Quantitative Electroencephalography Power Analysis in Subjective Idiopathic Tinnitus Patients: A Clinical Paradigm Shift in the Understanding of Tinnitus, An Electrophysiological Correlate

Abraham Shulman,[1,3] Matthew J. Avitable,[2] and Barbara Goldstein[1,3]

[1] *Martha Entenmann Tinnitus Research Center, Forest Hills, New York, and* [2] *Scientific Computing Center and* [3] *Department of Otolaryngology, Health Science Center at Brooklyn, State University of New York, Downstate Medical Center, Brooklyn, New York*

Abstract: We report a descriptive analysis-interpretation of quantitative electroencephalography (QEEG) data for the metric of power in patients with tinnitus of the severe disabling type (N = 61). The results are based on a statistical analysis of the data compared to a normative database as calculated in Z scores, controlling for the factors of age, gender, IQ, and the like. **Method:** We analyzed the QEEG data for the metric of power to measure (1) the number of significant recordings, normal and abnormal; (2) the significant recordings by electrode recording sites; (3) distribution of the electroencephalographic (EEG) frequency bands; and (4) occurrence of the EEG frequency bands correlated with the electrode recording sites. In the analysis of the occurrence of the EEG frequency bands by electrode recording area, we corrected for the number of recording sites. **Results:** We recorded normal power recordings in 20 of 61 patients (32.8%) and abnormal power recordings in 41 of 61 patients (67.2%); power distribution by frequency band in 41 of 61 patients, revealing the number of significant recordings of delta (119), alpha (69), beta (91), and theta (17); and the power distribution by location for all frequencies, which were revealed as recording site activity in the frontal greater than in the temporal sites, which in turn was greater than in the parietal site, and equal activity in parietal, occipital, and central sites. The analysis of the occurrence of the EEG frequency bands by electrode recording area as corrected for the number of recording sites reinforced our initial results. **Conclusions:** Z-score analyses of QEEG recordings—based on a large normative database—for the metric of power for patients having tinnitus of the severe disabling type (N = 61) revealed statistically significant abnormalities in frontal greater than temporal electrode recording sites. We reported no difference between male and female tinnitus patients in the number of abnormal power QEEG recordings. However, we observed significant differences in the average Z scores between males and females in the alpha and theta bands. The results suggest multiple central electrophysiological correlates for different clinical types of tinnitus identifiable with QEEG, for the metric of power, by frequencies of brain activity of delta greater than beta greater than alpha greater than theta bands of activity, reflecting physiologically the individuality of brain function and clinically the heterogeneity of the symptom of tinnitus for tinnitus patients. Clinical interpretation of the QEEG data in terms of brain function

Reprint requests: Abraham Shulman, MD, FACS, Department of Clinical Otolaryngology, Health Science Center at Brooklyn, State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Box 1239, Brooklyn, NY 11203-2098. Phone: 718-773-8888; Fax: 718-465-3669; E-mail: metrc@inch.com

in a tinnitus patient, with a focus on theories of a neuroanatomical homeostatic system that regulates baseline levels of local synchrony in multiple neuronal assemblies and on theories of consciousness, introduces a paradigm switch in our clinical understanding of the symptom of tinnitus and an application for tinnitus diagnosis and treatment.

Key Words: absolute power; coherence; phase; quantitative electroencephalography; relative power amplitude asymmetry; Z score

We report a descriptive analysis and interpretation of quantitative electroencephalography (QEEG) data for the metric of power in patients (N = 61) having tinnitus of the severe disabling type (subjective idiopathic tinnitus [SIT]). In a preliminary report, we cited the QEEG examination as a significant addition to the medical-audiological tinnitus patient protocol (MATPP) for patients with SIT [1,2]. Preliminary data from 21 SIT patients were found to support the hypothesis of the significant role of the temporal and temporofrontal regions of the brain.

QEEG is a quantitative analysis of brain function as reflected in electrophysiological measures via the electroencephalogram [3]. The metrics of analysis include absolute power, relative power in terms of percentage of power, Z scores of asymmetry power, coherence (reported as elevated or reduced), and phase (reported as phase delay, positive or negative, and as both intra- and interhemispheric homologous pairs).

The power metric is the total electrical activity recorded at the brain cortex with electroencephalography (EEG). The relative power measures the distribution of electrical activity over the delta, theta, alpha, and beta frequency bands. All these metrics can also be expressed in terms of the deviation of standardized scores based on a selected set of norms (i.e., Z scores). Z scores are observed scores transformed into a score with a common reference (i.e., Z mean = 0; standard deviation, Z = ±1) [4,5].

A significant increase in the average total power (in microvolts) recorded from 19 electrode sites in female patients and a decrease in male patients as compared to a group of subjects without any substantiated medical or neurological disease has been reported in tinnitus patients [6]. Abnormal spontaneous brain activity as measured by magnetoencephalography has demonstrated a pattern of marked reduction in alpha and an increase in delta, pronounced for temporal regions [7].

In this study, we analyze our attempt to identify and quantify Z scores of significant corticoelectrical dysfunction for the metric of power in patients with predominantly central-type severe, disabling SIT (N = 61). We use the following measures of analysis: (1) identification and distribution of the number of significant QEEG recordings (normal and abnormal); (2) identification and

distribution of specific electrode recording sites; (3) identification and distribution by band frequency; and (4) correlation of the distribution by band frequency and recording site. Analysis of the occurrence of the EEG frequency bands by electrode recording area corrected for the number of recording sites.

METHOD

We selected for analysis of the metric of power for the measures described patients who had SIT lasting 1 year or longer (N = 61) and in whom MATPP (including QEEG) established the diagnosis of a predominantly central-type tinnitus. We used the database that includes normative data for the metrics of relative power, amplitude asymmetry, phase, and coherence [6]. The ages represented in the database range from 2 months to 83 years, which represents 625 subjects. Delta was 0.5–3.5 Hz; theta was 3.7–7.5 Hz; alpha was 7.5–13.5 Hz; and beta was 13.5–22 Hz [4]. We performed the QEEG test with patients' eyes open and closed in a quiet, darkened room, with patients sitting relaxed in a chair in an upright position. This study included both male and female patients (mean age, 53.9 and 59.6 years, respectively; Table 1) with constant tinnitus.

