left lesion and 14 with right), was recorded to obtain spectral power analysis for several frequency bands. Multiple analysis of variance and receiver operating characteristic (ROC) curves were used to identify differences between post-stroke depression (PSD) and post-stroke non-depression (PSND), treating the different lesion hemispheres separately. Moreover, Pearson linear correlation analysis was conducted to test the severity of depressive symptoms and EEG indices. PSD with left-hemisphere lesion showed increased beta2 power in frontal and central areas, but PSD with right-hemisphere lesion showed increased theta and alpha power mainly in occipital and temporal regions. Additionally, for left-hemisphere lesions, beta2 power in central and right parietal regions provided high discrimination between PSD and PSND, and for right-hemisphere lesions, theta power was similarly discriminative in most regions, especially temporal regions. These researchers also explored the association between symptoms of depression and the power of abnormal bands, but found no such relationship. The authors concluded that the aberrant EEG oscillation in subjects with PSD differed between subjects with lesions of the left and right hemispheres, suggesting a complex association between depression and lesion location in stroke patients. The main drawbacks of this study were its relatively small sample size (n = 58) and the inclusion of participants with different lesions of the basal ganglia.

Screening for Depressed Mood after Stroke

Wang and colleagues (2018) examined the electrophysiological changes in post-stroke subjects with depressed mood. Resting-state electroencephalogram (rs-EEG) signals of 16 electrodes in 35 post-stroke depressed, 24 post-stroke non-depressed, and 35 age-matched healthy control subjects were analyzed by means of spectral power analysis, a qEEG measurement of different frequency bands. The relationship among depressed mood, functional status, lesion side, and post-stroke time was assessed by using variance and Spearman correlation analysis. Multiple analysis of variance was used to compare the differences among the 3 groups. Binary logistic regression analysis was used to establish a regression model to predict depressed mood in stroke subjects and to explore the association between depression and EEG band power; ROC curves were used to estimate the ability of spectral power selected by binary logistic regression to indicate depressed
mood in stroke subjects. These researchers found that the hemisphere in which the lesion was located and the time since stroke onset had no effect on depressed mood. Only the patient's functional status was related to emotional symptoms; qEEG analysis revealed increased delta, theta, and beta2 power in stroke subjects with depressed mood, particularly in temporal regions. The theta and beta2 power in the right temporal area were shown to be highly sensitive to depressed mood, and these parameters showed good discriminatory ability for depressed subjects following stroke. The authors concluded that depressed mood after stroke was associated with functional status; and qEEG parameters may be a useful tool in timely screening for depressed mood after stroke.

**BrainScope One System (Ahead 300) for Evaluation of Concussion / Traumatic Brain Injury**

Vincent et al (2017) stated that the BrainScope Ahead 300 is designed for use by health care professionals to aid in the assessment of patients suspected of a mild traumatic brain injury (TBI). These investigators established normative data for the cognitive test component of the Ahead 300 system and examined the role of demographic factors on test performance. Healthy, community-dwelling adults between the ages of 18 and 80 recruited from 5 geographically distributed sites were administered Android versions of the ANAM Matching to Sample and Procedural Reaction Time tests that comprise the cognitive test component of the Ahead 300 system by trained personnel. Scores were correlated with age, education, and race. Age accounted for the majority of the variance in test scores with additional significant, but minor, contributions of education and race. Gender did not account for a significant proportion of the variance for either test. Based on these results, the normative data for 551 individuals were presented stratified by age. The authors concluded that these were the first available normative data for these tests when administered using the Ahead 300 system and will assist health care professionals in determining the degree to which scores on the cognitive tests reflect impaired performance.

