Tuning the Brain: Neuromodulation as a Possible Panacea for treating non-pulsatile tinnitus?

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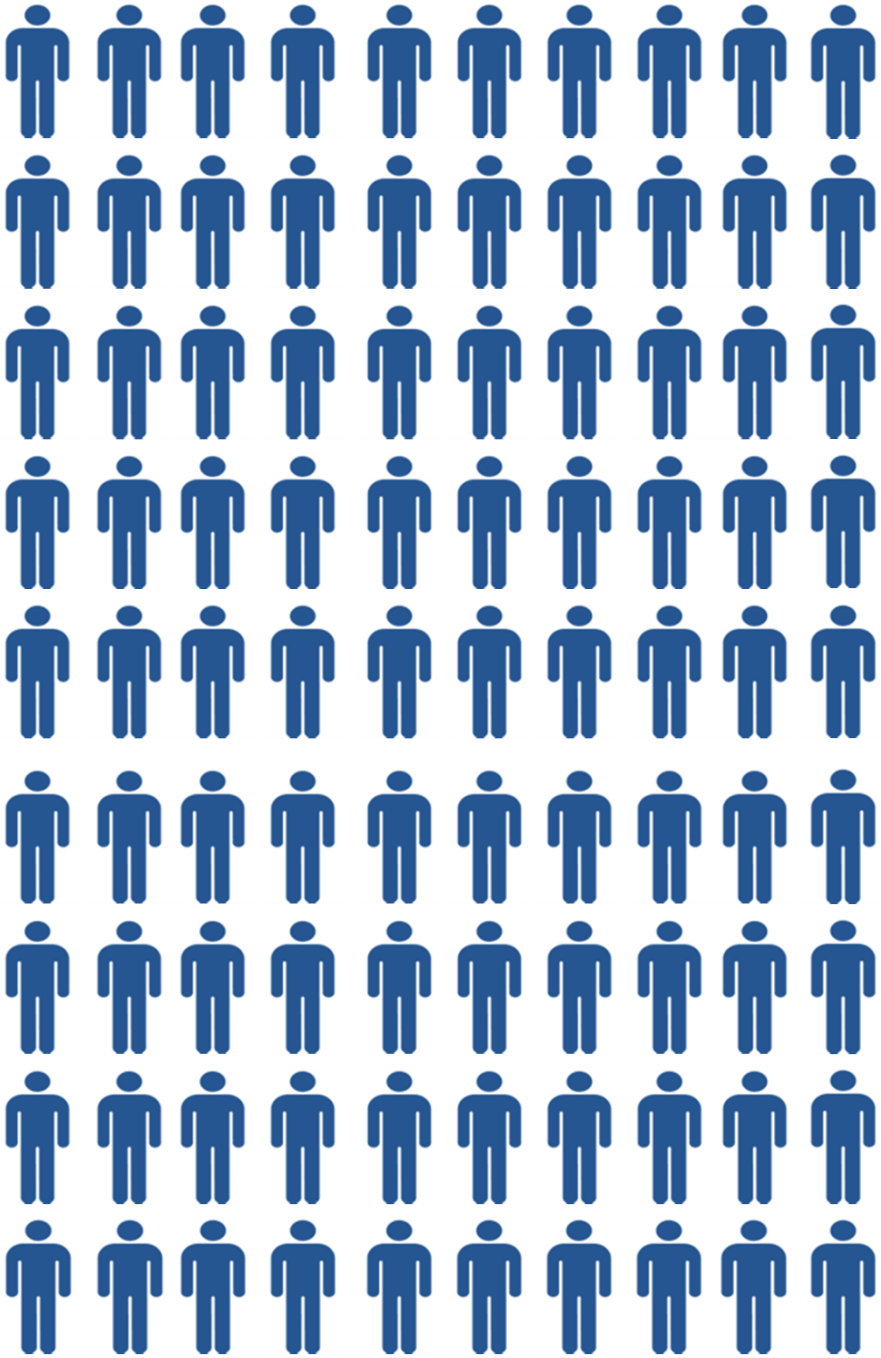
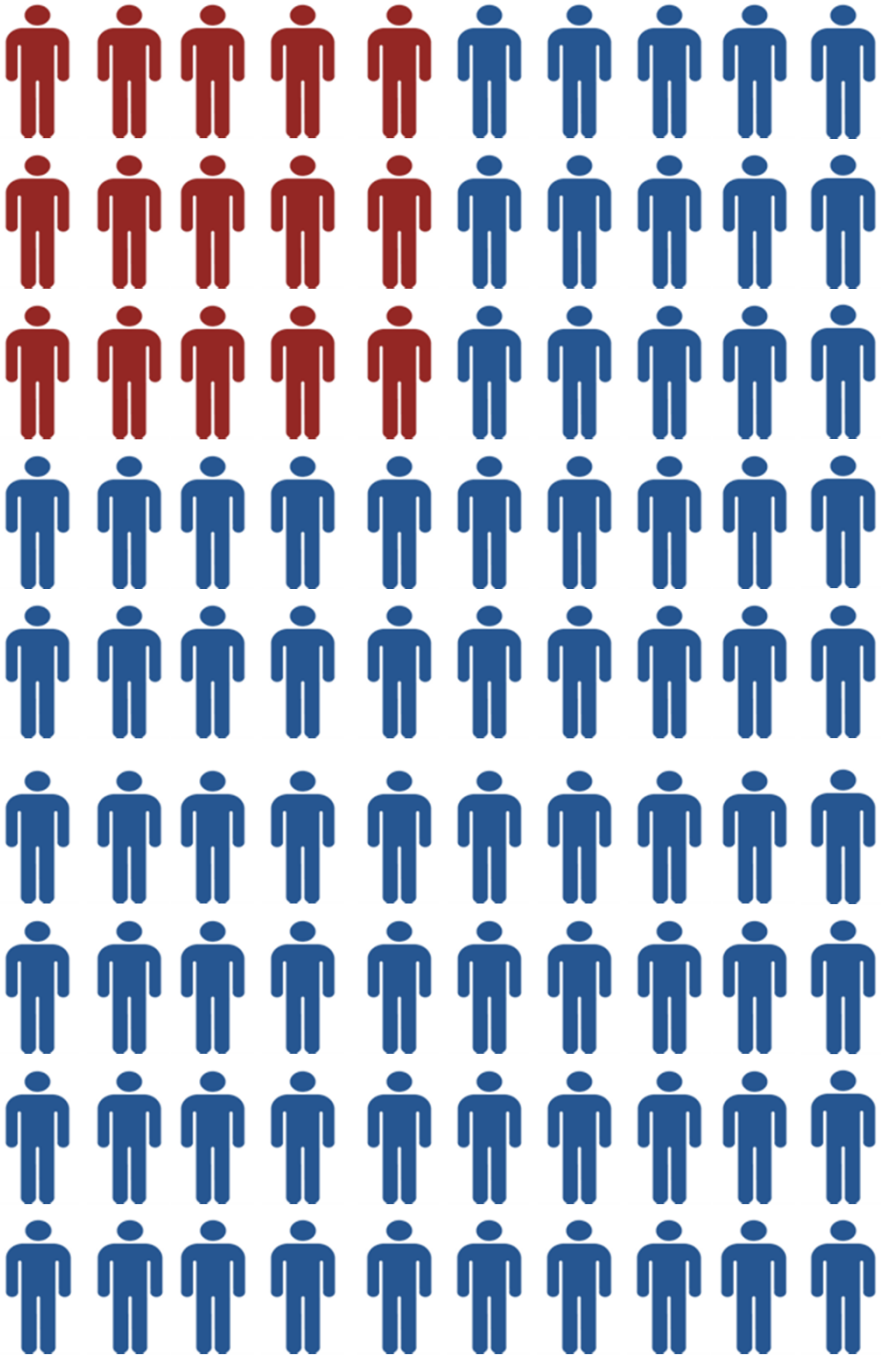


