QUANTITATIVE EEG ANALYSIS OF PATIENTS WITH CHRONIC PAIN: AN EXPLORATORY STUDY

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This study examined quantitative EEGs of six individuals with chronic pain and compared them to an age- and gender-matched normative database of healthy control subjects in an attempt to discern whether a particular pattern of resting state EEG activity is associated with chronic pain. In the chronic pain group, significantly reduced absolute power was seen in delta and theta bandwidths at frontal sites in the eyes-closed condition. In the eyes-open condition, significantly reduced absolute power was seen in delta, theta, and alpha bandwidths at frontal, central, and temporal sites, and increased relative high beta power was seen in the parietal region. Reduced theta/high beta and delta/high beta ratios were seen in the parietal region. Quantitative EEG neuromarkers of chronic pain are suggested.

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CHAPTER 1

INTRODUCTION

Historically, pain was understood as a peripheral phenomenon and a reflexive response to tissue injury or damage. Degree of pain experienced by an individual was expected to be commensurate with the degree of observable tissue damage present. In this model, the brain was not involved in the perception of pain other than as a passive receiver. In 1965, Melzack and Wall proposed the gate theory of pain perception. This model described nociceptive or painful input as being modulated by gating mechanisms in the spinal cord on its way to the brain. Later research began to point toward an increasingly important role for suprapsinal mechanisms in the perception of pain. Current understanding of pain processing involves multiple neurophysiological mechanisms of integration and modulation involving interaction among peripheral tissues, the spinal cord, and the brain (Jensen, Hakimian, Sherlin, & Fregni, 2008).

Literature Review

Measuring Brain Activity

There are several ways to measure and localize cerebral activation associated with states of pain. Neuroimaging techniques utilized for mapping brain regions associated with pain include functional magnetic resonance imaging and positron emission tomography. Functional magnetic resonance imaging (fMRI) measures localized changes to brain vasculature in response to neuronal activation based on the blood oxygen level dependent (BOLD) signal. The BOLD signal is produced by changes in levels of the magnetic endogenous molecule deoxyhemoglobin and changes in regional cerebral blood flow (rCBF). Positron emission tomography (PET) scanning measures localized metabolic changes based on regional cerebral blood flow via use of

radioactive isotypes which are injected intravenously and carried by the blood to the brain (Peyron, Laurent, & García-Larrea, 2000).

Techniques utilized to measure electrical activity in the brain include electroencephalography (EEG), including quantitative EEG (qEEG); magnetoencephalograpy (MEG); and evoked potentials (EPs). EEG is used to measure changes in cortical electrical activity. EEG scalp surface electrodes measure magnetic fields created by electrical dipoles generated by assemblies of neurons arranged in functional cortical columns. These columns are arranged perpendicularly to the surface of the cortex. The dipoles produced by electrical activity in the cortical columns are transferred via volume conduction through the surrounding tissues and are picked up and amplified by the EEG sensors (Rowan & Tolunsky, 2003). MEG also measures changes in cortical activity, but at a distance from the scalp via an array of supercooled superquantum induction devices (SQUIDS) (Chen, 2001).

Quantitative EEG is a more recent development in EEG technology which utilizes a fast Fourier transform (FFT) algorithm to convert analog EEG signals into digital signals, allowing for precise quantification and analysis of signals both at single electrode locations and across the scalp as a whole. These digitized recordings allow the identification of specific electrical waveform patterns within each signal. Measures assessed may include relative amplitude and power of the EEG signal within defined bandwidths as well as within single-hertz “bins”, as well as measurements of phase and coherence, which reflect speed of information transfer between sites and degree of functional connectivity between regions. In comparison with standard analog EEG, quantified EEG measurements can be analyzed statistically and can be presented as color-coded topographic maps for visual inspection of various aspects of brainwave activity. In addition, an important advance that has been permitted by qEEG analysis is the development of

lifespan normative databases against which individual qEEGs can be compared. The individual qEEG data can be compared with these age- and gender-matched norms, yielding Z-scores which assist in interpretation and treatment planning (Kaiser, 2006; Lubar, 2003).

Both PET scan and fMRI studies infer brain activation indirectly via changes in metabolism or local blood circulation, while EEG and MEG measure activation more directly via electromagnetic phenomena of activated assemblies of neurons. FMRI and PET technologies have greater spatial resolution, while EEG, MEG, and EPs have greater temporal resolution (Apkarian, Bushnell, Treede, & Zubieta, 2005).

Experimental Pain Induction

Researchers investigating the neurophysiological correlates of pain have utilized a variety of techniques to induce pain in the laboratory setting. These techniques have included application of contact heat, laser heat, cold, electric shock, pressure, muscular injections of hypertonic saline, capsaicin, esophageal distension, gastric distension, colonic distension, and rectal distension (Apkarian et al., 2005).

Acute Pain in the Normal Brain

Several brain regions have been consistently found to be activated in experimentally-induced pain. The most commonly implicated cortical regions include the somatosensory areas (the primary somatosensory cortex, the secondary somatosensory cortex, and the insular cortex), limbic areas (the anterior cingulate cortex and insular cortex), and associative areas (the prefrontal cortex) (Apkarian et al., 2005; Jensen, 2010).

Chen (2008) conducted a review of work on the activation of pain perception in the brain conducted between 1993 and 2008. He summarized areas of the brain found to be involved in pain activation in normal, healthy subjects. Sensory information about incoming pain stimuli

from the spinal cord is transmitted bilaterally from the thalamus to other parts of the brain. Peyron et al. (2000) have noted that this bilateral thalamic activation may induce an overall arousal of the cortex in response to pain.

Both the primary and secondary somatosensory cortices are involved in the pain phenomenon. The primary somatosensory cortex (SI), which is arranged somatotropically, has been shown to be the first cortical area to process somatosensory information following electrical nerve stimulation, and this processing occurs contralateral to the site of stimulation. Beyond this, considerable evidence supports the role of the secondary somatosensory cortex (SII) in the processing of pain (Bromm et al., 2000). The SII is involved in recognition, memory, and learning of pain information. Unlike the contralateral response of the SI region, however, stimuli are reflected in bilateral activation of specific, paired sites in the SII. Thus, for example, a painful stimulus applied to the right index finger would activate a different pair of sites than a painful stimulus applied to the left index finger. This is referred to as paired bilateral activation, and reflects an interhemispheric transfer of nociceptive information. Temporal analysis of neuronal signals suggests that the paired activation is more likely to result from simultaneous activation of the cortices by spinothalamic projections and thalamic relay stations rather than sequential activation via transcollosal fibers (Bromm et al., 2000).

Bromm et al. (2000) report that SII activity in response to pain appears to be related to overall arousal level, describing it as “tonically preprimed” by projections from other cortical and subcortical structures that control the arousal state of the brain. The responsiveness of the SII to painful stimuli has been shown to be attenuated by decreased vigilance, distraction, and administration of a sedative such as clonidine. In summary, they state that the SII reflects part of

the sensory-discriminative component of pain. This region is said to locate the site of pain on the body, explore the magnitude of the pain, and compare the hurting to the non-hurting side.

Other brain regions are also involved in the processing of pain in normal, healthy subjects. The cingulate gyrus (both anterior and posterior) has been found to be involved in the affective and attentional components of pain, as well as response selection (Peyron et al., 2000). The insular cortex (IC) is involved in the affective, aversive aspects of pain. Finally, the prefrontal cortex (PFC) has been found to be involved and is thought to exert executive control over cognitive-evaluative aspects of pain perception (Chen, 2008).

EEG Changes and Experimentally-Induced Acute Pain

The alpha rhythm is the dominant oscillation in the normal human EEG spectrum. It is reduced in power during physiologic events such as sensorimotor or cognitive processes and can be related to attention. The disruption of this oscillatory rhythm is known as alpha event-related desynchronization or alpha ERD. The lower the alpha power, the more effectively information is transferred through thalamo-cortical and cortico-cortical channels. This phenomenon has been referred to as thalamo-cortical gating. Suppression of the alpha rhythm has been said to "open the gates" to increased nociceptive input from the periphery (Babiloni et al., 2006; Pfurtscheller & da Silva, 1999). Suppression of alpha power or alpha ERD has been seen in the primary somatosensory cortex in anticipation of an aversive or painful electrical stimulus (Babiloni et al., 2003). In addition, magnitude of anticipatory alpha ERD in the primary somatosensory cortex prior to a painful stimulus predicted subjective evaluation of the intensity of the pain experience. The stronger the ERD in anticipation of pain, the greater the subjectively rated experience of pain (Babiloni et al., 2006).

The converse of alpha ERD or activation is alpha event-related synchronization or ERS. This occurs when, in anticipation of an event, synchronous alpha activity increases in power. It has been postulated that alpha desynchronization in anticipation of a painful stimulus reflects an alarm or activation preparation, while alpha synchronization in anticipation of a painful stimulus reflects either habituation or "defensive idling" as preparation. In the same study, increases in alpha synchronization by healthy individuals during experimentally-induced anticipation of a painful stimulus were associated with decreased subjective perception of pain (Babiloni et al., 2006). These findings may be relevant to chronic pain if it is the case that maintenance of chronic pain is facilitated by hypervigilance, appraisal of harm, and/or fear of pain (Roelofs, Peters, Zeegers, & Vlaeyen, 2002). In a similar vein, Zhuo (2008) has proposed that cortical hyperexcitability may be associated with increases in chronic pain.

Induction of pain in controlled laboratory settings generally results in decreases in alpha power over the somatosensory cortex and sometimes the visual cortex. For example, during an experimentally induced cold pain condition in which subjects placed their left hands in a bucket of ice water for 10 minutes, decreases in alpha amplitude were observed over the contralateral temporal scalp corresponding to the somatosensory cortex and increased over the posterior scalp corresponding to the visual cortex (Dowman, Rissacher, & Schuckers, 2008).

Findings have been mixed with regard to whether pain is an ipsilateral or contralateral event with regard to which hemisphere is activated. It appears that touch, like movement, is processed in the contralateral hemisphere, but there still appears to be some debate as to where pain itself is processed on the somatosensory cortex. One recent study attempted to discriminate between the cortical location of pain processing vs. the location of tactile processing. Ploner et al. (2006) conducted a study designed to differentiate the EEG effects of tactile stimulation from

painful stimulation. For the painful stimulus, they utilized forty painful cutaneous laser stimuli, which selectively activate nociceptive afferent fibers without activating tactile afferent fibers. They delivered the painful stimulus to the back of the right hand. In four of the 12 subjects, the left hand was stimulated as well. They used a tactile stimulus for the control condition. Application of the painful stimulus resulted in a suppression of the sensorimotor Mu rhythm (the idling synchronous rhythm) bilaterally. On the primary motor cortex, this was seen in suppression of synchronous alpha rhythm at about 10 Hz. On the primary somatosensory cortex, this was seen in suppression of the synchronous beta rhythm at about 20 Hz. In addition, the painful stimulus resulted in suppression of the posterior alpha rhythm. This is in distinction to the touch stimulus, which localized only to the contralateral hemisphere and did not suppress the posterior alpha rhythm. Interestingly, the painful stimulus primarily localized to the right somatosensory cortex, regardless of which hand was stimulated, indicating that perception of pain appeared to be primarily a function of the right hemisphere. Further, the overall suppression of the brain's cortical idling rhythms appeared to be a global phenomenon, indicating widespread changes in cortical function and excitability. Ploner et al. (2006) note that the right hemisphere is more involved in the processing of pain and negative affect, and that the alerting function of pain may be mediated by a right-lateralized cortical-subcortical network dedicated to the detection of salient events. They hypothesize that the alerting function of pain may have adaptive value for the organism by increasing hypervigilance under conditions of threat.

Neuroimaging and Electrophysiological Findings in Chronic Pain

Chronic pain has been shown to disrupt the default mode network (DMN) of the brain, a group of structures that are believed to maintain the normal resting state of the brain. The default mode network has been shown to be disrupted in a variety of pathological conditions, including

chronic pain (Baliki et al. 2008). In addition to examining abnormalities in brain function during rest and under task, researchers have also investigated the impact of both experimentally-induced acute pain as well as spontaneous pain exacerbations in chronic pain patients. Notably, the cortical networks involved in processing acute experimentally-induced pain in healthy subjects appear to differ from those involved in processing chronic pain in clinical populations. In a 2005 meta-analysis of research examining how activity in various brain regions "creates and modulates the experience of acute and chronic pain states," Apkarian et al. reviewed research investigating human brain activity during pain. Studies included in the review consisted of hemodynamic studies (fMRI, PET, SPECT), studies using neuroelectrical methods (EEG, MEG), and those which examined the neurochemistry of pain (e.g. receptor binding, neurotransmitter modulation). Of these studies, 68 examined experimentally-induced pain in normal subjects, and 30 examined brain activity in clinical pain states (e.g. chronic back pain, neuropathy, cardiac pain, migraine, cluster headache, spinal cord injury, cancer pain, complex regional pain syndrome). Of the studies examining brain activity in clinical pain states, some examined spontaneous pain, while others utilized methods for experimentally inducing pain episodes, such as use of nitroglycerin to induce cluster headache, presentation of visual stimuli to induce migraine, administration of dobutamine to induce cardiac pain, gastric or rectal distension to induce abdominal pain in IBS patients, or application of mechanical pressure in fibromyalgia patients. Comparison revealed differential activation of brain regions activated during experimentally induced pain in normal subjects versus brain regions activated during pain in clinical pain patients. Notably, in chronic pain patients, additional brain regions were found to be activated, particularly in the prefrontal cortex, which is postulated to be engaged in cognitive/emotional aspects of pain assessment.

Baliki et al. (2006) examined fMRI correlates of two types of pain, high sustained and increasing pain, in chronic back pain (CBP) patients. They found that sustained high pain resulted in increased activity in the medial prefrontal cortex (mPFC), including the rostral anterior cingulate. This activity was strongly correlated with intensity of CBP. Additional bilateral activity was observed in the posterior thalamus and the prefrontal cortex, as well the ventral striatum and amygdala. These authors remark that when pain level is high and sustained, it engages brain areas involved in emotion, cognition, and motivation. By contrast, during periods of increasing pain, cortical responses more closely reflected those seen in acute pain, involving regions associated with the sensory and discriminative aspects of pain: the primary and secondary somatosensory cortices, the right anterior and posterior insula, the mid-cingulate, and the cerebellum. Interestingly, intensity of activation in the insula was highly associated with number of years the individual had suffered with CBP, suggesting a long-term priming effect or sensitization of the insula in individuals with chronic pain. These differential findings indicate that increasing pain level activates areas involved in sensory processing of pain, while high sustained pain activates areas involved in emotional processing of pain. In this study, anxiety and depression showed no significant relationship with these conditions, nor did they influence ratings of pain intensity or duration.

