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AAO-HNS –Martha Entennan Tinnitus Research Center Tinnitus Miniseminar 2012

Brain Imaging and tinnitus

Location-Washington DC.

INTRODUCTION

The theme of the AAO HNS Martha Entenmann, Abraham Shulman, M.D., Barbara Goldstein, PhD, International Tinnitus Miniseminar 2012 was "Brain Imaging and Tinnitus.

The meeting, well attended , provided to the attendees a take home message that clinical application of the brain imaging technologies of nuclear medicine, single photon emission tomography, (SPECT), photon emission tomography(PET), functional MRI brain imaging ,fMRI, magnetoencephalography, (MEG), can provide an objectivity for tinnitus, a subjective sensory aberrant auditory complaint.

The meeting achieved the goal of the AAO-HNS, which is to provide state of the art information to the Otolaryngology community for continuing education dedicated to providing quality care to our patients.

The dilemma for all tinnitus professionals for tinnitus diagnosis and attempting treatment is how a sensory stimulus becomes translated into one of affect- behavior- a basic problem of sensory physiology. Specifically, this includes identification of the underlying structure and function relationships involved in this translation, and the interrelationships between both .i.e. identification of underlying neural signal circuitries, and the involved molecular genetic structures and mechanisms underlying the activated neuroanatomic substrates[1].

In general, the goals of brain imaging for tinnitus patients are to provide an objectivity for a subjective complaint, tinnitus. This miniseminar provided objective information to the otolaryngologist, tinnitus professional and tinnitus patients, with the technologies of: a) nuclear medicine single photon emission tomography, brain SPECT, b)photon emission tomography, brain PET; c) functional magnetic resolution imaging, fMRI; d)magnetic emission tomography (MEG), and e)low frequency resolution electromagnetic tomographic analysis (LORETA).

The brain images obtained serve as models of tinnitus activity in brain, reflecting with nuclear medicine SPECT cerebral perfusion and indirectly metabolism, with PET a direct measure metabolism, with fMRI, blood oxygenation, a indirect measure of neuronal activity, with MEG, a direct measure of neuronal activity, and with LORETA, a 3D tomographic representation of the spectral distribution of low frequencies of brain activities - all in the presence of the tinnitus signal, and individual for each tinnitus patient[1].

Clinically, the brain images find translation for establishment of an increase in the accuracy of the tinnitus diagnosis, for all clinical types of tinnitus, identification of patterns of brain activation reflecting underlying conditions in brain which provide a basis for identification of the medical significance of the tinnitus, a rationale for tinnitus treatment attempts to influence the clinical course of particular type(s) tinnitus, and a method to monitor the efficacy of modalities of treatment attempting tinnitus relief.

Clinically, all attempts for tinnitus treatment are directed to influence the aberrant auditory sensation, tinnitus, and its translation to one of behavior. Brain imaging is a start for clinical objective identification of the sensation and the behavior(s) that it evokes. The evolving brain imaging experience for tinnitus finds clinical translation for understanding an underlying biology, anatomy, and pathophysiology for tinnitus.

To explain the emotion/ behavior associated with the tinnitus, of interest are the brain imaging results reported for decision making processes in brain, clinically considered to have significance for consolidation of a memory. Specifically, the study of neural circuit dynamics that translate sensory inputs into behavior[2,3].

These results are part of an increasing list of publications in the literature clinically considered to support the hypothesis of a final common pathway for tinnitus, the transformation of a sensation to one of affect, the initial process being the establishment of a "paradoxical auditory memory for tinnitus, the translation of which has significance for tinnitus diagnosis and treatment[4].

PRESENTATIONS

Arnold M Strashun and Abraham Shulman reported their clinical experiences with nuclear medicine SPECT and PET brain imaging in predominantly central type severe disabling subjective idiopathic tinnitus in excess of 300 examinations, ongoing since 1989 at SUNY / Downstate.

The basic science and physics underlying of brain imaging nuclear medicine for SPECT and PET was reviewed. The clinical application of nuclear medicine brain

TcHmpao SPECT in tinnitus in 1989 was the first time that an increased activity (blood flow) was objectively demonstrated in multiple important auditory regions of interest in brain and provided a starting point to investigate pathophysiologic mechanisms of a predominantly central type tinnitus. Additional highlights included: a) Medial temporal lobe abnormality common to all; b) A complex pattern of disturbed neural connectivity; and c) Cerebral perfusion disturbance in many non auditory regions of interest in brain. Similar findings have been identified with brain PET including the additional frequent identification of a neurodegeneration pattern of senile dementia of the Alzheimer's type (SDAT).

