claeh FACULTAD DE MEDICINA

OTOHARMONICS

# Neurophysiologic bases of tinnitus treatment with sound stimulation during sleep

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## INTRODUCTION

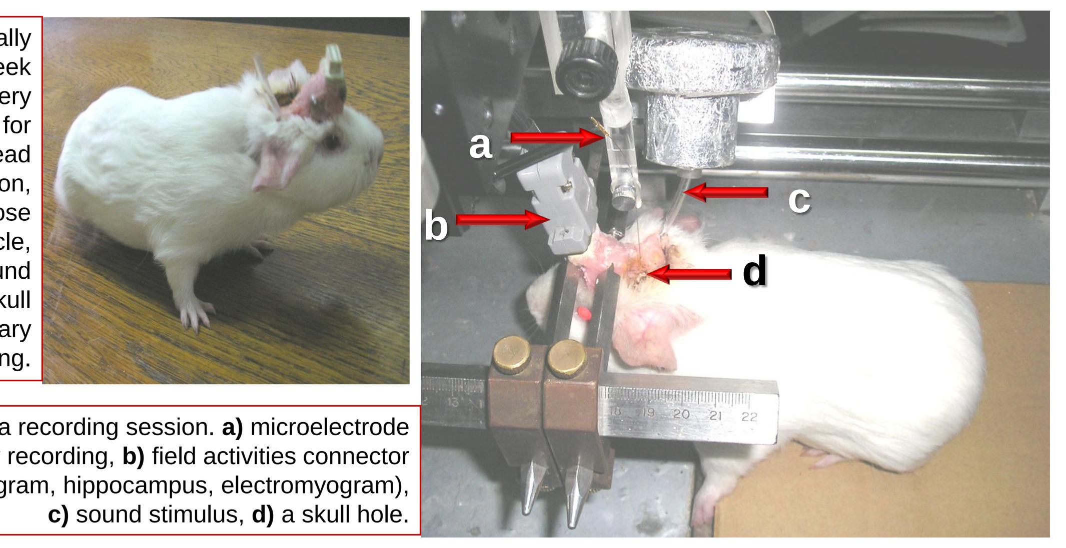
**H**earing is an important telereceptive modality active during sleep, which was fundamental in the phylogenetic evolution, acting as a continuous monitor of the environment.

**T**he auditory system has a conspicuous efferent pathway in parallel with the ascending system, functioning as an input controller (Velluti R.A. The Auditory System in Sleep. 2008. Acad Press-Elsevier).

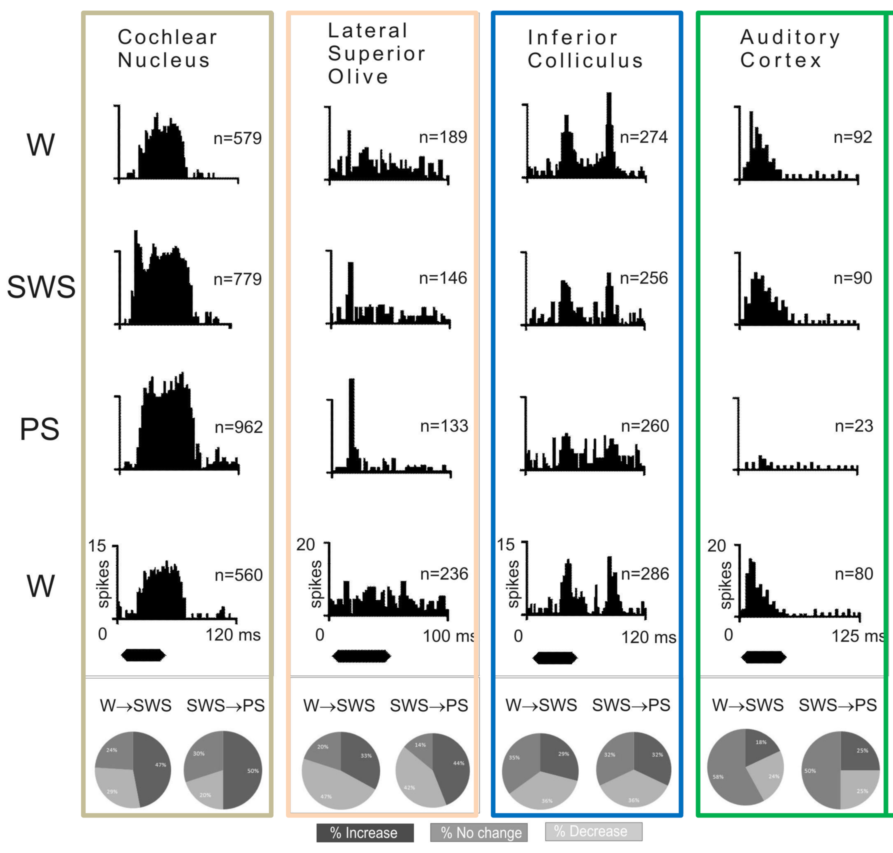
**T**he high sensitivity of the hair cells was not designed to tolerate the unnatural intensities provoked by human technologies. A minimal lesion of this delicate and sophisticated system may create a misbalance on the input information which could be misunderstood by the brain, creating the tinnitus as a phantom sensation.

