Quantitative EEG and swLORETA Analyses

PATIENT INFORMATION

Name:  
Exam#:  
Age: 31  
Gender: Male  
Handedness: Right  
Condition: Eyes-Closed

RECORDING

Date:  
Ref. By: Self  
Test Site:  
Duration: ~10 min.  
Ave. SH Reliability: 0.99  
Ave. TRT Reliability: 0.95

MEDICATION:  Sertraline 125 mg, Valacyclovir 500 mg, N-Acetyl Cysteine 600 mg.

meets the criteria for the following ICD-10 and DSM-5 diagnoses:

- G93.3 Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS; Postviral fatigue syndrome)
- G93.9 Non-traumatic Disease of the Brain (Encephalopathy), ME/CFS, Epstein-Barr and HHV-6 viral infection
- G90.9 Dysautonomia
- M79.7 Fibromyalgia

HISTORY:  became ill with severe flu-like symptoms typical of ME/CFS in early 2018 on a return flight from . Since that time, he has experienced chronic energy depletion and exhaustion, accompanied by cognitive deficits to attention (difficulties with concentration, inability to stay focused), language function (reading comprehension, word finding, autonomic dysfunction (orthostatic intolerance, urinary frequency, headaches, dyspnea), and diffuse chronic muscle/joint pain. His symptoms vary unpredictably day-by-day (even within the same day), with daily fluctuations in intensity, duration, and severity (moderate to severe/very severe levels). As a result of post-exertional malaise, he is unable to perform physical and cognitive demands on a predictable, reliable, and consistent basis. His initial baseline qEEG scan administered at the NCRI on showed significant bilateral dysregulation in the frontal lobes. This finding was later verified in his SPECT/CT scan showing regional mild diminished perfusion involving the frontal lobes bilaterally. A 2-day cardiopulmonary exercise test revealed the following: 1) VO₂ peak is 33-42% lower than normal for his age/sex, 2) low ventilatory/anaerobic threshold classifies him with mild to moderate impairment, 3) low ventilatory limitation consistent with muscle fatigue and/or lung/airway obstruction or restriction, 4) slow heart rate recovering following exercise, 5) dysautonomia indicated by abnormal blood pressure and ventilatory responses during exercise, 6) post-exertional malaise and exercise intolerance indicated by abnormal responses to exertion. The clinical findings presented in this report are based on his recent baseline qEEG recording.

SUMMARY:  The qEEG analyses were deviant from normal and showed dysregulation in the left frontal lobe, and the left temporal lobe. The frontal lobes are involved in executive functioning, abstract thinking, expressive language, sequential planning, mood control, and social skills. The temporal lobes are involved in auditory processing, short-term memory, receptive language on the left and face
recognition on the right. swLORETA 3-dimensional source analyses were consistent with the surface EEG and white-matter based on connectivity results. Elevated current sources were present in the left orbital gyrus and left superior and middle temporal pole. The temporal pole is a heterogeneous region implicated in different cognitive functions such as emotion, attention, behavior, and declarative memory. It is also involved in higher-order cognitive processes such as language function. His complaints of executive dysfunction are evidenced by significant dysregulation present in these regions. Additionally, swLORETA connectivity analyses revealed a highly significant reduction in global connectivity with a widespread and substantial reduction in information flow involving networks that govern cognitive, affective, sensorimotor, vestibular, and autonomic functions. These qEEG findings are consistent with marked or extreme limitations and impairments; together with his medical records and clinical history, findings provide clear, objective, and overwhelming evidence of severe disability due to ME/CFS.

Mark Zinn, Ph.D.

DETAILED NARRATIVE

**RAW EEG.** The raw EEG contained four potential myoclonic absence seizure events in brief duration (~1.5 seconds) with appearance of EMG artifact consistent with tonic neuromuscular contractions.

**SPECTRAL POWER:** The Linked Ears power spectral analyses were deviant from normal with excessive power in the left frontal region over a wide frequency range. Excessive power was also present in the left temporal region from 4 - 6 Hz and 8 Hz.