Baliki et al. (2006) then examined the brain activity of a separate group of CBP patients and controls in response to experimentally-induced thermal pain. In this study, thermal pain was most highly correlated with activity in the insular cortex in both CBP and control subjects. Again, sustained spontaneous CBP was correlated only with medial PFC (mPFC) activity. Taken together, these findings provide evidence that the sensory, affective, and cognitive properties of spontaneous CBP pain differ markedly from acute pain. It is argued that sustained high activity

in the mPFC most likely reflects a negative emotional state in reference to the self, i.e. suffering. In 1968, Melzack and Casey postulated a role for the frontal cortex in mediating between cognitive activities and the motivational-affective features of pain and it is suggested that the mPFC is the site reflecting that mediation (Baliki et al., 2006).

Somewhat consistent with the fMRI findings summarized above are the findings from EEG research in which sustained, high levels of spontaneous pain in neuropathic pain patients have been associated with increases in the high theta (6-8 hertz) and low beta (12-16 hertz) frequencies in the insular cortex, the anterior cingulate cortex, and the primary and secondary somatosensory cortices (Stern, Jeanmond & Sarnthein, 2006).

Clinical Improvements in Pain Following EEG Modulation

There have been reports of clinical improvements of pain following operant conditioning of the EEG using biofeedback. (EEG biofeedback is also termed neurofeedback.) Findings have been reported for a range of clinical pain syndromes (Jensen, Sherlin, Hakiman, & Fregni, 2009).

Jensen et al. (2007) have reported that patients treated with neurofeedback in addition to other pain management interventions have reported decreases in pain as well as decreased depression and anxiety and improved well-being. In an attempt to examine the role played by neurofeedback alone, they examined eighteen patients with severe long-standing Complex Regional Pain Syndrome Type 1 (CRPS-I). CRPS-1, formerly known as reflex sympathetic dystrophy, is a debilitating post-traumatic pain condition involving local neurogenic inflammation and severe pain in the skin, subcutaneous tissues, and joints. In this study, patients were examined before and after a single 30-minute session of neurofeedback and found to have significant decreases in pain intensity as well as improvements in secondary symptoms including muscle tension, muscle spasm, deep ache, skin sensitivity, and well-being. Treatment

protocols were individualized for each patient and utilized a variety of reinforcement frequencies and scalp locations, with T3-T4 bipolar training being the most common. These sites are located over the left and right temporal lobes, respectively. (See Figure 1 for an illustration of the International 10-20 System of EEG electrode placement.) These patients were current or former participants in a comprehensive 20-day pain treatment program and were undergoing neurofeedback therapy in addition to medication management, physical therapy, and psychotherapy. Due to the individualized and multimodal nature of the treatment program, the investigators limited their data collection for this study to immediately before and after a single neurofeedback session, in order to minimize any possible confounds from other treatment interventions. However, it should be noted that in addition to varying protocols, participants were in varying stages of ongoing neurofeedback training: the specific session number examined varied widely, from the 7th to the 143rd, with a median of the 20th session being examined.

Sime (2004) reported successful treatment of a patient with trigeminal neuralgia who was being treated with narcotics and was scheduled for surgery to sever the trigeminal nerve. The treatment protocol included neurofeedback, peripheral biofeedback, and stress management training. This patient experienced sufficient pain relief to not only cancel the surgery, but also to discontinue use of the narcotic pain medication. Improvements were also noted in bruxism and sleep quality. Benefits were maintained at one year post-treatment. In this patient, the greatest pain reductions were noted following training at T3-T4, enhancing 7.5-10.5 Hz, and inhibiting 2-7 Hz and 22-30Hz. (See Figure 1 for electrode site locations.)

Caro and Winter (2001) reported that 15 patients with fibromyalgia who received 40 or more sessions of neurofeedback training all reported significant improvement in self-reported pain and fatigue, as well as physician-assessed soft-tissue tenderness. Visual attention measures

on a continuous performance test also showed significant improvement. The protocol used consisted of enhancement of 12-15 Hz and inhibition of 4-7 Hz and 22-30 Hz at vertex location Cz. Cz is a central or midline site located at the top of the skull above the sensorimotor strip and over the cleft between the two hemispheres with access to subcortical regions. (See Figure 1 for electrode site locations.)

Walker reported successful treatment of 17 patients disabled by traumatic brain injury (TBI), all of whom were more than two years post-injury. All reported pain as their most prominent symptom, and none were expected to return to work. Self-reported improvements averaged >80%, and more than 60% of the patients returned to work following treatment (Walker, Norman, & Weber, 2002).

Othmer and Othmer (2006) report a clinical case history, from the practice of Richard Souter, Ph.D., of a male patient with multiple sclerosis and fibromyalgia who suffered from severe chronic pain accompanied by numbness, tingling, weakness, fatigue, and moderate depression. He was maintained on multiple medications for pain, sleep, and depression at intake. He was treated with 50 sessions of neurofeedback. His pain resolved completely by session 29 and he remained pain-free and was able to discontinue his medications. Souter reported that the patient continued to do well and was seen for occasional “booster” sessions to maintain his gains.

Ibric (2009), a physician, reported ten case studies of chronic pain treatment from her own practice utilizing neurofeedback for conditions including various neuropathies and pain secondary to TBI, spinal cord injury, meningitis, motor vehicle accident, surgery, peripheral injury, myofascial pain, head injury, Parkinson’s disease, cancer, leukemia, and rheumatoid arthritis, as well as idiopathic neuropathy. All patients achieved significant to complete remission of self-reported pain. Other improvements included return to work, school, or travel,

improvements in sleep, decreases in anxiety and depression, and reduction or elimination of pain medications.

The finding that patients are able to consciously alter brainwave activity to effect clinical change is not limited to the neurofeedback literature. It has also been shown that chronic pain patients can learn to alter activation of pain-related brain regions via use of feedback from real-time fMRI. In 2005, deCharms et al. reported the use of real-time fMRI feedback to help patients learn to decrease activation of the rostral anterior cingulate cortex, which as previously noted has been shown to be involved in the emotional aspects of pain processing. Patients able to achieve decreased activation of this region reported concomitant decreases in pain.

Supporting the observations made earlier that pain syndromes may be associated with disruptions or alterations in the default mode network of the brain (Baliki et al., 2008; Othmer and Othmer, 2006), Othmer and Othmer (2006) propose that several types of cortical dysregulation underlie various pain conditions. These underlying conditions include pain related to cortical hyperexcitability, including fibromyalgia and reflex sympathetic dystrophy (now known as complex regional pain syndrome); episodic pain associated with central nervous system instability such as migraines; pain exacerbated by prior traumatic experience such as traumatic brain injury or event-related psychological trauma; and finally, specific pain categories such as neuropathic pain. They describe three main neurofeedback approaches to pain remediation: mechanisms-based training, including enhancing alpha or the sensorimotor rhythm; qEEG-based training, which targets brainwave activity that deviates from database norms; and an approach based on conceptualizing brain function as a non-linear, dynamical (NLD) system described as NLD-based training. All of these approaches may promote deactivation of brain hyperexcitability.

Summary of Pain Findings in the Brain

In summary, pain has been found to be represented in the human brain in a number of areas. Findings from neuroimaging and electrophysiological studies converge in recognizing activation in the primary and secondary somatosensory cortices, the insular cortex, the anterior cingulate cortex, and the prefrontal cortex. Activation of the prefrontal cortex and the anterior cingulate cortex appear to be involved in the suffering or cognitive-emotional aspects of the pain experience, and these areas are more likely to be activated in individuals with chronic pain as opposed to experimentally-induced acute pain. In the EEG, activation of any kind is generally observed as a relative increase in fast wave or beta activity, notably desynchronized beta, and an associated decrease in slower wave activity, particularly alpha, which is considered to be an idling rhythm. In EEG research, it has been found that the subjective experience of pain is associated with a relative decrease in amplitude of the slower frequency bands (delta, theta, and alpha), and a relative increase in amplitude of faster wave (beta) activity. This is supportive of a theory of cortical hyperexcitability as a mechanism for maintaining the sensitization that is seen in chronic pain. In addition, it has been found that individuals are able to learn, via operant conditioning (or neurofeedback), to control their EEG brainwave activity, and neurofeedback interventions have been reported to be effective in cases of chronic pain.

Aims of the Current Study

The current study proposed to examine quantitative EEG (qEEG) measures of patients reporting chronic pain as a primary complaint and compare their qEEGs to a database of healthy, normal, age and gender-matched controls to determine whether specific patterns of alterations are observed in an at-rest condition. This was proposed as an exploratory or pilot study. The question to be answered was whether chronic pain patients present a specific qEEG pattern or

neuromarkers, identifiable as Z-scored deviations, which might be amenable to intervention. Based on the above-reviewed previous research findings, it was hypothesized that the qEEGs of pain patients would deviate from database norms, and would contain lower levels of alpha frequency brainwave activity (8-12 Hz) and higher levels of beta activity (12-30 Hz) than database norms. As noted above, decreases in alpha activity and increases in beta activity correspond to activation of the associated region (Babiloni et al., 2006), and chronic pain may be reflected in increased cortical excitation or overactivation (Zhuo, 2008). Activity in these bandwidths was examined in terms of both absolute power and relative power. Specific research hypotheses follow.

Hypotheses of the Current Study

Hypothesis 1

It is hypothesized that average qEEG Z-scores for the chronic pain group will show significant deviations in the alpha frequency range (8-12 hertz) from the normative database at one or more frontal and central cortical sites. Frontal sites to be examined will include FP1, FP2, Fz, F3, F4, F7, and F8. Central sites to be examined will include Cz, C3, C4, T3, and T4. This first hypothesis is based on the above reviewed work, including that of Apkarian et al., (2005), who found increased activation of the cingulate gyrus in pain, and particularly of the prefrontal cortex in chronic pain; Baliki et al., (2006), who found increased activity in the medial prefrontal cortex (mPFC) in chronic pain; Babiloni et al. (2006), who reported suppression of the alpha rhythm over the somatosensory cortex as a predictor of pain intensity, Chen (2008) who reported increased activation of the prefrontal cortex in chronic pain, Peyron et al., (2000) who reported increased activation of the cingulate gyrus, and Dowman, Rissacher, and Schuckers (2008), who

showed decreases in alpha amplitude over the somatosensory cortex in response to painful stimuli. A significant deviation is defined as a Z-score of $\pm$ 1.96 or greater.

Hypothesis 2

It is hypothesized that average qEEG Z-scores for the chronic pain group will show significant deviations in the beta range (12-30 hertz) from the normative database at one or more frontal and central cortical sites. Frontal and central sites to be examined include those listed above. This second hypothesis is also based on the above-reviewed work referenced in Hypothesis 1, as increased relative beta activity is also reflective of increased activation in the same regions. A significant deviation is defined as a Z-score of $\pm$ 1.96 or greater.

CHAPTER II

METHOD

Participants

Files of six clients who presented for evaluation and/or treatment at the UNT Neurotherapy Lab, located in the Department of Rehabilitation, Social Work, and Addictions at the University of North Texas in Denton, Texas, who indicated chronic pain as a major complaint were selected for analysis for this pilot study. The cases were drawn from archived client records. The chronic pain group included 2 males (33.3%) and 4 females (66.7%). Age ranged from 34.61 years to 58.89 years, with a mean age of 44.18 years (*SD* = 9.86). All participants were of European American ethnicity. Five were right-handed (83.33%) and one was left-handed (16.7%).

Procedure

As part of the standard intake process, all clients underwent an intake assessment battery which included a clinical interview and history, the completion of various paper and pencil measures, administration of continuous performance tests, other psychological assessments as indicated, and quantitative EEG (qEEG) recording. All clients were provided with verbal and written descriptions of the Lab's privacy practices and compliance with HIPAA regulations prior to intake assessment. All gave verbal and written informed consent for qEEG collection and evaluation and for psychological and/or cognitive assessment as part of the standard intake process. The purposes of the Lab as a research and training facility were described to them in detail, and they gave written consent for the anonymous use of their assessment and treatment records for current and future research and training purposes.

In order to protect the confidentiality of client information, all records were assigned a unique client identification number. All data collected were identified only with the client identification number. Clients' names, contact information, and any other personally identifiable information were not included with the research record or data analysis. Research and data analysis were conducted following approval from the UNT Institutional Review Board.

Apparatus and Measurement

For the EEG assessment, subjects were seated comfortably in a reclining chair in a quiet, semi-darkened room. EEG measures were recorded from nineteen scalp sites according to the International 10-20 system of electrode placement (Jasper, 1958) and digitally referenced to linked earlobes. Two additional electrodes were applied to peri-orbital sites to monitor eye movement for artifacting prior to data analysis. Electrode impedances were kept at or below 5 K ohms and within one K ohm of one another. The Deymed Tru-Scan 32 EEG System of hardware and software was used to collect the EEG recording. Bandpass filters were set at 0.5-80 Hz. Sampling rate was set at 128 samples per second. Subjects were instructed to minimize movement during the recordings. EEG data were collected for ten minutes under eyes-open and ten minutes under eyes-closed conditions. The Deymed raw EEG data files were then imported into the Neuroguide 2.2.5 software system (Thatcher, 2005) for artifacting and analysis.

In quantitative encephalography (qEEG), the analog EEG record is visually inspected in order to choose recording epochs that are free of artifacts such as eye movement, muscle activity, and drowsiness. The chosen epochs are then analyzed using fast Fourier transformation (FFT) to produce color topographic maps and spectral analysis that includes measures of absolute power, relative power, single band magnitude, coherence, asymmetry, and phase. For the current study, the analog EEG records were carefully examined for epochs containing eye movement, muscle,

or drowsiness artifacts, and these epochs were removed from the analog record before subjecting it to digital analysis and quantification. At least thirty epochs of each record were chosen via visual inspection for fast Fourier transformation. Artifact-free records were digitally analyzed using Neuroguide EEG analysis software (Thatcher, 2005). Reports were generated indicating relative and absolute power amplitudes in the 0.5-30 Hz frequency range at all 19 scalp sites in both the eyes open and eyes closed conditions. EEG records were then compared to the Neuroguide Lifespan Database (Thatcher, Biver, Walker, North, & Curtin, 2000) for Z-score analysis.