## Method: auditory processing during sleep

Guinea pig cronically implanted after a week of surgery recovery with: two bars for reproducing the head stereotaxic position, electrodes to diagnose wakefulness-sleep cycle, a tube for sound stimulation and a skull hole for unitary recording.




Guinea pig during a recording session. **a)** microelectrode for unitary recording, **b)** field activities connector (electroencephalogram, hippocampus, electromyogram), **c)** sound stimulus, **d)** a skull hole.




No auditory neuron exhibited a firing stop on passing from wakefulness (W) to slow wave sleep (SWS) and paradoxical sleep (PS).

They could increase, decrease or no change the firing rate and the discharge pattern comparing different behavioral states.

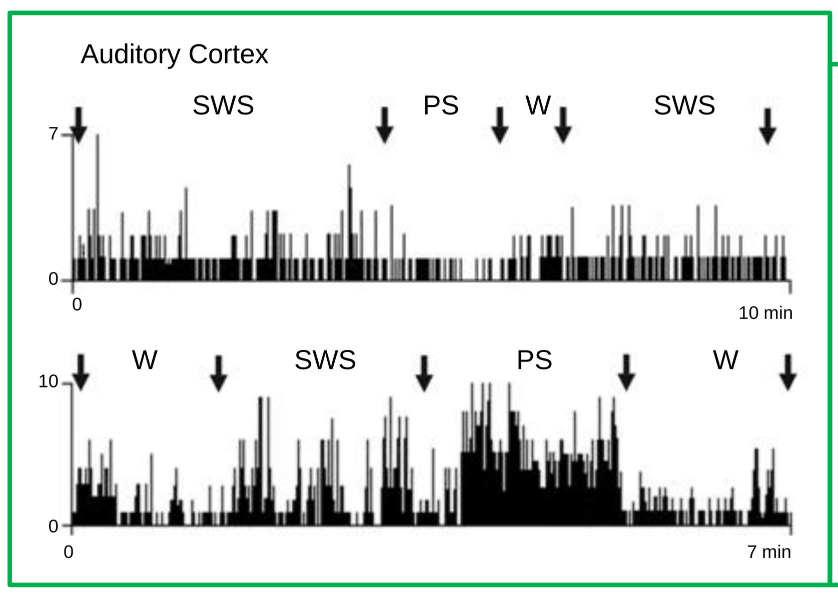
*Cell Mol Neurobiol 22 (2002): 501-516.*