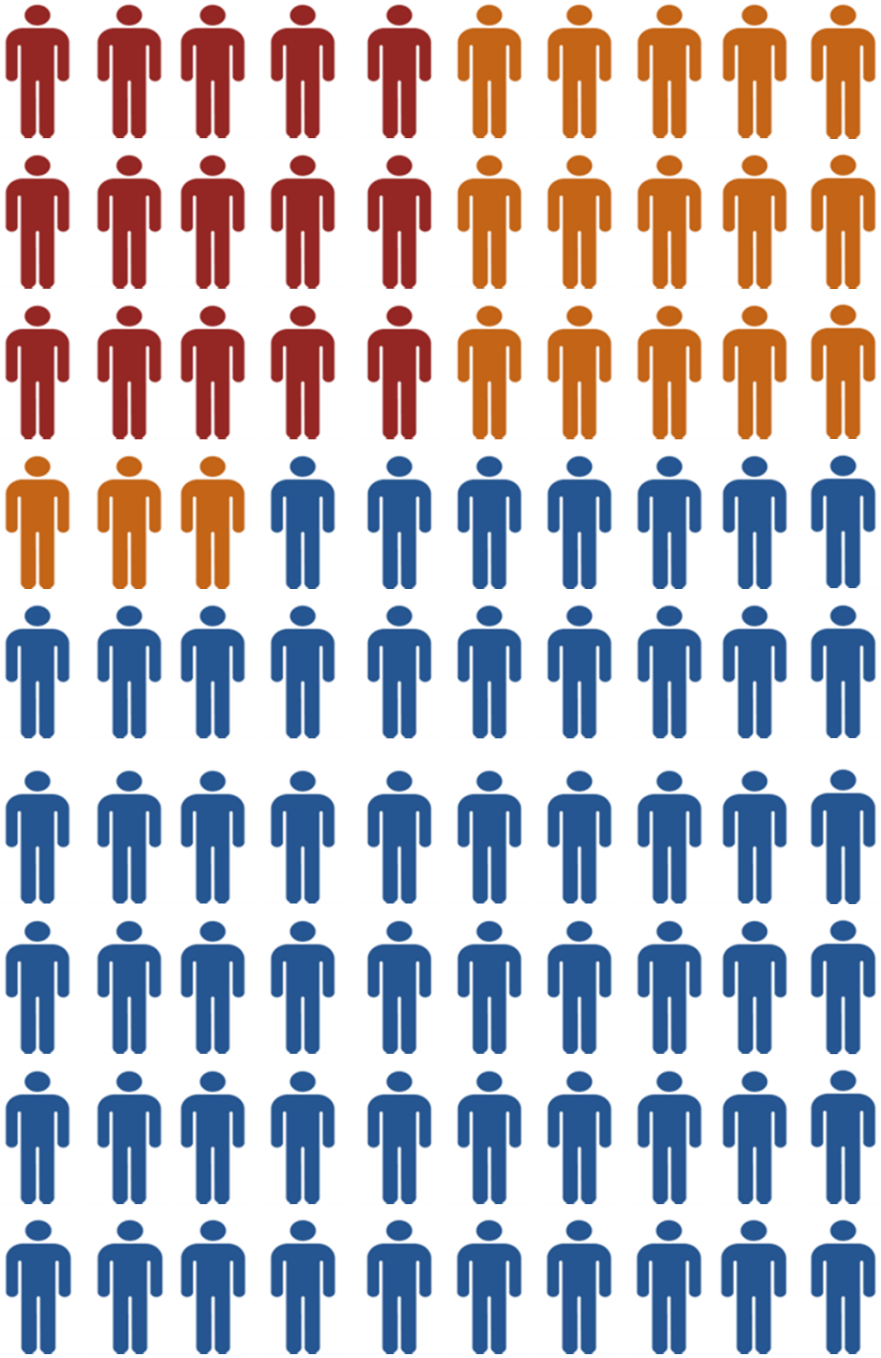
Tinnitus

- At some point most people experience tinnitus
- This has been related to listening to loud music, use of medication, trauma or other causes
- This sensation is reversible and subsides approximately between a few seconds to a few days