For the QEEG examination, we used the Neurosearch 24 (Lexicor Company, Boulder, CO) QEEG equipment [8]. We placed 19 electrodes on the patients' scalp using the international 10/20 montage (a montage being a standardized array of electrode sites used to ensure consistent results). The impedance measured at each electrode site with respect to the reference was less than 5,000 Ohms. We set the filter bandpass between 0.5 Hz and 32 Hz. We recorded 300 epochs, selected 25 as being representative and artifact-free, and processed and compared them with the normative database. The gain was 32,000, with a sampling rate of 128,000.

We submitted raw EEG results to the Lexicor Company for analysis, and that firm generated a report called the *Datalex report* for clinical application [9]. The Datalex report is presented in two sections. Section 1 includes normative reference database comparisons for the metrics of relative power, amplitude asymmetry, coherence, and phase [9]. Section 2 includes graphic representations of the raw data by means of color topo-

Table 1. Patient Data

Gender	No. of Patients	Mean Age (yr)	Age Range (yr)
Male	42	53.9	21.57–84.87
Female	19	59.6	32.11–83.18

Table 2. Z-Score Transformations

Band	Mean	SD	SEM
Delta			
Female	.0171	.86660	.19881
Male	.5904	1.34500	.20754
Theta			
Female*	.3395	.50934	.11685
Male	.0983	.65157	.10054
Alpha			
Female*	.5009	1.07562	.24676
Male	−.1948	.94128	.14524
Beta			
Female	−.1674	1.09277	.25070
Male	.0585	1.22843	.18955

SD = standard deviation; SEM = standard error of the mean.
* Differences significant at the 0.05 level.
Note: Between female (n = 19) and male (n = 42) patients.

graphical maps of absolute peak-peak microvolt amplitude at 1-Hz intervals in the frequency domain, along with a numerical table from which the topographical maps are derived. This section also includes eight topographical maps of the absolute power in eight defined bands in the frequency domain and is accompanied by a numerical table containing the data from which the maps were derived. Section 2 also includes percent power ratios computed at each of the 16 recording locations for each of the 4 bands compared to the total power measured at that location. Compressed spectral arrays are also displayed, illustrating the evolution of the frequency spectrum over time at each of the 16 electrode locations in the montage [9].

The Z score calculated in QEEG analysis is based on comparing an individual's EEG recording to the results of a disease-free sample of subjects [4,5]. The database is constructed with norms for both age and gender. The criteria to be included in the database were an uneventful prenatal, perinatal, and postnatal period, and absence of disorders of consciousness, head injury with cerebral symptoms, history of central nervous system diseases, convulsions of emotion (febrile or otherwise), and abnormal deviation with regard to mental and physical development. A Z score is calculated using the following formula:

$$Z = \frac{EEG_{Individual} - EEG_{Normative\ Mean}}{Standard\ Deviation_{Normative\ Mean}}$$

The Z distribution is normally distributed with a mean of 0 and a standard deviation of 1. If the value of an EEG recording is greater than +1.96 or less than −1.96, the recording is considered to occur in less than 5% of the normative population (two-tailed) and is considered statistically significant.

RESULTS

All results reported are based on an analysis of the data referenced to Z scores in the database described [4,5]. This type of analysis has the advantage of referring individual recordings to a normative database, thereby referencing affected individuals to their respective norms and not to the absolute EEG power, which varies owing to the influence of factors corrected for in the normative database. We included in this study both male and female patients with a mean age of 53.9 and 59.6 years, respectively (see Table 1).

We observed a significant difference in Z-score transformations between male and female patients (Table 2). Men significantly differed from women in both the alpha and theta bands. In the theta band, women were below the mean of the norm, whereas men were above the mean of the norm. In the alpha band, women were above the mean of the norm, whereas men were below the mean of the norm.

The analysis of distribution of the number of significant QEEG recordings (normal and abnormal) per tinnitus patient for all 61 patients revealed a significant degree of variability (Fig. 1). Significant considerations included the findings that 20 patients posted no abnormal EEG recording for the metric of power (i.e., 20 of 61 patients, or 32.8%, had normal power recordings) and that the remainder recorded one or more abnormal recordings with a range of 1–36 abnormal recordings
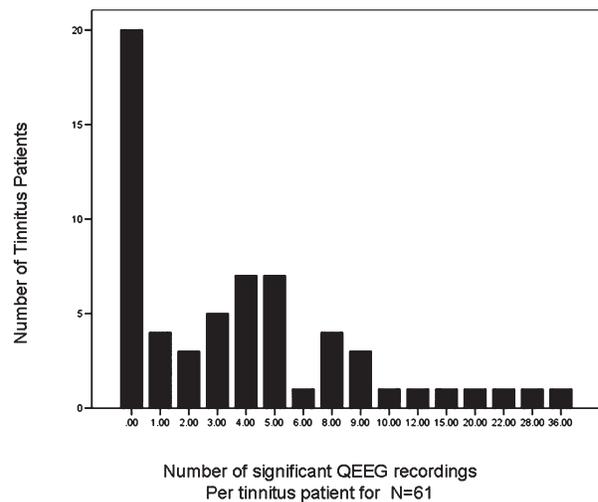

Figure 1. Analysis of distribution of the number of significant quantitative electroencephalography recordings.
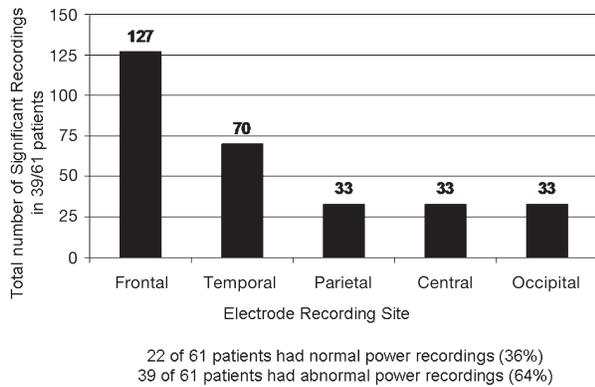
Figure 2. Distribution of response by electrode recording site of 296 significant recordings in 41 of 61 tinnitus patients.