*Brain Res 816 (1999):463-470.*

*J Sleep Res 4 (1995): 242-251.*

*Arch Ital Biol 132 (1994): 165-178.*

*Arch Ital Biol 130 (1992): 179-189.*



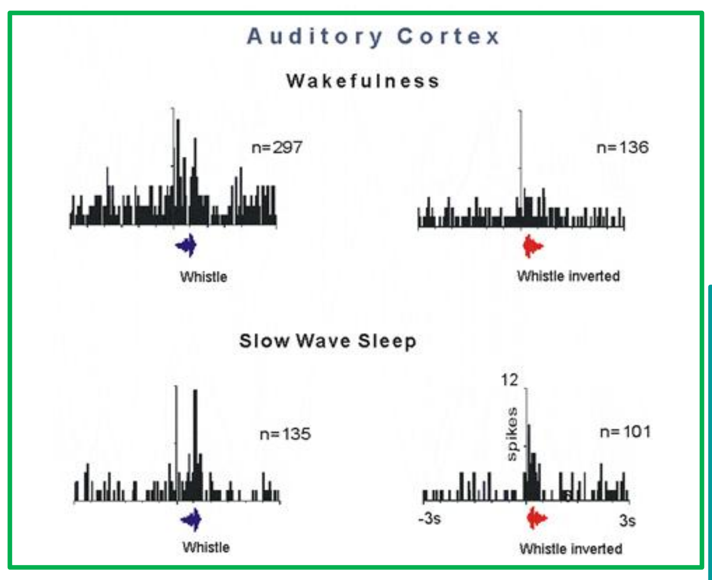

Spontaneous activity of two neurons recorded at the auditory cortex (A1) during wakefulness and sleep.

At the top, unit increases its firing during slow wave sleep (SWS).

At the bottom, the unit firing rate shows peaks during SWS and a quasi-tonic increment on passing to paradoxical sleep (PS). W: wakefulness.