The highlights of this experience were further demonstrated with case reports and included: a)objective identification of multifocal structure / function abnormalities of tinnitus in brain with SPECT and PET; b)support for the clinical diagnosis of multiple types of tinnitus and their medical significance; c)demonstration of activity in multiple neuroanatomic substrates reflective of brain functions elicited by the sensory-affect connectivity of an aberrant auditory sensory disorder, as clinically reflected in the symptomatology of the tinnitus patient; d)neurotologic neurologic implications for tinnitus diagnosis and treatment; e) the hypothesis for a final common pathway for all clinical types of tinnitus; and f) the identification of the GABA-A benzodiazepine chloride receptor distribution in severe disabling tinnitus with the radioisotope I 123 Iomazenil[4-10].

Take home messages for nuclear medicine imaging included:

A. What we are seeing with SPECT/PET of brain:

a) Different radioisotopes target different physiologic substrates, eg brain SPECT, Tc HMPAO, cerebral perfusion, indirect metabolism; PET, 18 F-fluorodeoxyglucose(18 F-FDG) garget metabolism direct; I-123 Iomazenil BZ-Cl/ GABA-A receptor;

b) Multiple activated brain regions reflect multiple brain functions activated in the presence of the tinnitus signal;

c) The multiple brain functions reflect components of an aberrant auditory sensation which are perceived by the patient and called tinnitus, i.e. sensory, affect, and psychomotor. The brain functions reflect response to a global arousal system (GA) in the presence of the tinnitus signal;

d) SPECT/PET images are individual for each patient;

e) Tinnitus is not a "phantom" sensation. A symptom qualifies to be "phantom" sensation when no neural substrates can be identified. Clinically, a symptom may be subclinical in its manifestation;

f) A final common pathway for tinnitus is not a theory of tinnitus production. Specifically, it is a hypothesis that attempts to explain how an aberrant auditory sensory stimulus becomes transformed into one of affect and somatomotor response;

g) The multifunctionality of the cytoarchitecture of brain- structure /function processes -are individual for each tinnitus patient, i.e. multiple functions expressed in same brain region of interest with SPECT, PET CT, fMRI, MEG, and LORETA. This was demonstrated by references in the literature to functions identified for the dorsolateral prefrontal cortex, for error related brain processing that overlaps partially but not completely with brain regions involved in response inhibition and competition[11]; for working memory- dorsolateral receives and codes the information inputs, the ventrolateral maintains the working memory[12].

h) A control of conflict circuit - anterior cingulate, dorsolateral prefrontal cortex, amygdala was demonstrated and considered clinically significant for the clinical interpretation of brain activation in tinnitus patients, and translation for tinnitus diagnosis and treatment[13].

B. What attendees learned for translation to clinical office based tinnitus practice:

a) Demonstration objectivity for an aberrant subjective sensory complaint, tinnitus, i.e. neural correlates multiple brain functions;

b) Identification multiple regions of interest (ROIs) for multiple brain functions are reflective of components of a sensation, the aberrant auditory sensation i.e. sensory, affect and psychomotor;

c) A final common pathway for tinnitus is hypothesized for all clinical types of tinnitus and may be extended to all sensations;

d) Translation of the nuclear medicine experience has critical application for tinnitus theory, improvement of the accuracy of the tinnitus diagnosis, increased efficacy of available modalities of tinnitus treatment, a monitor method for treatment efficacy and provides a basis for the identification of the medical significance of the brain for tinnitus.

C. Future nuclear medicine brain imaging and tinnitus:

Brain imaging for the future includes mapping of molecular brain imaging for identification of neural circuitries, neurotransmitters, their receptors and projection systems, to provide a basis for the diagnosis and treatment of all clinical types of tinnitus.

It is necessary to move beyond the stage of circuit centered views of regions of activation in brain to define the roles of these areas not only for the aberrant auditory stimulus, tinnitus, but also to be extended to all sensations, behavior and mental health.