The Neuroguide Lifespan Database (Thatcher et al., 2000) consists of 625 subjects ranging in age from 2 months to 82 years. Of the total number of normative database subjects, 56.8% were male and 43.2% were female. Database subjects were screened to determine that they had an uneventful prenatal, perinatal, and postnatal period, no disorders of consciousness, no history of central nervous system diseases, no convulsions either febrile or psychogenic, and no abnormal deviation with regard to mental and physical development.

Data Analysis

Absolute power and relative power at each of the 19 scalp EEG collection sites for each of the subject qEEGs were calculated in both eyes-open and eyes-closed conditions using a Laplacian reference montage. These calculations were then compared to an age- and gender-matched database of normal, healthy control subjects (Thatcher et al., 2000). Deviations from the normative database were converted to Z-scores for each site for all individuals.

EEG frequency bandwidths examined included delta (1.0-4.0 Hz), theta (4.0-8.0 Hz), alpha (8.0-12.0 Hz), beta (12.0-25.0 Hz), and high beta (25.0-30.0 Hz). The alpha bandwidth was further broken down into low frequency alpha (Alpha 1: 8.0-10.0 Hz) and fast frequency

alpha (Alpha 2: 10.0-12.0 Hz). The beta bandwidth was further broken down into Beta 1 (12.0-15.0 Hz), Beta 2 (15.0-18.0 Hz), and Beta 3 (18.0-25.0 Hz).

Individual qEEG Z-scores for each site in each bandwidth were pooled in order to obtain average Z-scores for the chronic pain group at each electrode site. These average Z-scores were then examined to identify the scalp locations and frequency ranges that deviated significantly from the normative database. Results were considered to be significant if there was an average Z-score difference at any site of greater than $\pm$ 1.96 from the database norm.

CHAPTER III

RESULTS

Hypothesis 1

It was hypothesized that average qEEG Z-scores for the chronic pain group would show significant deviations in the alpha frequency range (8-12 Hz) from the normative database at one or more frontal and central cortical sites. When the chronic pain group's Z-scores were averaged in the eyes-closed condition, significant deviations from the normative database were seen at four frontal sites. Specifically, the chronic pain group on average evidenced significantly lower absolute power in both the delta (1-4 Hz) and theta (4-8 Hz) frequency bandwidths at frontal sites, Fp1, F4, and F7 during the eyes closed condition. In addition, significantly lower absolute power was seen at frontal site Fp2 in the delta frequency range (See Table 1).

Inspection of the chronic pain group's average relative power Z-scores in the eyes-closed condition did not reveal any significant deviations from the normative database. However, a trend was seen in that the average relative power Z-scores for the chronic pain subjects at most sites in the eyes-closed condition in the low frequency ranges (i.e. delta, theta, and alpha) were negative (See Table 2).

When the chronic pain group's Z-scores were averaged in the eyes-open condition, significant deviations from the normative database were seen at six frontal sites, one central site, and two temporal sites. Significantly decreased absolute power in the delta, theta, and alpha frequency ranges was seen at frontal sites Fp1, Fp2, F4, and F7. Significantly decreased absolute power was seen at frontal site Fz in the alpha range. Significantly decreased absolute power was seen at central site C3 in the theta range. Significantly decreased alpha power at sites Fp1, Fp2, and F4 was seen in both the Alpha 1 (8-10 Hz) and Alpha 2 (10-12 Hz) ranges. Significantly

decreased alpha power at sites Fz, F7, and F8 was seen in the faster Alpha 2 range (10-12 Hz). Significantly decreased absolute power in the delta range was seen at temporal sites T5 and T6 (See Table 3).

Inspection of the chronic pain group's average relative power Z-scores in the eyes-open condition did not reveal any significant deviations from the normative database in the delta, theta, and alpha frequency ranges. However, a trend was seen in that the average relative power Z-scores for the chronic pain subjects at most sites in the eyes-open condition in the low frequency ranges (i.e. delta, theta, and alpha) fell in the negative direction (See Table 4).

Hypothesis 2

It was hypothesized that average qEEG Z-scores for the chronic pain group would show significant deviations in the beta range (12-30 Hz) from the normative database at one or more frontal and central cortical sites. When the chronic pain group's Z-scores were averaged in the eyes-closed condition, no significant deviations in the fast frequency ranges (i.e. beta or high beta) were seen at any sites (See Tables 1 and 2). When the chronic pain group's Z-scores were averaged in the eyes-open condition there was significantly increased relative power in the high beta range at parietal site Pz (See Tables 3 and 4).

Additional Findings

Significant group average deviations were seen in the absolute and relative power ratios of the proportion of slow waves to fast frequency or high beta waves in the parietal region. There were significant deviations from the norm in the ratio of theta/high beta power in both the eyes open and eyes closed conditions. In the eyes-open condition, the chronic pain group's average theta/high beta ratio was significantly lower than the norm at parietal site Pz (See Table 5). In the eyes closed condition, the chronic pain group's average theta/high beta ratio was also

significantly lower than the norm at parietal site Pz. In addition, at parietal site P3, the chronic pain group showed both a significantly decreased theta/high beta ratio and a significantly decreased delta/high beta ratio in the eyes closed condition (See Table 6).

Individual Topographic Maps

Individual summary topographic maps of Z-scored absolute and relative power in the main frequency bandwidths (delta, theta, alpha, beta, and high beta) in the eyes open condition are presented in Figures 2-13.

CHAPTER IV

DISCUSSION

This pilot study was undertaken to determine whether patients with chronic pain exhibit significant differences in cortical EEG activity from healthy subjects in a normative database. As hypothesized, quantitative EEG analysis of chronic pain patients did reveal significant differences, on average, in multiple frequency bands and in multiple cortical locations across the cortex.

Summary of Findings of the Current Study

It was expected that deficits in alpha activity would be seen at frontal and central sites, and these hypotheses were supported. Deficiencies in absolute alpha power were seen in the eyes open condition at six of the seven frontal sites examined. Although reduced alpha power was seen at all three central sites, indicating a trend in the expected direction, this difference did not reach the level of statistical significance. Notably, deficits in alpha activity were not observed in the eyes closed condition in terms of either absolute or relative power.

Furthermore, in addition to reductions in alpha power, significant deficits were also seen in the lower frequency ranges of delta and theta, particularly at frontal sites, but also in the central and temporal regions. Significantly decreased delta power was seen in five frontal sites and significantly decreased theta power was seen at six frontal sites. Significantly decreased theta power was observed at central site C3. We also saw significantly decreased bilateral delta power in the temporal region at sites T5 and T6. In addition, significantly reduced delta and theta activity was observed at four frontal sites in the eyes closed condition. However, patients with chronic pain exhibited more widespread abnormalities in these lower frequency ranges in the eyes open condition. In the eyes open condition, these reductions in power were seen in the

central and temporal regions as well. Thus patients exhibited a more widespread pattern of significantly reduced slow wave activity as compared to normal subjects when their eyes were open than when they were closed.

In addition to alterations in slow wave activity, we also hypothesized that chronic pain patients would exhibit increased fast frequency activity at frontal and central sites. We expected to see increased activity in the beta range, including fast frequency beta, at frontal and central sites. Although individual clients did display significant increases in the beta and high beta ranges in these locations, when grouped together, the overall group average trended in this direction but did not reach the level of statistical significance. However, we did see significantly elevated high beta power for the group in the parietal region at site Pz. In addition, we also saw a significantly increased proportion of high beta power relative to both delta and theta power in the parietal region at site P3, and an increased proportion of high beta power relative to theta power at site Pz.

Comparisons with Prior Research

Prior findings from neuroimaging research have shown that cortical brain regions involved in pain processing include the prefrontal cortex, the anterior cingulate cortex, the insular cortex, and the primary and secondary somatosensory cortices (Jensen et al., 2008). Further, it has been suggested that the experience of chronic pain may disrupt resting default networks in the brain (Baliki et al., 2008) and that individuals with chronic pain process and experience pain differently than healthy individuals (Apkarian et al., 2005). This line of research points to the theory that chronic pain changes the functional activity of the cortex at rest (Stern et al., 2006; Zhuo, 2008).

As previously discussed, increases in fast frequency activity or decreases in slow wave activity indicate increased levels of cortical arousal or activation of cortical regions. These increases are expected under demand conditions when subjects are instructed to perform particular tasks or mental operations, but we do not expect to see them in healthy subjects at rest. Comparison of the chronic pain patients to a large age and gender matched database of healthy, normal individuals allows us to more precisely quantify the location and extent of variations seen in clinical populations.

The current study found significantly deviant power in EEG recording sites corresponding to cortical regions involved in the processing of chronic pain. The primary somatosensory cortex receives incoming somatotropically organized pain information, and activation at central sites along the sensorimotor strip is therefore associated with the reception of incoming pain stimuli from specific locations in the body. In the chronic pain group, we saw decreased theta activity at C3, located over the left hemisphere on the sensorimotor strip, reflecting overactivation at this site.

Incoming sensory information, including pain, is also relayed to the secondary somatosensory cortex for integration and processing. We did find overactivation of this region as indicated by excessive high beta activity, as well as decreased ratios of slow to fast wave activity in the parietal region.

The current study also revealed decreased slow wave activity in the frontal, central, and temporal regions in the chronic pain group. Excessive anxiety or rumination has been associated with increased activation of the anterior cingulate cortex (Hammond, 2005). In chronic pain patients, the increased activation seen in this region may also correlate with the suffering state in chronic pain proposed by Melzack and Wall (1965). Real-time guided feedback utilizing fMRI

has been shown to be effective at reducing activation in this region, and this deactivation has been seen to be associated with decreased levels of pain (deCharms et al., 2005). These findings point to future research possibilities investigating potential relationships among EEG biofeedback training, anxiety, and pain in this population.

Decreased slow wave activity over the right frontal cortex in the alpha range, as well as in the delta and theta ranges was noted, indicating that the left frontal lobe may be underactive by comparison with the right frontal lobe. This pattern of underactivation of the left frontal lobe by comparison with the right frontal lobe is reminiscent of the now-classic findings by Davidson and colleagues of the frontal alpha asymmetry seen in depression (Davidson, 1995). As depression is a common complication of chronic pain, uptraining activity in the left frontal lobe may be of benefit in cases where this asymmetry is seen. Further research is warranted to clarify potential relationships between left frontal hypoactivation and depression in chronic pain patients.

We also found decreased activity in the theta range over the temporal lobes. This is consistent with a case study in the neurofeedback literature in which a patient with severe trigeminal neuralgia was successfully treated by reinforcing slow wave activity in the 8-11 Hz range in the temporal region (Sime, 2004).

Implications of the Current Study

Given that increased cortical excitability has been postulated as a potential mechanism for the sensitization of chronic pain patients to additional pain experiences and the perpetuation of the pain cycle, efforts to reduce this overall excitability may be fruitful areas for clinical intervention. Traditional intervention for chronic pain has included pharmacotherapy as well as more invasive surgical intervention. Modulation of the resting state activity of the brain through

behavioral modification of the EEG may present an additional or alternative treatment option. Additionally, since chronic pain patients often also experience emotional suffering, including increased rates of anxiety and depression, EEG modulation of cortical regions associated with excessive rumination, anxiety, and depression may also prove beneficial as an adjunctive treatment to pharmacotherapy and psychotherapeutic interventions for pain management and associated emotional symptoms.

Although conclusions from the current study are tentative because of the small sample size, these findings may provide some data regarding possible neuromarkers of chronic pain in the EEG as shown by quantitative analysis and comparison to a large normative database. The findings indicate that Z-score deviations from the normative database in this pilot group are consistent with imaging and prior EEG work implicating abnormal cortical activity in chronic pain. This study extends prior research from the neuroscience literature and connects it with clinical observations and case studies reporting the use of neurofeedback for chronic pain.

Normative databases are useful for research purposes, but they also hold promise for treatment planning and intervention. The Z-scored normative database is often utilized as a clinical tool thought to be useful in interpretation of quantitative EEG data and for neurofeedback treatment planning. The fact that the normative database yielded Z-scores consistent with symptoms and prior research findings on cortical areas which are overactive in chronic pain patients suggests that use of this database may provide a valuable adjunct to traditional pain management strategies in terms of assessment, planning, and as a possible treatment tool.

An important potential benefit of utilizing quantitative EEG for treatment planning is that it allows for individualized treatment intervention strategies best suited to an individual patient's

EEG signature. It is useful to begin to identify particular patterns of activity (or neuromarkers) in a given clinical population, such as pain patients, in order to provide support for understanding associations between given EEG patterns and clinical syndromes. Beyond this, further benefit may be gained by identifying variations within the population which may correspond to comorbid psychological symptoms that may also be amenable to intervention. Additional research with larger sample sizes is required to confirm the findings from this pilot study. Additional investigations correlating comorbid psychological symptoms with specific EEG variations may provide further insight into potential behavioral treatment interventions.