*Int J Bifurcation Chaos 20 (2010): 403-407*

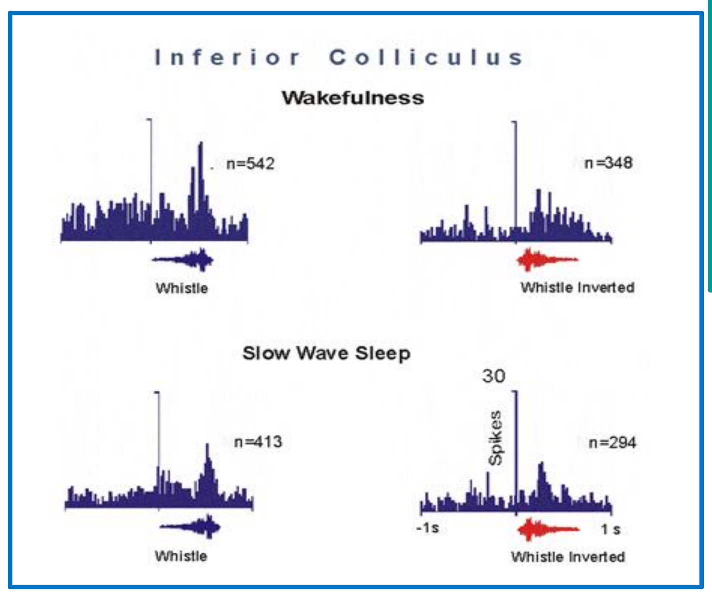
*Brain Res, 816 (1999): 463-470*

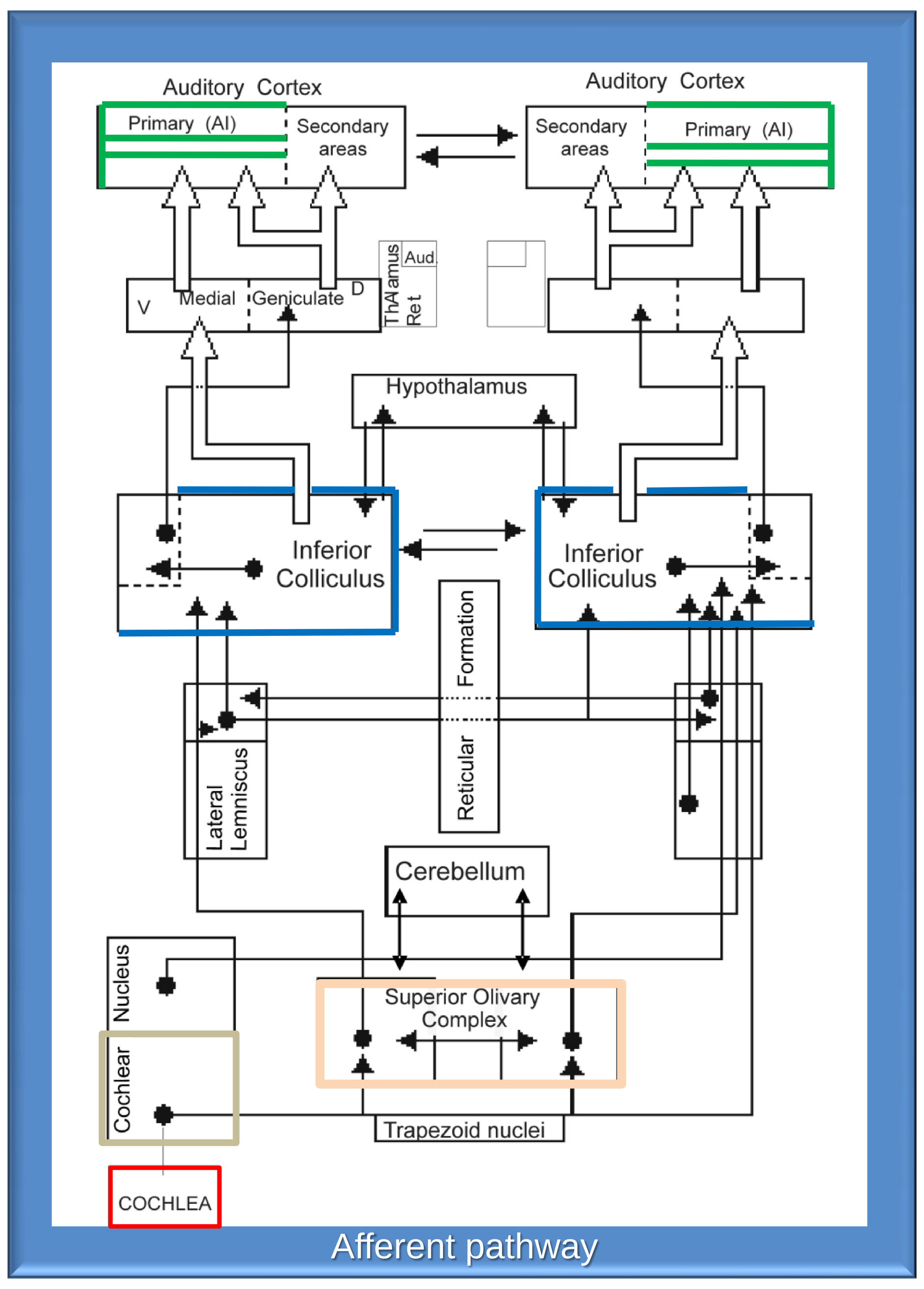



Both auditory cortex (top) and inferior colliculus neurons (bottom) show different responses evoked by the own guinea pig pre-recorded natural call when it is applied direct and reversed in time.

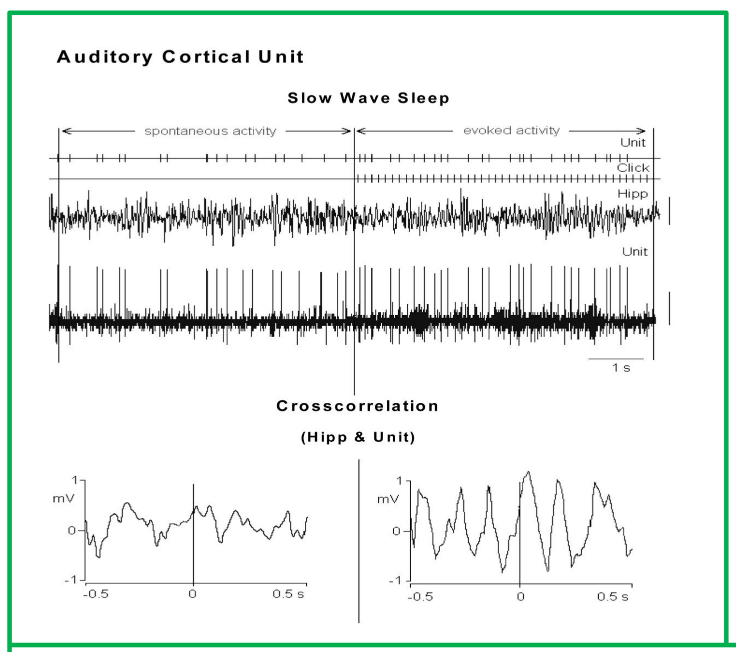
These changes are observed during wakefulness as well as in slow wave sleep.

