
REVIEW

Quantitative Electroencephalography for Tinnitus—A Means for Data Collection, Analysis, and Translation

Erik S. Viirre

Department of Neurosciences, School of Medicine, University of California–San Diego, San Diego, California, USA

Abstract: Quantitative electroencephalography (QEEG) is the technique whereby brain electrical activity in individuals is recorded as they sit quietly with their eyes closed. The electrical activity is quantified with a variety of statistical measures to characterize the huge variation in combinations of emissions from the brain. Neuroscience research has demonstrated that such resting brain activity measures may be consistently altered in conditions such as depression or dementia. A wide variety of ongoing efforts are attempting to find characterizations that reliably denote other neurological conditions. In research on tinnitus, a variety of groups have been working to characterize QEEG changes related to the presence of the abnormal sensation of sound and to the emotional distress associated with it. QEEG changes related to the tinnitus percept are in the gamma electroencephalography (EEG) band recorded from temporal lobes. Clinical depression has a reliable marker in the depression of posterior cerebral alpha EEG frequency band activity, and this same activity is found in patients with tinnitus of the severe disabling type. In the past, QEEG has suffered from inconsistent recording methods, closed data sets, and noncompatible analytical techniques. Now in the modern era, when reliable data sets are shared and hardware and software are less expensive, regular use of QEEG will be clinically important. Those prepared to make the minor investment in equipment and training will reap the benefit of objective measures of brain activity. Knowing patterns of QEEG activity related to tinnitus and its associated depression will help clinicians better manage these patients.

Key Words: depression; electroencephalography; quantitative; tinnitus

Electroencephalography (EEG) is a technology for recording the electrical potentials of the brain. QEEG is *quantitative* EEG, a means of quantifying those electrical potentials, and thus is a technique for comparing individuals or groups with common conditions against norms of recordings of large populations

Reprint requests: Erik S. Viirre, MD, Department of Neurosciences, Suite 1-B, Perlman Ambulatory Care Center, University of California, San Diego School of Medicine, 9350 Campus Point Drive, La Jolla, CA 92037. Phone: 858-657-8540; Fax: 858-270-0740; E-mail: eviirre@ucsd.edu

Disclosure: Erik Viirre is a consultant and shareholder in Otosound LLC and a consultant to Quasar USA Incorporated. Both companies and Dr. Viirre have financial interests in the EEG and the electrophysiology of tinnitus.

of nonaffected individuals. Unlike evoked potentials (EPs) or other recording techniques with EEG that provoke neural activity with stimuli, QEEG is simply a measure of ongoing activity in individuals while they sit quietly alert with their eyes closed. The promise of QEEG is the relative ease of obtaining such a recording: No large brain-imaging systems are required (as compared to positron emission tomography scanning or functional magnetic resonance imaging), and no computer-driven stimuli are needed (as in EP recordings). Caveats regarding QEEG use remain the establishment of a common baseline state for recording, wherein subjects are quietly alert (but not sleeping), and ensuring that no confounding conditions exist (such as ongoing medication use). Further, a well-characterized normative database must be available for the clinical comparisons, common

analytical techniques are necessary for statistical comparisons, and consistent statistical methods must be applied to the data [1].

An intriguing possibility is that of statistically detecting systematic differences in EEG related to a specific condition that nominally would involve only a small portion of the alert brain [2]. Tinnitus that is disruptive of an individual's life (tinnitus of the severe disabling type) is believed to be both a failure of feedback control of auditory pathways, resulting in the abnormal sound percept [3,4], and an alteration of activity in the limbic system that causes the heightened stress response to the percept [5,6]. The auditory percept of tinnitus is often just a single sound [7] that may represent overactivity of a single tonotopic pathway. Thus, simply in terms of numbers of neurons activated, on the order of only a few thousand cells may be active continuously and would be directly related to the sound percept. Further, in the stress response to tinnitus, activity of neurons of the structures deep in the brain in the limbic system, such as the amygdala and the hippocampus, are not conventionally believed to be measurable by EEG. How can one disentangle the firing activity of hundreds of millions of neurons active for all kinds of neural and body control processes for an activity as localized as tinnitus? What if the subject is not even "paying attention to" (attending to) the tinnitus percept or is not having a strong emotional response to it? Do systematic changes exist in brain activity related to tinnitus that can be detected by QEEG? Or might the diagnostic utility of QEEG in tinnitus syndromes be limited to individuals who have tinnitus of the severe disabling type and, thus, have concurrent psychological distress or even psychological disease related to the presence of tinnitus?