**SURFACE CONNECTIVITY:** EEG amplitude asymmetry, coherence and EEG phase were deviant from normal, especially in frontal, temporal, parietal and occipital relations. Elevated coherence was present in frontal, temporal, parietal and occipital regions which indicates reduced functional differentiation. Reduced coherence was present in frontal region which indicates reduced functional connectivity. Both conditions are often related to reduced speed and efficiency of information processing.

**swLORETA NEUROIMAGING:** swLORETA 3-D source analyses were consistent with the surface EEG and showed significantly elevated current density in the left orbital frontal gyrus (BA 11) of the prefrontal cortex and the left superior and middle temporal pole with a maximum at 5 Hz (BAs 36, 38). Other regions that were significantly elevated included the bi-lateral amygdala (BA 25), anterior insula, left hippocampus, and cerebellum areas IX and X.

**swLORETA FUNCTIONAL CONNECTIVITY:** Functional connectivity findings revealed widespread and significantly reduced information flow between regions of brain networks which play a vital role in neurocognitive (default-mode network, executive network, salience network, dorsal/ventral attention networks).

The salience network (SN) filters and directs our perception of external and internal relevant stimuli, representative sensations related to internal organ function and autonomic activity. It is closely related to the pain network (PN) which processes visceral sensation and sensory discriminatory
components of pain. Disruption to these networks may result in lower pain threshold and diffuse regional pain processing.

Attention can be thought of as the allocation of the brain’s processing resources to task-related stimuli, which is controlled by changes in the brain's state of arousal. The default-mode network (DMN) processes inward attention to self-related mental activity and experiential events and is anti-correlated with the executive network (EN) to shift attentional focus toward external stimuli which allows flexibility of responses in accordance with changing task demands. The dorsal attention network (DAN) is engaged during externally directed attentional tasks, whereas the ventral attention network (VAN) responds when behaviorally relevant stimuli are detected which are initially outside the focus of attention and are initially unattended to. The ventral attention network redirects the DAN toward behaviorally relevant stimuli. DAN and VAN together help to initiate state changes in arousal and allocation of task-related stimuli needed for sustained concentration and multi-tasking.

Mr. Albertini also suffers from post-exertional malaise (PEM), which is a cardinal feature of ME/CFS characterized by rapid and severe mental or physical fatigue from exposure to even minimal activity—the prolonged recovery period may last for days or weeks at a time. Examples of PEM-induced by cognitive exertion include just reading a few pages from a book or just trying to follow a conversation. Consistent with severe PEM, functional connectivity findings revealed significant dysregulation in his central autonomic network (CAN), a set of cortical regions which include the anterior, middle, and posterior insula, amygdala, medial frontal gyrus, anterior and posterior cingulate cortex, hippocampus, orbital frontal gyrus. Subcortical areas include the thalamus, and cerebellum. Together these regions coordinate top-down maintenance of peripheral ANS outflow (parasympathetic, sympathetic, and enteric branches of the ANS) to ensure survival and adaptive flexibility to momentary challenges. CAN dysregulation is related to homeostatic instability with neurological consequences that manifest wide-ranging symptoms reported by Mr. Albertini, including but not limited to the following: orthostatic intolerance, unstable regulation of body temperature, headaches, neckaches, cardiac irregularities (heart palpitations and tachycardia), sensory hypersensitivities (light, sound, taste, touch, and smell), GI motility problems, excessive sweating, and a host of other autonomic symptoms.

Mr. Albertini also contends with severe dizziness and nausea, balance problems, and muscle weakness on a daily basis. Significant reductions in information flow were found in his ataxia network, which is involved in motor sequencing, coordination, vestibular balance, and precise movement control. It includes the cerebellum which is linked to the vestibular system for coordinating movement and balance. It also plays a vital role in cortical sensorimotor/spatial processing of the parietal lobe, memory and auditory functions of the temporal lobe, and visual/spatial processing of the occipital lobe. Additionally, recent findings demonstrate lateral cerebellar involvement in coordinating cognitive executive functions (e.g., attention and default-mode networks).

Significant reductions in information flow were present in mood network and anxiety network. This is consistent with neurological sequelae that impact limbic function. Disease of the CNS typically interferes with brain mechanisms that underlie emotion. The widespread dysregulation found in this evaluation combined with his clinical history of neurotropic viral infection, CPET evaluation, SPECT results, and other testing results on record clearly and overwhelmingly evidences the physiological basis for his severe limitations and disability.