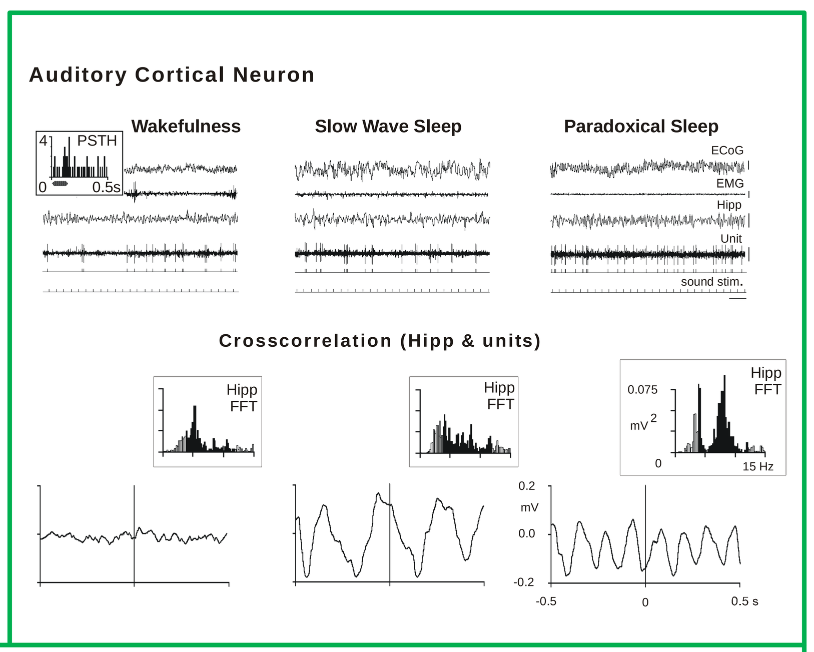
*The Auditory System in Sleep. 2008. Acad Press-Elsevier*