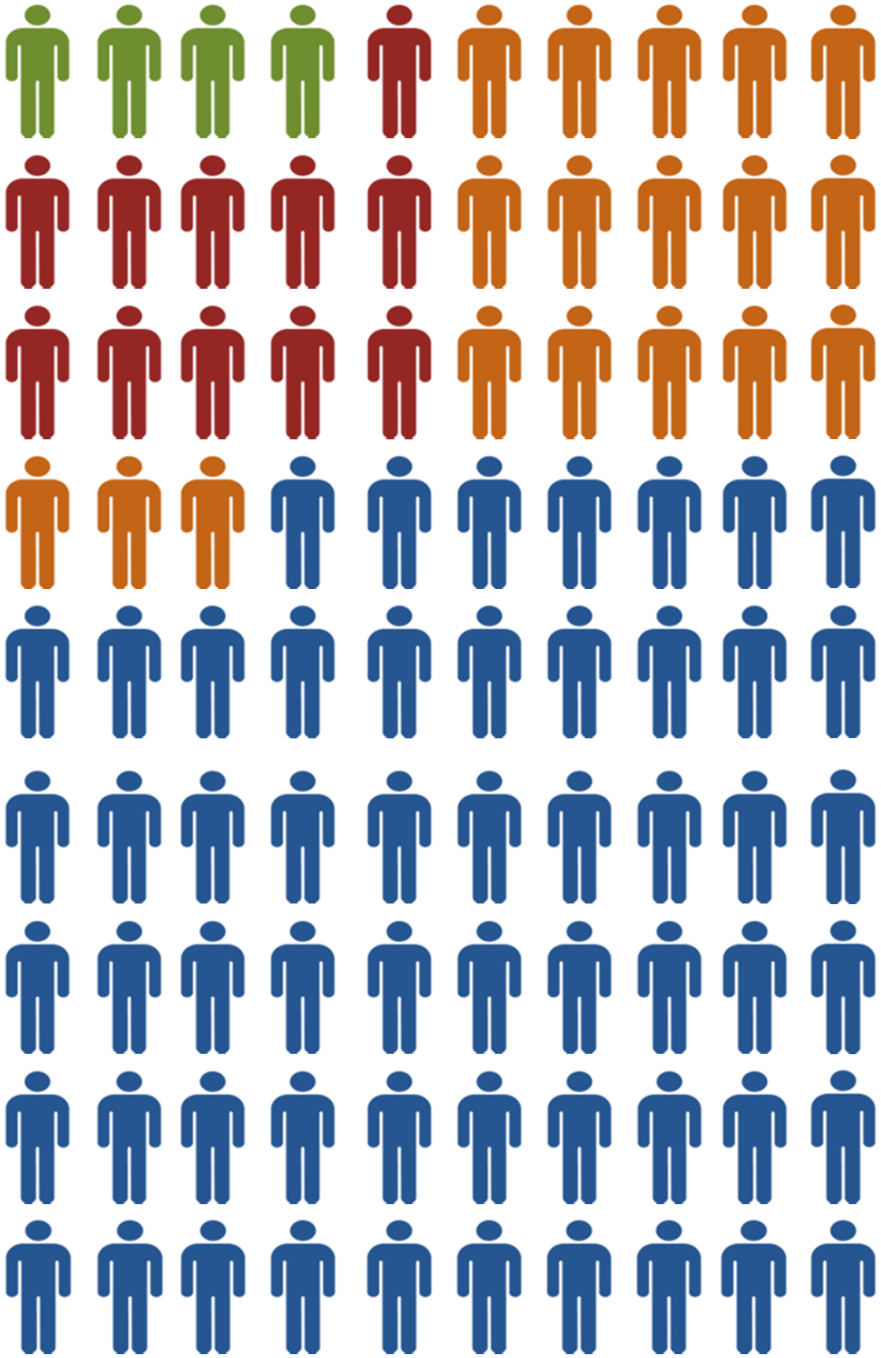
Tinnitus

- In an adult population 10 to 15% perceives tinnitus continuously



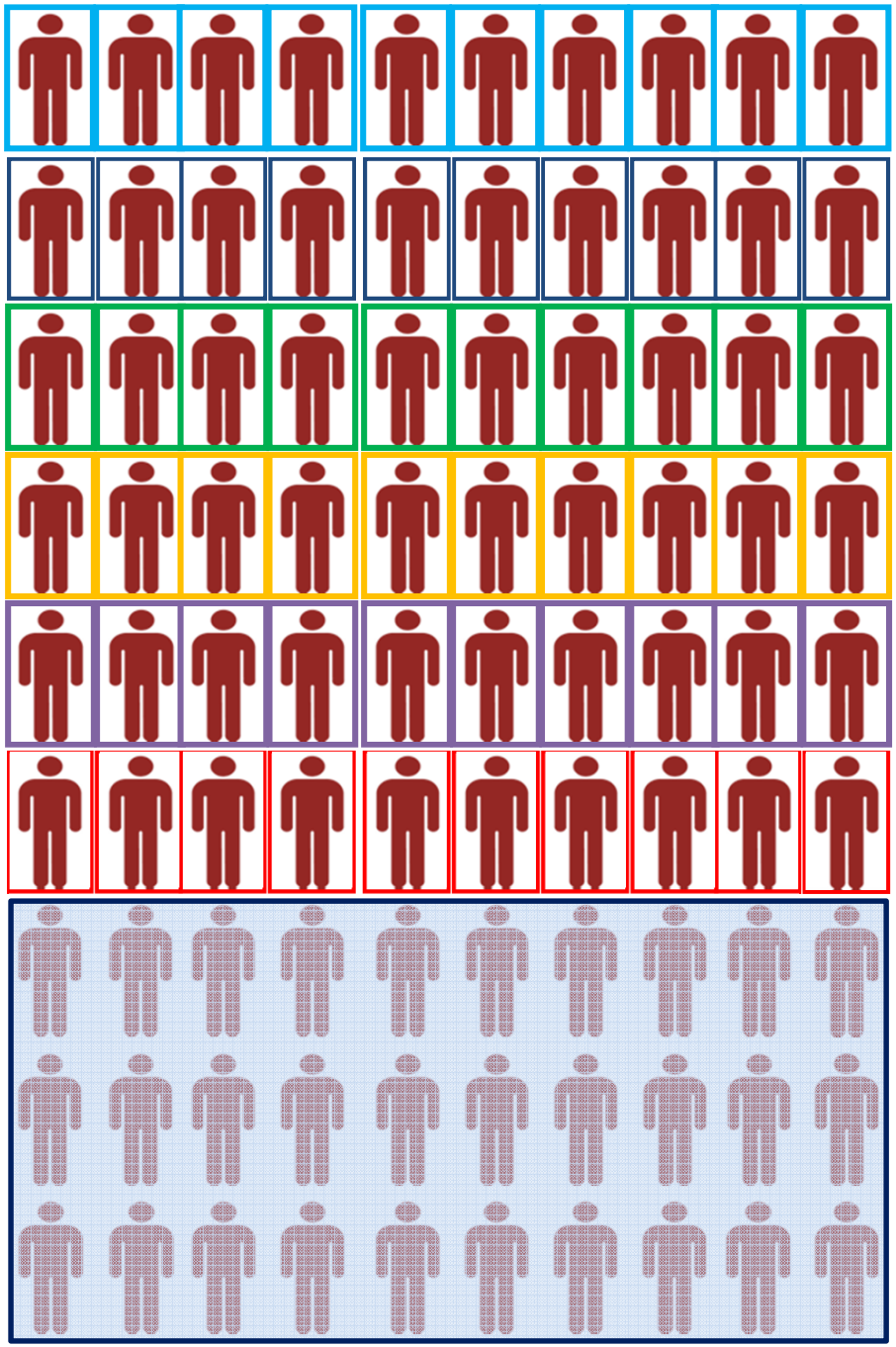
Tinnitus

- In an adult population 10 to 15% perceives tinnitus continuously
- Increasing up to 33% in the elderly population



Tinnitus

- In an adult population 10 to 15% perceives tinnitus continuously
- Increasing up to 33% in the elderly population