**DTI Findings.** swLORETA connectivity results were mapped onto white-matter fiber tracts modeled from diffusion tensor imaging (DTI), which is an MRI technique used to measure the diffusion of water molecules. Significantly reduced information flow was present in crossing fibers of the corpus callosum which is the largest white-matter bundle in the brain and it is responsible for interhemispheric information flow between cortical and subcortical regions of each hemisphere. Other fiber tracts that were significantly affected include the left superior longitudinal fasciculus (SLF) and left arcuate fasciculus tracts. The SLF is an extensive white-matter tract that connects to nearly all cortical areas of
each hemisphere and it is involved in working memory and executive functions. The left arcuate
connects Broca’s area to Wernicke’s area and it plays a key role in language processing.

**Frequency Bands.** Location of abnormality is primarily important for understanding
neurological symptoms, but the frequency band provides an added layer of information. Abnormalities were found in the delta and theta frequency bands. **Delta rhythms (1-3 Hz)** are slow oscillations that are produced by cortico-cortical and cortico-thalamic networks involved in basic homeostatic processing, restorative sleep, salience recognition, and language. Slowing of EEG background activity is consistent with neuroinflammatory conditions and neurotropic virus infections. Abnormal delta activity has also been implicated in studies of Alzheimer’s disease and may demonstrate a link between brain states, arousal, and efficiency, with decrements in information processing speed, which is typically found in patients with ME/CFS. **Theta rhythms (4 – 7 Hz)** originate in the thalamus and associated with arousal, affective states originating from synchronized neurons (pacemakers) in the limbic system, including the cingulate gyrus and the parahippocampal cortex. It is considered important for a variety of cognitive functions including memory consolidation, spatial navigation, working memory and memory encoding/retrieval. Together, findings of this evaluation point to signs of slowing of EEG background activity that is consistent with neuroinflammatory conditions.

**Raw EEG and Spectral Analyses**

Baseline Linked Ears EEG and Absolute Power – Eyes Closed Condition
swLORETA Electrical Neuroimaging

Linking a patient's symptoms and complaints to functional systems in the brain is important in evaluating the health and efficiency of cognitive and perceptual functions. The electrical rhythms in the EEG arise from many sources but approximately 50% of the power arises directly beneath each recording electrode. Standardized-weighted low-resolution electromagnetic tomography (swLORETA) is an advanced electrical neuroimaging tool which uses a mathematical method called an "inverse solution" to accurately estimate the originating sources of the surface EEG (Pascual-Marqui et al, 1994; Pascual-Marqui, 1999; Soler et al., 2007). swLORETA allows one to examine of deeper brain structures (e.g. cerebellum) with similar spatial localization characteristics and co-registration of other neuroimaging modalities (e.g. fMRI) (Bougariou et al., 2015). Where fMRI measures blood flow, EEG measures direct neuronal activity, adding high temporal resolution for detecting millisecond changes in the electrical sources in the brain that are associated with changes in blood flow. Below is a Brodmann map of anatomical brain regions that lie near to each 10/20 scalp electrode with associated functions as evidenced by fMRI, EEG/MEG and PET neuroimaging methods.

A healthy brain will show very few, if any, significant connections at baseline which are deviant from the normal. Z-score color scale has range of ± 3 standard deviations.

Z-scores are based on normalized distribution with a mean of 0 and standard deviation of 1. Z-scores greater than 1.96 are above the 95th percentile at 2 standard deviations. Significance at the .05 level, means, hypothetically, if an analysis were performed an infinite number of times in the same person, the same results would happen at least 95% of the time.
BRAIN BRODMANN REGIONS

FRONTAL BRODMANN AREAS

TEMPORAL BRODMANN AREAS

PARietal BRODMANN AREAS

OCCIPITAL BRODMANN AREAS

LEFT  RIGHT
Maximal theta activity at 5 Hz present in the left middle temporal pole area (BA 38, max. z-score = 2.64) significant above 2 standard deviations. Other significantly elevated regions were found to include the left orbital frontal gyrus (BA 11) of the prefrontal cortex, the bi-lateral amygdala (BA 25), anterior insula, left hippocampus, and cerebellum areas IX and X.
**Z Scored swLORETA Connectivity Analysis**