Afferent pathway



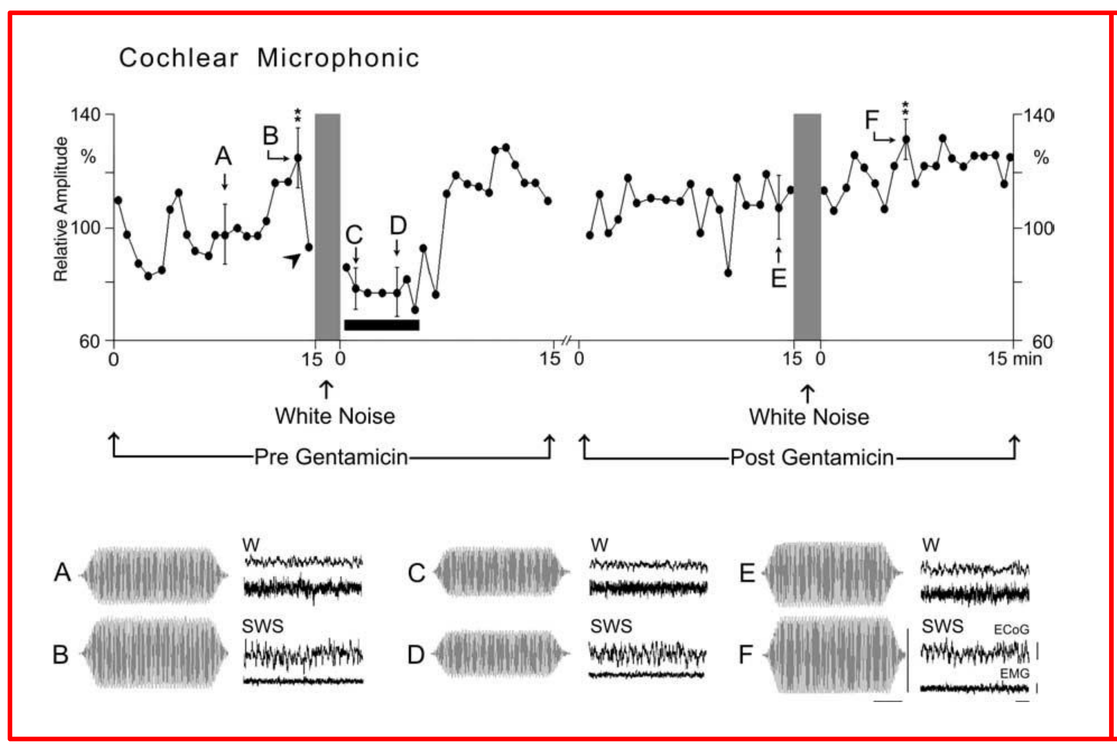




Auditory units discharge phase-locked with hippocampus theta rhythm all along the auditory pathways. This temporal correlation appears and disappears induced by sensory inputs changes and different CNS influences as wakefulness-sleep cycle.

At the left, phase-locking appears when start the sound stimulation during slow wave sleep.

At the right, unitary discharge provoked by a constant sound change its temporal correlation with theta depending on the behavioral state.

*Int J Bifurcation Chaos 20 (2010): 403-407; Sleep Res OnLine 4 (2001): 51-57; Biol Sign recept 9 (2000): 297-308.*



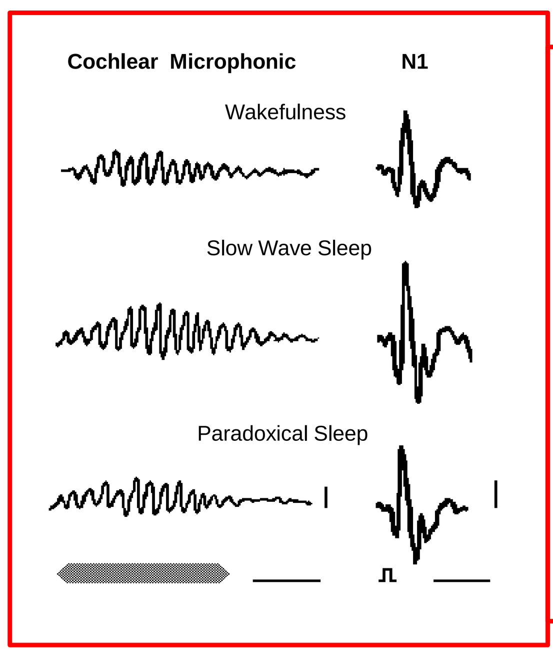

White noise effect on the cochlear microphonic (CM) amplitude during pre- and post-gentamicin administration.

The black bar indicates the change to a less variable pattern and a significant decrease in CM amplitude ($p < 0.05$) after white noise presentation between points C and D and the previous one (arrowhead).

After gentamicin administration (right) the white noise effect did not appear.

During the white noise effect (C, D) the sleep/waking cycle does not modulate the CM amplitude. This modulation reappears when white noise effect was blocked by gentamicin.