- Up to 25% of the affected people report interference with their lives as tinnitus causes a considerable amount of distress

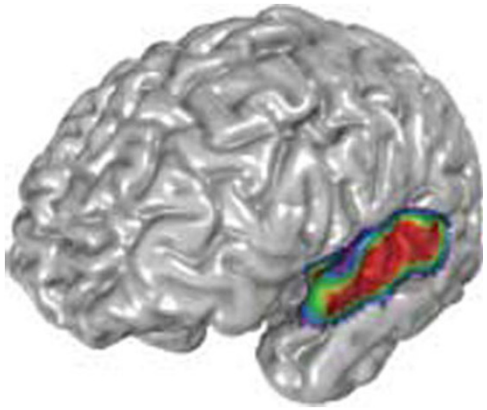


Tinnitus treatments

- Counseling
- Hearing aid
- Masking
- Active amplification
- Medication
- Neuromodulation (Non-invasive)

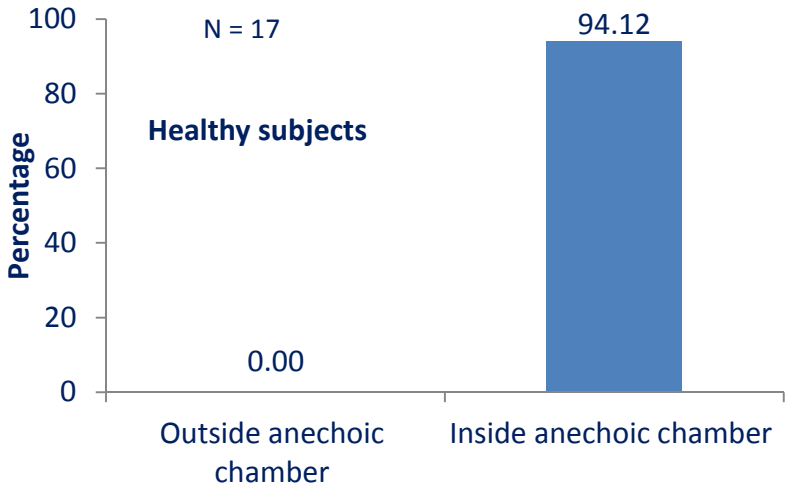
- **30% no treatment**
- Most treatment are based on symptomatic relief.
- **No causal treatment**
- **Subtypes?**