Table 1
Averaged Absolute Power Z-Scores in the Eyes Closed Condition

Z Scored FFT Absolute Power - Eyes Closed - Laplacian										
	Delta 1.0 - 4.0 Hz	Theta 4.0 - 8.0 Hz	Alpha 8.0 - 12.0 Hz	Beta 12.0 - 25.0 Hz	High Beta 25.0 - 30.0 Hz	Alpha 1 8.0 - 10.0 Hz	Alpha 2 10.0 - 12.0 Hz	Beta 1 12.0 - 15.0 Hz	Beta 2 15.0 - 18.0 Hz	Beta 3 18.0 - 25.0 Hz
FP1	-2.026	-2.025	-1.481	-0.724	-0.261	-1.649	-1.318	-1.151	-0.792	-0.567
FP2	-2.011	-1.753	-1.476	-0.900	-0.519	-1.395	-1.645	-1.208	-0.964	-0.742
F3	-1.541	-1.608	-1.133	-0.355	-0.063	-1.273	-0.942	-0.535	-0.395	-0.262
F4	-1.983	-2.138	-1.554	-0.756	-0.397	-1.585	-1.440	-1.095	-0.906	-0.586
C3	-1.579	-1.352	-0.600	-0.232	0.150	-0.480	-0.713	-0.553	-0.139	-0.089
C4	-1.360	-1.271	-0.732	-0.388	-0.022	-0.702	-0.743	-0.599	-0.322	-0.275
P3	-1.648	-1.120	-0.625	-0.121	0.172	-0.634	-0.665	-0.499	-0.182	0.188
P4	-1.440	-1.225	-0.629	-0.244	0.065	-0.725	-0.570	-0.372	-0.324	-0.075
O1	-1.137	-0.855	-0.479	-0.292	-0.240	-0.580	-0.452	-0.339	-0.197	-0.274
O2	-1.450	-0.837	-0.452	-0.243	-0.527	-0.629	-0.371	-0.277	-0.079	-0.279
F7	-2.100	-1.992	-1.482	-0.805	-0.241	-1.411	-1.529	-1.416	-0.863	-0.564
F8	-1.734	-1.686	-1.355	-0.954	-0.495	-1.397	-1.318	-1.465	-0.976	-0.731
T3	-1.372	-1.328	-0.846	-0.745	-0.339	-0.848	-0.861	-0.890	-0.610	-0.688
T4	-1.266	-0.973	-0.934	-0.453	-0.127	-0.869	-0.961	-0.755	-0.468	-0.316
T5	-1.612	-1.028	-0.684	-0.509	-0.326	-0.737	-0.633	-0.671	-0.368	-0.422
T6	-1.712	-1.092	-0.631	-0.500	-0.227	-0.757	-0.551	-0.602	-0.372	-0.392
Fz	-1.296	-1.341	-0.895	-0.188	0.161	-0.939	-0.816	-0.459	-0.296	-0.032
Cz	-0.931	-0.353	-0.403	0.368	0.735	-0.279	-0.514	-0.125	0.164	0.533
Pz	-1.291	-0.978	-0.595	-0.215	0.591	-0.548	-0.613	-0.609	-0.393	0.080

Table 2
Averaged Relative Power Z-Scores in the Eyes Closed Condition

Z Scored FFT Relative Power Average - Eyes Closed - Laplacian										
	Delta 1.0 - 4.0 Hz	Theta 4.0 - 8.0 Hz	Alpha 8.0 - 12.0 Hz	Beta 12.0 - 25.0 Hz	High Beta 25.0 - 30.0 Hz	Alpha 1 8.0 - 10.0 Hz	Alpha 2 10.0 - 12.0 Hz	Beta 1 12.0 - 15.0 Hz	Beta 2 15.0 - 18.0 Hz	Beta 3 18.0 - 25.0 Hz
FP1	-0.780	-0.433	-0.059	0.847	1.122	-0.243	0.060	0.810	0.888	0.824
FP2	-0.662	-0.223	0.014	0.985	1.104	-0.032	-0.028	0.962	1.054	0.930
F3	-0.868	-0.472	-0.076	0.931	1.144	-0.202	0.093	0.987	0.859	0.906
F4	-0.700	0.159	0.146	0.845	1.000	0.238	0.055	0.704	0.689	0.858
C3	-0.929	-0.634	-0.002	0.931	1.136	0.308	-0.230	0.339	0.975	0.952
C4	-0.537	-0.338	-0.278	0.659	0.932	-0.110	-0.341	0.159	0.684	0.705
P3	-0.980	-0.569	-0.244	1.652	1.529	-0.243	-0.325	0.497	1.230	1.823
P4	-0.617	-0.457	-0.185	1.272	1.310	-0.345	-0.094	0.846	0.923	1.335
O1	-0.473	-0.326	-0.114	0.856	0.657	-0.283	-0.088	0.616	0.900	0.796
O2	-0.655	-0.335	-0.031	0.940	0.298	-0.383	0.078	0.732	1.093	0.731
F7	-0.840	-0.403	-0.225	0.967	1.324	-0.174	-0.316	0.511	0.882	0.994
F8	-0.401	0.153	-0.029	0.692	0.947	-0.045	-0.071	0.282	0.693	0.738
T3	-0.222	0.114	0.178	0.469	0.752	0.146	0.127	0.763	0.737	0.276
T4	-0.468	0.006	-0.262	0.461	0.665	-0.208	-0.319	0.271	0.397	0.479
T5	-0.545	-0.021	-0.108	0.999	0.641	-0.227	-0.029	0.750	1.166	0.782
T6	-0.777	-0.379	-0.026	0.933	0.749	-0.311	0.097	0.739	0.931	0.821
Fz	-0.969	-0.606	-0.090	1.314	1.458	-0.050	-0.056	0.808	1.112	1.346
Cz	-1.021	-0.475	-0.571	1.109	1.325	-0.368	-0.699	-0.016	0.563	1.189
Pz	-0.638	-0.310	-0.207	1.297	1.774	-0.024	-0.233	0.176	0.691	1.577

Table 3
Averaged Absolute Power Z-Scores in the Eyes Open Condition

Z Scored FFT Absolute Power Average - Eyes Open - Laplacian										
	Delta 1.0 - 4.0 Hz	Theta 4.0 - 8.0 Hz	Alpha 8.0 - 12.0 Hz	Beta 12.0 - 25.0 Hz	High Beta 25.0 - 30.0 Hz	Alpha 1 8.0 - 10.0 Hz	Alpha 2 10.0 - 12.0 Hz	Beta 1 12.0 - 15.0 Hz	Beta 2 15.0 - 18.0 Hz	Beta 3 18.0 - 25.0 Hz
FP1	-2.520	-2.799	-2.193	-0.912	-0.528	-2.181	-2.070	-1.492	-1.076	-0.761
FP2	-2.128	-2.738	-2.356	-1.069	-0.656	-2.310	-2.311	-1.568	-1.134	-0.921
F3	-1.499	-1.779	-1.673	-0.830	-0.387	-1.696	-1.566	-1.158	-0.979	-0.677
F4	-2.686	-2.825	-2.245	-1.211	-0.687	-2.246	-2.124	-1.672	-1.413	-1.030
C3	-1.784	-2.079	-1.184	-0.971	-0.425	-0.992	-1.311	-1.456	-1.064	-0.733
C4	-1.953	-1.785	-1.094	-1.143	-0.475	-0.951	-1.137	-1.403	-1.082	-0.966
P3	-1.729	-1.621	-1.066	-0.713	-0.130	-0.996	-1.080	-1.060	-0.999	-0.275
P4	-1.527	-1.647	-1.164	-0.969	-0.357	-1.134	-1.125	-1.021	-1.054	-0.805
O1	-1.364	-0.995	-0.931	-0.904	-0.750	-0.956	-0.867	-0.820	-0.813	-0.940
O2	-1.627	-1.065	-0.943	-0.980	-1.056	-0.913	-0.919	-0.775	-0.823	-1.176
F7	-2.400	-2.285	-2.019	-1.005	-0.467	-1.950	-2.027	-1.933	-1.174	-0.696
F8	-2.033	-2.284	-1.987	-1.144	-0.554	-1.878	-2.059	-1.702	-1.342	-0.899
T3	-1.924	-1.859	-1.620	-1.187	-0.679	-1.501	-1.629	-1.539	-1.121	-1.010
T4	-1.698	-1.512	-1.393	-1.242	-0.744	-1.284	-1.421	-1.390	-1.367	-1.012
T5	-2.075	-1.428	-1.217	-1.027	-0.526	-1.146	-1.227	-1.039	-1.008	-0.869
T6	-2.039	-1.592	-1.205	-1.342	-0.984	-1.136	-1.219	-1.271	-1.275	-1.255
Fz	-1.757	-1.920	-2.049	-1.069	-0.356	-1.919	-2.032	-1.648	-1.418	-0.690
Cz	-1.012	-0.572	-0.731	0.188	0.593	-0.611	-0.810	-0.470	-0.240	0.443
Pz	-1.432	-1.401	-1.091	-0.716	0.273	-0.985	-1.167	-1.115	-0.930	-0.374

Table 4
Averaged Relative Power Z-Scores in the Eyes Open Condition

Z Scored FFT Relative Power Average - Eyes Open - Laplacian										
	Delta 1.0 - 4.0 Hz	Theta 4.0 - 8.0 Hz	Alpha 8.0 - 12.0 Hz	Beta 12.0 - 25.0 Hz	High Beta 25.0 - 30.0 Hz	Alpha 1 8.0 - 10.0 Hz	Alpha 2 10.0 - 12.0 Hz	Beta 1 12.0 - 15.0 Hz	Beta 2 15.0 - 18.0 Hz	Beta 3 18.0 - 25.0 Hz
FP1	-0.959	-0.118	0.014	0.824	0.948	-0.035	0.133	0.938	1.015	0.753
FP2	-0.595	-0.012	0.105	0.648	0.842	0.038	0.232	0.891	0.911	0.564
F3	-0.361	0.102	0.131	0.612	0.723	0.071	0.232	0.803	0.586	0.596
F4	-0.829	0.260	0.415	0.594	0.754	0.467	0.336	0.803	0.549	0.561
C3	-0.517	-0.237	0.083	0.705	0.728	0.321	-0.096	0.289	0.680	0.722
C4	-0.806	-0.259	-0.038	0.498	0.832	0.167	-0.133	0.128	0.495	0.555
P3	-0.595	-0.882	-0.395	1.461	1.519	-0.324	-0.339	0.396	0.802	1.792
P4	-0.360	-0.388	-0.414	1.132	1.502	-0.366	-0.312	0.983	0.869	1.283
O1	-0.119	0.475	-0.359	0.867	0.794	-0.368	-0.259	0.616	0.915	0.848
O2	-0.135	0.661	-0.250	0.969	0.592	-0.113	-0.239	1.009	1.193	0.642
F7	-1.238	-0.438	-0.202	0.958	0.855	-0.294	-0.104	0.576	0.955	0.952
F8	-0.756	-0.174	0.000	0.651	0.829	-0.060	0.089	0.726	0.574	0.648
T3	-0.454	-0.072	0.009	0.540	0.496	0.014	0.071	0.733	0.808	0.382
T4	-0.359	0.256	-0.085	0.303	0.377	-0.047	-0.035	0.707	0.288	0.227
T5	-0.525	0.089	-0.276	1.056	0.675	-0.224	-0.237	1.140	1.239	0.801
T6	-0.303	0.125	-0.142	0.830	0.534	-0.090	-0.059	0.903	0.925	0.635
Fz	-0.679	-0.252	-0.428	0.947	1.056	-0.365	-0.358	0.542	0.768	1.045
Cz	-0.835	-0.504	-0.745	0.986	1.231	-0.570	-0.790	-0.159	0.298	1.135
Pz	-0.507	-0.554	-0.375	1.219	2.124	-0.183	-0.412	0.291	0.613	1.570

Table 5
Averaged Power Ratio Z-Scores in the Eyes Open Condition

Z Scored FFT Power Ratio Average - Eyes Open - Laplacian										
	Delta / Theta	Delta / Alpha	Delta / Beta	Delta / High Beta	Theta / Alpha	Theta / Beta	Theta / High Beta	Alpha / Beta	Alpha / High Beta	Beta / High Beta
FP1	-1.077	-0.699	-0.930	-1.019	-0.130	-0.485	-0.610	-0.435	-0.557	-0.691
FP2	-0.740	-0.482	-0.640	-0.801	-0.128	-0.361	-0.519	-0.324	-0.470	-0.691
F3	-0.540	-0.359	-0.500	-0.594	-0.021	-0.332	-0.465	-0.386	-0.505	-0.627
F4	-1.054	-0.753	-0.621	-0.720	-0.143	-0.154	-0.350	-0.107	-0.343	-0.663
C3	-0.497	-0.346	-0.646	-0.713	-0.192	-0.521	-0.599	-0.329	-0.421	-0.484
C4	-0.726	-0.369	-0.760	-0.993	-0.054	-0.444	-0.699	-0.251	-0.493	-0.834
P3	-0.203	-0.055	-1.243	-1.899	0.023	-1.557	-1.765	-1.041	-1.087	-0.743
P4	-0.246	0.032	-0.815	-1.327	0.194	-1.051	-1.527	-0.975	-1.149	-1.034
O1	-0.501	0.123	-0.547	-0.799	0.434	-0.254	-0.502	-0.662	-0.676	-0.434
O2	-0.858	0.065	-0.585	-0.609	0.446	-0.168	-0.203	-0.610	-0.473	-0.069
F7	-0.931	-0.591	-1.147	-1.069	-0.120	-0.797	-0.745	-0.741	-0.694	-0.504
F8	-0.809	-0.478	-0.746	-0.869	-0.135	-0.517	-0.654	-0.439	-0.578	-0.718
T3	-0.498	-0.279	-0.520	-0.529	-0.062	-0.314	-0.343	-0.292	-0.320	-0.328
T4	-0.677	-0.154	-0.367	-0.415	0.273	-0.031	-0.160	-0.220	-0.288	-0.363
T5	-0.544	-0.079	-0.937	-0.832	0.320	-0.529	-0.466	-0.662	-0.549	-0.205
T6	-0.486	-0.079	-0.602	-0.565	0.231	-0.382	-0.330	-0.487	-0.402	-0.148
Fz	-0.293	-0.040	-0.879	-1.006	0.296	-0.804	-0.926	-1.022	-1.062	-0.865
Cz	-0.589	0.052	-1.091	-1.286	0.494	-0.965	-1.165	-1.105	-1.310	-0.945
Pz	-0.482	-0.063	-0.956	-1.759	0.076	-1.138	-1.973	-1.015	-1.498	-1.631

Table 6
Averaged Power Ratio Z-Scores in the Eyes Closed Condition

Z Scored FFT Power Ratio Average - Eyes Closed -Laplacian										
	Delta / Theta	Delta / Alpha	Delta / Beta	Delta / High Beta	Theta / Alpha	Theta / Beta	Theta / High Beta	Alpha / Beta	Alpha / High Beta	Beta / High Beta
FP1	-0.604	-0.441	-0.855	-1.039	-0.208	-0.755	-0.952	-0.646	-0.875	-1.009
FP2	-0.627	-0.429	-0.861	-0.990	-0.186	-0.682	-0.826	-0.548	-0.739	-0.794
F3	-0.511	-0.488	-0.874	-1.016	-0.306	-0.781	-0.938	-0.753	-0.905	-0.869
F4	-0.889	-0.538	-0.800	-0.922	-0.028	-0.456	-0.640	-0.510	-0.700	-0.734
C3	-0.777	-0.556	-0.994	-1.291	-0.336	-0.879	-1.151	-0.576	-0.708	-0.685
C4	-0.416	-0.162	-0.630	-0.901	0.024	-0.560	-0.851	-0.546	-0.697	-0.709
P3	-0.857	-0.391	-1.541	-2.235	-0.067	-1.556	-2.087	-0.984	-0.943	-0.511
P4	-0.453	-0.254	-1.074	-1.496	-0.080	-1.267	-1.742	-0.788	-0.819	-0.519
O1	-0.406	-0.214	-0.851	-0.950	-0.053	-0.850	-0.856	-0.487	-0.431	-0.144
O2	-0.721	-0.370	-1.064	-0.858	-0.118	-0.854	-0.478	-0.467	-0.179	0.457
F7	-0.503	-0.240	-0.977	-1.269	0.007	-0.798	-1.088	-0.713	-0.976	-1.193
F8	-0.612	-0.155	-0.578	-0.798	0.123	-0.352	-0.611	-0.382	-0.626	-0.874
T3	-0.471	-0.256	-0.354	-0.575	-0.084	-0.174	-0.438	-0.087	-0.339	-0.755
T4	-0.758	-0.096	-0.516	-0.641	0.301	-0.226	-0.424	-0.407	-0.570	-0.640
T5	-0.624	-0.247	-0.880	-0.868	0.068	-0.599	-0.527	-0.500	-0.420	-0.184
T6	-0.650	-0.451	-1.089	-1.061	-0.152	-0.782	-0.759	-0.445	-0.446	-0.311
Fz	-0.468	-0.413	-1.244	-1.492	-0.388	-1.329	-1.458	-1.052	-1.113	-0.813
Cz	-0.879	-0.182	-1.268	-1.581	0.259	-1.015	-1.300	-1.000	-1.097	-0.758
Pz	-0.611	-0.255	-1.078	-1.947	-0.003	-1.115	-2.124	-0.807	-1.081	-1.204

