

Phantom Sound of Tinnitus: Human Brain Imaging and Animal Models

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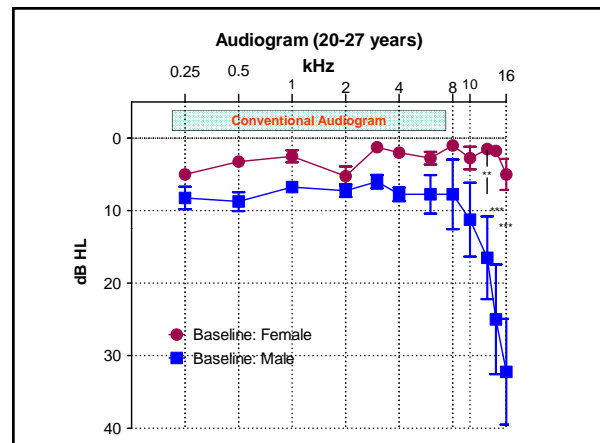
Inner Ear Damage Induces Tinnitus

- **Cisplatin**
- **Noise Exposure**
- **Presbycusis**
Significant Central Effects
 - **Cell Death in Hippocampus**
 - **Suppress Neurogenesis**
 - **Decrease synapses with age**

Tinnitus & Hearing Loss

555 Patients (Nicolas-Puel et al. 2002)

• Presbycusis	42%
• Noise Trauma	22%
• Meniere's	6.3%
• Sudden Onset	4.0%



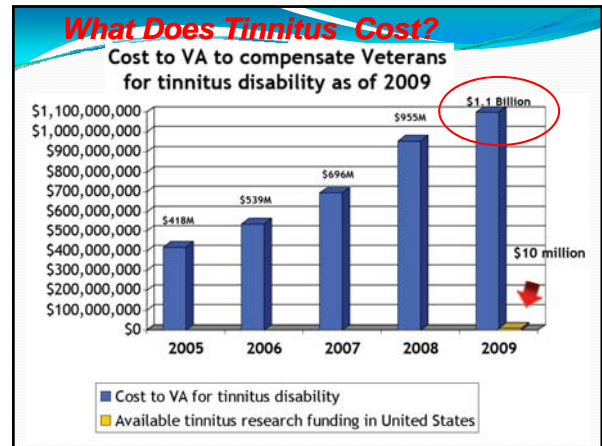
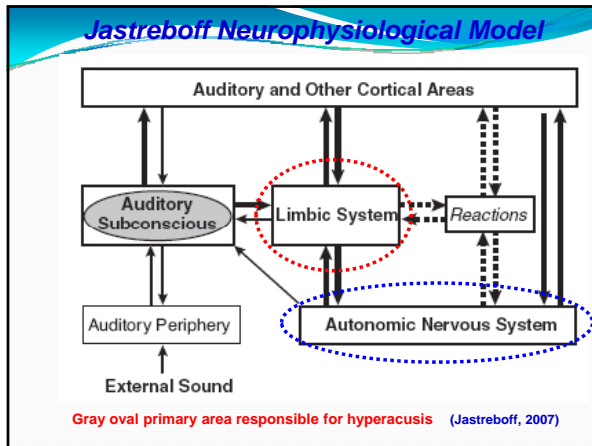
Tinnitus Who Gets it?

- ✓ 12-14% of general population-tinnitus
 - ✓ 1 of 4 seek medical treatment
 - ✓ 1% experience-debilitating tinnitus
- ✓ 50% combat soldiers develop tinnitus
- ✓ 55% Patients with Cochlear Implant
 - ✓ Severe or debilitating tinnitus

- **Hyperacusis-Loudness Intolerance**
 - ~70 of Tinnitus patients have hyperacusis

Debilitating Tinnitus

"I remember waking up on the morning of April 12, 1994, with a high-pitched squealing in my ears, I thought it was the microwave going off downstairs, but I wasn't able to find the sound anywhere. Ultimately, I went into a state of depression and couldn't even work. I have spent the last four years looking for help, but I have been told to learn to live with it."



