Long-term Inhibition of Tinnitus by UltraQuiet™ Therapy
Preliminary Report

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Abstract: Masking of tinnitus by noise can produce residual inhibition, a persistence in the reduction in tinnitus after the noise is removed. Typically this is very short-lived, on the order of minutes. This paper reports long-term inhibition of tinnitus by UltraQuiet™ therapy, a new technique that employs patterned sound in the 10-20 kHz range, presented through bone conduction. Nine subjects participated in a study of the efficacy of this tinnitus suppression technique. Eight reported improvement in tinnitus symptoms; one did not complete the study. The duration of the improvement ranged from days to weeks. This long-term inhibition may involve a truly plastic change in the brain at the central level.

Keywords: tinnitus, residual inhibition, masking, cortical plasticity, UltraQuiet™

Introduction

The ultimate goal in tinnitus therapy is the long-term inhibition or elimination of the tinnitus. Masking of tinnitus by noise delivered through a tinnitus masker either alone or in conjunction with a hearing aid has been one of the most effective therapies, but in most cases the relief is short-term, primarily occurring while the masking noise is present [1]. There is a phenomenon called residual inhibition (RI), however, in which the reduced intensity of the tinnitus persists for some time after the masking noise is removed. This paper presents the preliminary results of tinnitus treatment with a new technique intended to induce residual inhibition, UltraQuiet™ therapy⁴, provides a basis for continued studies, and discusses central mechanisms that may lead to long-term inhibition of tinnitus.

Masking and Residual Inhibition:
A. Masking

For masking of an externally applied tone, only energy in a critical band around the tone frequency, corresponding to the filtering capability of the basilar membrane, should be effective in masking (i.e., a conventional psychophysical tuning curve) [2]. However, Feldmann, Shailer et al., Tyler et al., Penner, Smith et al. and others, using maskers of varying bandwidths, have shown that tinnitus is not masked like a tone in many
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B. Residual Inhibition

Forward masking of tones is a well-known psychophysical effect, in which a masking tone can prevent detection of a tone after the masker is cut off. This is a very short-duration phenomenon, however, normally lasting less than 100 milliseconds, and may correspond to the time required for the receptors to regain their sensitivity [2]. Residual inhibition (RI), a postmasking effect with much longer duration, was first reported by Feldmann [3]. The term refers to a decrease in the perceived intensity of the tinnitus for a time after the masking noise stops.

Typically, residual inhibition lasts only for a few seconds or minutes, but occasionally can persist substantially longer. Hazell and Wood report a few cases in which 15 minutes of masking noise resulted in residual inhibition of tinnitus for the entire day [13]. Clearly a therapeutic technique for tinnitus that did not require continuous masking noise would be of great benefit. However, the factors resulting in persistence of inhibition and the mechanism are not well understood.

Tyler et al. note that factors influencing residual inhibition include the duration of the masker over a period of 60 seconds and possibly more [5]. They contrast this with forward masking of two acoustic tones, where increasing masker duration beyond about 400 milliseconds generally produces no increase in the amount of forward masking.

Terry et al. conducted a parametric study of residual inhibition to determine the dependence of RI on masker characteristics such as center frequency, bandwidth, intensity and duration [14]. They wanted to know if maskers could be designed to be maximally efficient in producing RI, and if the incidence and extent of RI could be predicted from the type of tinnitus. They found that RI increased with masker intensity, but the relationship to duration was not clear. Duration only increased RI when a relatively intense masker was used, and it is not known if this holds for masker durations greater than 10 minutes. The relationship of RI to tinnitus frequency and to masker center frequency and bandwidth was complex and varied between individuals. No attempt was made to assess the effect of masking noise outside the tinnitus frequency. In contrast to Feldmann [3] they did not find evidence of contralateral masking. They found that there was no obvious predictor of whether a particular subject would exhibit RI.

The UltraQuiet™ Therapy

A. Background: The ‘UltraQuiet™’ therapy (Figure 1) provides patterned auditory stimulation in the high audio and ultrasonic ranges (10-20 kHz), using a bone conduction transducer. It is based on the work of Lenhardt et al., demonstrating ultrasonic perception by humans through bone conduction up to 100 kHz [10]. It differs from the conventional masker in that none of the sound overlaps the range of reported tinnitus. Nevertheless, ultrasound was even more effective than speech-range masking noise for tinnitus masking and producing residual...
Inhibition in a study by Meikle et al. [9]. In the UltraQuiet™ therapy, the auditory stimulation, rather than a band of noise as is commonly used for masking, is music that has been processed and shifted in pitch. Davis and Wilde demonstrated music to be a more effective tinnitus masker than noise [15]. They attribute the greater effectiveness of music in part to the involvement of more central and cognitive processes. In the UltraQuiet™ therapy, the processed music is presented through a bone conduction transducer at a low level – about 6 dB above threshold - for periods of 30 minutes to 1 hour, two times per week. The goal is to effect changes in the central nervous system mechanisms of tinnitus, resulting in long-term inhibition.