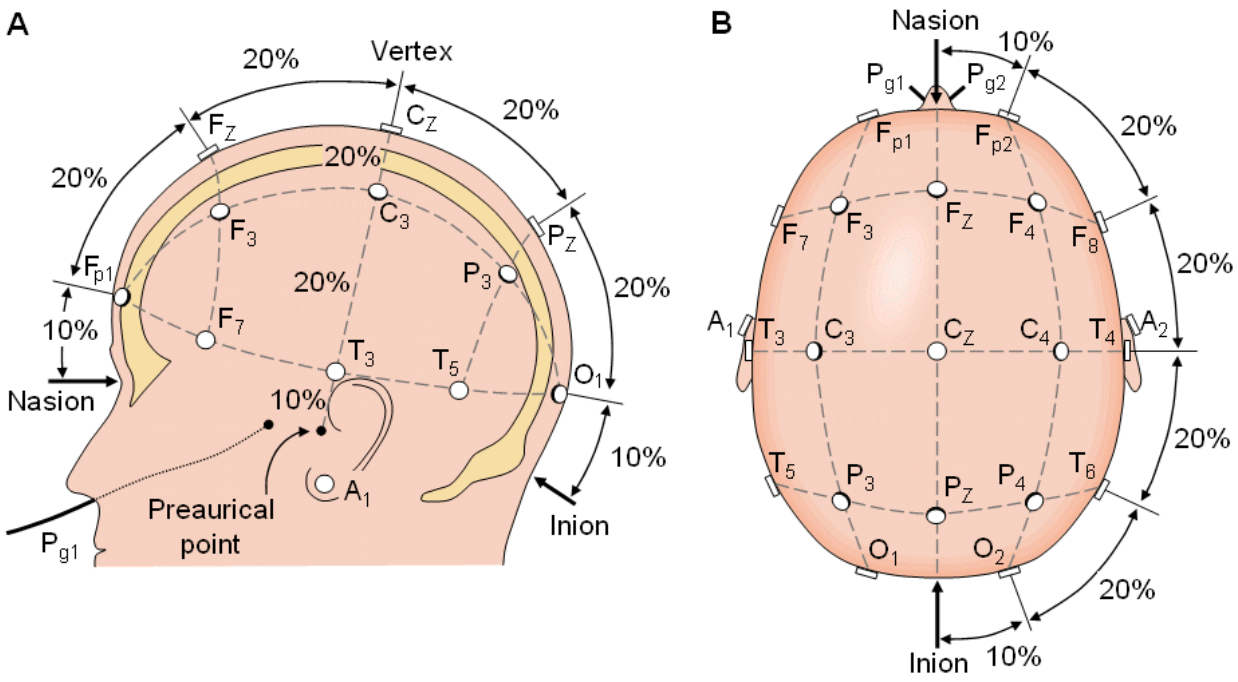

Figure 1. The International 10-20 System seen from (A) left and (B) above the head.

Fp = Frontal Polar, F = Frontal, C = Central, T = Temporal, P = Parietal, O = Occipital,