Hanley et al (2017) noted that a brain electrical activity biomarker for identifying TBI in emergency department (ED) patients presenting with high Glasgow Coma Scale (GCS) after sustaining a head injury has shown promise for objective, rapid triage. In an observational study, these investigators prospectively evaluated the efficacy of an automated classification algorithm to determine the likelihood of being computed tomography (CT)-positive, in high-functioning TBI patients in the acute
state. Adult patients admitted to the ED for evaluation within 72 hours of sustaining a closed head injury with GCS 12 to 15 were candidates for study. A total of 720 patients (18 to 85 years) meeting inclusion/exclusion criteria were enrolled in this validation trial at 11 U.S. EDs; GCS was 15 in 97 %, with the 1st and 3rd quartiles being 15 (interquartile range [IQR] = 0) in the study population at the time of the evaluation. Standard clinical evaluations were conducted and 5 to 10 minutes of EEG was acquired from frontal and frontal-temporal scalp locations. Using an a priori derived EEG-based classification algorithm developed on an independent population and applied to this validation population prospectively, the likelihood of each subject being CT+ was determined, and performance metrics were computed relative to adjudicated CT findings. Sensitivity of the binary classifier (likely CT+ or CT-) was 92.3 % (95 % confidence interval [CI]: 87.8 % to 95.5 %) for detection of any intra-cranial injury visible on CT (CT+), with specificity of 51.6 % (95 % CI: 48.1 % to 55.1 %) and negative predictive value (NPV) of 96.0 % (95 % CI: 93.2 % to 97.9 %). Using ternary classification (likely CT+, equivocal, likely CT-) demonstrated enhanced sensitivity to traumatic hematomas (greater than or equal to 1 ml of blood), 98.6 % (95 % CI: 92.6 % to 100.0 %), and NPV of 98.2 % (95 % CI: 95.5 % to 99.5 %). The authors concluded that using an EEG-based biomarker high accuracy of predicting the likelihood of being CT+ was obtained, with high NPV and sensitivity to any traumatic bleeding and to hematomas; specificity was significantly higher than standard CT decision rules. They stated that the short time to acquire results and the ease of use in the ED environment suggested that EEG-based classifier algorithms have potential to impact triage and clinical management of head-injured patients.

Hack et al (2017) compared the predictive power using that algorithm (which includes loss of consciousness [LOC] and amnesia) to the predictive power of LOC alone or LOC plus traumatic amnesia. ED patients 18 to 85 years presenting within 72 hours of closed head injury, with GCS 12 to 15, were study candidates. A total of 680 patients with known absence or presence of LOC were enrolled (145 CT+ and 535 CT- patients); 5 to 10 mins of eyes closed EEG was acquired using the Ahead 300 hand-held device, from frontal and fronto-temporal regions. The same classification algorithm methodology was used for both the EEG-based and the LOC-based algorithms. Predictive power was evaluated using area under the ROC curve (AUC) and odds ratios (ORs). The quantitative EEG (QEEG)-based classification algorithm demonstrated significant improvement in predictive power compared with LOC alone, both in improved AUC (83 % improvement) and OR (increase from 4.65 to 16.22). Adding RGA and/or PTA to LOC was not improved

http://www.aetna.com/cpb/medical/data/200_299/0221.html 05/30/2019
over LOC alone. The authors concluded that rapid triage of TBI relies on strong initial predictors. Addition of an EEG-based marker was shown to out-perform report of LOC alone or LOC plus amnesia, in determining risk of an intra-cranial bleed. Moreover, they stated that ease of use at point-of-care, non-invasive, and rapid result using such technology suggested significant value added to standard clinical prediction.

Hanley et al (2018) stated that the potential clinical utility of a novel QEEG-based Brain Function Index (BFI) as a measure of the presence and severity of functional brain injury was studied as part of an independent prospective validation trial. The BFI was derived using QEEG features associated with functional brain impairment reflecting current consensus on the physiology of concussive injury. A total of 720 adult patients (18 to 85 years of age) evaluated within 72 hours of sustaining a closed head injury were enrolled at 11 U.S. EDs; GCS score was 15 in 97%. Standard clinical evaluations were conducted and 5 to 10 mins of EEG acquired from frontal locations. Clinical utility of the BFI was assessed for raw scores and percentile values. A multi-nomial logistic regression analysis demonstrated that the ORs (computed against controls) of the mild and moderate functionally impaired groups were significantly different from the OR of the CT-positive (CT+, structural injury visible on CT) group (p = 0.0009 and p = 0.0026, respectively). However, no significant differences were observed between the ORs of the mild and moderately functionally impaired groups. Analysis of variance (ANOVA) demonstrated significant differences in BFI among normal (16.8 %), mild TBI (mTBI)/concussed with mild or moderate functional impairment, (61.3 %), and CT+ (21.9 %) patients (p potential to aid in early diagnosis and thereby potential to impact the sequelae of TBI by providing an objective marker that is available at the point-of-care, hand-held, non-invasive, and rapid to obtain.

