

Medical Significance of Tinnitus

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Abstract: The medical significance of a symptom or disease process in a patient is defined as a clinical manifestation of abnormal function of a living cell, tissue, organ or organ system(s). Tinnitus, an aberrant perception of sound unrelated to an external source of sound, has been identified to have a medical significance. The medical significance of tinnitus has been identified with a Medical Audiologic Tinnitus Patient Protocol since 1979. The highlights of this clinical experience include for diagnosis: tinnitus not to be a unitary symptom; the identification of clinical type and subtypes of tinnitus and a Final Common Pathway for Tinnitus of all clinical types particularly of the severe disabling type. For treatment a multidisciplinary approach has evolved including neurology, otology and psychiatry; a combined treatment protocol of drug therapy and instrumentation, based on differentiation between the components of the symptom of tinnitus i.e. sensory, affect, and psychomotor. Two diagnostic categories are identified: otologic/neurotologic and neurologic. The application of SPECT Imaging of Brain which has identified a Final Common Pathway for tinnitus and provides an increased diagnostic accuracy for tinnitus and a basis for selection of a neuropharmacology for tinnitus is discussed.

Keywords: Medical Significance; Medical Audiologic Tinnitus Patient Protocol; Clinical Types of Tinnitus; Final Common Pathway for Tinnitus; SPECT of Brain

INTRODUCTION

I appreciate the opportunity to present what we consider to be a highlight of our tinnitus experience i.e. the medical significance of tinnitus. This clinical experience reflects a medical audiologic team approach. My co-worker in this effort is Dr. Barbara Goldstein, audiologist. The medical significance of a symptom or disease process in a patient is defined as a clinical manifestation of abnormal function of a living cell, tissue, organ or organ system(s).

Our clinical experience for tinnitus diagnosis and treatment has clinically identified tinnitus, particularly of the severe disabling type, to have medical signifi-

cance.¹ This medical and audiologic experience has been ongoing since 1977.² An excess of 4,000 patients with tinnitus particularly of the severe disabling type have been evaluated with a Medical Audiologic Tinnitus Patient Protocol (MATPP) at the Tinnitus Clinic of the Health Sciences Center at Brooklyn, State University of New York.¹⁻⁴

The definition of tinnitus is considered to be dynamic and reflects the integration of clinical efforts of observation and neuroscience/ nuclear medicine identification of underlying mechanisms of tinnitus production. Tinnitus is defined in 1996 as a sensory disorder of auditory perception reflecting an aberrant auditory signal produced by interference in the excitatory/inhibitory processes involved in neurotransmission.⁵ Since 1979 the underlying mechanism is hypothesized as a dysynchronization which may occur in the peripheral or central nervous system, or both. Dysynchronization is a lack of synchrony or interference in timing of the discharge rate and phase locking of the auditory signal. This definition identifies tinnitus as a medical audiologic complaint and a symptom of neurotologic disease.^{1,2}

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Classical teaching of the symptom of tinnitus has been primarily from the audiologic perspective in terms of the psychoacoustic and psychophysical characteristics/attributes of tinnitus. From the perspective of a physician, specifically an otologist/neurotologist, the symptom of tinnitus should be considered as a symptom of neurotologic disease occurring either alone and/or in combination with hearing loss, vertigo, ear blockage alone and/or in combination. The integration of clinical observations with recent neuroscience reports of interruption in the homeostasis of neurotransmitter systems at specific anatomic sites with resultant alteration in sensory/affect and memory function, supports the neurotologic clinical observations that tinnitus has a medical significance.

Tinnitus at this time is considered not only in terms of the classical description of its psychophysical and psychoacoustical characteristics but also from the perspective of a neurotologist. Specifically, respect for disease of the ear and brain; interactions of ear and brain, mind and brain; and integration of the multifactorial characteristics of the symptom of tinnitus with the clinical histories of tinnitus patients. Such a clinical medical/audiologic approach reflects our clinical experience and identifies tinnitus to have multiple etiologies and underlying mechanisms of tinnitus production some of which may or may not be shared by single clinical types and/or subtypes of tinnitus.