Tinnitus Perceived in Damage Ear

-Tinnitus Generator in Ear

Tumor-Cut Auditory Nerve

- **No Activity Sent to Brain**
- **Tinnitus Persists**

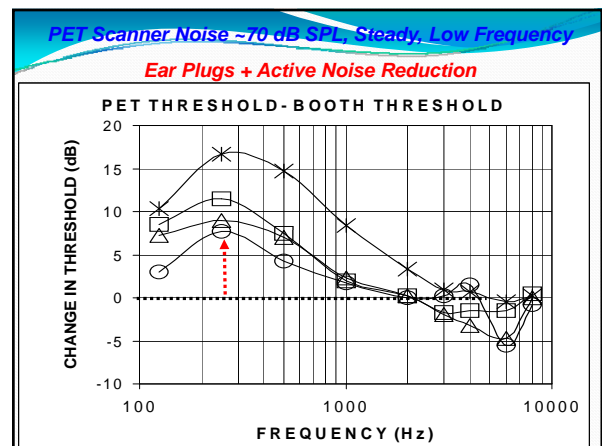
• **Maybe Tinnitus Generated in CNS**

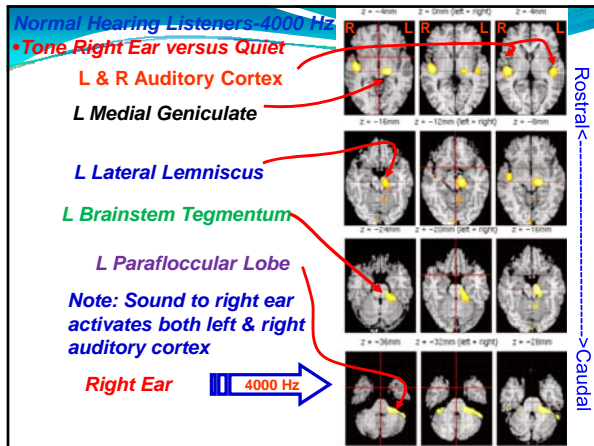
Positron Emission Tomography

- Utilizes radioisotope-isotope is unstable
- Gives off positrons (positively charged electron)
- Annihilation-occurs when positron (+) collides with electrons .
- Disintegration of positron gives off 2 gamma rays that move in opposite directions

Positron Emission Tomography (PET)

- **Functional Imaging-Sound Evoked**
- ^{15}O labeled water-estimate rCBF, neural activity
- **Conditions**
- **Rest-Quiet scanner**
- **Tone bursts**
- **SPM-Statistics**



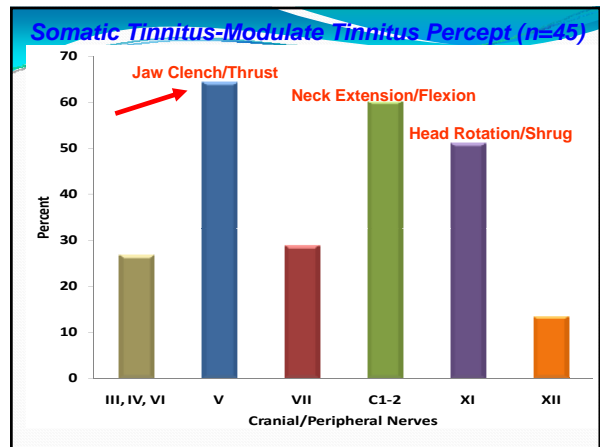
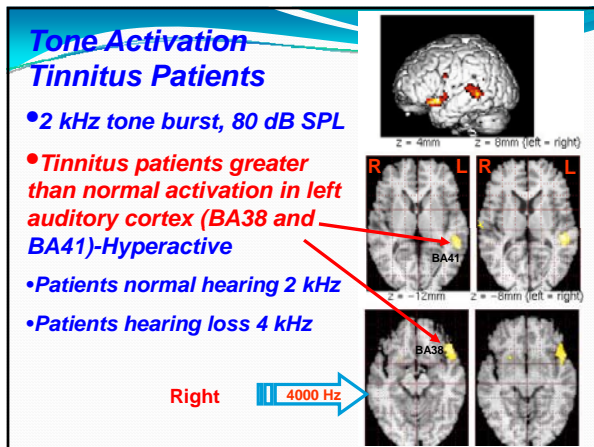
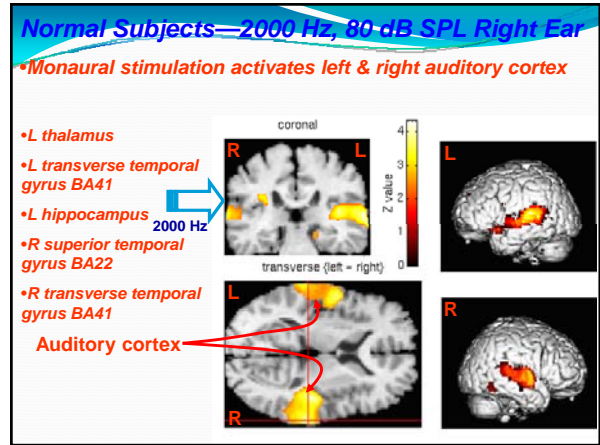
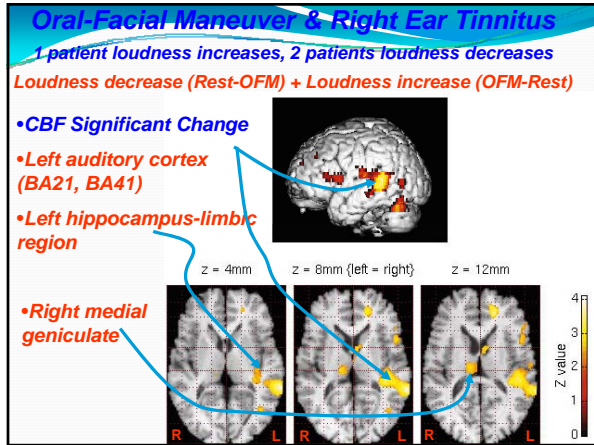