A = Auricular, Pg = Nasopharyngeal

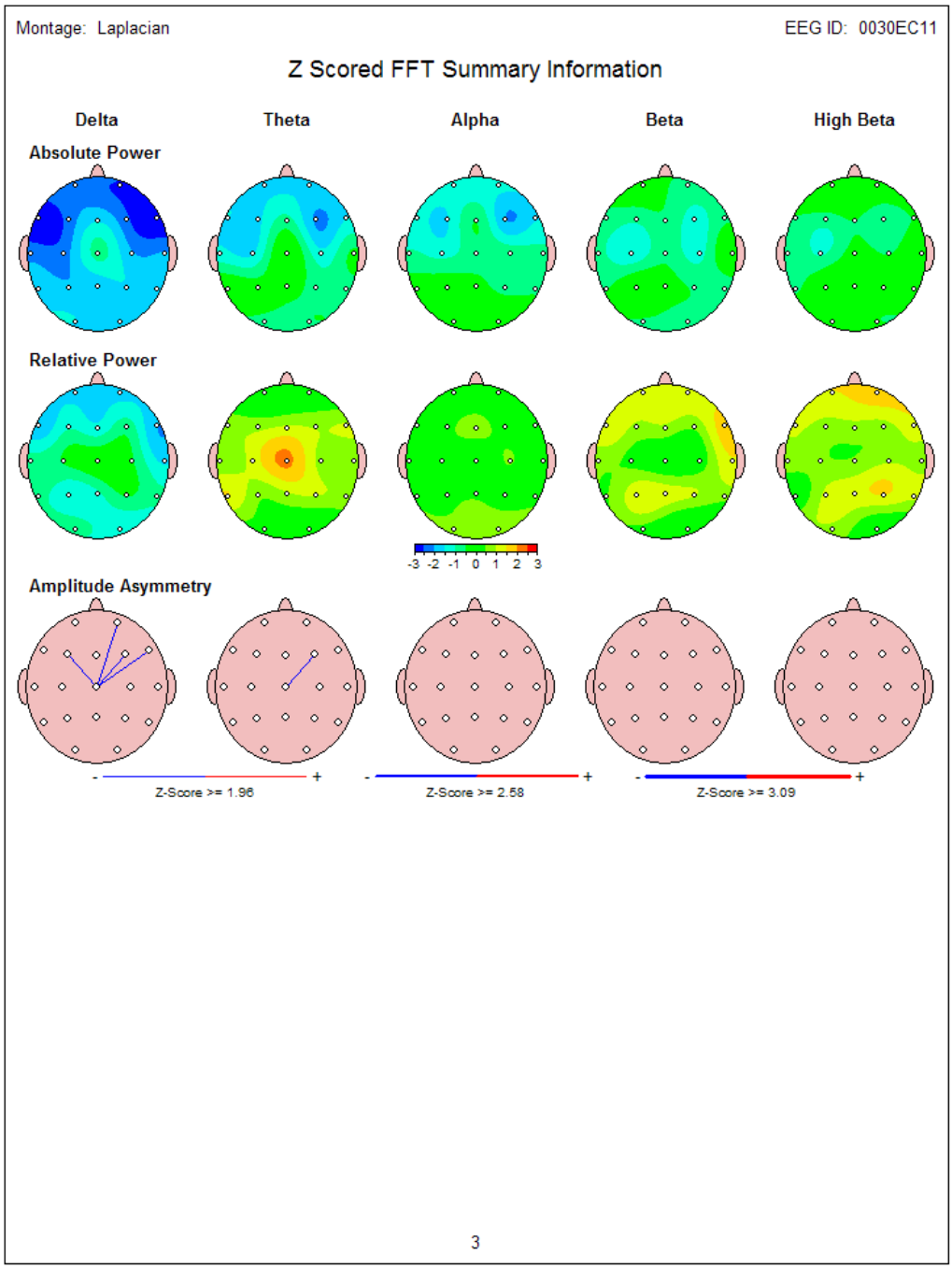

Figure 1. Subject 1: Eyes closed Z score summary topographic map

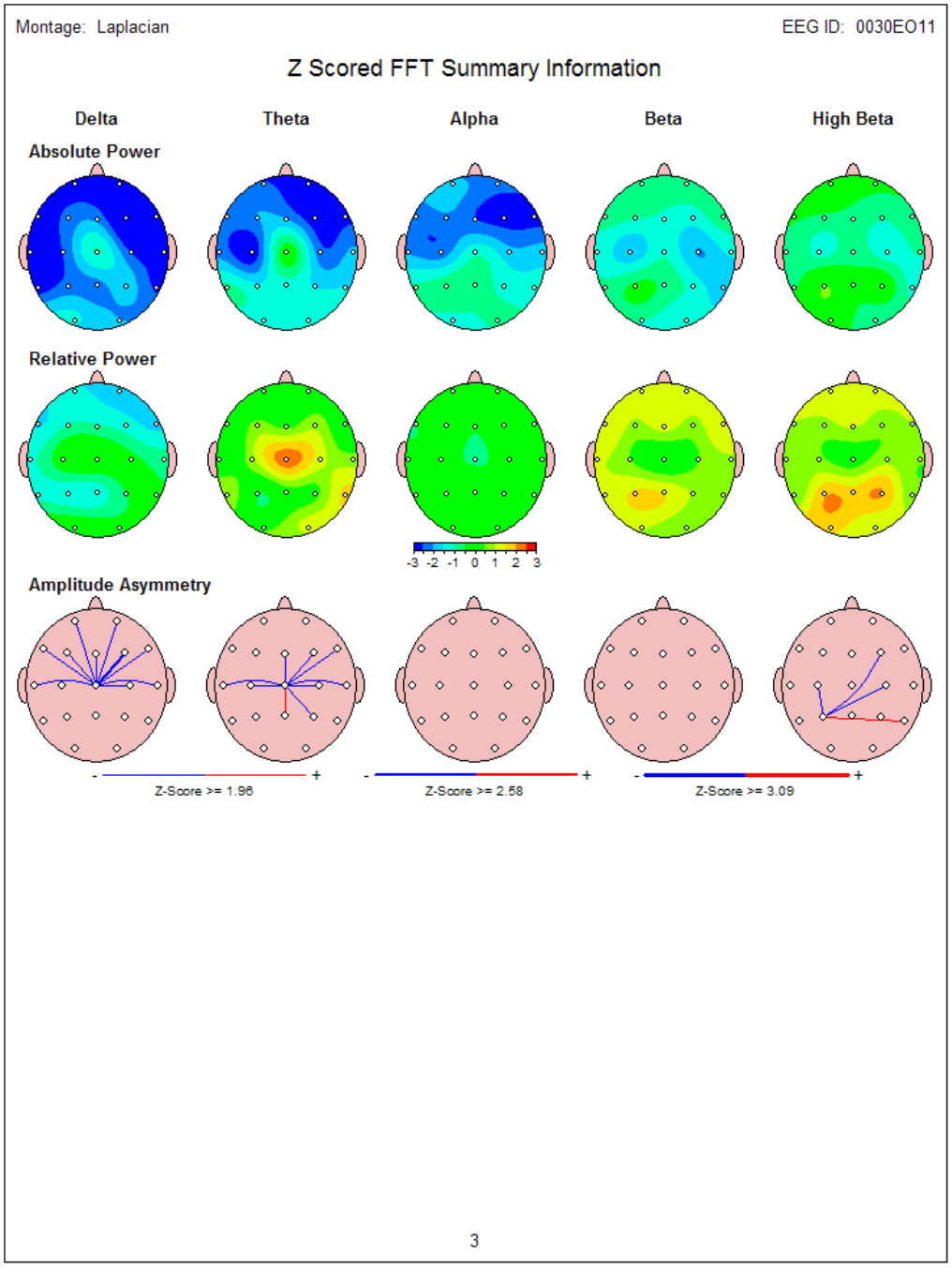

Figure 2. Subject 1: Eyes open Z score summary topographic map

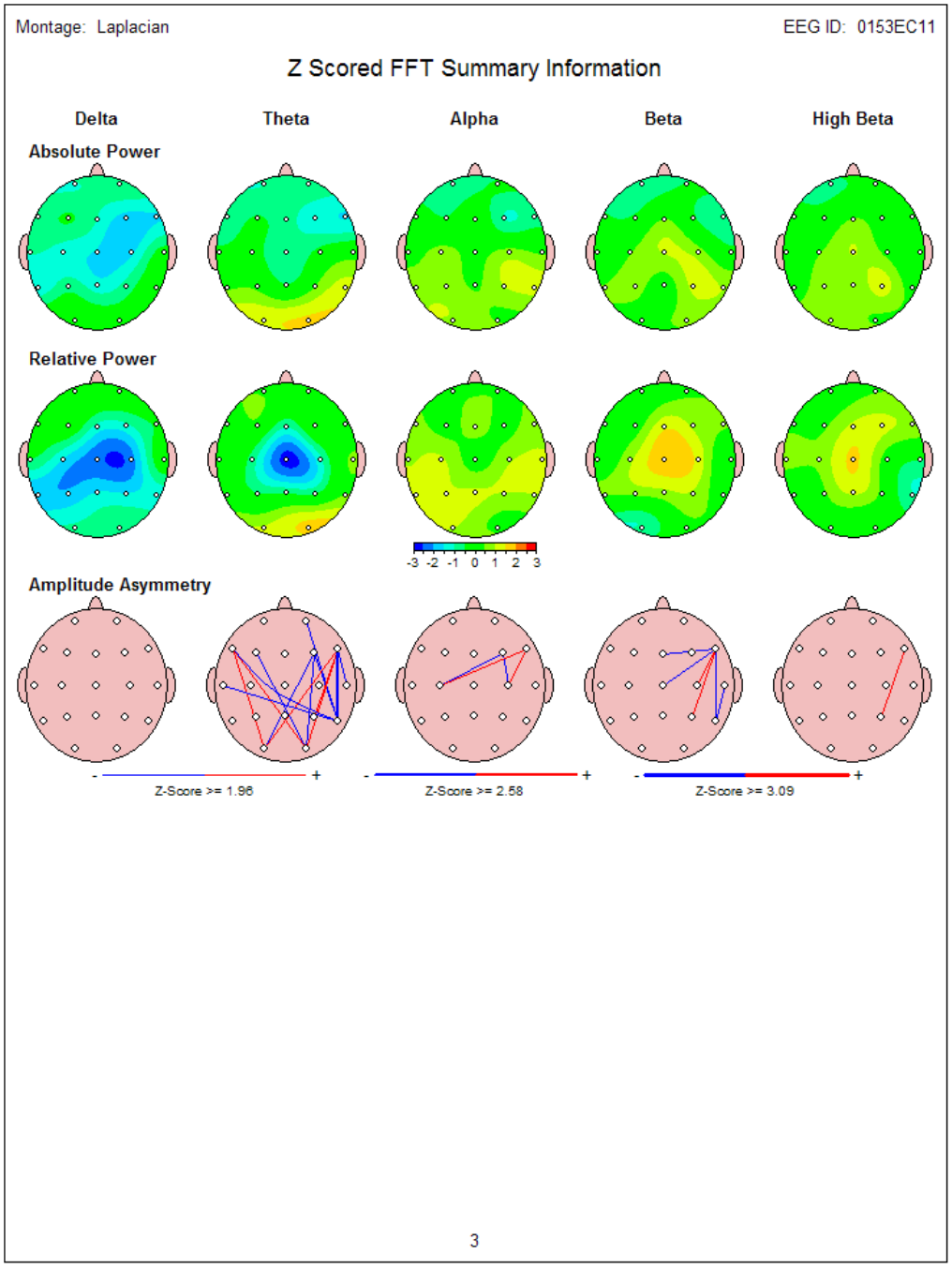

Figure 3. Subject 2: Eyes closed Z score summary topographic map

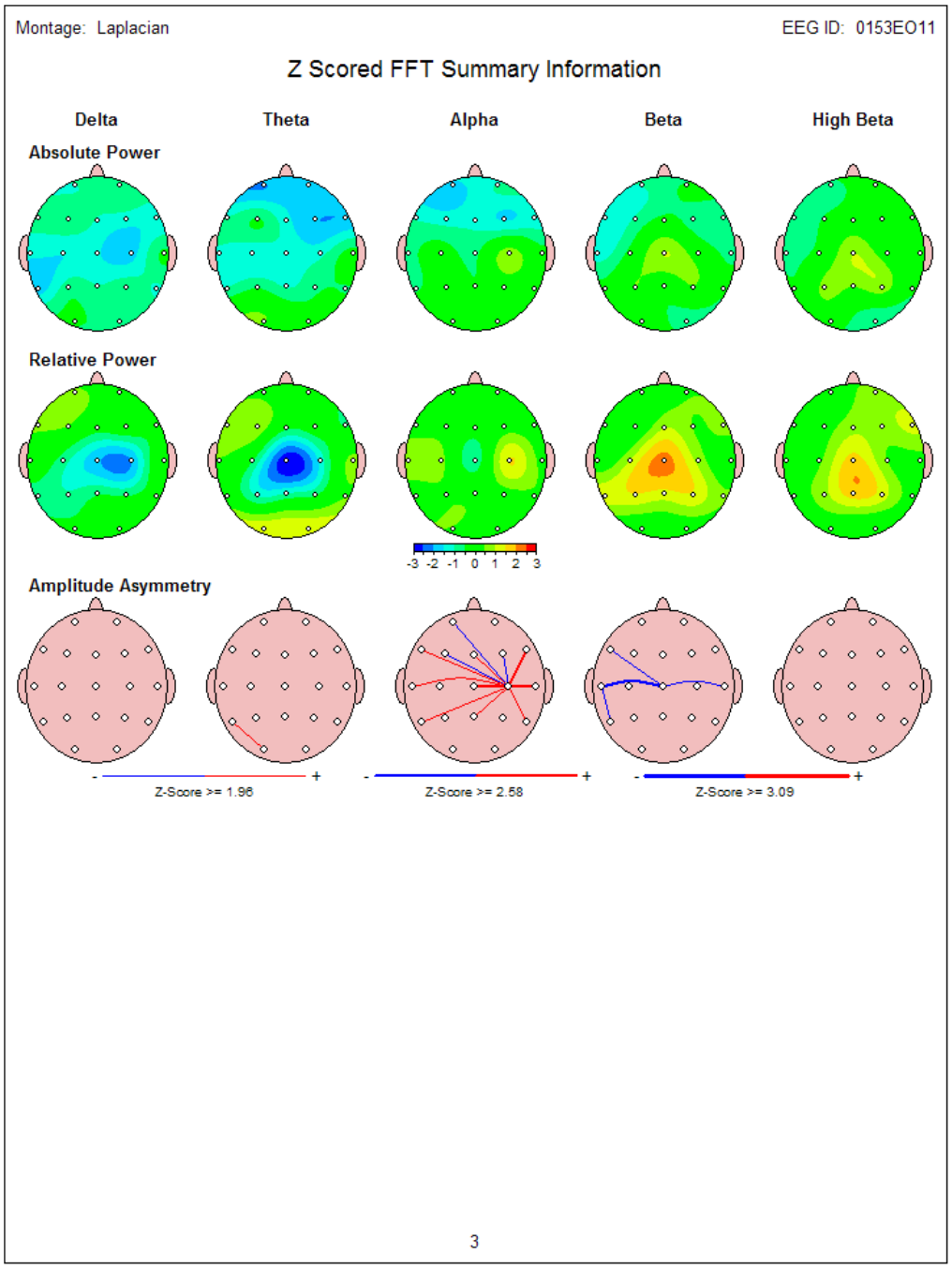

Figure 4. Subject 2: Eyes open Z score summary topographic map

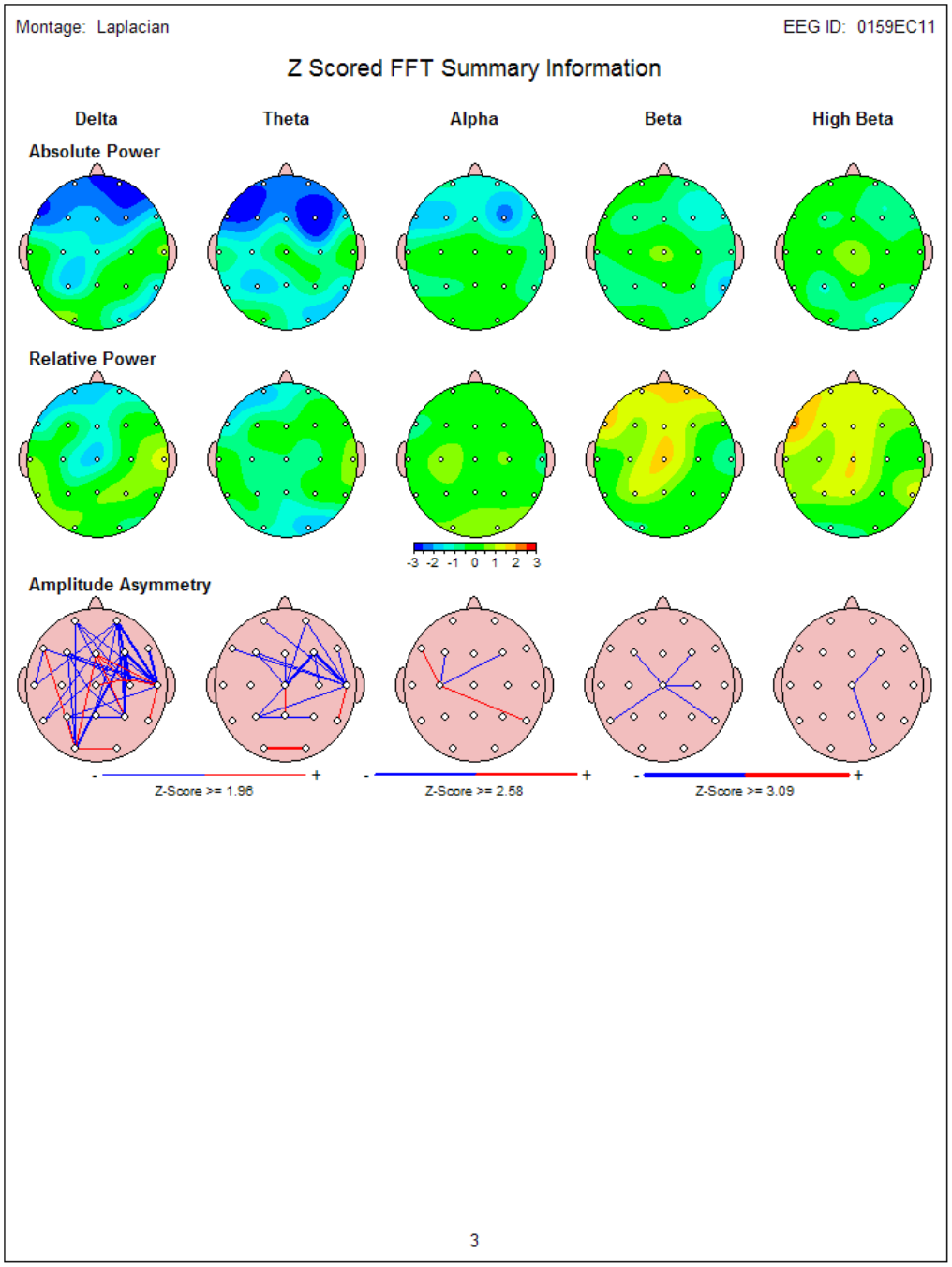

Figure 5. Subject 3: Eyes closed Z score summary topographic map

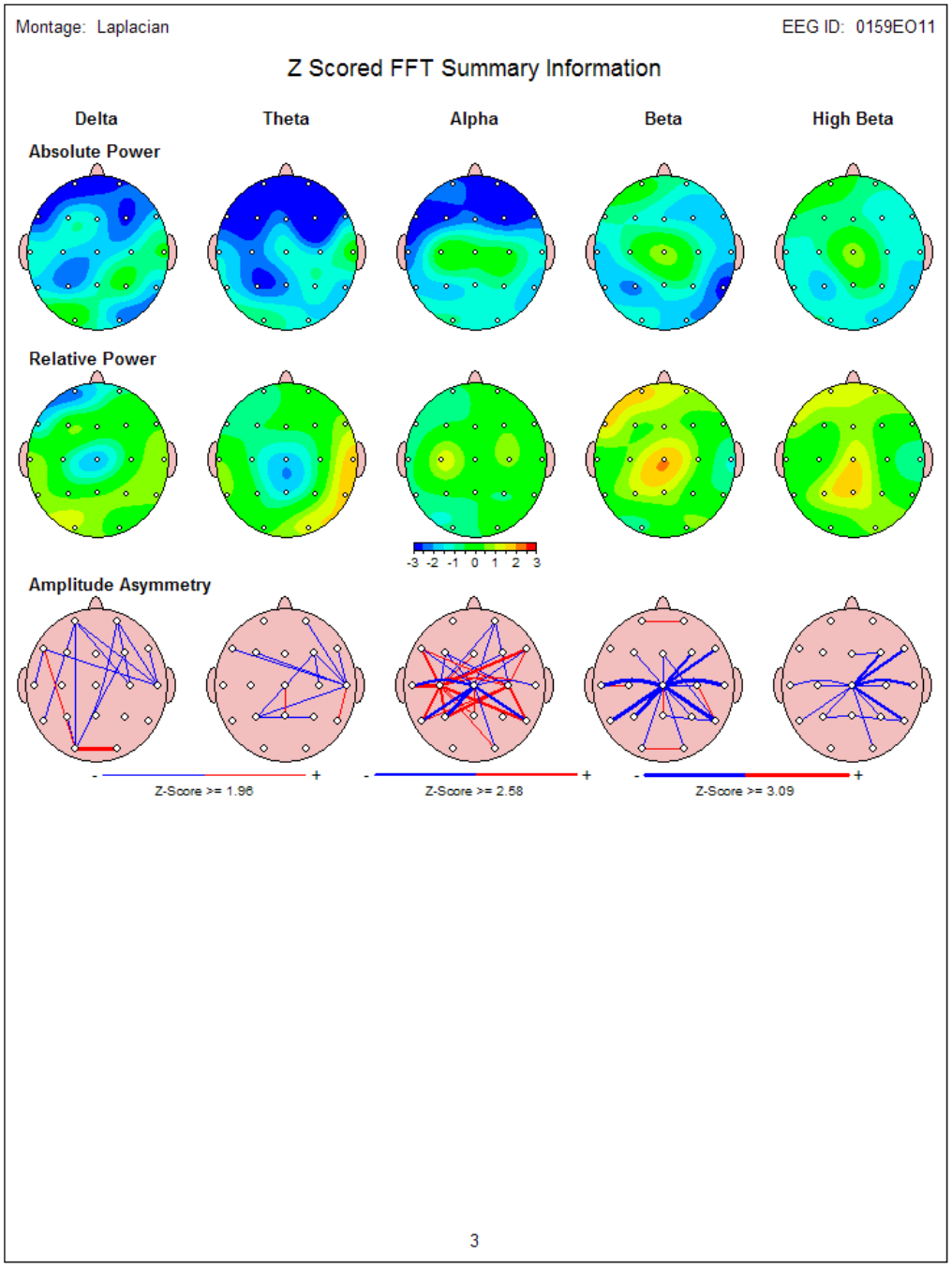

Figure 6. Subject 3: Eyes open Z score summary topographic map

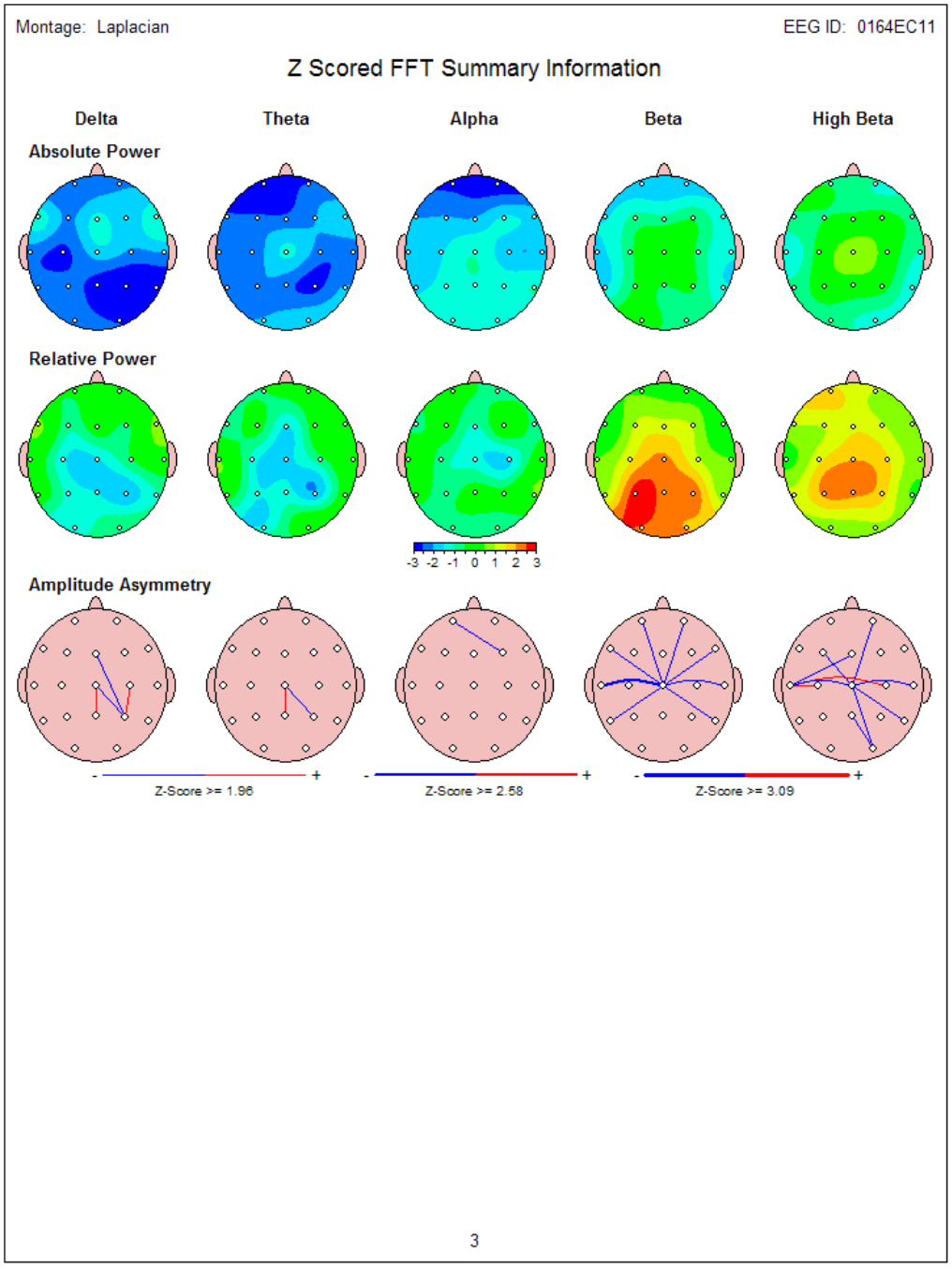

Figure 7. Subject 4: Eyes closed Z score summary topographic map

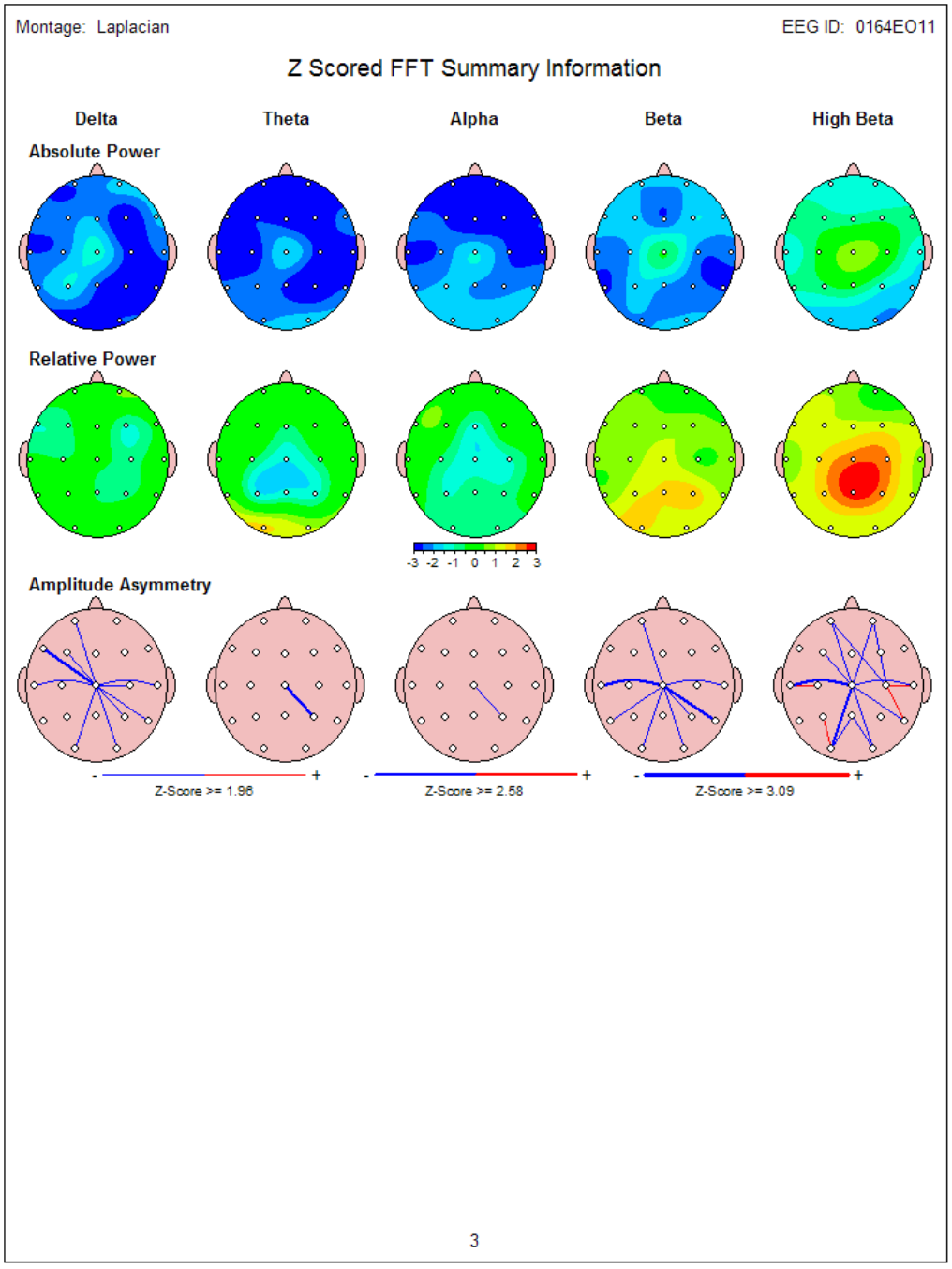

Figure 8. Subject 4: Eyes open Z score summary topographic map

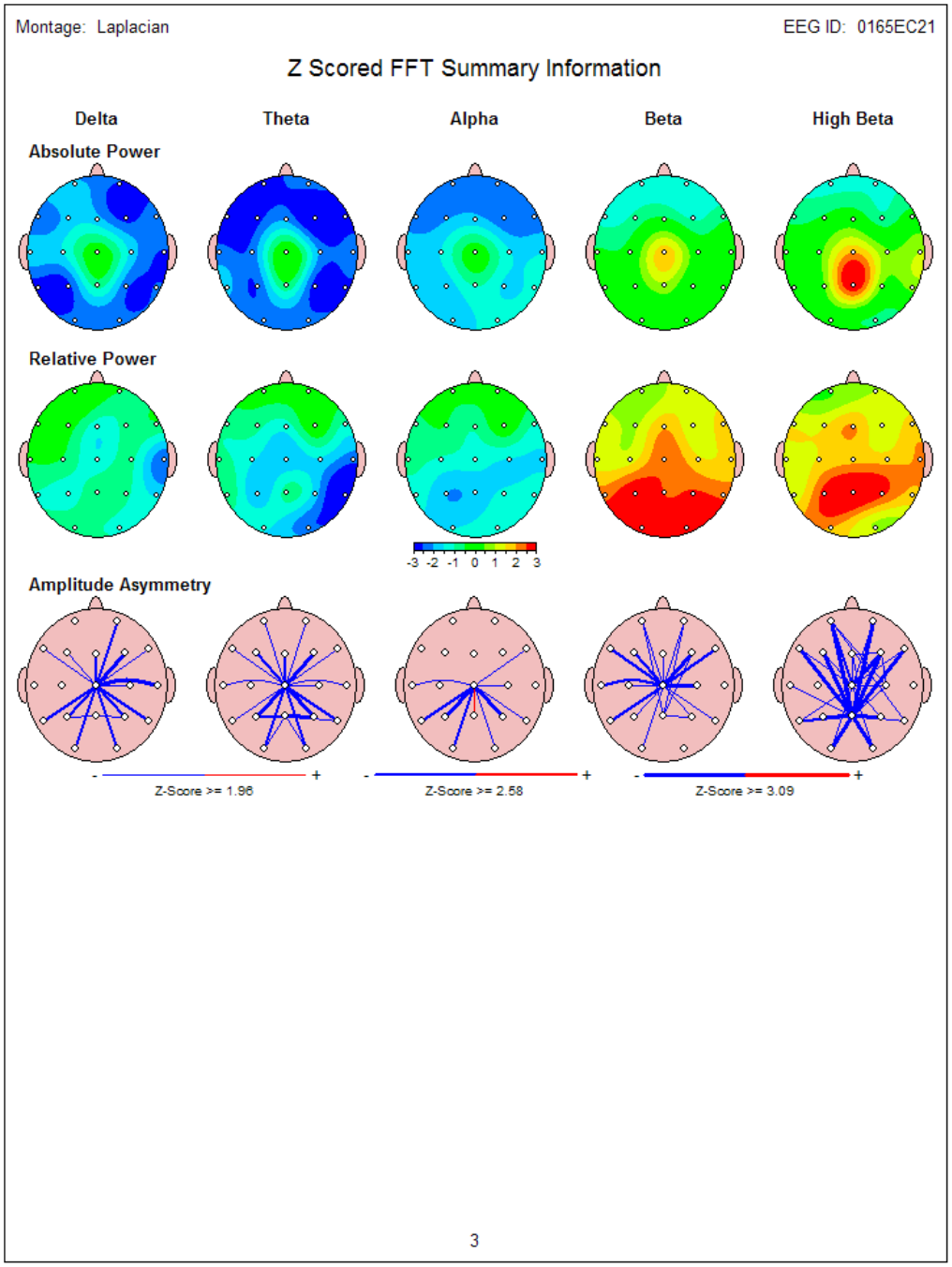

Figure 9. Subject 5: Eyes closed Z score summary topographic map

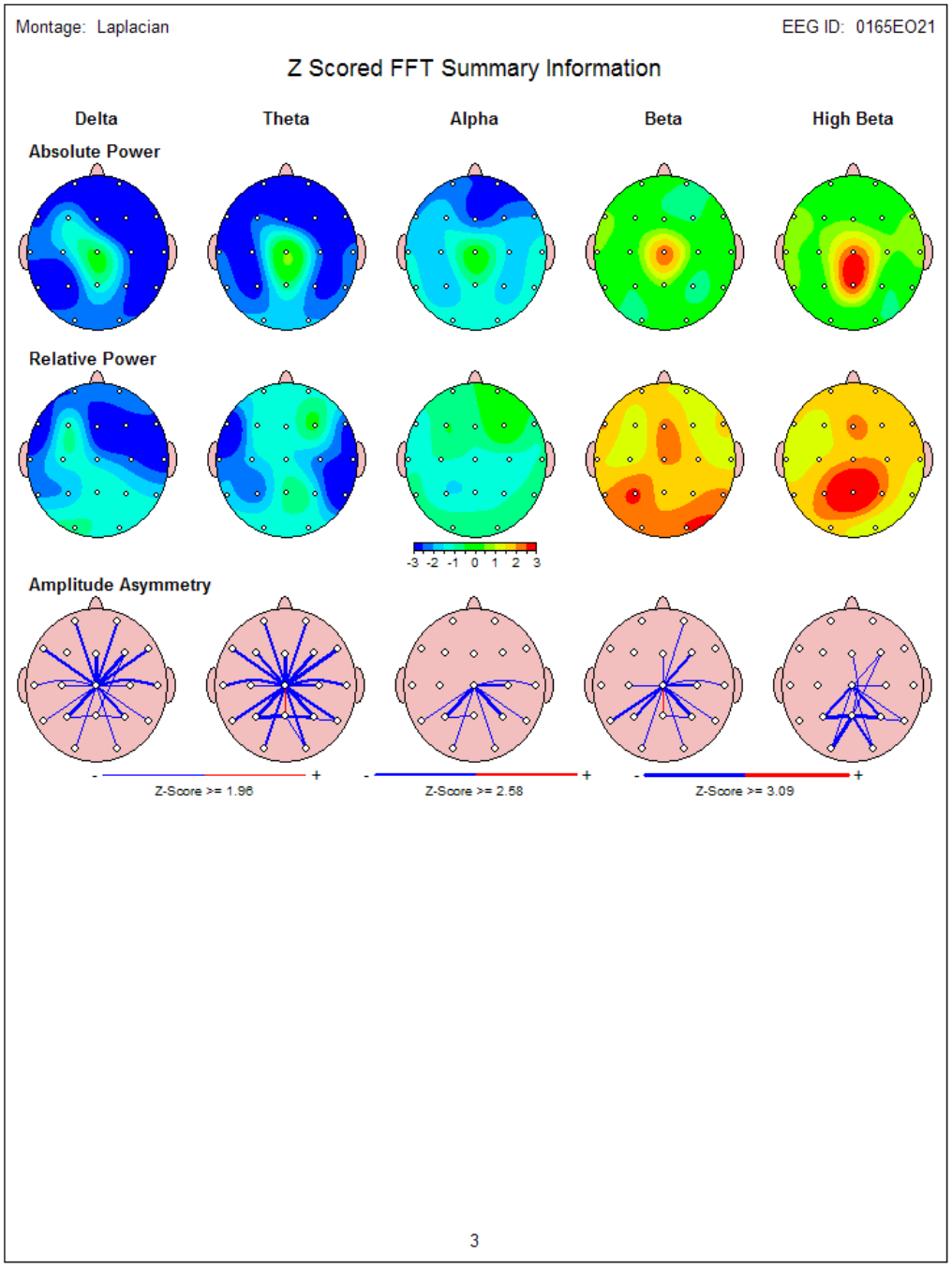

Figure 10. Subject 5: Eyes open Z score summary topographic map

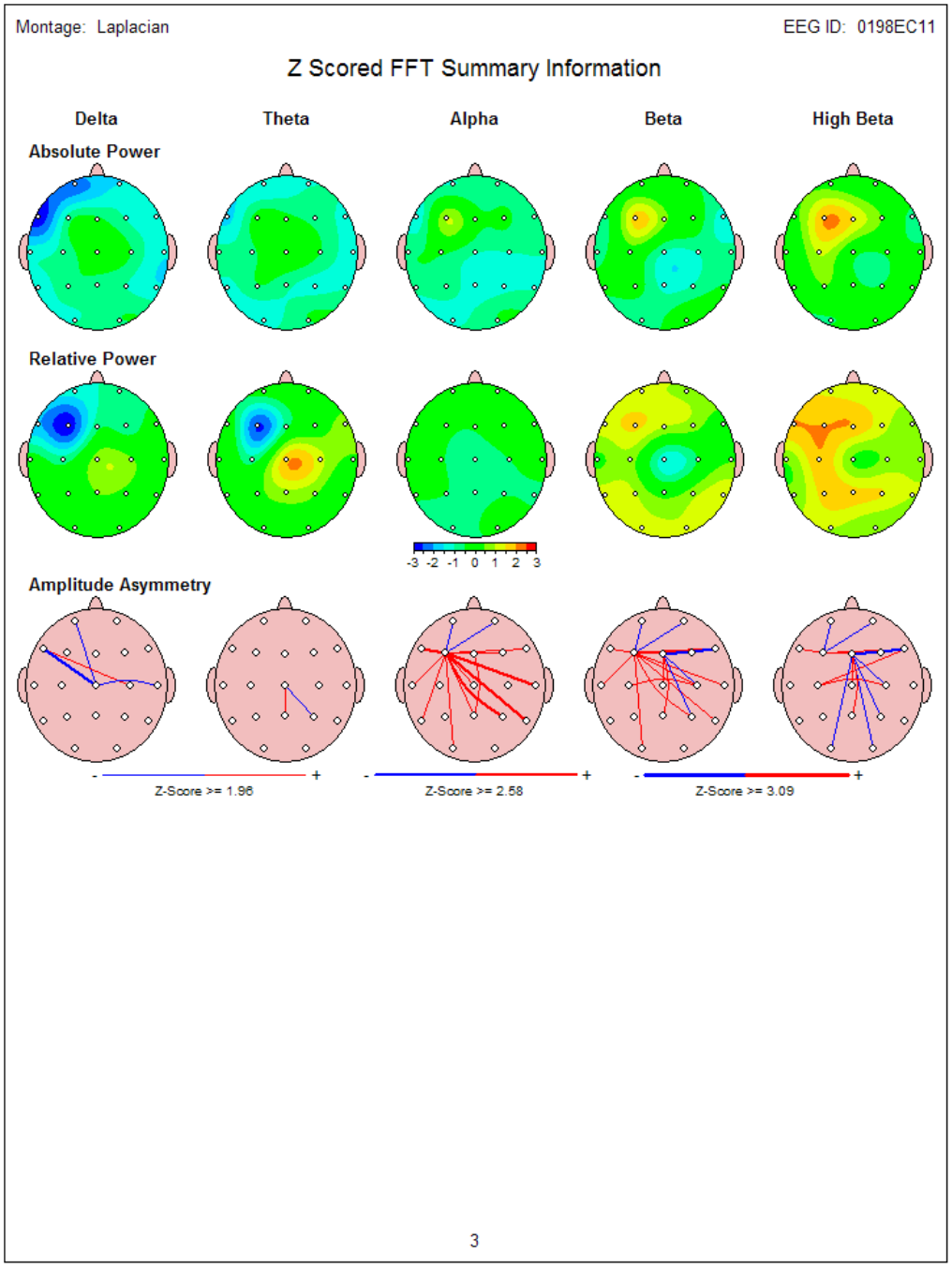

Figure 11. Subject 6: Eyes closed Z score summary topographic map

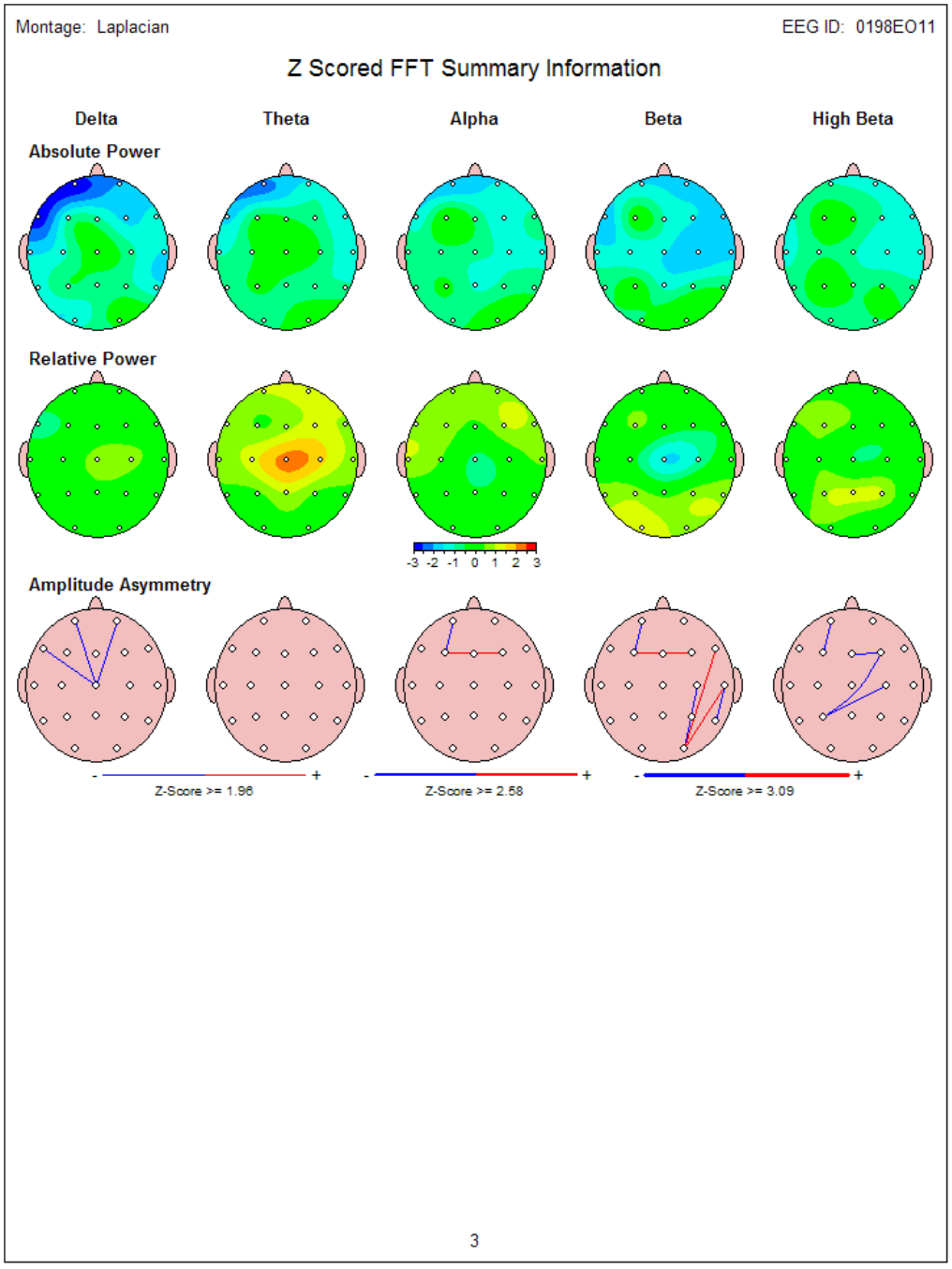

Figure 12. Subject 6: Eyes open Z score summary topographic map

REFERENCES

Apkarian, A. V., Bushnell, M. C., Treede, R. D., & Zubieta, J. K. (2005). Human brain mechanisms of pain perception and regulation in health and disease. *European Journal of Pain (London, England), 9*(4), 463-484.

Babiloni, C., Brancucci, A., Capotosto, P., Arendt-Nielsen, L., Chen, A. C. N., & Rossini, P. M. (2005). Expectancy of pain is influenced by motor preparation: A high-resolution EEG study of cortical alpha rhythms. *Behavioral Neuroscience, 119*(2), 503-511.

Babiloni, C., Brancucci, A., Del Percio, C., Capotosto, P., Arendt-Nielsen, L., Chen, A. C. N., et al. (2006). Anticipatory electroencephalography alpha rhythm predicts subjective perception of pain intensity. *Journal of Pain, 7*(10), 709-717.

Babiloni, C., Brancucci, A., Babiloni, F., Capotosto, P., Carducci, F., Cincotti, F., et al. (2003). Anticipatory cortical responses during the expectancy of a predictable painful stimulation. A high-resolution electroencephalography study. *European Journal of Neuroscience, 18*(6), 1692-1700.

Baliki, M. N., Chialvo, D. R., Geha, P. Y., Levy, R. M., Harden, R. N., Parrish, T. B., et al. (2006). Chronic pain and the emotional brain: Specific brain activity associated with spontaneous fluctuations of intensity of chronic back pain. *Journal of Neuroscience, 26*(47), 12165-12173.