Loss of auditory input

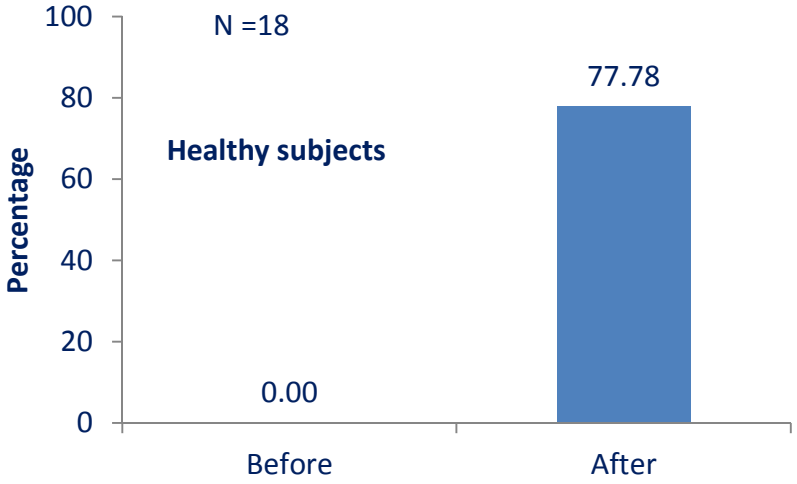


Loss of auditory input sets up a cascade of neurophysiologic changes in the central auditory system culminating to the perception of a phantom sound