(i.e., 41 of 61 patients, or 67.2%, had abnormal power recordings).

In the 296 significant recordings in those same 41 patients, analysis of response distribution by electrode recording site revealed frontal (127), temporal (70), parietal (33), central (33), and occipital (33) recording sites (Fig. 2). Of those 296 recordings in these same 41 patients, the analysis by frequency band revealed delta (119), theta (17), alpha (69), and beta (91) (Fig. 3). The analysis of power response distribution and correlation of EEG frequency band with recording site (Table 3; Fig. 4) revealed (1) occurrence of all frequencies in all recording areas; (2) pattern of brain rhythm activity of delta greater than beta, greater than alpha, greater than theta in frontal greater than temporal greater than occipital recording sites and the same brain activity in occipital, parietal, and central recording sites; (3) delta response distribution that was greater in the frontal than temporal than parietal and occipital recording sites and equal in parietal and occipital sites, which was greater than in the central recording sites; (4) theta response
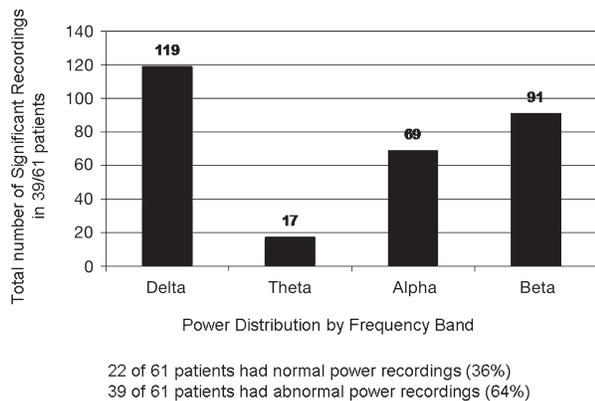
Table 3. Cross-Tabulation Analysis of Power Response Distribution and Correlation of Electroencephalography Frequency Band with Recording Area

Band	Area					Total
---	Central	Frontal	Occipital	Parietal	Temporal	
Alpha	9	29	7	6	18	69
Beta	14	40	8	10	19	91
Delta	8	48	16	16	31	119
Theta	2	10	2	1	2	17
Total	33	127	33	33	70	296

that was minimal and distribution that was greater in the frontal than in the occipital recording sites and equal in the occipital, temporal, and central recording sites, which was greater than in the parietal recording sites; (5) alpha response that was greater in the frontal than temporal than central than occipital than parietal recording sites; (6) beta response distribution that was greater in the frontal than temporal than central than parieto-occipital recording sites; and (7) beta response that was greater than alpha response in the frontal than temporal than central than parietal than occipital recording sites.

Analysis of the number of significant recordings with correlation of EEG frequency bands and the recording area when corrected for the number of recording electrode sites (i.e., total 16 but, of this number, 6 frontal, 2 central, 4 temporal, 2 parietal, and 2 occipital) revealed similar but increased responses, as previously described (Fig. 5).

DISCUSSION

The distribution of increased electrical activity recorded from multiple sites and its correlation with specific brain rhythms (i.e., frequencies) in patients with predominantly central-type SIT has not previously been reported with Z-score analysis based on a normative
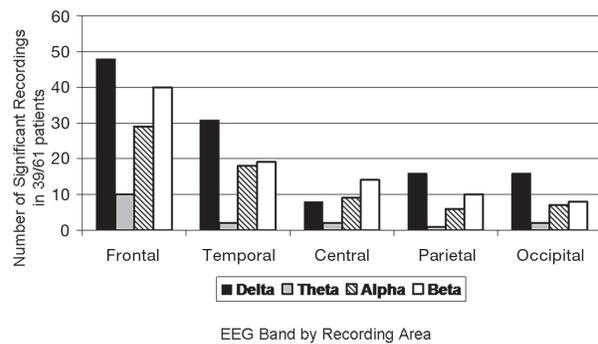

Figure 3. Analysis of power distribution by frequency band of 296 significant recordings in 41 of 61 tinnitus patients.

Figure 4. Distribution of power response and correlation of electroencephalography frequency band with recording area.

22 of 61 patients had normal power recordings (36%)
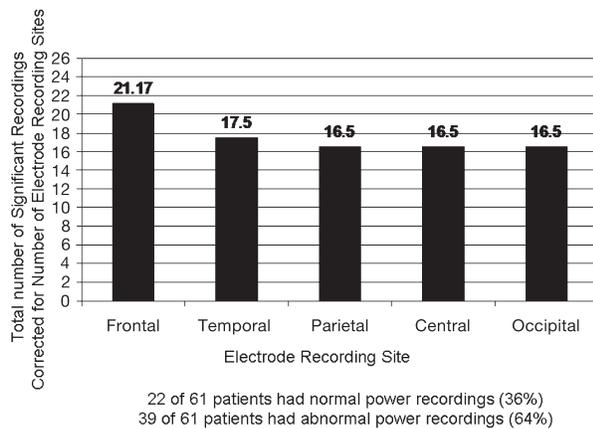39 of 61 patients had abnormal power recordings (64%)

Figure 5. Analysis of the number of significant recordings with correlation of electroencephalography frequency bands and the recording area when corrected for the number of recording electrode sites.

database of EEG activity. The importance of the results reported here is that the significant recordings observed are not only statistically significant but clinically significant, because the significant Z-score transformations indicate that the recordings occur in less than 5% of the population norm.