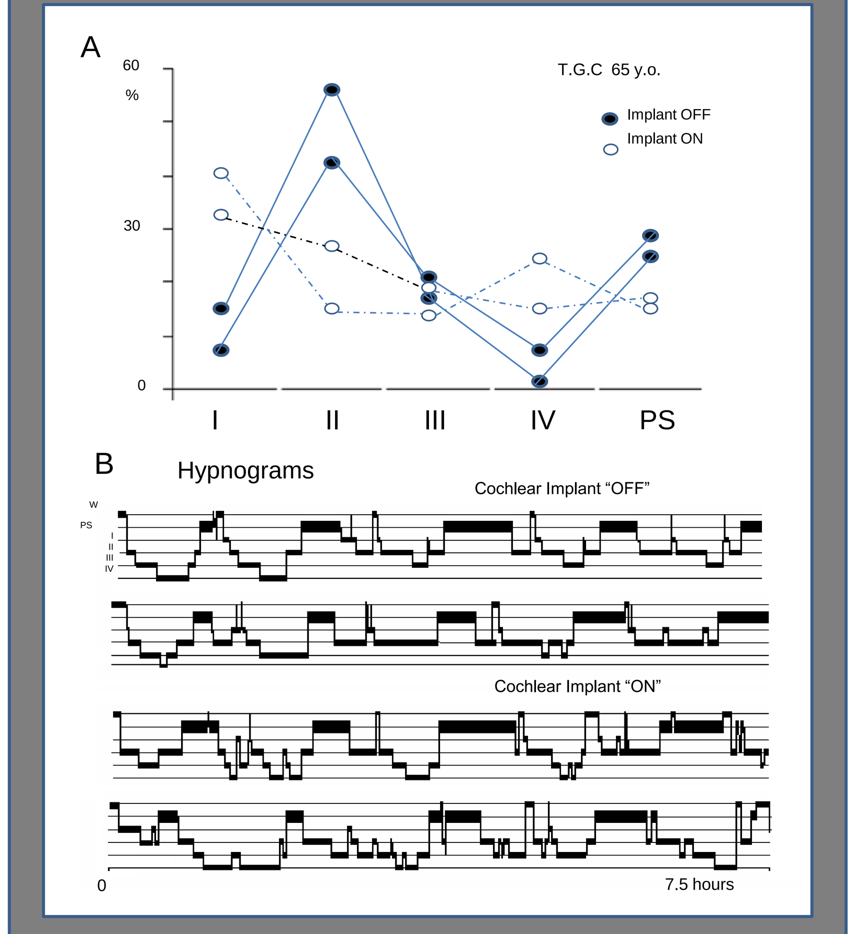
*Hear Res, 194 (2004) 25–30.*




Cochlear microphonic and compound auditory nerve action potential amplitud of a quiet waking period increase during slow wave sleep and decrease again during paradoxical sleep.

*Hear Res, 39 (1989) 203–208.*

## Human study




Example of sleep stages organization in a deaf implanted patient.

A. The filled circles show control recording nights with the implant OFF, that is, recorded as a deaf patient, and the open circles, implant ON, that is, as a hearing patient. Sleep stages are I, II, III, IV (equivalent to SWS or non-REM sleep), and PS (equivalent to REM sleep).

B, Hypnograms of each recorded night.

*J. Sleep Res 19, (2010) 585–590*

## RESULTS and CONCLUSIONS

♦ Cochlear potentials exhibited amplitude increment during slow wave sleep (SWS), compared with wakefulness (W) and paradoxical sleep (REM).

♦ Fifty percent of the auditory cortical units recorded during SWS and REM maintained a firing similar to the W while 50% increased or decreased their firing when the animal was asleep.

♦ Neuronal discharge rate shifts were found in the brainstem nuclei in different percentage than in the auditory cortex.

♦ The auditory neurons that increase/decrease firing in sleep are postulated to be engaged in some sleep processes, participating in sleep-active cell assemblies/networks.

♦ No auditory neuron exhibited a firing stop on passing to sleep.

♦ Hippocampal theta rhythm has temporal relationship with auditory units (phase-locking) all along the auditory pathway, appearing as a time-giver to organize auditory storage, also during attention changes and sleep.

♦ In human studies, we demonstrated that sleep architecture changes when profound post-lingual deaf patients with an intra-cochlear implant maintained the implant "on" during the night.

♦ Sleep and sound are closely related. As well as regular environmental auditory stimuli (e.g. mother lullaby) facilitate sleep, sound stimulation during sleep could improve sleep disorders caused by tinnitus and decreases tinnitus perception.

♦ Since the auditory processing happens during both wakefulness and sleep, the reorganization of neural networks –taking advantage of neural plasticity- could be induced by sound stimulation during sleep.