Loss of auditory input

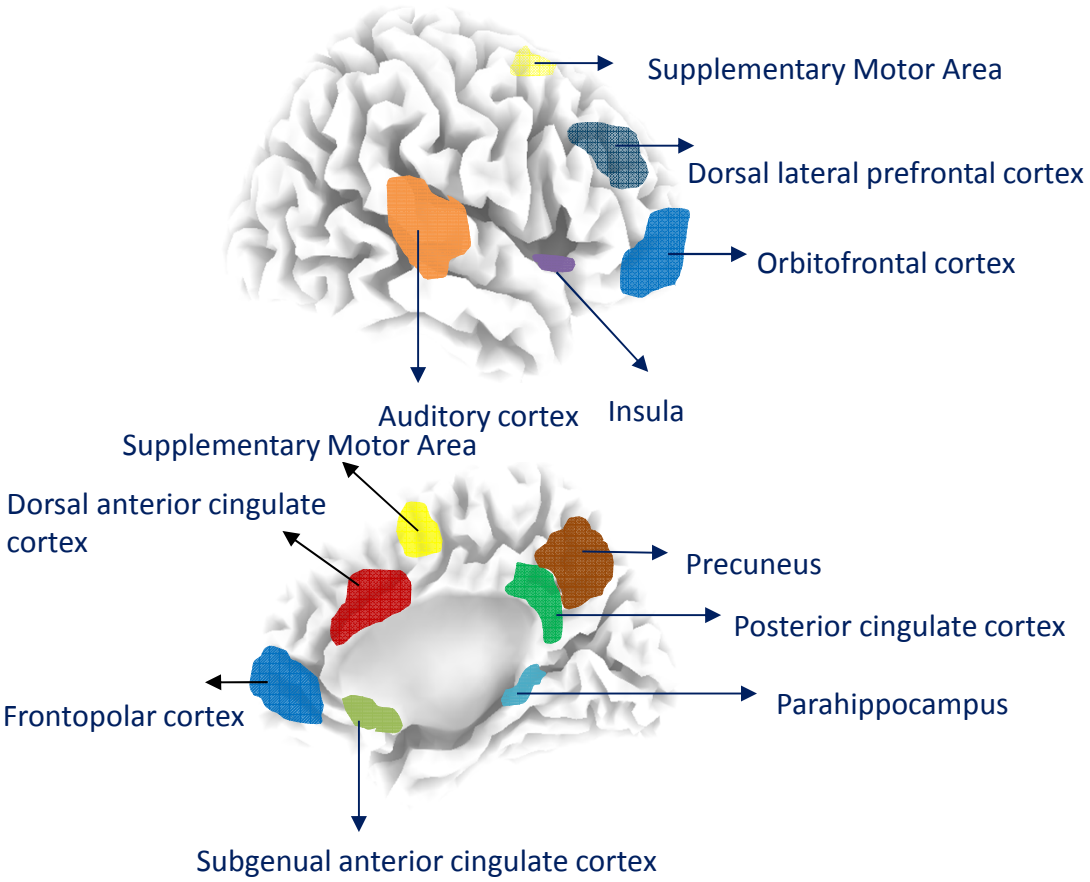


Gilles & Vanneste, submitted

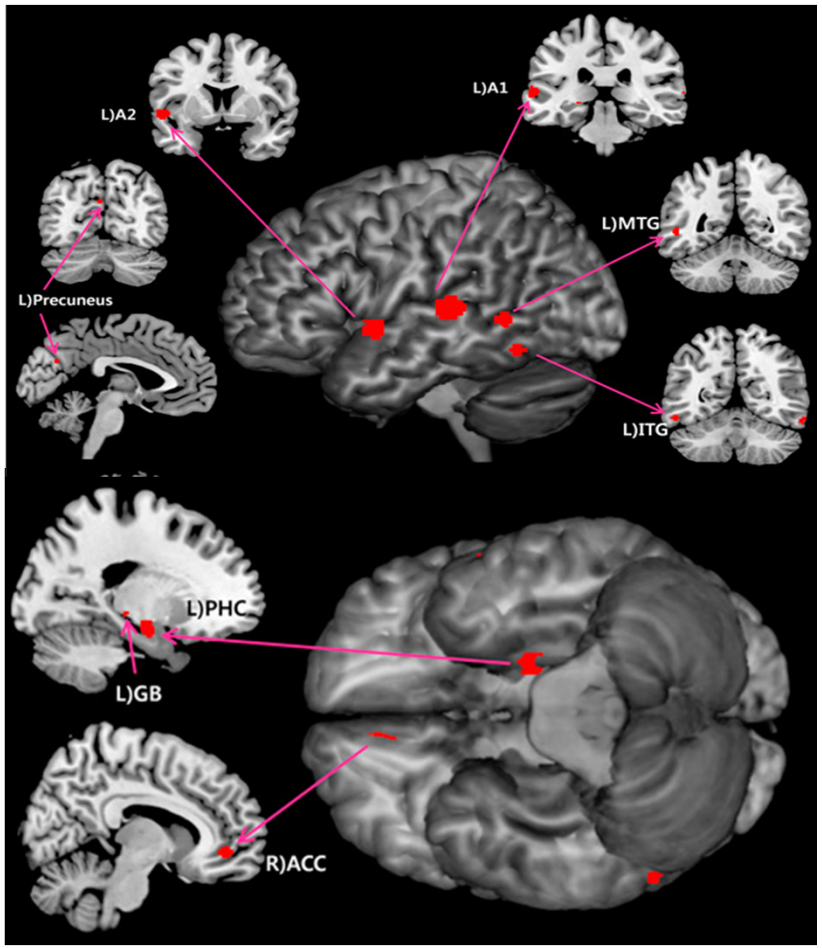


Schaette et al., Plos One, 2012

The brain involved in tinnitus