Somatic Tinnitus

-Modulate Tinnitus with Oral Facial Maneuver

Conditions

- Resting Brain Activity
- 2000 Hz tone, 80 dB
- OFM-Jaw Clench



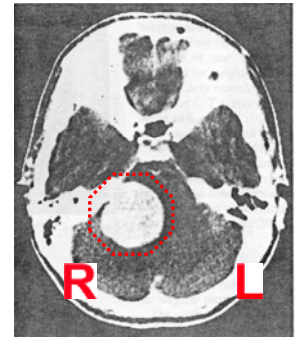
Gaze-Evoked/Modulated Tinnitus

- Tumor on Acoustic-Vestibular Nerve
- Surgical Removal
 - Cut Auditory Nerve: Deafness
- Gaze-Evoked Tinnitus
 - Lateral gaze: tinnitus appears/get louder
- 125 Gaze-Evoked Tinnitus Patients
 - Acoustic Neuroma Newsletters

First Case Report-Whittaker (1982)

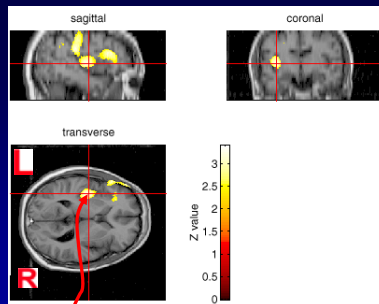
Contrast-enhanced CT scan

- 44 year old woman
- 3.6 cm tumor
- GET - right lateral



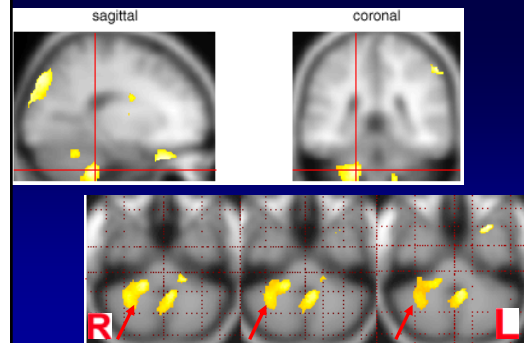
Single subject SPM analysis

Left AN, gaze to left.
Clockwise rotatory nystagmus on R gaze



- Activation-Angular Gyrus Next to Auditory Cortex

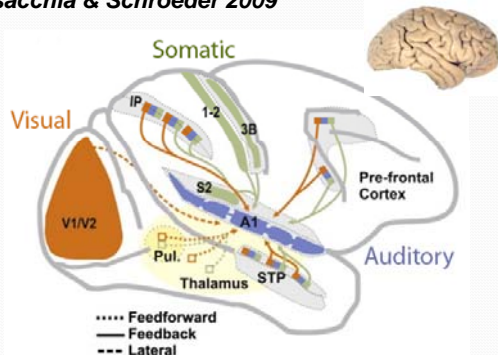
3 Subject SPM, R Acoustic Neuroma



Brainstem-near Cochlear Nucleus & Superior Olive

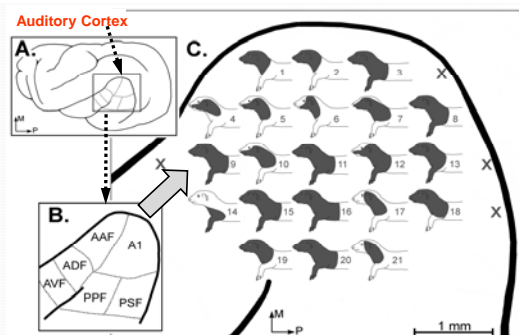
Pre-Existing Somatic and Visual Input to Auditory Cortex in Non-Human Primate

Musacchia & Schroeder 2009



Somatosensory Invasion of Deaf Auditory Cortex

Allman & Meredith, 2009



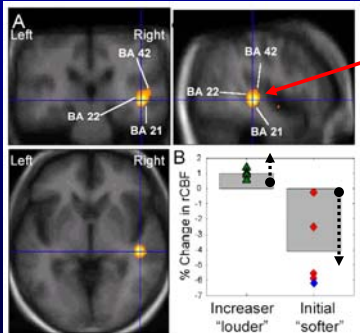
Lidocaine & Tinnitus

- **Otology-Suppresses Tinnitus!**



- **Cardiology-Induces Tinnitus!**

- **Lidocaine-Increases & Decreases Tinnitus Loudness**
- **Reduction in tinnitus decrease in rCBF**
- **Increases in tinnitus increase in rCBF**



Right Auditory Cortex-Only region that shows a change in rCBF with change in tinnitus loudness

Tinnitus Trigger

Loss Sensory Input

- Alters Central Auditory System
- Abnormal Plasticity
- Analogous to Phantom Limb Pain

Animal Models

- Physiology
- Biochemical
- Molecular



Animal Model of Tinnitus (SIPAC)