Jennifer Melcher presented: 1) the results of a recent fMRI study "Tinnitus, Diminished Sound-Level Tolerance, and Elevated Auditory Activity in Humans With Clinically Normal Hearing Sensitivity[14] and 2) Brainstem auditory evoked potentials suggest a role for the Ventral Cochlear Nucleus in Tinnitus[15].

Initially, highlights of the basics of fMRI were presented. Briefly, the fMRI identifies the Blood Oxygenation Level Dependent (BOLD) signal -a indirect measure of neural activity. Increased neural activity results in an increase in blood flow, decreases in the concentration of deoxyhemoglobin, and an increase in the fMRI signal. In this study an attempt was made to identify previously reported documented elevations in sound-evoked activation in midbrain and cortex to be a reflection of two physiological correlates of auditory sound perception, i.e. tinnitus, hypercusis or both.

The study of sound level tolerance is the first to directly demonstrate the abnormal physiological correlate of an abnormal sound level tolerance, i.e. hypercusis. Previous demonstrations of elevated sound evoked fMRI activation in the inferior colliculus of tinnitus subjects were likely related to abnormal perception of the sound stimulus rather than tinnitus. fMRI brain imaging measured sound evoked activation in the following auditory centers: auditory midbrain, thalamus, and primary auditory cortex compared with subjects with normal tolerance.

Specifically, the clinical implications of the results of this study provide a basis for translation to sound therapies attempting tinnitus and/or hypercusis relief, i.e. quantification and understanding of basic mechanisms underlying tinnitus and hypercusis. Also different clinical conditions with disorders of perception, hypothesized to reflect increased neural activity in brain, e g phantom limb pain, chronic neuropathic pain, photophobia accompanying migraine, suggest a common physiology "not entirely unique to the auditory system but also involving the visual and somatosensory domains[16,17]".

The auditory brainstem responses were evaluated in human patients with/without tinnitus

Tinnitus patients demonstrated a reduced amplitude of P1 and a increased amplitude of response for P5, when compared to non tinnitus subjects matched in age, sex, and pure tone threshold.

The degree of amplitude is considered to reflect the degree of auditory activity, i.e. increased amplitude reflective of increased auditory activity and reduced amplitude an increased input to the inferior colliculus auditory activity. In tinnitus patients, the transformation from the reduced peripheral activity identified with P1 to the central hyperactivity identified in P5 was further apparent in the V/1 and III/1 amplitude ratios.

A third group of non tinnitus patients, both tinnitus, and matched non tinnitus groups demonstrated elevated thresholds above 4 kHz and a reduced P1 amplitude. This is interpreted as indicating that the "differences between tinnitus and matched non tinnitus subjects occurred against a backdrop of shared peripheral dysfunction, that while not tinnitus specific, cannot be discounted as a factor in tinnitus development".

The animal lesion and human data literature are referenced as indicating that P3 and P5 activity originate in a pathway in the ventral cochlear nucleus, particularly with the spherical bushy cells. It is concluded that the elevated amplitude of P3/P1 and P5 /P1 reflect a disproportionately high activity in spherical bushy cells for a given amount of input from the periphery. A role is suggested for the ventral cochlear nucleus and specifically to target the spherical bushy cells for treatment[15].

To be considered for the result of the third group of non tinnitus patients, both tinnitus, and matched non tinnitus groups who demonstrated elevated thresholds above 4kHz and a reduced P1 amplitude, is the ongoing SUNY / DMC ongoing tinnitus clinical experience since which has reported the need to clinically identify and differentiate between the subclinical and clinical stage of all clinical types of tinnitus. Specifically, the reported "differences between tinnitus and matched non tinnitus subjects occurred against a backdrop of shared peripheral dysfunction, that while not tinnitus specific, cannot be discounted as a factor in tinnitus development" may reflect the following:

a) Clinically, this paper may have demonstrated a subclinical manifestation of tinnitus;
b) All patients with a peripheral sensorineural hearing loss have tinnitus, clinically manifest or subclinical. The underlying mechanism being a research issue, hypothesized to be related to auditory masking.
c) Future inclusion of ultra high frequency audiometric threshold testing 10-20 kHz into the classical hearing threshold determination of 250-8000 Hz , particularly in tinnitus and non tinnitus patients with reported "normal hearing".