Baliki, M. N., Geha, P. Y., Apkarian, A. V., & Chialvo, D. R. (2008). Beyond feeling: Chronic pain hurts the brain, disrupting the default-mode network dynamics. *Journal of Neuroscience, 28*(6), 1398-1403.

Bromm, B., Scharein, E., & Vahle-Hinz, C. (2000). Cortex areas involved in the processing of normal and altered pain. *Progress in Brain Research, 129*, 289-302.

Caro, X. J. & Winter, E. F. (2001). Attention measures improve in fibromyalgia patients receiving EEG biofeedback training: A pilot study. *Arthritis and Rheumatism, 44 (Supplement),* S71.

Chen, A. (2001). New perspectives in EEG/MEG brain mapping and PET/fMRI neuroimaging of human pain. *International Journal of Psychophysiology*, *42*(2), 147-159.

Chen, A. C. (2008). Pain perception and its genesis in the human brain. *Sheng Li Xue Bao: [Acta Physiologica Sinica]*, *60*(5), 677-685.

Davidson, R.J. (1995). Cerebral asymmetry, emotion and affective style. In R. J. Davidson & K. Hugdahl, (Eds.), *Brain asymmetry*. (pp. 361-387). Cambridge, MA: MIT Press.

deCharms, R. C., Maeda, F., Glover, G. H., Ludlow, D., Pauly, J. M., Soneji, D., et al. (2005). Control over brain activation and pain learned by using real-time functional MRI. *Proceedings of the National Academy of Sciences of the United States of America, 102*(51), 18626-18631.

Dowman, R., Rissacher, D., & Schuckers, S. (2008). EEG indices of tonic pain-related activity in the somatosensory cortices. *Clinical Neurophysiology*, *119*(5), 1201-1212.

Hammond, D.C. (2005). Neurofeedback with anxiety and affective disorders. *Child and Adolescent Psychiatry Clinics of North America*, *14*(1):105-123, vii.

Ibric, V. L. & Dragomirescu, L. G. (2009). Neurofeedback in pain management. In T.H. Budzinski, H. K. Budzinski, J. R. Evans, & A. Abarbanel (Eds.), *Introduction to quantitative EEG and neurofeedback: Advanced theory and applications* (2nd ed.), (pp.417-451). New York: Elsevier Press.

Jasper, H. H. (1958). The 10-20 system of the International Federation. *Electroencephalography and Clinical Neurophysiology*, *10*, 371-375.

Jensen, M.P. (2010). A neuropsychological model of pain: Research and clinical implications. *The Journal of Pain, 11*(1), 2-12.

Jensen, M. P., Grierson, C., Tracy-Smith, V., Bacigalupi, S. C., & Othmer, S. (2007). Neurofeedback treatment for pain associated with complex regional pain syndrome type I. *Journal of Neurotherapy, 11*(1), 45-53.

Jensen, M. P., Hakimian, S., Sherlin, L. H., & Fregni, F. (2008). New insights into neuromodulatory approaches for the treatment of pain. *Journal of Pain, 9*(3), 193-199.