The descriptive analysis of the QEEG results in 61 SIT patients is highlighted by the findings of (1) significant abnormal QEEG recordings in SIT patients (64%); (2) a significant number of abnormal power recordings in multiple electrode recording sites; (3) a clinical suggestion, by the power distribution of multiple frequency bands in multiple recording sites, of the heterogeneity of the tinnitus symptom; (4) support for a hypothesis to explain the heterogeneity of brain activity in tinnitus patients [10,11]; (5) a method to objectify SIT (i.e., electrophysiological correlates in terms of frequencies of brain activity for the metric of power with QEEG); and (6) a paradigm alteration in understanding tinnitus based not on the psychoacoustic and psychophysical attributes of tinnitus but on multiple brain functions in response to and in presence of tinnitus, with a focus on consciousness.

Theoretical Considerations

Male-Female Differences

We observed significant average Z-score differences between men and women in the alpha and theta bands (see Table 2). At this time, we have not arrived at a conclusion as to its significance. Male and female tinnitus patients have been reported to differ significantly from "normals" (i.e., those without tinnitus), but no comparison was in the report between male versus female

tinnitus patients [6]. To be considered are profound changes reported in the neurobiological basis of the mind accompanying hormonal changes during the estrous cycle [12]. Alterations in physical substrates that subserve brain functions with fluctuating levels of progesterone or estrogen include alterations in excitatory synapse density in the hippocampus [13], changes in GABA inhibitory neurotransmitter receptors and their modulators [14,15], and neurons that express different subsets of GABA-A receptor subunits during different phases of the estrous cycle [16].

Brain Function and the Heterogeneity of Tinnitus

QEEG studies in SIT patients, reported originally by Weiler et al. [17,18], provided an insight into electrical brain activity and a technique to objectify the SIT symptom in terms of its psychophysical and psychoacoustic characteristics. The results in this report contribute to and enlarge the understanding of the SIT symptom beyond that of its psychophysical and psychoacoustic characteristics as projected to brain. They provide a basis for understanding the clinical heterogeneity of the SIT symptom by demonstration of multiple brain frequencies of activity recorded in multiple electrode recording sites, all in response to an aberrant auditory stimulus: tinnitus. Clinically, the results reflect attempts of reestablishment of a homeostasis in brain activity for multiple brain functions, including plastic alterations in multiple neural substrates resulting in neuronal transmission in interneuronal networks. The brain functions include consciousness, attention, concentration, cognition, learning, memory, perception, affect, and psychomotor activity [19–21].

The brain's response to environmental stimulation is global in nature and individual for each patient. Each of us accepts our individuality with pride, and this individuality is maintained and manifested clinically in how each of us reacts to bodily symptoms, all reflected in various brain function activities. This reality of the individuality of brain function is reported by each tinnitus patient and is manifested clinically by its heterogeneity.

The QEEG results we reported of frequency band distribution in different recording sites are clinically considered to reflect this heterogeneity and the individuality of brain function for each tinnitus patient. All professionals involved in attempts to establish accuracy for tinnitus diagnosis—to establish its medical significance and attempts for tinnitus relief—have reported the clinical heterogeneity of the tinnitus symptom [21].

Z Scores and Referenced Normative Database: Statistical and Clinical Significance

Our reported results are based on Z scores referenced to a normative database [4]. The Z scores are observed

scores transformed into a score with a common reference. For the QEEG, the raw power data were transformed into a Z score against a normative database corrected for age and other factors. Significant in the interpretation of QEEG results is the need not to confuse *statistical* significance and *clinical* significance. Statistical significance is a mathematical statement. The true "test" of significance is the answer to the question, "Are the results clinically meaningful?" For example, a study of fluctuation of blood pressure may report a statistical significance for systolic-diastolic values ranging from 160/100 to 150/100 in a given population. Clinically, this is not significant (i.e., the patient is still hypertensive). In this report, the statistically significant QEEG Z-score results *are* clinically significant and correlate with the reported clinical course of the 61 tinnitus patients and the diagnosis of the clinical type of tinnitus (i.e., predominantly central-type SIT). In addition, clinical application of QEEG as an in-office, outpatient monitoring procedure for providing an objective determination of the efficacy of therapy attempting tinnitus relief has been identified [22].

Tinnitus Neural Substrates, A Final Common Pathway for Tinnitus, and Tinnitus Circuit

The power distribution by frequency bands and electrode sites correlates with our reported clinical experience of identifying neural substrates with nuclear medicine (single-photon emission computed tomography [SPECT]) brain imaging in patients with SIT. The first reported and demonstrated alterations in perfusion in multiple regions of interest in the brain—in frontal, temporal, and parietal lobes, basal ganglia, and cerebellum, and highlighted by hypoperfusion in the medial temporal lobe system of brain—has been and continues to be significant. These alterations have provided the basis for the hypothesis or concept of a final common pathway for tinnitus [23,24]. A final common pathway for tinnitus has been hypothesized for transformation of a sensory aberrant auditory stimulus to one of affect. It is highlighted by the medial temporal lobe system, the initial processes being the establishment of a paradoxical auditory memory for the aberrant auditory stimulus.

Specifically, the QEEG results reflect activation of multiple electrode recording sites, providing objective evidence for an interneuronal cortical network highlighted by the frontal and temporal recording sites modulated by the thalamus (i.e., a thalamo-fronto-temporal circuit). The brain rhythms are clinically considered to reflect a complexity of corticothalamic neuronal function both "top down" and "bottom up" [10,11]. The thalamic generators are amplified by the cortex.