The original and basic neurotologic teaching of the need to associate complaints of hearing loss, tinnitus, vertigo, ear blockage alone and/or in combination now requires an expansion to include the associated complaint of hyperacusis, an increased sensitivity to the perception of sound; other abnormal auditory sensations; and dysfunction of central nervous system processes of cognition, memory, anxiety, depression and fear.

The factor of stress is significant for all tinnitus patients particularly of the severe disabling type.⁵ The Stress Diathesis Model for depression has been modified and applied for the symptom of tinnitus.^{6,7} Specifically increasing stress results in an increased level of cortisol i.e., hypercortisolemia.⁸ When not controlled, hypercortisolemia is manifested clinically by an increased sense of anxiety progressing to depression and increased tinnitus. Tinnitus is a stressor to patients with tinnitus of the severe disabling type. Stress, fear, sleep disorders marked by insomnia before or after an accompanying tinnitus - alone or in any combination - have a significant incidence of occurrence in patients with tinnitus of the severe disabling type.⁵

As neurotologists we must accept the challenge of the tinnitus symptom to provide the tinnitus patient a protocol for diagnosis and treatment; to eliminate the

phrase "nothing is available," "live with it"; and to actively apply the principles of otology and neurotology to tinnitus, as we do for hearing loss and vertigo complaints, in the tradition of our teachers like Lempert, Shambaugh, House, Shea, and Schuknecht.

HIGHLIGHTS OF HSCB-SUNY— TINNITUS CLINIC EXPERIENCE

The highlights of our clinical experience with tinnitus reflect the goals of a neurotologic and audiologic team approach for tinnitus diagnosis and treatment. Specifically to identify the medical significance of the symptom of tinnitus and to attempt to provide a treatment for tinnitus relief and/or elimination. In order to achieve this goal for a subjective idiopathic complaint, i.e., tinnitus, a Medical Audiologic Tinnitus Patient Protocol (MATPP) was introduced in 1979 and has been followed to date.^{1-4,9} It is dynamic and reflects our ongoing clinical tinnitus experience. The highlights include the following for:

a. Diagnosis:

- Tinnitus is not a unitary symptom.¹
- Clinical types and subtypes of tinnitus exist and have been identified.^{1-4,9-11}
- A Final Common Pathway has been identified for tinnitus which we consider to be basic for all clinical types of tinnitus particularly of the severe disabling type. The basic process is considered to be the establishment of a paradoxical auditory memory for tinnitus. It provides a model for the identification of the underlying neurochemistry involved in the production of tinnitus.⁵

b. Treatment:

- Identification of components of the symptom of tinnitus - sensory, affect and psychomotor¹;
- A combined treatment protocol which has increased the efficacy of tinnitus control and treatment¹; and
- A multidisciplinary approach including neurology, otology, and psychiatry.^{1,4}

c. Clinical Course of Tinnitus¹:

The clinical classification of the stages of the natural history of a chronic disease has been applied to attempt to understand the natural history of the symptom of tinnitus:

- Susceptibility.
- Subclinical pre-symptomatic.
- Clinically manifest.
- Handicap and disability.

The medical significance of SIT can be characterized at this time as a spectrum of clinical manifestations of sensory, behavioral, and psychomotor components.

The symptom of tinnitus is not considered to be a unitary symptom. To date the following components have been identified: a) sensory; b) affect; and c) psychomotor. All sensory complaints have a sensory and affect component. Specifically for tinnitus the sensory component is the sound itself. The affect component is primarily that of the behavioral response of the patient to the presence or absence of tinnitus. The psychomotor component is considered clinically to contribute to the interference in communicative difficulties of patients with severe tinnitus.