QEEG has been used and validated for a wide variety of conditions from clinical depression [8] and attention deficit disorder [9] to dementia [10]. The statistical techniques that find correlations to these conditions point to the same use of QEEG for tinnitus. For example, depression results in asymmetrical changes in frontal cortex EEG power [11–13].

QEEG technology has been surrounded by controversy in its development, application, and interpretation [14]. A task force of the American Psychiatric Association pointed out that conditions that affect broad regions of the cerebral cortex, such as dementia or intoxication, can be reliably detected with QEEG systems. However, lack of standardized equipment, analytical techniques, and common databases made QEEG detection and interpretation of more subtle conditions, such as mood disorders, less certain. A review 10 years ago by the American Academy of Neurology affirmed the absence of sufficient evidence to use QEEG outside of a research setting for more moderate disorders of the brain, such as

mild traumatic brain injury, mood disorders, and childhood attention problems [15]. However, a 2006 review by the Committee on Research of the American Neuropsychiatric Association concluded that the quality of normative databases had improved and that cautious use of QEEG as a clinical laboratory test in developmental disorders in childhood and in mood disorders of adults was justified [1]. Thus, QEEG has emerged as a means of reliably assessing neurological function in neurological conditions that more subtly affect the brain than do conditions such as global dementia.

QEEG IN CONDITIONS RELATED TO TINNITUS

As mentioned, reliable QEEG indices appear to be related to depression [8,11–13]. Interestingly, some of these indices appear to be predictive of efficacy of selective serotonin reuptake inhibitor treatments within 7 days of use, which is weeks in advance of clinically determinable effects [16].

In the area of somatoform disorders, the only report so far is that posterior alpha rhythm depression appears in migraine headache patients [17]. No systematic reports cite the diagnostic utility of QEEG in chronic pain or other conditions. Similarly, no reports on QEEG diagnostics for stress or anxiety disorders are found.

QEEG IN TINNITUS

Since the first report of the use of QEEG in tinnitus patients [2], some effort has been made in using techniques of quiet brain EEG recording in the characterization of tinnitus. Shulman [2,18] found varied changes in spectral content in the EEG of patients with tinnitus throughout the frontal and temporal lobes. The most common significant changes were seen in frontal lobes. Given the heterogeneity reported by Shulman, apparently other conditions must modify the EEG content in these tinnitus patients. The most obvious confounding factor appears to be the coincidence of depression with the condition of tinnitus.

Interestingly, Ashton et. al. [19] found localized "hot spots" of increased EEG gamma-band activity in temporal lobes of tinnitus patients in the resting QEEG paradigm. This corresponds to the magnetoencephalographic (MEG) findings of Weisz et al. [20]. Gamma-band is conventionally considered "high-frequency" EEG recording (typically above 30 Hz). These findings point out both that research investigation into more parameters of EEG recording may be profitable and that QEEG techniques may be sensitive enough to pick up small signal sources for which the expensive and difficult-to-use MEG technology has been used until now.