Brain networks are multifunctional and no cortical region supports only one, specific, isolated cognitive process such as attention. Topological changes in connectivity within the network can serve as indicators for adaptations to disease processes and provide a marker for symptoms. Thus, linking a patient's symptoms and complaints to functional connectivity in the brain is important in evaluating the health and cognitive behavioral functions. Especially important for these functions is understanding the momentary changes in the network that are adaptively reconfigured in response to task demands.

This assessment of network connectivity is based on the phase-slope index (Pascual-Marqui et al., 2011) a measure of the magnitude of information flow occurring between two given brain regions (nodes). Cyan-blue color lines (edges) indicate regions that are significantly hypo-connected (reduced information flow) whereas yellow-red color lines indicate significantly hyper-connected (increased information flow). Significant deviations from normal in either positive or negative direction indicate abnormal connectivity occurring between different nodes within the networks of the brain. The purple dots are nodes which represent different Brodmann areas. Greater disability is expected to the extent there is significantly higher or lower deviation from normal electrical connectivity patterns within and across these networks.

**Example of a neuro-typical individual (healthy person)**
In the delta band (1-3 Hz), the above connectivity map and connectome diagram with 88 Brodmann areas show a significant mixture of hyper and hypoconnectivity at baseline for all large-scale brain networks. Blue lines indicate an overall significantly reduced amount of information flow on a widespread spatial scale. Yellow-red lines indicate compensatory connections.

In the delta band, hyperconnectivity (compensatory activity) is present between bi-lateral areas of the parietal lobe and both hemispheres of the cerebellar vermis region. This region receives somatosensory input from ascending spinal pathways and descending pathways from primary motor cortex.
In Delta 1-3 Hz in the axial model above, fiber tracts are based on values from the connectome figure with 88 Brodmann areas. Both figures show a generalized significant reduction of information flow (blue color) in the U-shaped crossing fibers of the corpus callosum tract are indicated with ovals. This indicates a widespread substantial reduction in cross-hemispheric communication.

In Delta 1-3 Hz, the left sagittal view illustrates reduced information flow in the U-shaped corpus collosom (circle), and left cerebellar hemisphere (circle). Back view also shows reduced information flow in the U-shaped corpus collosom tract and the left cerebellar hemisphere (circle).
In Theta 4-7 Hz, the above connectivity model and connectome map with 88 Brodmann areas shows significantly reduced information flow mainly in the left hemisphere, crossing over to certain nodes in the right hemisphere.

In Theta 4-7 Hz, substantially reduced magnitude of information flow is present between many nodes of the left frontal/temporal/parietal lobes and nodes of both cerebellar hemispheres which are responsible for motor, attentional, and default-mode processing.
In Theta 4-7 Hz, the above fiber tracts are based on values from the connectome figure with 88 Brodmann areas. The figures above show a left-lateralized reduction in information flow (blue color) in the left superior longitudinal fasciculus and left arcuate fasciculus tracts (indicated with black square), and in the U-shaped crossing fibers of the corpus callosum tract (indicated with circle). This indicates an overall and significantly reduced cross-hemispheric communication.

In Theta 4-7 Hz, the left side view illustrates significant abnormality in the U-shaped uncinate fasciculus (circle), superior longitudinal fasciculus, arcuate fasciculus, inferior fronto-occipital fasciculus, and cingulum (oval).

The above figure shows significantly reduced fiber tracts of the left figure, superimposed onto 3-D source analysis Theta results (see p. 9), shown here in light red-orange color. This concordance of both findings is highly consistent and it includes the left cingulum.
Delta 1-3 Hz. Reduced information is present in the executive network, which is involved in goal-directed attention, working memory, and performance monitoring during situations that call for planning, problem solving, and decision making.