The symptom of tinnitus is considered to be a medical disorder involving primarily the cochleovestibular system either in its periphery and/or central nervous system. Tinnitus is not considered a psychiatric disorder. It is considered in some patients to be a symptom of neuropsychiatric disease.¹

The clinical identification of types and subtypes of tinnitus are considered to reflect multiple neuronal and interneuronal systems, the underlying mechanisms of which may manifest themselves with associated affect complaints, highlighted by behavior, fear, interference in cognition, mentation, speech expression, communication disorders, anxiety, depression and interference in memory.

Classical medical teaching stresses the need to establish an accurate medical diagnosis which includes identification of a specific etiology or etiologies and the underlying pathophysiologic mechanisms involved to provide a basis for successful therapy. This approach has, in general, not been successful in our experience. The identification and treatment of factors influencing the clinical course of tinnitus has resulted in significant tinnitus relief, e.g., a) noise exposure; b) fluctuation in aeration of the middle ear; and c) Secondary Endolymphatic Hydrops.^{1,2,3,9,11}

These factors are not etiologies for the symptom of tinnitus. The identification with vestibular testing of a reduced vestibular response in the peripheral vestibular labyrinth when correlated particularly with the clinical history of the associated complaint of ear blockage and cochleovestibular test findings, which we accept as indicative of Meniere's Disease, have been the basis for diagnosis for a Secondary Endolymphatic Hydrops. Treatment for Endolymphatic Hydrops has in our experience improved the efficacy of recommendations of instrumentation, particularly hearing aid and/or masking^{1,9} and/or habituators.

Systemic disease which has been found to have a high degree of correlation with tinnitus includes: a) cardiovascular disease (particularly fluctuating hypertension); b) metabolic disease (hyperlipidemias; thyroid disease; elevated blood glucose); c) neuropsychiatric disorders. Identification and treatment, when appropriate, has resulted in a significant incidence of reported tinnitus relief.

In summary, the identification and appropriate treatment of factors known to influence the clinical course of tinnitus will provide to your patients, as it has to ours, a significant incidence of tinnitus control. Our identification of these factors and treatment has resulted in tinnitus control of 25–35%. Coordination of efforts of multiple medical disciplines, when integrated with the neurotologic and audiologic findings, has increased the results for tinnitus control by medical means to 40%. Accordingly, the need for instrumentation has been reduced.¹

For both diagnosis and treatment we are increasingly recommending a combined protocol which is multidisciplinary, i.e., neurology, otology, audiology, and psychiatry.

CLINICAL SUPPORT OF THE MEDICAL SIGNIFICANCE OF TINNITUS

Tinnitus has been clinically identified as a "soft" sign of the following neurotologic and neurologic diagnostic categories^{12–17}:

A. Otologic and Neurotologic:

1. Inflammatory Middle Ear/Mastoid/Inner Ear Disease
2. Meniere's Disease
3. Acoustic Tumor
4. Sensorineural Hearing Loss
5. Attributes of Hearing/Tinnitus

Attributes of both hearing and tinnitus are considered to have appropriate cortical representation in specific anatomical regions of brain, which when differentiated and identified appropriately provide a basis for increased accuracy of tinnitus diagnosis and its clinical application for treatment.¹⁴ Presently investigations in our laboratory are in progress for the development of a neuropharmacologic approach for tinnitus particularly of the central type(s).

B. Neurologic Disease^{1,12–17}:

Five categories of diagnosis are included.