Yoshimura and Calloway [25] reported precision of cortical connections manifested at multiple and different levels of organization, demonstrating a "fine-scale specificity" for excitation and inhibition dependent on the type of inhibitory neuron and connectivity to neighboring pyramidal-inhibitory neuron pairs. Considered significant is the correlation of the predominant findings in both SPECT of brain and QEEG (i.e., frontal and temporal brain regions of interest). These two sites account for the majority of abnormal power recordings by frequency bands (127 frontal and 70 temporal from a total of 296). The two functional clinical measures, nuclear medicine imaging and electrophysiological data, provide objective evidence of dynamic maps of brain activity of the interaction of the frontal and temporal lobes and support the final common pathway for tinnitus [2,23, 24]. In addition, positron emission tomography of brain study in tinnitus patients attempting to achieve tinnitus relief with ultra-high-frequency acoustic stimulation reported frontotemporal interaction consistent with the dynamic maps of brain activity reported in this QEEG analysis [26].

Definition of Tinnitus; Consciousness and Tinnitus

The QEEG results of frequency band distribution of tinnitus patients in this report are considered to be clinical support for a new definition for tinnitus and a recent integrative theory of consciousness [10,11].

Tinnitus is a conscious, abnormal, auditory percept reflecting a dyssynchrony in development of, or neural transmission within, the peripheral or central nervous system. By interference in the excitatory-inhibitory processes involved in maintaining homeostasis in neural function, tinnitus acts as a stimulus to express its dysfunction via the auditory system. Tinnitus is not a "phantom" but an active physical process in multiple neural substrates in response to a peripheral or central stimulus. It is identifiable both in electrophysiological recordings (cortical and subcortical) and metabolic activated neural substrates, reflecting a synchrony or dyssynchrony in homeostatic mechanisms involved in maintenance of "normal" individual brain function.

Consciousness and Tinnitus

The theory of homeostatically regulated thresholds for every neuronal population in brain and how this activity is transformed into a subjective experience is the problem of consciousness [10,11]. QEEG results provide a basis for understanding the clinical heterogeneity of SIT in terms of brain function, highlighted by consciousness and not by measures of its psychophysical and psychoacoustic characteristics. This is a paradigm

shift in clinical thinking, which now explains tinnitus in terms of neurobiological processes underlying electrical recordings of spontaneous neuronal activity as reflected in the brain function of consciousness.

Initially, our clinical efforts for attempting tinnitus diagnosis and treatment of SIT recognized the need to find answers to what was considered a key question: How does a sensory phenomenon become transposed or transformed into one of affect? This question had a historical background in the writings of Descartes [27]. We have come to realize and have reported that the answers to this question of attaining increased accuracy for tinnitus diagnosis and efficacy for tinnitus treatment have been reflected in clinical translation of advances in neuroscience for brain function and specifically for consciousness [23,24].

The establishment of the concept of brain function called *consciousness* is a work in progress. One of the past definitions has been that consciousness is the perception of the remembered present [28]. The theory of consciousness of John [10] and John and Prichep [11] is considered to be supported by the QEEG results in this report and provides a basis for clinical translation for tinnitus diagnosis and treatment and clinical interpretation and understanding of the QEEG data.

Advances in Neuroscience and QEEG Power Analysis

Certain advances have been made in the neuroscience of understanding brain function and the integrative theory of consciousness that is considered to support the clinical conclusions of this report.

Background

A neuroanatomical homeostatic system regulates baseline levels of local synchrony [29,30], global interactions among regions [31], and periodic sampling of the signal space [31]. Perception is an active process that specifies the content of consciousness. It reflects a "ground state" of activity of brain function in multiple brain regions that allows the normal brain to achieve adaptive and normal behavior. Alterations in the homeostatic regulation of the ground state reflect response in the brain of a "sensory exogenous system" to multiple stimuli [10,11, 29–32]. The response originates within or outside the brain, which is combined with an "endogenous system" and provides to the signal continuous episodic and short-term memories and emotional content [10,11,29,30]. The signal of neuronal activity received from neuronal assemblies and to be applied for the brain's adaptive response is separated from the spontaneous neural activity, or noise, to restore the ground state. Failures in this

self-organizing system for the encoding of the signal result in a deviation of brain activity for reestablishment of the ground state of brain activity. Such failure may become clinically manifest in seizure activity, inappropriate behavior, misperceptions, delusions, or other psychiatric symptoms. Consciousness is an inherent property of an electric field resonating in a critical mass of coherently coupled cells [10,11].

The QEEG data demonstrate rhythmic voltage oscillations derived from the electrical activity of the subjacent neuronal populations [33]. This reflects the nonrandom synchronization of postsynaptic potentials regulated by interactions of a homeostatic system mediated by different neurotransmitters consisting of rhythmic oscillations in broad frequency bands called delta (1.5–3.5 Hz), theta (3.5–7.5 Hz), alpha (7.5–12.5 Hz), beta (12.5–25 Hz), and gamma (25–50 Hz) [29,30].

The homeostatic system, hypothesized to generate and regulate the EEG power spectrum, exhibits a complex dependence on ionic currents, causing a sequence of hyperpolarizations followed by depolarizations that influence the thalamocortical circuits to act as pacemakers in response to network interactions [34–37]. Sensory input received by the relay nuclei in the thalamus are pacemaker neurons that oscillate in the frequency range of alpha (8–12 Hz) and regulate and synchronize the excitability of cells in the thalamocortical pathways. This modulation is further distributed throughout the cortex by corticocortical interactions.

The alpha rhythm dominates the resting QEEG. The alpha activity arises from interaction between the neurons on the thalamus and certain areas of the cortex. The intrinsic property of these thalamic cells is oscillatory activity in the alpha range (7.5–12.5 Hz). The reticular nucleus of the thalamus mediates GABA influences that can hyperpolarize cell membranes of these cells and result in a slowing of the alpha rhythm to the theta range (3.5–7.5 Hz).

The theta activity is generated in the limbic system by pacemakers in the septal nuclei. They are inhibited by collaterals from the mesolimbic system entorhinal and hippocampal theta rhythmic influences [38] and propagated to the cortex by the anterior cingulate and medialis dorsalis.