B. Case Reports

1. Methods

a. Subjects

The subjects were 9 adults with severe disabling tinnitus, 7 male and 2 female, ranging in age from 35 to 72. All subjects were evaluated for tinnitus, including audiograms and pitch matches. All subjects had mild to moderate high frequency hearing loss. Figure 2 shows the average of the audiograms for the 9 subjects. The pitch match to the tinnitus for all subjects was high pitched, matching to either a pure tone or narrow band noise with frequencies between 5-16 kHz (mean 7.3 kHz).

b. Stimulus

The tinnitus treatment stimulus was produced using Kyma Version 5 software with a Capybara 320 Sound Computation Engine, and recorded on a compact disk. The stimulus consisted of music digitally processed and used to modulate a signal in the 10 – 20 kHz range. The compact disk was played through a custom made amplifier into a piezoelectric bone conduction transducer. The transducer was held in place on the mastoid bone of the subject by a headband. Although the stimulus is presented on only one side of the head, it is heard binaurally through bone conduction.

c. Procedure

The subjects listened to the tinnitus treatment stimulus for eight sessions (two times per week for four weeks), beginning with 30 minute sessions, and increasing to 60 minute sessions. The stimulus was presented at 6 dB above the threshold of each individual.

2. Results

All eight subjects who completed the study reported improvement in their tinnitus symptoms during the course of treatment. (One subject dropped out for reasons unrelated to the tinnitus study.) The duration of the improvement varied. For two patients the improvement lasted for two or more weeks. For the others it lasted for 1-2 hours up to three days (Figure 3). A long-term follow-up questionnaire was administered 2 to 8 months after the end of the treatment, with the following results: On the question, “How do you feel that your overall tinnitus symptoms have changed since before you began the tinnitus treatment?” one person answered “moderately improved,” five people answered “slightly improved,” and two answered, “about the same.” One person reported benefit lasting 4 weeks following the last treatment, one 1
week, four 3-5 days, and two reported no lasting benefit. No one reported any adverse effects or worsening of symptoms (Figure 4). The mean change between the pre-treatment and post-treatment audiograms was less than 5 dB (Figure 5), and not statistically significant. None of the individual audiograms showed any notable change.

Subjects occasionally reported an “after image” of the stimulus following the sessions, but this was not perceived as aversive, and in some cases seemed to enhance the suppression of tinnitus. Some subjects also reported a subjective improvement in hearing, but this was not supported by the post-treatment audiometric results. However, discrimination was not assessed.

Discussion

The response of the patients suggests that the UltraQuiet™ therapy is able to induce residual inhibition of tinnitus for a substantially longer duration than conventional masking noise. There is the potential that the improvement reported by the patients is truly a plastic change at the central level, which may, over time, reflect the establishment of a “new” inter-neuronal network for auditory perception, and elimination of the aberrant auditory phenomenon, i.e., tinnitus. Central nervous system involvement in tinnitus has been found at both subcortical and cortical levels. Both levels could potentially play a role in long-term inhibition.

Subcortical habituation

Jastreboff and colleagues have developed a neurophysiological approach to tinnitus based on subcortical habituation, called Tinnitus Retraining Therapy (TRT) [16, 17]. The concept is that the annoyance of tinnitus depends on a subcortical conditioned response that creates distress through a link to the limbic system. The goal of the therapy is to habituate this response so that the tinnitus is no longer perceived. In TRT, the role of the sound is not to mask the tinnitus, but to accomplish changes in the auditory system including (1) decreasing the contrast between the neuronal activity that represents tinnitus and the background neuronal activity, (2) interfering with the brain’s ability to detect the tinnitus signal, and (3) reducing the abnormal gain in the auditory system and thus reducing hypersensitivity.
The Jastreboff approach uses broadband noise, but at levels that are adjusted low enough to avoid masking the tinnitus. The intent is to facilitate habituation with enriched sound stimulation. The idea is to enhance background neural activity within the auditory pathways, and habituate the tinnitus signal at a subcortical level. They use noise with stable temporal characteristics; the spectrum is not as important as the stability of the signal, since in their model, fluctuation of the sound level might attract the attention of the patient and create problems with adapting to the sound. This contrasts with the form of cortical reprogramming discussed below where attention may be necessary for the changes to take place, relevant to the effect of the UltraQuiet™.

Habituation of tinnitus by TRT requires long-term treatment. Sheldrake et al. report that tinnitus awareness is reduced by 61% and virtually abolished in 16% of cases, but that this can take up to two years of wearing the device from 8 to 10 hours per day [18]. The much more rapid reduction of tinnitus by the UltraQuiet™ therapy suggests that subcortical habituation is not a sufficient explanation.

Cortical and limbic system mechanisms

There is evidence for considerable cortical plasticity after hearing loss. For example, in monkeys, Schwaber et al. mapped the tonotopic organization of the cortex before and three months after cochlear deafening for high frequencies. The deprived area of the cortex reorganized and became responsive to chiefly the frequencies intact at the cochlea. The low frequency region did not change [19].