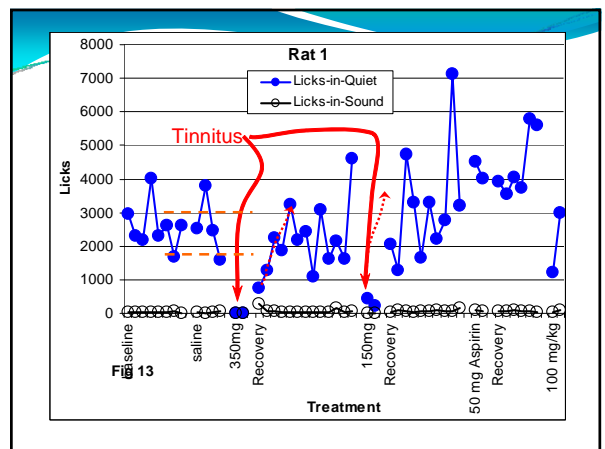
Schedule Induced Polydipsia (SIP)

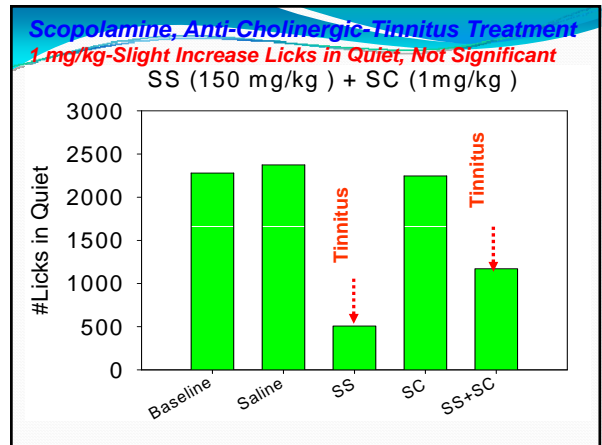
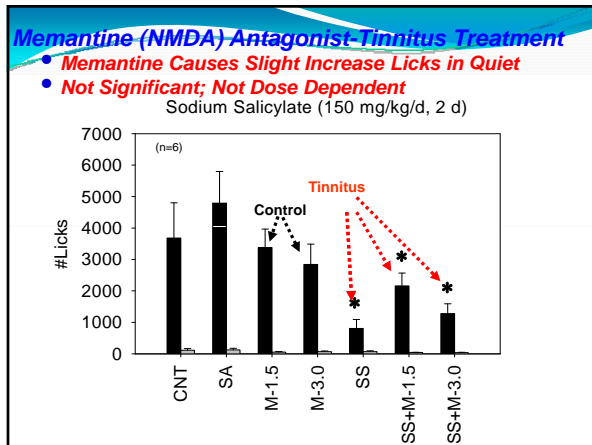
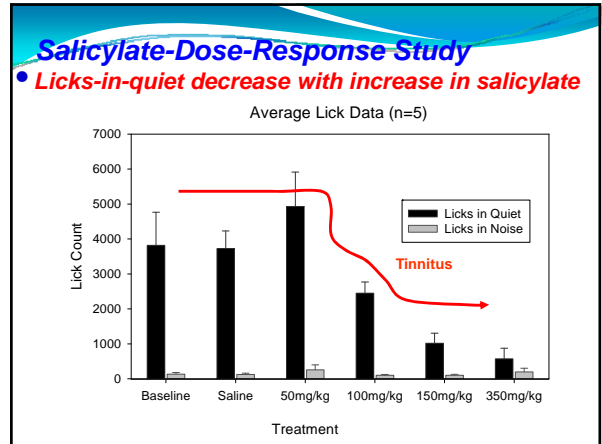
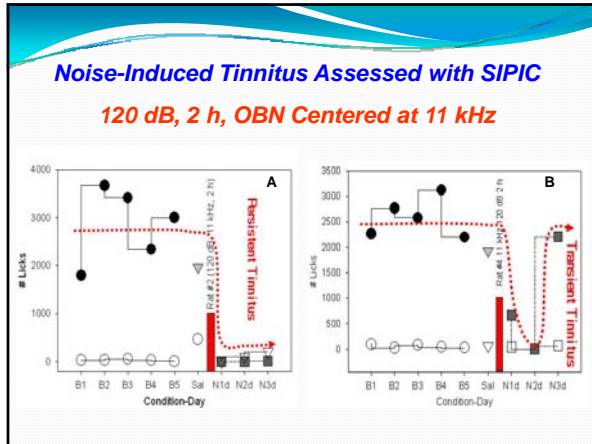
- Intermittent pellet delivery (1/min) is used to drive drinking in food deprived rats
- **Avoidance Conditioning (AC)**