Delta activity (0.5–4 Hz) is generated in the cortex when cortical neurons are deprived of input (i.e., extreme depression of thalamic gates together with decreased activity of the brainstem reticular formation, also called the *ascending reticular activating system* (ARAS). Significant is the inhibition of ARAS by descending pathways from the cortex via the striatum.

Beta activity largely reflects intracortical interactions, which receive collaterals from all afferent sensory pathways and exert cholinergic influences resulting in a

diminution of the GABAergic influence of the reticular thalamic nucleus neurons. This diminution can, in turn, be initiated by glutaminergic influences from the cortex and result in a depolarizing effect on the thalamic cells and an increase of the alpha rhythm, which is expressed on the thalamocortical circuit in the beta range. The beta band reflects corticocortical and thalamocortical oscillations related to specific information processing. Gamma activity (25–39 Hz) reflects corticocortical and corticothalamic transactions. Its significance is in perceptual processes.

Normal conscious function is proposed to require activation among the ARAS, intralaminar nuclei of the thalamus, and the cortex. The binding together of fragments of perception from dispersed neuronal assemblies into a unifying reverberating system comprises the perceptual content of consciousness [10,11].

Clinical Interpretation of QEEG Results: Speculations for Tinnitus

Clinically, the interpretation of QEEG results for the metric of power in relation to the theory of consciousness is considered to demonstrate how the brain, in response to a dyssynchronous auditory signal (tinnitus), is attempting to reestablish homeostasis in multiple neuroanatomical substrates with a synchrony of activity reflected clinically by a subjective awareness or consciousness.

Brain function activity recorded in patients with a severe, predominantly central-type tinnitus revealed electrical activity in multiple sites that reflected multiple neuroanatomical substrates, highlighted by frontal and temporal sites, with mainly delta and beta bands of activity. The predominance of frontal and temporal recording sites provides objective evidence to support the clinical consideration of a frontotemporal thalamic circuit in SIT patients, modulated by the thalamus (i.e., a thalamo-fronto-temporal circuit).

The clinical application of the theory of homeostasis of brain activity and consciousness, when integrated with the tinnitus dyssynchrony and synchrony theory [22], provides a basis for translation to tinnitus diagnosis and treatment. The delta and beta band predominance in frontal and temporal recording sites reflects thalamic response to the aberrant dyssynchronous auditory sensory stimulus within the exogenous system. Specifically, in patients with the delta band responses, hyperpolarization at the level of the thalamus, mediated by an increased GABA response, resulted in reduction of the activity of the alpha band to that of the delta band. In patients with the beta band of activity, the GABA response was reduced and resulted in an increase of the alpha band of activity to that of the beta band. Thalamocortical and corticocortical oscillations of each are recorded from multiple electrical sites, highlighted by fron-

tal and temporal sites. In both cases, correlation of the incidence of occurrence of the different band frequencies in the recording electrical sites has been hypothesized to reflect the degree of severity of the tinnitus complaint, the ability or attempt of the brain to reestablish the ground state of brain activity, and homeostasis of brain activity in multiple neuroanatomical substrates. The beta activity is clinically considered to reflect reverberating activity at the cortex and may point to seizure-type activity, misperceptions, and alterations in affect.

The theta band of activity is considered to be the activity of the endogenous system and clinically signals attempts to establish a paradoxical auditory memory. The theta band of activity is clinically hypothesized to reflect an increased synchrony of activity of cortical neurons not involved in informational processing. Rather, they are involved in the sensory-affect transformation receiving collateral inputs from multiple neuroanatomical electrical recording sites, highlighted by frontal and temporal sites. In our cohort of tinnitus patients, the establishment of the paradoxical memory is considered to be in progress. We hypothesized that successful attempts for tinnitus relief may be increased by demonstration in a tinnitus patient of low, not high, theta band activity. High theta band activity may indicate the establishment or consolidation of a memory that is difficult to influence or erase.

A rationale for treatment options of medication or instrumentation attempting tinnitus relief based on a theory of homeostasis of brain activity finds support for biofeedback attempts to increase the alpha band activity [17,18] and receptor-targeted therapy directed to the GABA receptor [39].

Electrophysiological Correlates for Tinnitus

Shulman et al. [40] reported an electrophysiological correlate for tinnitus based on short latency responses with auditory evoked potentials to a broad-band click stimulus. The responses signaled responses to an acoustic stimulus, not a reflection of brain function in response to an aberrant auditory stimulus (i.e., tinnitus). The QEEG power analysis results explain and provide a basis for clinically understanding the difficulty in attempts to establish a single electrophysiological metabolic correlate for SIT [20].

The distribution of the frequency bands in this report is heterogeneous and demonstrates patterns of brain activities responding to an aberrant auditory stimulus (i.e., variations in a common pattern). The integrative theory of consciousness has provided an understanding of the heterogeneity of the tinnitus symptom in terms of brain function responses to an aberrant auditory stimulus. These electrophysiological QEEG results demon-

strate a definite pattern of such responses at specific electrode sites, with a pattern of distribution of frequency bands (i.e., not a single electrophysiological correlate). The pattern of brain rhythm activity of delta greater than beta than alpha than theta in frontal greater than temporal than occipital recording sites and occipital equal to parietal and central recording sites is clinically considered to reflect multiple neuroanatomical ensembles of activity in patients with predominantly central-type SIT.

We hypothesized that tinnitus patients will have variations in the general pattern of the electrophysiological response as manifested in the distribution of the frequencies (i.e., different or multiple electrophysiological correlates for different clinical types of tinnitus, denoting the degree of severity of the tinnitus complaint).