Conley and co-workers (2018) noted that sports-related concussion is associated with a range of short-term functional deficits that are commonly thought to recover within a 2-week post-injury period for most, but certainly not all, persons; and rs-EEG may prove to be an affordable, accessible, and sensitive method of assessing severity of brain injury and rate of recovery after a concussion. These investigators presented a systematic review of rs-EEG in sports-related concussion. A systematic review of articles published in the English language, up to June 2017, was retrieved via PsychINFO, Medline, Medline In Process, Embase, SportDiscus, CINAHL, and Cochrane Library, Reviews, and Trials. The following key words were used for database searches: electroencephalography, quantitative
electroencephalography, qEEG, cranio-cerebral trauma, mild traumatic brain injury, mTBI, traumatic brain injury, brain concussion, concussion, brain damage, sport, athletic, and athlete. Observational, cohort, correlational, cross-sectional, and longitudinal studies were all included in the current review. A total of 16 articles met inclusion criteria, which included data on 504 athletes and 367 controls. All 16 articles reported some abnormality in rs-EEG activity after a concussion; however, the cortical rhythms that were affected varied. The authors concluded that despite substantial methodological and analytical differences across the 16 studies, the current review suggested that rs-EEG may provide a reliable technique to identify persistent functional changes in athletes after a concussion. Moreover, they stated that because of the varied approaches, however, considerable work is needed to establish a systematic methodology to assess its efficacy as a marker of return-to-play.

Furthermore, an UpToDate review on “Acute mild traumatic brain injury (concussion) in adults” (Evans and Whitlow, 2018) does not mention BrainScope / EEG-based technology as a diagnostic tool.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by”+”:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>95961</td>
<td>Functional cortical and subcortical mapping by stimulation and/or recording of electrodes on brain surface, or of depth electrodes, to provoke seizures or identify vital brain structures; initial hour of attendance by a physician or other qualified health care professional.</td>
</tr>
<tr>
<td>+ 95962</td>
<td>each additional hour of attendance by a physician or other qualified health care professional (List separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>95812 - 95830</td>
<td>Electroencephalography</td>
</tr>
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</table>