1. Cerebrovascular Disease
2. Neurodegenerative Disorders and Associated Dementia
3. Neuropsychiatric Disorders, specifically dementia, schizophrenia, and the affective disorder of depression
4. Migraine
5. Epilepsy

Although no conclusion has yet been established with respect to the association between tinnitus and cerebrovascular, neurodegenerative, and some neuropsychiatric disorders, there is strong clinical support as

manifested by the correlation of SPECT imaging of brain findings with the clinical history and long-term follow-up of the clinical course of tinnitus in patients from initial visit to a period of more than two years. The identification of subtypes of a central type tinnitus can only be accomplished by the scoring of neurons in brain, ganglion cells in the Organ of Corti and other factors. It is agreed that such conclusions await neuropathologic confirmation with attention to the demonstration of a neuropathologic correlate.^{5,12-17}

An underlying basic mechanism is speculated to be that of glutamate neurotoxicity. Such glutamate receptors mediate excitatory neurotransmission in brain and/or ear and are important in memory, speech and sound acquisition, learning, certain neurodegenerative disorders, neuronal plasticity, and neurotoxicity. Similarly the dopamine/serotonin system particularly highlighted by their function as modulators for affective behavior are considered significant in tinnitus production with involvement of the autonomic nervous system.

It is hypothesized that a clinical type of temporomandibular joint tinnitus is an auditory migraine phenomenon. Trigeminal stimulation of brainstem level is considered to be the mechanism involved resulting in a migraine type effect.¹⁸

Similarities have been identified clinically between some central types of tinnitus and epilepsy. Tinnitogenesis, a state of hyperexcitability with epileptic characteristics at the cortex, has been identified with SPECT.⁵

Our clinical reported observations find a continuous uninterrupted stream of support from neuroscience investigations of basic processes of sensation, memory, stress, fear which find clinical application for diagnosis and attempts for tinnitus control.¹⁹⁻²²

It is satisfying to us that clinically our reported observations now find support by others for a neurophysiological theory of tinnitus²³; and objective evidence based on perfusion changes in brain hypothesized to reflect a Final Common Pathway for Tinnitus.^{5,12-17}

SPECT IMAGING OF BRAIN/FINAL COMMON PATHWAY FOR TINNITUS/MEDICAL SIGNIFICANCE

Single Photon Emission Computerized Tomography (SPECT) of brain with the radio isotope technetium 99m hexamethyl propyleneamine oxine (TC-99-HMPAO) is a functional brain imaging technique which was introduced in 1990 for the identification of abnormalities of regional cerebral blood flow (rCBF) in patients with a central type subjective idiopathic tinnitus characterized as severe and disabling. It has been the one single diagnostic technique which has increased the accuracy of

our tinnitus diagnosis and provided a method to monitor the efficacy of tinnitus treatment. It has provided objective support for clinical speculations that tinnitus is a "soft" sign of CNS Disease as reflected in associated CNS complaints, for example, anxiety, depression, cognition, memory, fear.^{5,12-17}

All patients with tinnitus, particularly of the severe disabling type, have as a common denominator a disorder in affect. Specifically, a behavioral disorder in response to or as an accompaniment of an aberrant auditory sensory stimulus, i.e., tinnitus. The heterogeneity of response of tinnitus patients both for sensory and affect have been reported by professionals of all disciplines involved in this diagnosis and treatment. The change from sensory to affect suggests components of a Final Common Pathway. At this time neuroscience reports anatomical substrates wherein mechanisms of interchange of processes, involved in the transition of sensory to affect may occur, to include: a) the temporal medial lobe system (MTLS); and b) the limbic lobe.^{19,20}

It is hypothesized that a Final Common Pathway for Tinnitus exists in all patients with tinnitus. Its chief function is the transition of an aberrant dysynchronous auditory sensory signal to behavioral response identified as an affective behavioral change. The basic transition is considered to have at least three essential components: a) sensory; b) affect; and c) memory. The sensory and affect components are in a constant state of reciprocal interaction. The MTLS is considered to be the key anatomic substrate in this Final Common Pathway. It is hypothesized to be involved in the establishment of a paradoxical memory for the aberrant dysynchronous sensory auditory stimulus. The establishment of a paradoxical memory provides a linkage that is a "bridge" between the sensory and affect components. A paradoxical memory modulates the transition between the sensory and behavioral component of tinnitus and is considered to be the initial process.⁵