Several studies have demonstrated changes in the cerebral cortex specifically associated with tinnitus. These include changes in both the auditory cortex and the limbic system. Recent studies that are especially significant include those of Shulman, Llinas and Pare, Jeanmonod et al., Muhlnickel et al., and Lockwood et al. [20-26].

Shulman hypothesized that a final common pathway for tinnitus exists for all patients with tinnitus, based on the identification with Single Photon Emission Computerized Tomography (SPECT) of Brain of side to side perfusion asymmetries highlighted by the medial temporal lobe which includes the amygdala-hippocampal complex. Its function is the transition of the sensory to affect component of the symptom of tinnitus. The initial process is the development of a paradoxical memory for an aberrant auditory stimulus. The anatomical substrate is the medial temporal lobe system of the brain. Adjacent perfusion asymmetries involving the frontal, temporal, and parietal lobes suggest an interneuronal network resulting in the transition of the sensory to the affect component of the symptom of tinnitus. Underlying mechanisms are hypothesized to exist and to be highlighted by a diminution of inhibition mediated by gamma amino butyric acid (GABA) due to a disconnection from excitatory (glutamate) inputs. Blockage of GABA mediated inhibition with antagonists results in Tinnitogenesis, a epileptiform auditory phenomenon [20] as well as broadening of cortical neural tuning curves [21]. Treatment with the anticonvulsive GABA agonist drug, Gabapentin, reversed high frequency specific tinnitus and reduced hearing loss in animals [22]. Although only anecdotal, some of our subjects reported the perception of better hearing after the UltraQuiet™ trial, a finding to be investigated.

Shulman et al. reported identification of a biochemical marker for tinnitus, the GABA-A/Benzodiazepine/Chloride receptor and long term tinnitus control with a receptor targeted therapy binding to GABAR receptors in patients identified to have predominately central tinnitus [23] [24]. Llinas and Pare hypothesized that low threshold calcium spike bursts (LTS) were at the origin of Parkinsonian tremor, action tremor, neurogenic pain or absence epilepsy and tinnitus [25]. Jeanmonod et al. reported LTS in the human thalamus, which following medial thalamotomy resulted in a 50-100% relief in three of six patients with tinnitus, with a complete relief in only one [26].

Muhlnickel et al. explored the reorganization of the auditory cortex in tinnitus, using magnetoencephalography [27]. They found that there was a marked shift of the cortical representation of the tinnitus frequency into an area adjacent to the expected tonotopic location. There was also a strong positive correlation between the strength of the tinnitus and the amount of cortical reorganization. They point out the similarities between tinnitus and phantom limb pain. In both cases there is a loss of input from peripheral nerves, accompanied by a similar reorganization of the cortex. Muhlnickel et al. suggest a possible therapeutic approach in which patients attend to and discriminate some features of acoustic stimuli that are close to the tinnitus frequency to drive cortical reorganization of the non-tinnitus frequencies into the tinnitus representation, thereby reducing it. Note that this is quite different from conventional masking, where the
acoustic stimuli encompass the tinnitus frequency, and also different from the TRT paradigm, in which the point is to learn to not attend to the sounds. It does, however, resemble the UltraQuiet™ system, which uses patterned stimuli well-removed from the tinnitus frequency.

Lockwood et al. provide additional evidence for cortical plasticity in tinnitus, as well as evidence for limbic system links [28]. They used PET imaging techniques to look at cerebral blood flow in patients with tinnitus, and mapped neural responses to probe tones. They confirmed the SPECT findings of Shulman [20] of limbic and auditory system links. They noted more widespread activation in patients with tinnitus, as compared with controls, and aberrant links between the limbic and auditory systems. Like Muhlnickel et al. [27], Lockwood et al. make an analogy with phantom limb pain. Although they make no treatment recommendations, they note as already demonstrated by Shulman that pre- and post-treatment functional imaging studies may provide objective measures of tinnitus, and thus be useful in evaluating treatments.

Llinas et al recorded spontaneous magnetoencephalographic activity in awake, healthy human controls and in patients suffering from neurogenic pain, tinnitus, Parkinson’s disease, or depression. They reported a thalamocortical dysrhythmia marked by an increased low frequency rhythmicity, in the frequency band of 4-8 Hz [29].

Two other recent papers make a good case for treatment-induced cortical reorganization as therapy for neurological conditions. Liepert et al. looked at rehabilitation of muscles following stroke in humans [30]. They noted that injury-induced cortical reorganization is a widely recognized phenomenon, but that there is almost no information on treatment-induced plastic changes in the human brain. In their study, hand-muscle training led to significant enlargement of the muscle output area in the affected hemisphere. Menning et al. documented plastic changes in the auditory cortex induced by intensive frequency discrimination training [31].

Tinnitus is different from simple cortical reorganization in which adjacent areas expand to fill the region no longer receiving input from the cochlea. A region of the cortex is spuriously responding in a manner analogous to epileptiform activity, but we contend it can be remapped to patterned auditory stimuli above the frequency of the tinnitus, presented through bone conduction, with a consequent reduction in tinnitus.

References


Footnote

1. UltraQuiet™ is a proprietary tinnitus treatment with pending patents of Sound Technique Systems, LLC.

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