HCPCS code covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S8040</td>
<td>Topographic brain mapping</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>HCPCS codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>BrainScope One system (Ahead 300) - no specific code:</td>
<td></td>
</tr>
<tr>
<td>ICD-10 codes covered if selection criteria are met (not all-inclusive):</td>
<td></td>
</tr>
<tr>
<td>F02.80</td>
<td>Dementia in other diseases classified elsewhere, without behavioral disturbance</td>
</tr>
<tr>
<td>F02.81</td>
<td>Dementia in other diseases classified elsewhere, with behavioral disturbance</td>
</tr>
<tr>
<td>F03.90 - F03.91</td>
<td>Unspecified dementia</td>
</tr>
<tr>
<td>F06.1, F06.8</td>
<td>Psychotic disorders with hallucinations and other specified mental disorders due to known physiological conditions</td>
</tr>
<tr>
<td>G40.00 - G40.919</td>
<td>Epilepsy and recurrent seizures</td>
</tr>
<tr>
<td>G92</td>
<td>Toxic encephalopathy</td>
</tr>
<tr>
<td>G93.1</td>
<td>Anoxic brain damage, not elsewhere classified</td>
</tr>
<tr>
<td>G93.40 - G93.49</td>
<td>Encephalopathy, not elsewhere classified [not covered for assessing prognosis of sepsis-associated encephalopathy]</td>
</tr>
<tr>
<td>G97.31 - G97.32</td>
<td>Intraoperative hemorrhage and hematoma of a nervous system organ or structure complicating a procedure</td>
</tr>
<tr>
<td>I65.01 - I69.998</td>
<td>Occlusion and stenosis of precerebral arteries, occlusion of cerebral arteries, transient cerebral ischemia, acute, but ill-defined cerebrovascular disease, other and ill-defined cerebrovascular disease, and late effects of cerebrovascular disease</td>
</tr>
<tr>
<td>I97.810 - I97.821</td>
<td>Other intraoperative and postprocedural cerebrovascular infarction during surgery</td>
</tr>
<tr>
<td>R40.3</td>
<td>Persistent vegetative state</td>
</tr>
<tr>
<td>R56.1</td>
<td>Post traumatic seizures</td>
</tr>
<tr>
<td>R56.9</td>
<td>Unspecified convulsions</td>
</tr>
<tr>
<td>T56.0x1+</td>
<td>Toxic effect of lead and its compounds, accidental (unintentional)</td>
</tr>
<tr>
<td>ICD-10 codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>A81.00 - A81.9</td>
<td>Atypical virus infections of central nervous system [Prion diseases]</td>
</tr>
<tr>
<td>F07.81</td>
<td>Postconcussional syndrome</td>
</tr>
<tr>
<td>F10.121</td>
<td>Alcohol abuse with intoxication delirium</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>F10.14</td>
<td>Alcohol abuse with alcohol-induced mood disorder</td>
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<tr>
<td>F10.150 -</td>
<td>Alcohol abuse with alcohol-induced psychotic disorder</td>
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<tr>
<td>F10.159</td>
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<tr>
<td>F10.180 - F10.19</td>
<td>Alcohol abuse with other alcohol-induced disorders</td>
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<tr>
<td>F10.221</td>
<td>Alcohol dependence with intoxication delirium</td>
</tr>
<tr>
<td>F10.230 - F10.24</td>
<td>Alcohol dependence with withdrawal and alcohol-induced mood disorder</td>
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<tr>
<td>F10.250 - F10.29</td>
<td>Alcohol dependence with alcohol-induced psychotic, persisting amnestic, persisting dementia and other and unspecified alcohol-induced disorders</td>
</tr>
<tr>
<td>F10.920 - F10.99</td>
<td>Alcohol use, unspecified, with intoxication, alcohol-induced mood, psychotic, persisting amnestic, persisting dementia and other and unspecified alcohol-induced disorders</td>
</tr>
<tr>
<td>F11.10 - F19.999</td>
<td>Drug induced mental disorders</td>
</tr>
<tr>
<td>F20.0 - F20.9</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>F25.0 - F25.9</td>
<td>Schizoaffective disorders</td>
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<tr>
<td>F30.10 - F39</td>
<td>Mood [affective] disorders</td>
</tr>
<tr>
<td>F34.1</td>
<td>Dysthymic disorder</td>
</tr>
<tr>
<td>F41.0</td>
<td>Panic disorder [episodic paroxysmal anxiety]</td>
</tr>
<tr>
<td>F51.01</td>
<td>Primary insomnia</td>
</tr>
<tr>
<td>F51.02</td>
<td>Adjustment insomnia</td>
</tr>
<tr>
<td>F51.03</td>
<td>Paradoxical insomnia</td>
</tr>
<tr>
<td>F51.09</td>
<td>Other insomnia not due to a substance or known physiological condition</td>
</tr>
<tr>
<td>F80.0 - F89</td>
<td>Pervasive and specific developmental disorders</td>
</tr>
<tr>
<td>F90.0 - F90.9</td>
<td>Attention-deficit hyperactivity disorders</td>
</tr>
<tr>
<td>G20 - G21.9</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td>G47.00</td>
<td>Insomnia, unspecified</td>
</tr>
<tr>
<td>G89.21 - G89.29</td>
<td>Chronic pain not elsewhere classified</td>
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<tr>
<td>H93.11 - H93.9</td>
<td>Tinnitus</td>
</tr>
<tr>
<td>M79.7</td>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>P91.60</td>
<td>Hypoxic-ischemic encephalopathy (HIE), unspecified</td>
</tr>
</tbody>
</table>
The above policy is based on the following references:


37. Krull KR. Attention deficit hyperactivity disorder in children and adolescents: Clinical features and evaluation. Last reviewed December 2013. UpToDate Inc., Waltham, MA.


Amendment to
Aetna Clinical Policy Bulletin Number: 0221 Quantitative EEG (Brain Mapping)

There are no amendments for Medicaid.