The establishment of an accurate medical diagnosis for tinnitus and for symptoms associated with tinnitus, particularly of the central nervous system, can provide a basis for selection of medication to be used in an innovative application to attempt tinnitus control. This is the basis for the psychopharmacology that is now being used in our practice to attempt tinnitus control. Significant tinnitus relief has resulted from the use of drug medication based upon a Final Common Pathway which differentiates between the sensory and affect components of tinnitus; recognizing that all tinnitus patients, particularly of the severe disabling type, share in common the factor of stress and fright, and associated behavior of mood changes of anxiety and depression.

The medical significance for tinnitus is recommended to be approached not only as a "soft" sign of

associated disease either of ear, brain or other organ systems, but also a prognostic sign for local and/or systemic disease. Our clinical experiences as neurotologists have filled the literature with the identification of tinnitus as an early sign of acoustic tumor; its association with inflammatory ear disease; and its accompaniment of sensorineural hearing loss and increase in the presence of noise. Now, increased clinical exposure of professionals to the problem of tinnitus of the severe disabling type demonstrates its medical significance to involve not only the peripheral area of the cochleovestibular system but also the CNS. Specifically, we have considered and reported since 1979 that tinnitus should be considered to reflect a dysynchrony either within the peripheral and/or central cochleovestibular system, and that in addition to the cochleovestibular system other organ systems may utilize the central nervous system to express their dysfunction.^{1,2,24}

Our research for identification of the medical significance of tinnitus continues. It is not new. We realize that our search is similar to the search by those who over centuries attempted to understand the transition from sensory to affect in brain. Descartes regarded the mind as something immaterial, separate from brain but interacting with it in some manner.

CONCLUSIONS

The symptom of tinnitus particularly of the severe disabling type has a medical significance for the identification and treatment of the presence of disease highlighted at the present time both for ear, brain. In 1996, tinnitus is considered to be a symptom of neurotologic disease and a neuropsychiatric disorder.

SPECT Imaging of Brain in patients with tinnitus demonstrates for the first time the in-vivo significance of the organicity of brain for a central type tinnitus.

Neurotologic and neurologic implications for tinnitus are suggested by the results of SPECT Imaging of Brain which can be applied to both diagnosis and treatment for different types and subtypes of central tinnitus.

A Final Common Pathway for Tinnitus is hypothesized to exist for all patients with tinnitus. Its function is the transition of the sensory to the affect component of the symptom of tinnitus. It is hypothesized that the anatomical substrate is in the medial temporal lobe system and involves the transition of the sensory to the affect component of tinnitus. The initial processes are the establishment of a paradoxical auditory memory.

Nuclear Medicine, by application of radiotracers for SPECT and PET imaging, is expected to provide identification of specific receptors of neurotransmitter systems, which are speculated to form the basis for identi-

fication of specific disease processes on a cellular level. It should also provide a basis for the development of a neuropharmacology for a specific central type(s) or subtypes of tinnitus. This supports the contention that we as physicians recognize the medical significance of tinnitus.

Otologists and neurotologists need to recognize that tinnitus provides an opportunity to apply the basic science of sensory physiology to clinical disorders of sensory perception. No longer should patients come to our offices and be told that "they should live with it" or "nothing is available." Significant advances have been made for both diagnosis and treatment and should be shared with tinnitus patients in 1996 and in the next century.

The future is bright for the development of surgical techniques specifically for a cochlear type tinnitus and the achievement of a cure, not for all tinnitus but for a specific type of tinnitus reflecting a specific etiology and a specific underlying mechanism of tinnitus production.

The processes involved in the establishment of tinnitus particularly of the severe disabling type and the problems encountered, relate to the eternal problem of what the relationship is of mind and brain and what the processes are involved in such identification. The problem is not only scientific but also philosophical. This is the reason for the complexity encountered in tinnitus diagnosis and treatment.

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