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# The Impact of Sound on Electroencephalographic Waves during Sleep in Patients Suffering from Tinnitus

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ABSTRACT

Based on the knowledge that sensory processing continues during sleep and that a relationship exists between sleep and learning, a new strategy for treatment of idiopathic subjective tinnitus, consisted of customized sound stimulation presented during sleep, was tested. It has been previously shown that this treatment induces a sustained decrease in tinnitus intensity; however, its effect on brain activity has not yet been studied. In this work, we compared the impact of sound stimulation in tinnitus patients in the different sleep stages.

Ten patients with idiopathic tinnitus were treated with sound stimulation mimicking tinnitus during sleep. Power spectra and intra- and inter-hemispheric coherence of electroencephalographic waves from frontal and temporal electrodes were measured with and without sound stimulation for each sleep stage (stages N2 with sleep spindles; N3 with slow wave sleep and REM sleep with Rapid Eye Movements).

The main results found were that the largest number of changes, considering both the power spectrum and wave's coherence, occurred in stages N2 and N3. The delta and theta bands were the most changed, with important changes also in coherence of spindles during N2. All changes were more frequent in temporal areas. The differences between the two hemispheres do not depend, at least exclusively, on the side where the tinnitus is perceived and, hence, of the stimulated side. These results demonstrate that sound stimulation during sleep in tinnitus patients' influences brain activity and open an avenue for investigating the mechanism underlying tinnitus and its treatment.



## 1. Introduction

While all sensory processing persists during sleep, the auditory input is particularly relevant for continuously monitoring the environment [1,2].

Several treatment strategies of tinnitus are based on sound stimulation and evidence indicates that they are more effective if sound mimics the tinnitus [3]. All these protocols conduct sound stimulation during the day, while patients are awake. Based on the knowledge that auditory processing continues during sleep [2] and that a relationship between learning and memory and sleep stages has been established, our group has embarked a new strategy for the treatment of idiopathic subjective tinnitus. A protocol of customized

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sound stimulation during sleep has resulted in a decrease in the subjective intensity, significantly improving the patients' quality of life [4].

It has been argued that slow wave sleep is important for declarative memory and that working memory is processed mainly during REM (Rapid Eyes Movements) sleep; however, the integrity and interaction of the different sleep stages for learning and memory process have also been suggested [5–8]. Slow EEG oscillations (less than 1 Hz) have been involved in the consolidation of long-term memory [9] and in the homeostatic regulation of synaptic connections [10]. Rhythmic acoustic stimulation induces K-complexes, which are considered a "forerunner" of slow oscillations in slow wave sleep stage [6,11]. Slow oscillation during slow wave sleep promotes consolidation of memory and the post-sleep facilitation of encoding new memories [12]. Slow waves may be modulated by low-frequency auditory stimulation [13]. Studies with functional magnetic resonance showed that auditory cortical activity is maintained during sleep but varies with stimulus significance [14,15].

The goal of this study was to explore the changes on brain activity induced by the sound stimulation during sleep in tinnitus patients.

## 2. Material and methods

### 2.1. *Polysomnographic recording*

Ten patients with idiopathic tinnitus, treated with sound stimulation mimicking tinnitus during sleep were studied [4]. The inclusion criteria were (1) adult patients with unilateral or bilateral subjective idiopathic tinnitus, (2) evolution of more than 6 months and (3) Tinnitus Handicap Inventory score above 17. The exclusion criteria included patients that demonstrated (1) objective or subjective secondary tinnitus, (2) hearing loss of 50 dB hearing threshold level (HTL) or worse in more than one frequency of the audiogram, (3) those that had undergone other treatments for tinnitus in the past year, (4) current use of hearing aids, (5) use of psychoactive drugs, (6) depression (Hamilton scale test above 13), and (7) sleep disorders not related to tinnitus (apnea, periodic limb movements, narcolepsy, etc.).

All of them were recorded with a complete Polysomnography throughout the night (patient characteristics are shown in Table 1). Polysomnographic recording were done when patients were habituated to treatment and had the largest decrease in the intensity of tinnitus, in the second or third months of treatment.

The Polysomnography (PSG) was carried out with the usual clinical protocol through computerized Polysomnograph (Bio PC V11/V12, Akonic S.A.), recording 10 electroencephalographic channels (frontals: F3, F4; centrals: C3, C4; parietals: P3, P4; temporal: T3, T4, T5, T6, following the internationally accepted standard denomination), electrocardiogram, electromyogram, eye movements and oxygen saturation. All EEG recordings were monopolar, recorded from scalp electrodes and separate ear electrodes A1 and A2, with electrodes referenced to linked ear lobes. The sampling frequency was set at 256 Hz. The EEG acquisition system is equipped with hardware high-pass filters with cut-off frequency at 0.5 Hz and hardware low-pass filters with cut-off frequency at 100 Hz. In addition, there is a selectable notch filter to suppress 50/60 Hz power line noise. No digital post-processing filters were applied. One researcher accompanied the patient all night, diagnosing the sleep stages online.

After beginning the night with the usual sound stimulation for tinnitus treatment, sounds are stopped after a minimum of one pass through each of the sleep stages: somnolence (stage N1), stage N2 with sleep spindles, stage N3 with slow wave sleep and sleep with Rapid Eye Movements (REM). The rest of the night the patients continue to sleep in silence (Fig. 1). All patients were started with sound stimulation because they are habituated and improve sleep onset with the sound. This enhances the disturbances caused by tinnitus, e.g., anxiety, increased sleep latency, awakenings, shallow sleep the first few hours.

### 2.2. *Sound stimulation*

Each patient was stimulated with a sound created through special software combining different types of sounds (pure tones, band noises, white noise) designed with the specific aim of being able to match their perception. Each night patients fixed the sound intensity in the same level that feel the tinnitus. These sounds are applied in a continuous way (sound stimulation for each patient is shown in Table 1, third column) [4]. Customized ear buds with flat response in the range of 0.125–16 kHz were created for each of the patients studied. These ear buds provide a reliable output, are comfortable for the patient and ensure a fixed distance between the source of sound and the eardrum. The specific sound was loaded onto the patient's devices (iPod Touch). The whole system output was measured using an artificial ear (Ear Simulator 43AC, GRAS sound and vibration) and a sound level meter (Bruel & Kjaer type 2250) and calibrated with a sound calibrator (Bruel & Kjaer type 4231@1 kHz, 94 dB SPL).

### 2.3. *Data processing*

Twenty temporal windows (2 sec duration each one) were selected in each sleep stage (N2, N3 and REM); 10 of them during silence and the other 10 during sound stimulation. Always data were compared in the same patient.

We analyzed the power spectra and the coherence in electroencephalographic waves recorded by electrodes F3, F4, T3 and T4. We compared the power spectra during noiseless (as a "Control") versus sound stimulation, exploring different electroencephalographic frequency bands (delta: 0.5–3.5 cps; theta: 4–7.5 cps; alpha: 8–12 cps) in the same sleep stage. A comparison between the left and right hemispheres (T3 vs. T4 and F3 vs. F4) was also carried out.

We studied the wave's coherence percentages, analyzing pair of intra-hemispheric electrodes (F3-T3 and F4-T4) and inter-hemispheric electrodes (F3-F4 and T3-T4). The overall coherence (considering all frequencies, from 0.5 to 12 cps, together) and the coherence of each range of frequency were considered, comparing temporal windows