As of this writing (2009), preliminary results of QEEG recordings in tinnitus patients have been reported by a group in Belgium. Vanneste et al. [21] looked at two groups of six patients with tinnitus (one group with duration of less than 4 years and the other group with duration of greater than 4 years) with the tinnitus percept on only the left side. Interestingly, they report that the early group was characterized by QEEG changes on the left side, whereas the later group was characterized by QEEG changes on the right. In particular, the later or chronic group exhibited decreased gamma-band activity in the left-sided auditory cortex and increased theta in bilateral auditory cortices. Thus, the QEEG indices may have value in understanding the evolution of tinnitus.

The same Belgian research group also reviewed tinnitus patients with high distress and low distress [22]. One important finding was a decrease in alpha activity in posterior cingulate cortex. Such a decrease corresponds to the alpha-wave changes found in clinical depression, as mentioned earlier. Those authors also described increased alpha activity in QEEG measures of deep limbic activity. Conventional QEEG metrics usually do not report deep limbic structures, but the low-resolution brain electromagnetic tomography analytical technique [23] used by Vanneste et al. [21] gives some possibility of interpretation of activity of deep structures. Using MEG technology, Schlee et al. [24] found decreased alpha-frequency-band coupling in distant cortical sites but increased gamma-band coupling. Concordance or other coupling metrics can be found in QEEG analytical techniques, so these MEG findings may also be detectable with QEEG.

CONCLUSIONS

The foregoing results suggest that though measurable QEEG changes may be related to the sound percept of tinnitus, they are poorly consistent and have not been described to the point of utility in the clinical setting. However, in particular, gamma-band changes in the temporal lobe appear promising for a marker of tinnitus sound percepts. In contrast, tinnitus of the disabling type demonstrates more reliably detected changes, especially the depression of alpha-range activity in the posterior lobes. As depression of posterior alpha is also a marker of clinical depression, this QEEG metric may be critically important in the clinical distinction of people with tinnitus, with implications for their management. Indeed, suppression of posterior alpha-frequency activity may be the signature finding of tinnitus of the severe disabling type.

QEEG is an important technology with a difficult history in neuroscience. Some problems stand in the way of QEEG's development as a common technology for clin-

ical use. However, clinicians dedicated to seeing tinnitus patients can find equipment, analytical tools, and assistance in results interpretation to make the technology an adjunct to their clinical armamentarium. The provocative results found in QEEG data in many neurological conditions and in tinnitus suggest that continued effort is justified in bringing it to the clinic. Beyond QEEG, electrical activity of the brain stimulated in EP and event-related potential paradigms in electrical recordings and in the MEG means of recording are also important and will continue to be developed in tinnitus. Electrophysiology is important for understanding tinnitus because of the high temporal resolution needed to understand brain dynamics of audio processing and because electrophysiological signals (particularly EEG) can be simultaneously recorded during stimulation with sound, unlike positron emission tomography and functional magnetic resonance imaging, for example.

QEEG has a variety of limitations. The basic physical characteristics of electrical potentials of the brain are that they are low voltage and low current and are substantially attenuated and distorted by the tissues of the head, skull, and scalp. This makes directly measuring deep structures of the brain difficult. However, advanced electrode technologies afford high conductivity for improved signal-to-noise ratios and have small size, so that orders of magnitude more electrodes can be placed on the head than in traditional EEG. Further, advanced viewing and analytical techniques enable better localization and characterization of signal sources, including deep sources in the brain.

QEEG is *quantitative* EEG. Unfortunately, the quantification remains problematic. Traditional EEG relies on signal localization to electrode locations and analysis by frequency content with crude subdivisions into "bands." Advanced statistical comparisons are possible via a plethora of techniques. Adherence to EEG standards in the research community is only poor in the ever-ongoing search for better techniques. Witness the increase in attention and research in the "gamma" band of EEG in recent years, with important findings there. Meaningful comparisons across studies are difficult. However, the simplicity of the QEEG paradigm—quietly alert with eyes closed—is its power. It should be readily possible to establish community databases of raw EEG data, with electrode placement and other recording settings well described. The raw data sets would be of great value in cross-comparison of populations and questions. Having the raw data would enable researchers to apply not only conventional analytical paradigms but whatever pet flavor of technique they would like. An open data set would allow analyses not by the data gatherer but by others. Coburn et al. [1] point out the fundamental difficulty whereby population data are melded

for analytical needs and the underlying data are obscured. By combining group members, statistical features are brought out, but the same aggregation reduces the ability to compare a test subject or control against the data set. Again, open databases would enable appropriate comparisons.