Delta 1-3 Hz. Highly significant reduction to information flow (dark blue) is shown here in the somatosensory nodes of the pain network for visceral sensation and sensory discrimination of pain processing. Disruption is related to widespread chronic muscle/joint pain and fibromyalgia symptoms.
Delta (1-3 Hz). Reduced information flow present in nodes of the DMN. This network is engaged during self-referential cognitive activity and suppression of this network is needed when engaging external attention for environmental tasks. Dysregulation of this network results in episodic memory deficits and task-switching.

Delta 1-3 Hz. Reduced information flow present between the bi-lateral posterior insula and salience recognition association regions of the frontal lobe. Increased information flow is present between the bi-lateral posterior cingulate and the left insula and anterior cingulate (compensatory response). The SN directs our attention to external and internal relevant stimuli, including autonomic and emotional challenge. The insula (circles) is a key region for integrating and filters incoming sensory stimuli, interoceptive awareness, and reward information. Dysregulation of this network may result in aberrant control of attention and working memory resources and hypersensitive perception of light, noise, smell, and touch.
### CENTRAL AUTONOMIC NETWORK

Delta 1-3 Hz. The CAN is involved in top-down control and maintenance of the peripheral autonomic nervous system (ANS) outflow to target organs. Dysregulation shown here explains wide ranging symptoms and rapid fluctuations in symptoms which include severe fatigue and stamina loss, cold extremities, fluctuating body temperature, nausea, dizziness, headache, neckache, cardiac irregularities and palpitations, visual acuity problems, hypersensitivity to light, noise, smell, touch.

### ATAXIA NETWORK

Delta 1-3 Hz. Reduced information flow is present across each cerebellar hemisphere (oval). Ataxia is a primary symptom of cerebellar dysfunction. Connections from the cerebellum mainly convey information to the cerebral motor cortices. However, reduced information is present in the primary motor cortex (square).
**DORSAL ATTENTION NETWORK**

Delta 1-3 Hz. Significantly reduced information flow is present between most regions of the DAN. This network is engaged during externally directed attentional tasks.

**VENTRAL ATTENTION NETWORK**

Delta 1-3 Hz. Significantly reduced information flow is present between nearly all regions of the VAN. This network responds when behaviorally relevant stimuli are detected which are initially outside the focus of attention and are initially unattended to. It also redirects the DAN toward behaviorally relevant stimuli.
The mood network is involved in mood maintenance. It includes the habenula which is involved in nociception, sleep-wake cycles, reproductive behavior. It is known to influence virtually all monoaminergic systems in the brainstem, such as dopamine, norepinephrine, and serotonin.

The anxiety network regulates fear responses. It involves the amygdala which sends projections to the hypothalamic-pituitary-adrenal axis and locus coeruleus for mediating stress hormones of the neuroendocrine system.
This record supports the following reliability estimates:

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<tr>
<td><strong>Technical Information</strong></td>
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<td>Record Length:</td>
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<td>Edit Length:</td>
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**Reliability:**

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<th>Test Rel.</th>
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<td>FP1</td>
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<td>FP4</td>
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<td>C4</td>
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**Sampling Rate:** 256

**Collection Hardware:** BrainMaster Discovery

Appendix

Important Disclaimer:

QEEG tests are ancillary tests similar to blood tests, that are not intended to provide a diagnosis by themselves, but are used to evaluate the nature and severity of dysregulation in the brain such as in ME/CFS or in any of the other 600+ neurological disorders. The QEEG tests provide a quantitative assessment of regions of brain dysfunction and information regarding impaired conduction and connectivity between different regional neural networks in the brain. The assessment of impaired connectivity is based on abnormal measurements of Coherence and Phase. The diagnosis of MTBI is a clinical one and is not based on any one test. A diagnosis is performed by the clinician, who integrates the medical history, clinical symptoms, neurocognitive tests with the above-mentioned brain function tests as well as other information to render a diagnosis. The information on impaired brain connectivity is derived primarily from abnormal measurements of Coherence and Phase. Assessments of regional abnormality rely also on abnormal amplitude (power) distribution across the spectrum of EEG frequencies as compared to norms.