QEEG, Tinnitus Severity, and "Normal" Brain Function: A Hypothesis

We hypothesized that analysis of the distribution of the power response and correlation of the EEG frequency band with the recording area (Table 3; see Fig. 4) is a clinical manifestation of the severity of the tinnitus and the attempt of the brain—on an individual basis—to reestablish homeostatic mechanisms that result in consciousness as demonstrated by "normal" brain rhythm in a severely disabled tinnitus patient. The relationships among the delta, beta, and alpha rhythms in both the frontal and temporal recording sites are the measures hypothesized to clinically demonstrate the severity of the tinnitus complaint and the degree of interference in homeostatic mechanisms resulting in normal brain rhythms in severely disabled tinnitus patients.

Specifically, when the brain rhythm pattern of activity is delta greater than beta than alpha than theta bands in frontal greater than temporal recording sites, we hypothesized the tinnitus severity to point to an "ongoing" or "early" attempt to reestablish normal brain rhythms (i.e., alpha) in a severely disabled tinnitus patient. The preponderance of the frontal and temporal recording sites suggests a functional interaction (i.e., a circuitry and coupling of activity between the two regions).

The increase in brain activity of beta rhythm relative to or greater than delta in frontal and temporal recording sites is clinically hypothesized to reflect an increased severity of tinnitus. The relative increase in theta in the recording sites is clinically hypothesized to reflect the sensory-affect translation of the sensory response. The relative increase of the alpha band in sequential QEEG recordings and reduction in both delta and beta rhythms (or both) is hypothesized to clinically reflect a reduction in severity of the tinnitus and increased reestablishment of homeostatic mechanisms for normal brain rhythms (i.e., function in a SIT patient).

The theta frequency (4–8 Hz) is an ongoing frequency of activity from the limbic system of the temporal lobe. Is this the final common pathway for tinnitus? Consciousness has been associated with the gamma frequency of activity (>30 Hz). The correlation of the beta and gamma bands to delta, theta, and alpha may clinically reflect the most severe disabling tinnitus (i.e., preponderance of recording sites frontal greater than temporal of the gamma greater than beta, or gamma greater than beta than delta than alpha than theta).

Questions

Some questions remain about the relevance of QEEG analysis to tinnitus diagnosis and treatment.

- What correlations with QEEG may be established between the incidence of occurrence of distribution of the frequencies and recording sites and the degree of tinnitus severity? We have hypothesized that the greater degree of tinnitus severity may be seen in a preponderance of the beta band and the incidence of occurrence or preponderance (or both) of the gamma band.
- What correlations with QEEG for objectively identifying electrophysiological correlates for tinnitus, the severity of the tinnitus, and a monitoring system for tinnitus treatment efficacy may be established by a multimetric analysis of the QEEG data? Preliminary evaluation in tinnitus patients with a multimetric analysis identified abnormalities in metrics of coherence and phase other than or in addition to power [2].
- What is the significance of the gamma band activity and its clinical correlation with theta and the severity of tinnitus?
- Is the establishment of a paradoxical memory for the aberrant auditory stimulus an objective indicator for tinnitus severity and prognosis and signaled in theta and gamma band activities?
- Does the establishment of a paradoxical auditory memory reflect an inability of the homeostatic regulation of brain activity, and is that objectively demonstrated in high delta, theta, beta, and gamma bands and low alpha bands of brain activity?

SUMMARY

Our clinical experiences with QEEG recording in tinnitus patients is the basis for our recommending its routine inclusion into the MATPP both for tinnitus diagnosis and as an in-office monitor to establish the efficacy of therapeutic modalities attempting tinnitus relief [1]. This report clinically confirms our preliminary report; supports the significance of QEEG for identifying brain

function in tinnitus patients; and provides an improvement in the accuracy of the clinical tinnitus diagnosis, an electrophysiological correlate for SIT, and a monitor for the clinical course of tinnitus and response to attempts to establish tinnitus relief. The electrophysiological information obtained with a multimetric analysis (including not only absolute power but Z scores of relative power, amplitude asymmetry, coherence, and phase) may provide additional measures for objective clinical analysis of the tinnitus complaint. We suggest that the reports of QEEG results in tinnitus patients specify the normative database being referenced for the Z-score analysis of the data.

CONCLUSIONS

The results of the Z-score analysis of QEEG recordings—for the metric of power for SIT patients—based on a large normative database are clinically considered to be a global response of interneuronal cortical networks, reflecting multiple brain functions to an aberrant sensory, conscious, perceptive auditory disorder. The pattern of an electrophysiological correlate for SIT has been identified, highlighting the individuality of brain function for each tinnitus patient and different clinical types of tinnitus. Specifically, we point to a cortical interneuronal network pattern of spontaneous brain function activity (i.e., delta greater than beta greater than alpha greater than theta in frontal greater than temporal greater than occipital recording sites and equal in occipital, parietal, and central recording sites).

These Z-score analyses of QEEG recordings in 61 patients revealed 20 of 61 as normal (32.8%) and 41 of 61 as abnormal (67.2%), with demonstration of statistically significant abnormalities in both frontal and temporal recording sites—frontal greater than temporal—for brain activity rhythms of delta greater than beta. This pattern of brain rhythm activity is clinically considered to reflect multiple neuroanatomical ensembles of activity in patients with predominantly central-type SIT. We recommend a paradigm shift in understanding tinnitus: from a focus on its psychoacoustic and psychophysical characteristics to that of brain function response to tinnitus, with a focus on consciousness.

REFERENCES

1. Shulman A. Medical Audiologic Tinnitus Patient Protocol. In A Shulman et al. (eds), *Tinnitus—Diagnosis/Treatment*. Philadelphia: Lea & Febiger, 1991:319–321.

2. Shulman A, Goldstein B. Quantitative electroencephalography: Preliminary report. Tinnitus. *Int Tinnitus J* 8(2):77–86, 2002.

3. Speckmann EJ, Elger CE. Introduction to the Neurophysiological Basis of the EEG and DC Potentials. In E Niedermeyer, F Lopes-DaSilva (eds), *Electroencephalography*, 4th ed. Baltimore: Lippincott, Williams & Wilkins, 1999: 15–47.