Drinking (Licks) is put under stimulus control by pairing sound with foot shock

Schedule Induced Polydipsia-Avoidance Conditioning

Quiet = Lick-for-Water Food Pellet 1/minute

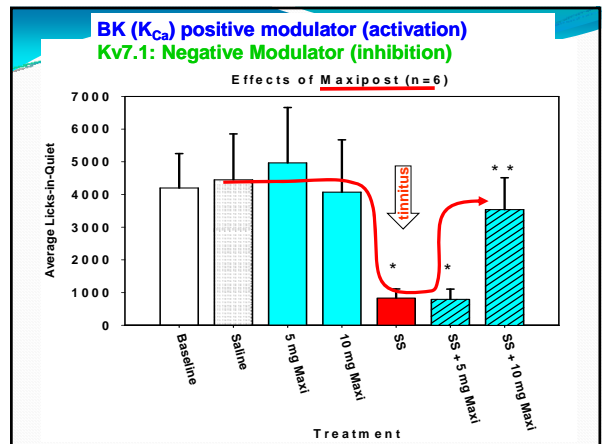



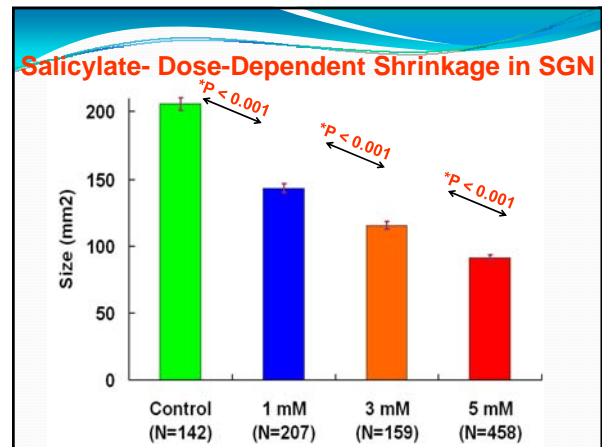
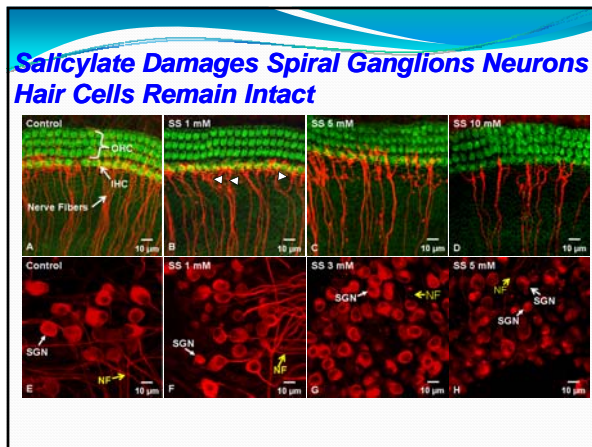
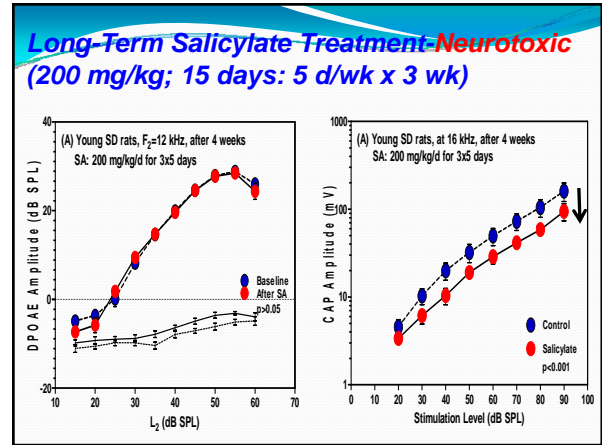
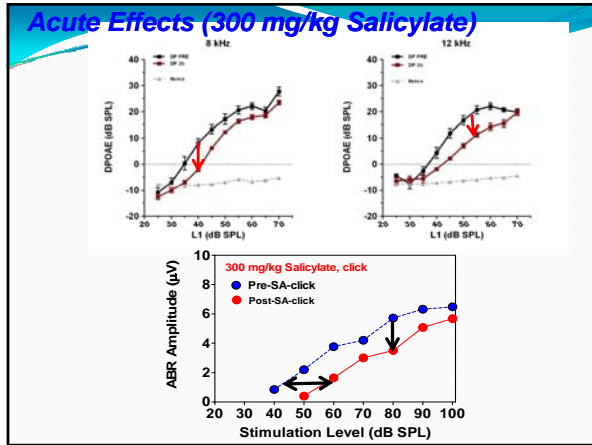
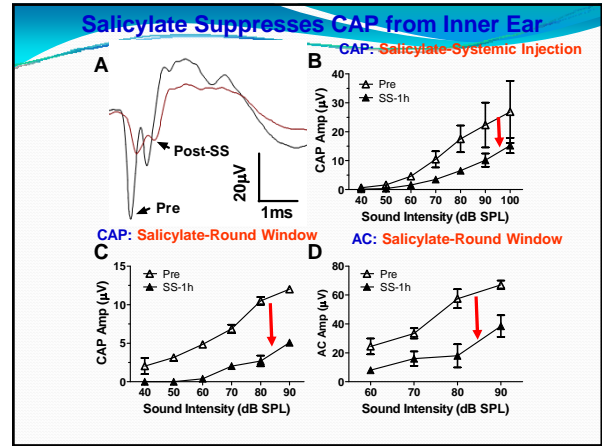
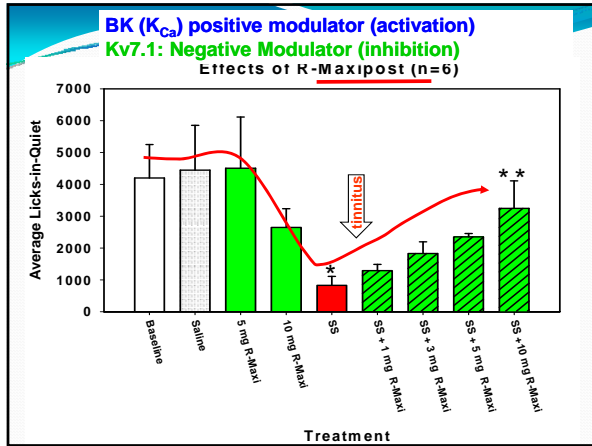