Artifact Rejection:

NeuroGuide uses the standard deletion of artifact method to only select artifact free EEG data for analyses. View the Test Re-Test reliability which must be at least 0.90 NeuroGuide does not use any regression methods to allegedly remove artifact such as ICA/PCA or Blind Source or unpublished methods like SARA that distort Phase and Coherence, thus invaliding the results. Details and tutorials demonstrating how the ICA and regression methods distort Phase and Coherence are available at: https://www.appliedneuroscience.com/PDFs/Tutorial_Adulteration_Phase_Relations_when_using_ICA.pdf.

Split Half and Test Re-Test Reliability:

Split-Half (SH) reliability is the ratio of variance between the even and odd seconds of the time series of selected digital EEG (variance = sum of the square of the deviation of each timepoint from the mean of the time points). Test Re-Test reliability is an excellent statistic to compare. Brain state changes such as drowsiness as well as the consistency of a measure independent of changes in brain state.

Description of the NeuroGuide Normative Database:

The NeuroGuide normative database in versions 1.0 to 2.4.6 included a total of 678 carefully screened individual subjects ranging in age from 2 months to 82 years. NG 2.6.8 involved the addition of 49 adult subjects ranging in age from 18.3 years to 72.6 years resulting in a normative database of 727 subjects. The inclusion/exclusion criteria, demographics, neuropsychological tests, Gaussian distribution tests and cross-validation tests are described in several peer reviewed publications (Thatcher et al, 1983; 1987; 2003). Two year means were computed using a sliding average with 6 month overlap of subjects. This produced a stable and higher age resolution normative database with a total of 21 different age groups. The 21 age groups and age ranges and number of subjects per age group is shown in the bar graph in Appendix F figure 2 in the NeuroGuide Manual (click Help > NeuroGuide Help).

The individuals used to create the normative database met specific clinical standards of no history of neurological disorders, no history of behavioral disorders, performed at grade level in school, etc. Most of the subjects in the normative database were given extensive neuropsychological tests. Details of the normative database are published at: Thatcher, R.W., Walker, R.A. and Guidice, S. Human cerebral hemispheres develop at different rates and ages. Science, 236: 1110-1113, 1987 and Thatcher R.W., Biver, C.L., North, D., Curtin, R. and Walker, R.W. Quantitative EEG Normative Databases: Validation and Clinical Correlation. Journal of Neurotherapy, 2003, 7(3-4): 87-121. You can download a description of the normative database by going to https://appliedneuroscience.com/scientific-articles/ and clicking on Article #5.
Is there a normative database for different montages including bipolar montages?

Yes. The raw digital data from the same group of normal subjects is analyzed using different montages such as Average Reference, Laplacian current source density, a common reference based on all 19 channels of the 10/20 system and standard clinical bipolar montages (e.g., longitudinal, circular, transverse). Users can create any montage that they wish and there will be a normative reference database comparison available for both eyes closed and eyes open conditions.

Age range of the swLORETA Current Density and Source Correlation Normative Databases

The swLORETA current density and source correlation norms use the same subjects as are used for the surface EEG norms and the age range is 2 months to 82 years. The computational details of the LORETA current density norms are published at: Thatcher, R.W., North, D., Biver, C. EEG inverse solutions and parametric vs. non-parametric statistics of Low Resolution Electromagnetic Tomography (LORETA). Clin. EEG and Neuroscience, 36(1): 1-9, 2005 and Thatcher, R.W., North, D., Biver, C. Evaluation and Validity of a LORETA normative EEG database. Clin. EEG and Neuroscience, 2005, 36(2): 116-122. Copies of these publications are available to download from https://appliedneuroscience.com/scientific-articles/ by clicking on article nos. 11 and 12.

Amplifier Matching is Necessary

This stems from the fact that amplifiers have different frequency gain characteristics. The matching of amplifiers to the NeuroGuide database amplifier was done by injecting microvolt calibration signals of different amplitudes and frequencies into the input of the respective EEG machines and then computing correction curves to exactly match the amplifier characteristics of the norms and discriminant functions. The units of comparison are in microvolts and a match within 3% is generally achieved. The NeuroGuide research team double checked the amplifier match by computing FFT and digital spectral analyses on calibration signals used to acquire the norms with the calibration signals used to evaluate a given manufacturer's amplifiers.

History of the Scientific Standards of QEEG Normative Databases


References