Susan M Bowyer presented the clinical experience of Magnetoencephalography (MEG) and tinnitus of the Departments of Neurology, Henry Ford Hospital, Wayne State University, Department of Physics, Oakland University, Michigan and the Department of Neurosurgery of University of Antwerp, Belgium. The neuroscience of MEG was reviewed. MEG is a brain imaging technique which can identify a specific site in brain that is generating the tinnitus symptom by measurement of small magnetic fields of activity, which are generated by intracellular electrical currents of the brain, with magnetometers, i.e. superconducting quantum interference devices (SQUIDs). Brain activity, reflective of a localized or functionally connected neural network can be identified at each instant in time. "Using MEG, we can actually see the areas in the brain that are generating the patient's tinnitus, which allows us to target it and treat it."(Susan M. Bowyer).

Demonstrations of MEG localization of suspected cortical generators images in a pilot study of 2 severe disabling tinnitus patients were presented. The objective of the study was to determine the effect of electrical stimulation on specific areas of the auditory cortex in tinnitus patients.

Each patient had bilateral tinnitus, intensity fluctuant, occasionally more in one ear than the other. The protocol followed by each patient included completion of tinnitus questionnaires and psychoacoustic measures to establish the frequency and loudness of their tinnitus. Tones at these frequencies and loudness were then represented to each patient while having magnetoencephalography (MEG) performed to determine the tonotopic map for these frequencies. MEG data was analyzed by Single Equivalent Current Dipole. The surgical navigational MRI images with MEG localization for the 6 and 8 kHz tones responses were demonstrated. Functional magnetic resonance imaging (fMRI) was performed and the images were demonstrated during presentation of music to identify the entire auditory cortex. The fMRI data was analyzed by SPM.

Patient #1 rated his tinnitus at 8/10 for pitch and 9/10 for loudness prior to surgery, with frequencies at 6 kHz and 8 kHz. He noted that occasionally his tinnitus was worse in his right ear. Patient #1 had the tinnitus frequency locations localized by MEG on the right hemisphere. The MEG images for Patient #1 were uploaded to the operating room neuronavigational system to guide the implantation of a Medtronics neurostimulator with a Pisces quadripolar electrode for electrical stimulation.

Patient #2 rated his tinnitus 10/10 for pitch and 9/10 for loudness prior to surgery, with frequencies at 8 kHz and 10 kHz. Patient #2 had his tinnitus frequencies localized by MEG and fMRI in the left auditory cortex and was also implanted with a quadripolar electrode. Medtroincs neurostimulators allow stimulations to be presented in a random pattern to the auditory cortex.

The results were positive in both cases with reduction /near elimination in patient #1 short term; which has persisted post op in excess of 2 years. In patient #2, post op 2 months, the tinnitus was eliminated in ear lt, and increased in intensity ear rt .-

Although no cure is available for tinnitus at this time this pilot study demonstrated that the described methodology of electrical stimulation of the auditory cortex can reduce the tinnitus perception and annoyance as identified with MEG.

Dirk de Ridder presentation was entitled "fMRI Guided implantation for tinnitus".

Introductory remarks included the following:

The concept of thalamocortical dysrhythmia was proposed as a possible pathophysiological mechanism for both tinnitus and pain. A prerequisite for conscious auditory perception was stated to be the frequency of gamma activity, i.e. 30 hz and higher frequencies of brain activity. Decrease in the gamma frequency is accompanied by and increase in loudness perception. The underlying mechanism is a thalamo cortical dysrhythmia, a possible mechanism for both tinnitus and pain.

Tinnitus an aberrant auditory sensory stimulus is related to a reorganization and hyperactivity in the primary auditory cortex. This is supported by nuclear medicine imaging and magnetoencephalography (MEG). The problem for localization of electrode placement in brain attempting tinnitus suppression is that the tinnitus is not limited to the primary auditory cortex (PAC), but can be in multiple overlying neural networks or the parahippocampus, and respond to stimulation at different frequencies. Stimulation of the amygdala and hippocampus may influence an auditory memory for the tinnitus. The dorsolateral prefrontal cortex (DLPFC) may influence the primary auditory cortex (PAC) and parahippocampus (PH) in a top down model. Chronic tinnitus may be reflected electro physiologically by the beta frequency and activation of the parahippocampus - not the primary auditory cortex.