The populations for QEEG studies are difficult to characterize, and this is true in tinnitus. Even defining normal populations is difficult [25]. Clinical populations are even more problematic for a variety of reasons:

- Disorders are not clearly defined.
- Severity is difficult to assess.
- Multiple comorbidities are possible [26].
- Prescription or illicit drug use make analyses difficult.

All these complications are present in tinnitus. Ironically, the difficulty is a chicken-and-egg problem. QEEG may well be the “epigenome” of the nervous system, but establishing the clinical criteria for disorders will be necessary for defining QEEG, and we might not find the clinical criteria without the QEEG. The combinatorial explosion of QEEG features, actual genetics, neural environmental history, and plain cussedness of the difficult mind-brain problem make feature identification a challenge.

Finally, a significant problem is that of resistance to adoption of QEEG techniques. As pointed out by Coburn et al. [1], again in their excellent review, substantial acrimony—including legal action—has dogged the history of QEEG. Such history must give any clinician pause in considering pursuing research for fear of being tarred with the wrong brush. Beyond scientific acceptance of what should ultimately be the highest-quality data-driven medical evidence lies resistance to adoption in the clinical community because of QEEG’s history, begging the question of whether more questionable claims are found in the history of EEG than in other medical technologies and, if so, why. Further, the research funding and technology funding communities may similarly have some hesitation in the development of electrophysiological technologies. Can such objections be overcome?

The answer is that QEEG is a viable technology for clinical use now. It is validated for conditions such as depression. Clinicians dedicated to their patients need objective tools for diagnosis and assessment of treatment efficacy. Successful examples of earlier technologies give hope for broad adoption of QEEG and development and validation of more markers of neurological conditions, such as the tinnitus percept. The example of electrocardiograms shows that knowledge is developed, technology is created, and a critical technique becomes available for the good of all at a very low cost.