4. Thatcher RW. Normative EEG database and EEG biofeedback. *J Neurotherapy* 2(4):8–39, 1998.

5. Thatcher RW. EEG Database-Guided Neurotherapy. In JR Evans, A Abarbanel (eds), *Introduction to Quantitative EEG and Neurofeedback*. San Diego: Academic Press, 1999:29–64.

6. Weiler EWJ, Brill K. Quantitative electroencephalography patterns in patients suffering from tinnitus. *Int Tinnitus J* 10(2):127–131, 2004.

7. Weisz N, Moratti S, et al. Tinnitus perception and distress is related to abnormal spontaneous brain activity as measured by magnetoencephalography. *PLOS Med* 2(6):2–25, 2005.

8. Lexicor Medical Technology, Inc., Boulder, CO.

9. Lexicor Medical Technology, Inc. "Datalex On Line EEG Analysis—The Future of Mental Health Diagnosis." Training Seminar, New York City, April 21, 2001.

10. John ER. From synchronous neuronal discharges to subjective awareness? *Prog Brain Res* 150:143–171, 2005.

11. John ER, Prichep L. The anesthetic cascade. A theory of how anesthesia suppresses consciousness. *Anesthesiology* 102:447–471, 2005.

12. Staley K, Scharfman H. A woman's prerogative. *Nat Neurosci* 8(6):697–698, 2005.

13. Wooley CS, McEwen BS. Changes in GABA receptors and their modulators. *J Neurosci* 12:2549–2554, 1992.

14. Smith J, Woolley SS, Cleve CS. *Clin J Med* 71(suppl): S4–S10, 2004.

15. Nakamura NH, Rosell DR, et al. *Neuroendocrinology* 80:308–323, 2004.

16. Maguire JL, Stell BM, et al. *Nat Neurosci* 8:797–804, 2005.

17. Weiler EWJ, Brill K, Tachiki KH, Wiegand R. Electroencephalography correlates in tinnitus. *Int Tinnitus J* 6(1): 21–24, 2000.

18. Weiler EWJ, Brill K, Tachiki KH. Quantitative electroencephalography and tinnitus: A case study. *Int Tinnitus J* 6(2):124–126, 2000.

19. Shulman A. Medical Evaluation. In A Shulman et al. (eds), *Tinnitus—Diagnosis/Treatment*. Philadelphia: Lea & Febiger, 1991:257.

20. Shulman A. *Auditory Brainstem Response and Tinnitus*. Philadelphia: Lea & Febiger, 1991:138–183.

21. Shulman A. Medical-Audiologic Tinnitus Patient Protocol. In A Shulman et al. (eds), *Tinnitus—Diagnosis/Treatment*. Philadelphia: Lea & Febiger, 1991:319–321.

22. Shulman A, et al. Tinnitus dyssynchrony-synchrony theory: a translational concept for diagnosis and treatment. *Int Tinnitus J* 12(2):101–114, 2006.

23. Shulman A. A final common pathway for tinnitus: The medial temporal lobe system. *Int Tinnitus J* 1(1):115–126, 1995.

24. Shulman A. Tinnitus neural substrates: An addendum. *Int Tinnitus J* 11(1):1–3, 2005.

25. Yoshimura Y, Calloway EM. Fine scale specificity of cortical networks depends on inhibitory cell type and connectivity. *Nat Neurosci* 8(11):1552–1560, 2005.

26. Shulman A, Strashun AM, Avitable MJ, et al. Ultra-high-frequency acoustic stimulation and tinnitus control: A positron emission tomography study. *Int Tinnitus J* 10(2): 113–125, 2004.

27. Descartes R. *The Philosophical Writings of Descartes*, vol 3 (J Cottingham, R Stoothoff, D Murdoch, transl). Cambridge: Cambridge University Press, 1988.

28. Edelman G. Consciousness: The remembered present. *Ann NY Acad Sci* 929:111–122, 2001.

29. Hughes JR, John ER. Conventional and quantitative electroencephalography in psychiatry. *J Neuropsychiatry Clin Neurosci* 11:190–208, 1999.

30. John ER, Prichep L, et al. *Neurometrics Sci* 293:162–169, 1988.

31. Duffy FH, Jones K, et al. Spectral coherence in normal adults. *Clin Electroencephalogr* 26:30–46, 1995.

32. Koenig T, Prichep L, et al. Millisecond by millisecond, year by year: Normative EEG microstates and developmental stages. *Neuroimage* 16:41–48, 2002.

33. Berger HA. Electroencephalogram of man. *Arch Psychiar Nervenkr* 106:577–584, 1937.

34. Llinas R. The intrinsic properties of mammalian neurons: Insights into central nervous system function. *Science* 242: 1654–1664, 1988.

35. Steriade M, Gloor P, Llinas RR, et al. Basic mechanisms of cerebral rhythmic activities. *Electroencephalogr Clin Neurophysiol* 76:481–508, 1990.

36. McCormick DA. Neurotransmitter actions in the thalamus and cerebral cortex and their role in neuromodulation of thalamocortical activity. *Prog Neurobiol* 39:337–338, 1992.

37. McCormick DA. Cortical and subcortical generators of normal and abnormal rhythmicity. *Int Rev Neurobiol* 49: 99–113, 2002.

38. Buzsaki G. Theta oscillations in the hippocampus. *Neuron* 33:325–340, 2002.

39. Shulman A, Strashun AM, Goldstein BA. GABA-A-benzodiazepine-chloride receptor-targeted therapy for tinnitus control: Preliminary report. *Int Tinnitus J* 8(1):30–36, 2002.

40. Shulman A, Seitz M. Central tinnitus diagnosis–treatment. Observations of simultaneous brain stem responses with monaural stimulation in the tinnitus patient. *Laryngoscope* 91:2025–2035, 1981.