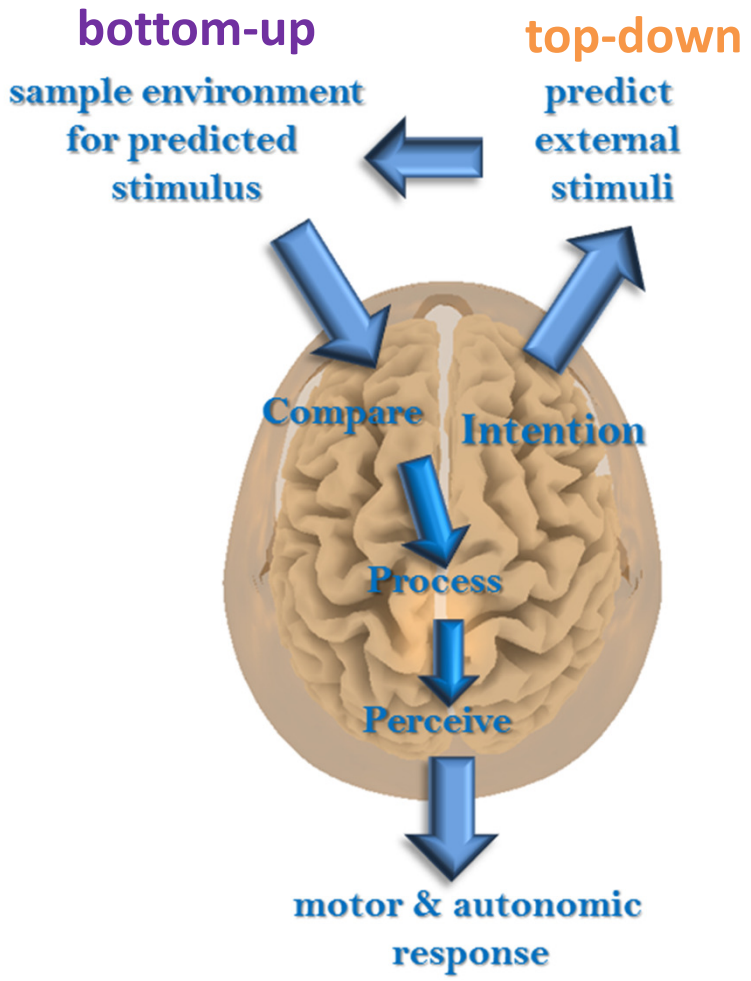


Vanneste & De Ridder, Frontiers in System Neuroscience, 2012



Song, De Ridder & Vanneste, Journal Nuclear Medicine, 2012

Why a phantom sound?