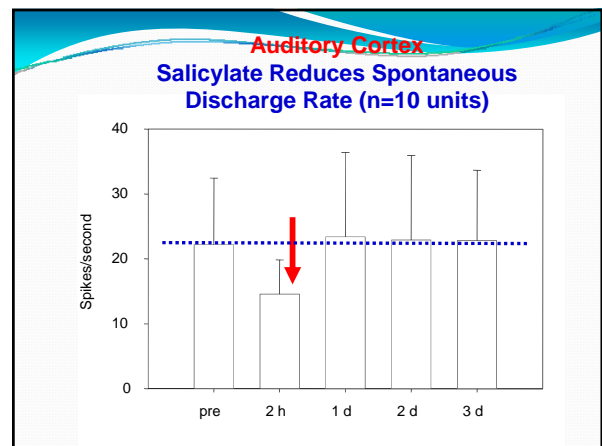
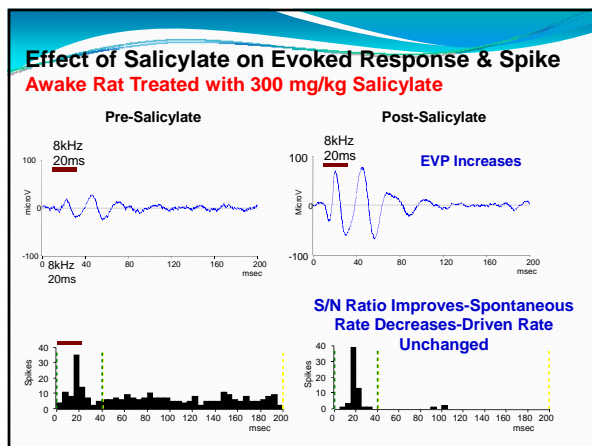
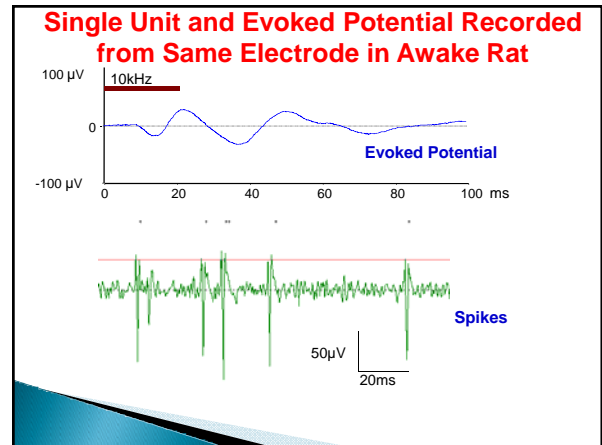
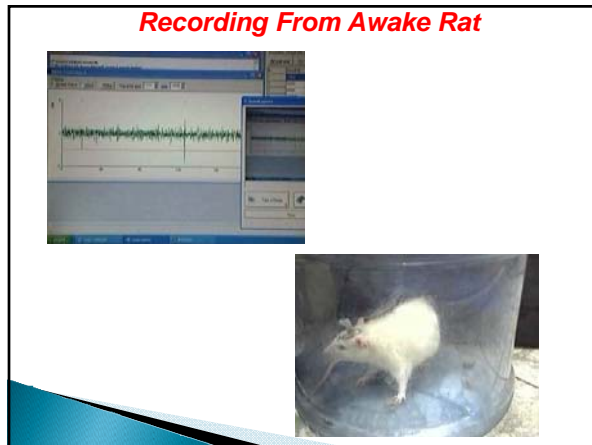
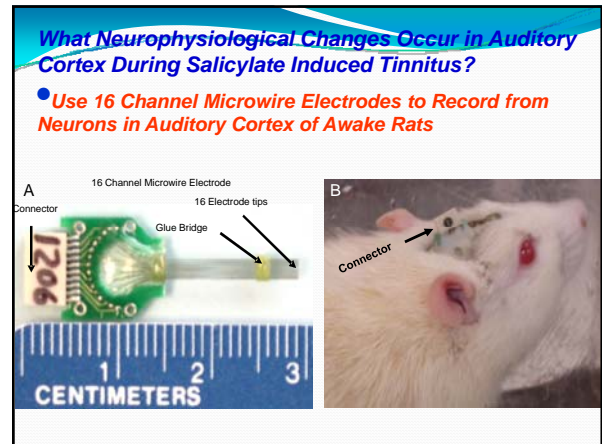
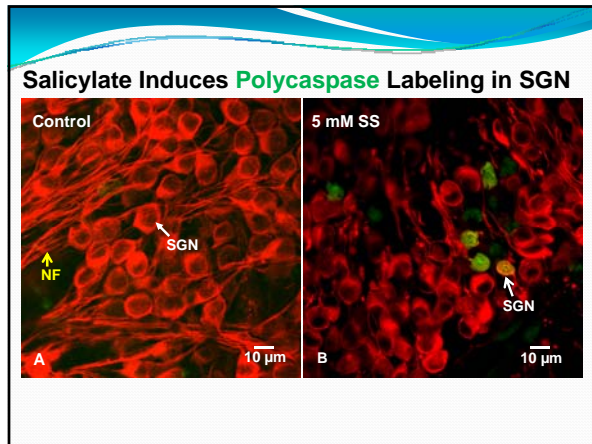
Potassium Channels