REFERENCES

1. Coburn KL, Lauterbach EC, Boutros NN, et al. The value of quantitative electroencephalography in clinical psychiatry: A report by the Committee on Research of the American Neuropsychiatric Association. *J Neuropsychiatry Clin Neurosci* 18(4):460–500, 2006.
2. Shulman A, Goldstein B. Quantitative electroencephalography: Preliminary report—tinnitus. *Int Tinnitus J* 8(2):77–86, 2002.
3. Llinás RR, Ribary U, Jeanmonod D, et al. Thalamocortical dysrhythmia: A neurological and neuropsychiatric syndrome characterized by magnetoencephalography. *Proc Natl Acad Sci U S A* 96(26):15222–15227, 1999.
4. Lobarinas E, Sun W, Stolzberg D, et al. Human brain imaging of tinnitus and animal models. *Semin Hear* 29(4):333–349, 2008.
5. Shulman A, Goldstein B. A final common pathway for tinnitus—implications for treatment. *Int Tinnitus J* 2:137–142, 1996.
6. Jastreboff PJ, Gray WC, Gold SL. Neurophysiological approach to tinnitus patients. *Am J Otol* 17(2):236–240, 1996.
7. Shailer MJ, Tyler RS, Coles RR. Critical masking bands for sensorineural tinnitus. *Scand Audiol* 10(3):157–162, 1981.
8. John ER, Pritchard LS. The relevance of QEEG to the evaluation of behavioral disorders and pharmacological interventions. *Clin EEG Neurosci* 37(2):135–143, 2006.
9. Chabot RJ, di Michele F, Pritchard L. The role of quantitative electroencephalography in child and adolescent psychiatric disorders. *Child Adolesc Psychiatr Clin North Am* 14(1):v–vi, 21–53, 2005.
10. Hughes JR, John ER. Conventional and quantitative electroencephalography in psychiatry. *J Neuropsychiatry Clin Neurosci* 11(2):190–208, 1999.
11. Bares M, Brunovsky M, Kopecek M, et al. Early reduction in prefrontal theta QEEG cordance value predicts response to venlafaxine treatment in patients with resistant depressive disorder. *Eur Psychiatry* 23(5):350–355, 2008.
12. Spronk D, Arns M, Bootsma A, et al. Long-term effects of left frontal rTMS on EEG and ERPs in patients with depression. *Clin EEG Neurosci* 39(3):118–124, 2008.
13. Hunter AM, Muthén BO, Cook IA, Leuchter AF. Anti-depressant response trajectories and quantitative electroencephalography (QEEG) biomarkers in major depressive disorder. *J Psychiatr Res* 2009 (in press).
14. American Psychiatric Association Task Force on Quantitative Electrophysiological Assessment. Quantitative electroencephalography: A report on the present state of computerized EEG techniques. *Am J Psychiatry* 148(7):961–964, 1991.
15. Nuwer M. Assessment of digital EEG, quantitative EEG, and EEG brain mapping: Report of the American Academy of Neurology and the American Clinical Neurophysiology Society. *Neurology* 49(1):277–292, 1997.
16. Leuchter AF, Cook IA, Marangell LB, et al. Comparative effectiveness of biomarkers and clinical indicators for predicting outcomes of SSRI treatment in major depressive disorder: Results of the BRITE-MD study. *Psychiatr Res* 169(2):124–131, 2009.

17. Bjørk MH, Stovner LJ, Nilsen BM, et al. The occipital alpha rhythm related to the “migraine cycle” and headache burden: A blinded, controlled longitudinal study. *Clin Neurophysiol* 120(3):464–471, 2009.
18. Shulman A, Avitable MJ, Goldstein B. Quantitative electroencephalography power analysis in subjective idiopathic tinnitus patients: A clinical paradigm shift in the understanding of tinnitus, an electrophysiological correlate. *Int Tinnitus J* 12(2):121–131, 2006.
19. Ashton H, Reid K, Marsh R, et al. High frequency localised “hot spots” in temporal lobes of patients with intractable tinnitus: A quantitative electroencephalographic (QEEG) study. *Neurosci Lett* 426(1):23–28, 2007.
20. Weisz N, Müller S, Schlee W, et al. The neural code of auditory phantom perception. *J Neurosci* 27(6):1479–1484, 2007.
21. Vanneste S, Plazier M, et al. The neural correlates of acute and chronic tinnitus [abstract]. Third Conference of the Tinnitus Research Initiative, La Stessa, Italy, 2009.
22. Vanneste S, Plazier M, et al. The neural correlates of distress in tinnitus [abstract]. Third Conference of the Tinnitus Research Initiative, La Stessa, Italy, 2009.
23. Pascual-Marqui RD. Standardized low resolution brain electromagnetic tomography (sLORETA): Technical details. *Exp Clin Pharmacol* 24D:5–12, 2002.
24. Schlee W, Hartmann T, Langguth B, Weisz N. Abnormal resting-state cortical coupling in chronic tinnitus. *BMC Neurosci* 10:11, 2009.
25. Coutin-Churchman P, Añez Y, Uzcátegui M, et al. Quantitative spectral analysis of EEG in psychiatry revisited: Drawing signs out of numbers in a clinical setting. *Clin Neurophysiol* 114(12):2294–2306, 2003.
26. Lechtenberg R, Shulman A. The neurologic implications of tinnitus. *Arch Neurol* 41(7):718–721, 1984.