A case report and a fMRI technique was presented for electrode site selection for attempting electrical cortical tinnitus suppression. Thalamocortical dysrhythmia refers to a persistent pathological resting state theta-gamma coupling that is spatially localized at an area where normally alpha oscillations predominate. The fMRI technique demonstrates a "fusion" of gamma and the BOLD response. Specifically, the brain fMRI identifies regions of the BOLD activity elicited by a tinnitus matched sound presentation. The BOLD fMRI response in brain is stated to be reflective of gamma activity. The gamma response is highest at the BOLD response.

The site of the fMRI Bold response may be a "hot spot" for electrode placement attempting tinnitus suppression. Source localized electroencephalography

recordings, (LORETA) identify the increased theta gamma activity which colocalized with the fMRI "hot spot". Current was applied to an intracranial electrode "exactly" at the "hot" spot which had been identified to be colocalized with an increased gamma and theta. With tinnitus suppression the spectral EEG changes normalized both at the site of the stimulating electrode and the source localized EEG recordings, in contrast to the other electrode poles which demonstrated a normal alpha peak. It is hypothesized that a normal "resting" alpha brain frequency may be replaced by tinnitus with a beta and an altered alpha frequency. Significant is the identification in responders of the connectivity or lack of the phase connectivity between brain regions of activation related to the tinnitus. Specifically, the data suggests that identification of a theta gamma coupling as hypothesized by the thalamocortical dysrhythmia and the reverting to a normal alpha peak with electrical stimulation results in maximal tinnitus suppression. It is suggested, based on preliminary investigations, attempting electrical cortical stimulation for tinnitus suppression, that the state of the brain, as identified by source localization and the fMRI technique as described, is critical for site selection and placement of the electrodes, and the resulting identification of responders or non responders[18].

SUMMARY

The AAO HNS International tinnitus Miniseminar 2012 informed otolaryngologists and tinnitus professionals of the clinical application for tinnitus diagnosis and treatment of brain imaging techniques available to objectivize the subjective aberrant auditory sensory percept- tinnitus - for all patients with subjective idiopathic tinnitus of the severe disabling type.

One has with brain imaging technologies an objective insight into the complexity of the underlying biology and pathophysiology of tinnitus, both of which are basic for clinical translation to establish an increased accuracy for the tinnitus diagnosis and attempts for tinnitus control and treatment. The Brian imaging technologies presented at this Miniseminar, provided for a broad diagnostic category, tinnitus, an objective identification and understanding of subgroups of tinnitus as defined by combinations of biological and behavioral characteristics. In addition, an understanding for additional multiple brain functions accompanying tinnitus, highlighted in the clinical history by the perception of the sensation, tinnitus, and its transformation to behavior, i.e. emotion, anxiety, depression, memory, i.e. a final common pathway for tinnitus.

Of the goals as set forth for this AAO-HNS Int Tinnitus Miniseminar 2012, the highlight to be considered is the demonstration that an Otolaryngologist and all tinnitus professionals can objectivize, with brain imaging, the subjective sensory aberrant auditory complaint tinnitus in terms of multiple brain functions. The brain imaging techniques and models presented at this Miniseminar which started with nuclear medicine SPECT and PET imaging in 1989 and are ongoing at SUNY/DMC, and worldwide, have advanced with fMRI, and MEG and have provided: a) a theoretical basis for mechanism(s) of tinnitus production ; b) an evolving neurobiology and pathophysiology for tinnitus of all clinical types; c) identification of neuroanatomical substrates and brain functions activated in the presence of the tinnitus signal; d) a basis for investigation and identification of underlying signal processing and molecular mechanisms involved in the clinical manifestation of subjective idiopathic tinnitus; and e) clinical translation for increase in the accuracy of the tinnitus diagnosis and modalities of treatment attempting tinnitus relief of all clinical types - all-for the ultimate benefit of the tinnitus patient.

Each brain imaging technique has advantages and limitations. The limitations of treatment results attempting tinnitus relief are reflected of what is and is not known of ear and brain function. The brain imaging techniques are recommended to be considered as models of tinnitus activity, reflecting with nuclear medicine SPECT cerebral perfusion and indirectly metabolism, with PET a direct measure metabolism, with fMRI, blood oxygenation, a indirect measure of neuronal activity, with MEG, a direct measure of neuronal activity, and with LORETA, a 3D tomographic representation of the spectral distribution of low frequencies of the EEG brain activities - all in the presence of the tinnitus signal, and individual for each tinnitus patient. The fMRI has application for identification of regional brain activation for specific tasks, and a clinical tool when used in combination with MEG and cortical electrical stimulation attempting tinnitus relief. Specific ligands, e.g. I 123 Iomazenil for the identification of regions of brain activation of the GABA - A receptor. The clinical application of all the presented technologies for tinnitus patients, particularly of a predominant central type tinnitus, are significant advances for the diagnosis and treatment for all clinical types of tinnitus, and reflective of the expanding new discipline of Tinnitology.