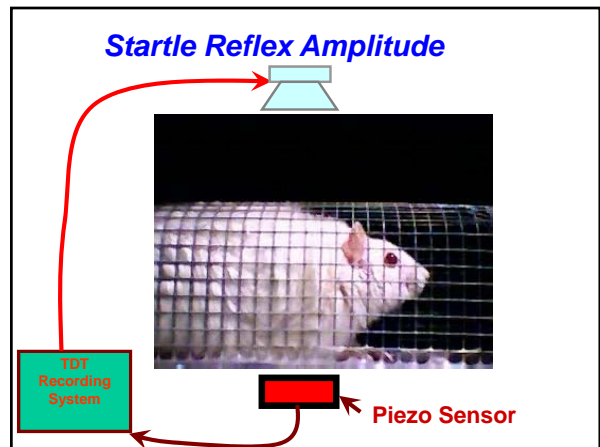
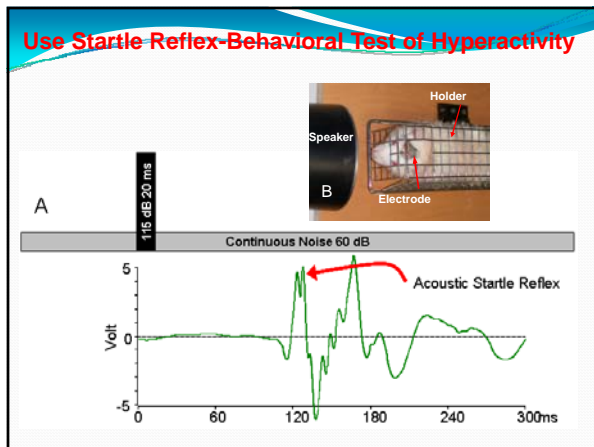
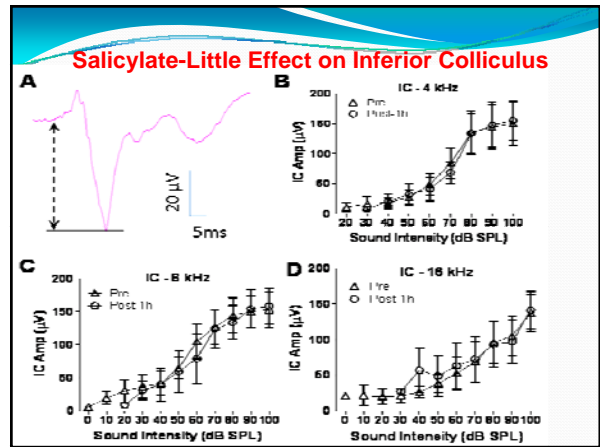
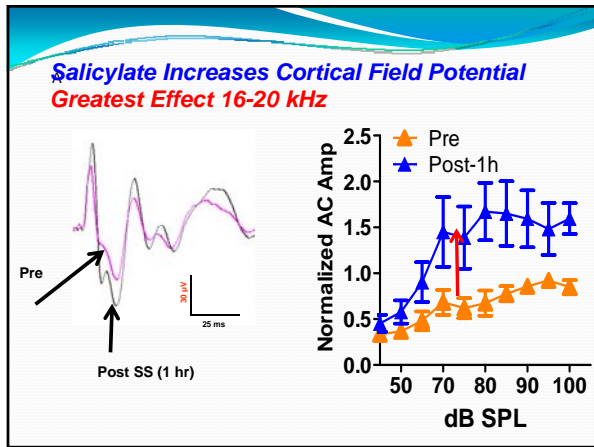
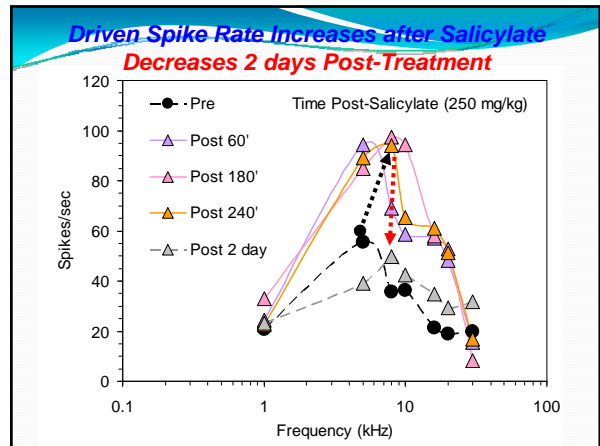
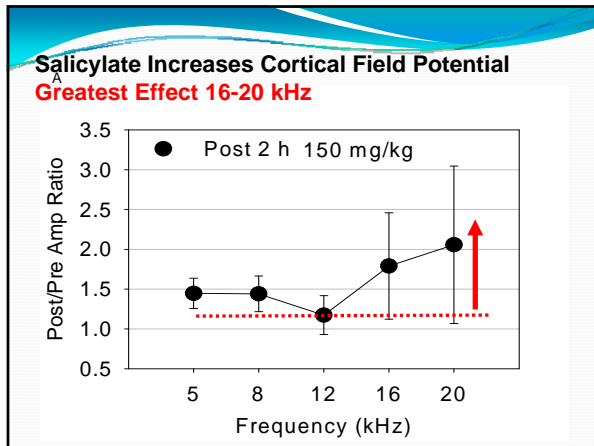
- Greatest Ion Channel Diversity
- Important targets for therapy
- Kv7.2-7.5 in cochlea