Jensen, M.P., Sherlin, L.H., Hakiman, S., & Fregni, F. (2009). Neuromodulatory approaches for chronic pain management: Research findings and clinical implications. *Journal of Neurotherapy, 13*(4), 196-213.

Kaiser, D. (2007). What is quantitative EEG? *Journal of Neurotherapy, 10*(4), 37-52.

Lubar, J. (2004). *Quantitative electroencephalographic analysis (QEEG) databases for neurotherapy: Description, validation, and application*. New York, NY US: Haworth Press.

Melzack, R., & Wall, P.D. (1965). Pain mechanisms: A new theory. *Science, 150*(699), 971-979.

Othmer, S. & Othmer S. F. (2006). Efficacy of neurofeedback for pain management. In M. V. Boswell & B. E. Cole (Eds.), *Weiner's pain management: A practical guide for clinicians* (7th ed.). Boca Raton, FL: CRC Press, pp. 713-739.

Peyron, R, Laurent, B, and García-Larrea, L. (2000). Functional imaging of brain responses to pain. A review and meta-analysis (2000). *Clinical Neurophysiology, 30*(5), 263-288.

Pfurtscheller, G., & da Silva, L. (1999). Event-related EEG/MEG synchronization and desynchronization: Basic principles. *Clinical Neurophysiology, 110*(11), 1842-1857.

Ploner, M., Gross, J., Timmermann, L., Pollok, B., & Schnitzler, A. (2006). Pain suppresses spontaneous brain rhythms. *Cerebral Cortex, 16*(4), 537-540.

Roelofs, J., Peters, M. L., Zeegers, M. P. A., & Vlaeyen, J. W. S. (2002). The modified Stroop paradigm as a measure of selective attention towards pain-related stimuli among chronic pain patients: A meta-analysis. *European Journal of Pain, 6*(4), 273-281.

Rowan, A. J. & Tolunsky, E. (2003). *Primer of EEG*. Philadelphia, PA: Butterworth Heinemann.

Sime, A. (2004). Case study of trigeminal neuralgia using neurofeedback and peripheral biofeedback. *Journal of Neurotherapy, 8*(1), 59-71.

Stern, J., Jeanmonod, D., & Sarnthein, J. (2006). Persistent EEG overactivation in the cortical pain matrix of neurogenic pain patients. *NeuroImage, 31*(2), 721-731.

Thatcher, R.W. (2005). Neuroguide software package. Applied Neurosciences, Inc.

Thatcher, R.W., Biver, C.J., Walker, R.A., North, D.M., & Curtin, B.S. (2000). Quantitative EEG normative databases: Validation and clinical correlation, *Journal of Neurotherapy, 7*, 87-121.

Walker, J. E., Norman, C. A., & Weber, R. K. (2002). Impact of qEEG-guided coherence training for patients with a mild closed head injury. *Journal of Neurotherapy, 6*(2), 31-43.

Zhuo, M. (2008). Cortical excitation and chronic pain. *Trends in Neurosciences, 31*(4), 199-207.