In 2012 one must be cautious in the interpretation of what we are seeing with each of these brain imaging technologies. First, in our clinical experience, nuclear medicine imaging, fMRI is identifying activation of regions of interest in brain of multiple brain functions in the presence of the tinnitus signal - not the tinnitus signal. The literature for the MEG for tinnitus is evolving and has great potential for the identification not only of brain function in the presence of the tinnitus signal - but of the specific tinnitus signal. Second, is to respect the multifunctionality of the cytoarchitecture of the brain, i.e. multiple functions in the same region of interest.

The identified brain regions of activation in the tinnitus patient with SPECT, fMRI, PET, MEG, are to be considered to be not "tinnitus" but multiple brain function(s) in the presence of the tinnitus signal. For example, the dorsolateral prefrontal cortex (DLFC) and ventral lateral prefrontal cortex have been identified with brain fMRI and nuclear medicine as regions of activation in brain in tinnitus patients. The clinical significance of this activation for tinnitus is recommended to not rush to judgment specifically for tinnitus but to evaluate reports from sensory physiology and cognitive neuroscience of: a) DLFC involvement in a "conflict circuit" in brain; b) the DLPFC receives /codes information in working memory; and c) the ventral lateral prefrontal cortex consolidates the information.

FUTURE

It is anticipated that ongoing advances in existing brain imaging techniques presented at this meeting are and will continue, the results which will increase the diagnostic accuracy and treatment efficacy of existing modalities attempting tinnitus relief of instrumentation and medication, and the development of an emerging new field of pharmacology dedicated to different clinical types of tinnitus, i.e. tinnitopharmacogenomics.

Such advances will include: 1) a multimodal approach of fiberoptic recordings of fluorescent calcium signal indicators in combination with fMRI which have measures of signals not accessible with electrophysiologic recordings[19]. 2) Optogenetics, the integration of optics and genetics to control precisely defined events within specific cells of living tissue even within freely moving animals[20].

The brain imaging for tinnitus extends beyond the models presented at the Miniseminar 2012. What needs to be included into our otologic/ neurotologic evaluation of the subjective idiopathic tinnitus is the individual electromagnetic encephalographic (EEG) pattern of brain activity.

The theme of the AAO-HNS Intl Tinnitus Miniseminar 2013 is planned to be "Electrophysiology and Tinnitus". The meeting will provide to the otolaryngologist and tinnitus professionals state of the art clinical electrophysiologic ear and brain imaging models that have translation for tinnitus diagnosis and treatment. Specifically, office based objective measurement in ear of electrophysiologic responses with hearing and balance testing in the presence of the tinnitus signal, and in brain a focus on the individual electromagnetic electroencephalographic (EEG) pattern of brain activity, the quantitative spectral analysis of the raw EEG data (QEEG), and the low frequency resolution electromagnetic tomographic analysis (LORETA) - all with application for tinnitus diagnosis and treatment.

It is particularly gratifying to our tinnitus team at the Department of Otolaryngology and Radiology Nuclear medicine SUNY/Downstate to be witness to the growth and development of the brain imaging technique of nuclear medicine brain SPECT/PET imaging in tinnitus patients, worldwide. This application, originated at SUNY /Downstate with brain SPECT in 1989, was initially reported in 1991, and has been followed with brain PET since 2000. From the start, the application and findings of nuclear medicine technology for the tinnitus patient were recognized to have implications not only for tinnitus diagnosis and treatment but translation for all sensations and to contribute to the neuroscience of brain function in general and specific brain functions in the presence of the tinnitus signal.

On behalf of the program committee of the AAO--HNS Intl Tinnitus Miniseminar we welcome you to the upcoming meeting in Vancouver, B.C.2013, Wednesday, 10/2/13, Title: New Concepts in Electrophysiology and Tinnitus -Translation Diagnosis and Treatment.

Abraham Shulman, M.D.,
Michael E. Hoffer, M.D., Capt. USN,
Barbara Goldstein, PhD.

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