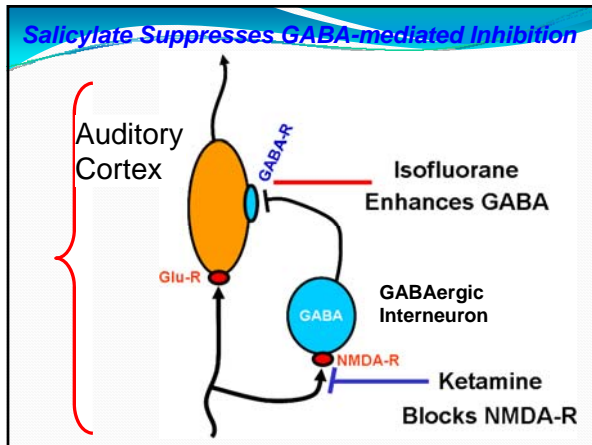
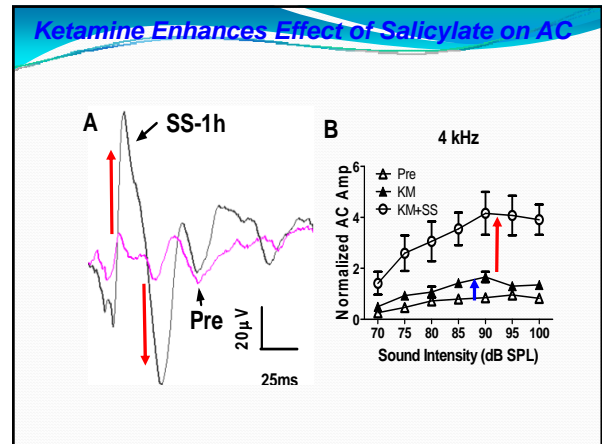
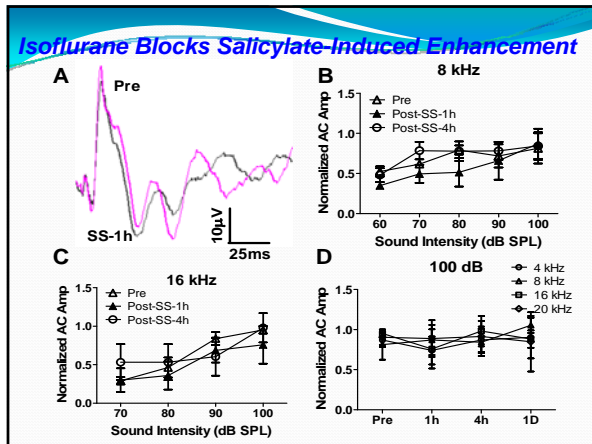
Drug	Kv7.2-7.5	Kv7.1	BK (K _{Ca})
Maxipost (BMS 204342)	Positive modulator (activation)	Negative Modulator (inhibition)	Positive modulator (activation)
R-Maxipost	Negative modulator (inhibition)	Negative Modulator (inhibition)	Positive modulator (activation)











Tinnitus-Loss of Cochlear Input

- ✓ Cochlear damage reduces input to central auditory system (gas pedal)
- ✓ Auditory system turns up its gain (Reduced Inhibition) to compensate for hearing loss and lack of cochlear input

CNS Inhibition Decreased (indicated by a red upward arrow)

Cochlear Activity Decreased (indicated by a blue downward arrow)

Fifth International TRI Tinnitus Conference

The Neuroscience of Tinnitus

Holiday Inn Grand Island Resort and Conference Center
Grand Island, New York, U.S.A.
August 19-21, 2011

To obtain a Registration Form, e-mail or call Carol Altman (caltman@buffalo.edu; 716-829-5291) or you can download the form from <http://wings.buffalo.edu/faculty/research/chd/>

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