Active "Bayesian" Brain

- The predictive brain - the architecture of the cortex implements a **top-down prediction algorithm** that **constantly anticipates incoming bottom-up sensory stimuli** (Wacongne et al., PNAS, 2011).

Prediction ↔ External Stimuli
↓
Prediction error
(Bayesian updating)

To reduce the uncertainty of future events

Prediction = External Stimuli
↓
No Prediction error
(No updating)

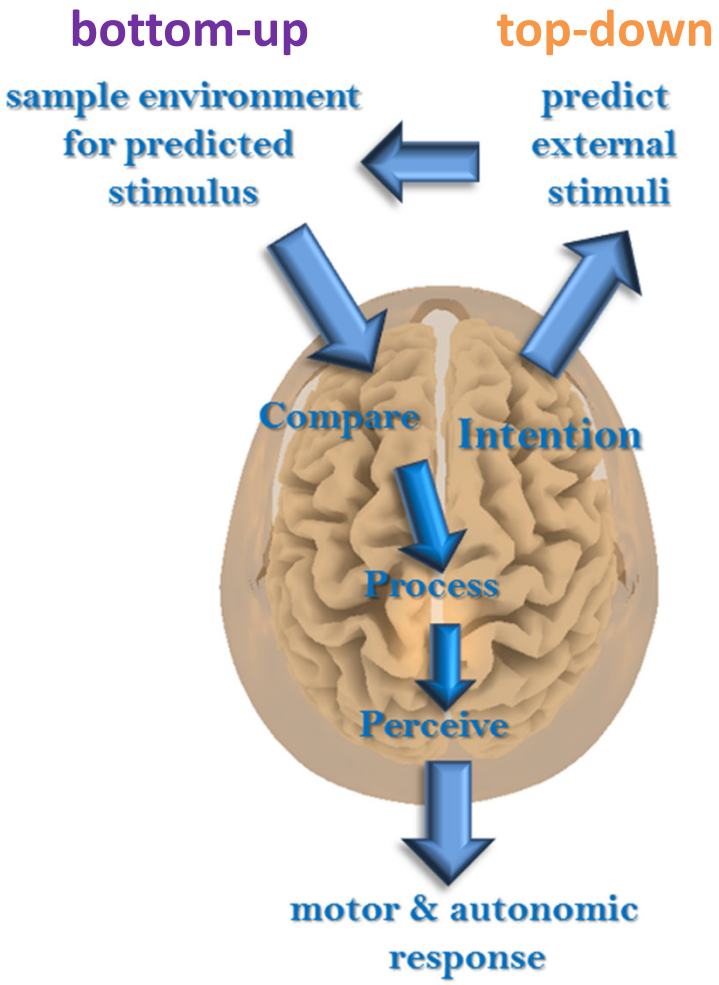
No reduce the uncertainty of future events

De Ridder, Vanneste & Freeman, Neuroscience & Biobehavioral Reviews, 2014

Why phantom sound?

Why does the brain generates tinnitus?

1. **Sensory deprivation** leads to limits the amount of information the brain can acquire
2. **increases uncertainty** present in the environment
3. to **reduce the uncertainty** will **look for information** or **fill in the missing information**
4. **reduction the prediction error**



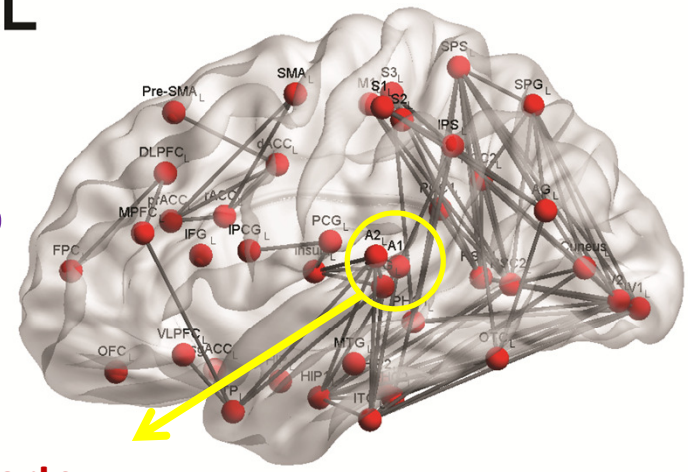
De Ridder, Vanneste & Freeman, Neuroscience & Biobehavioral Reviews, 2014

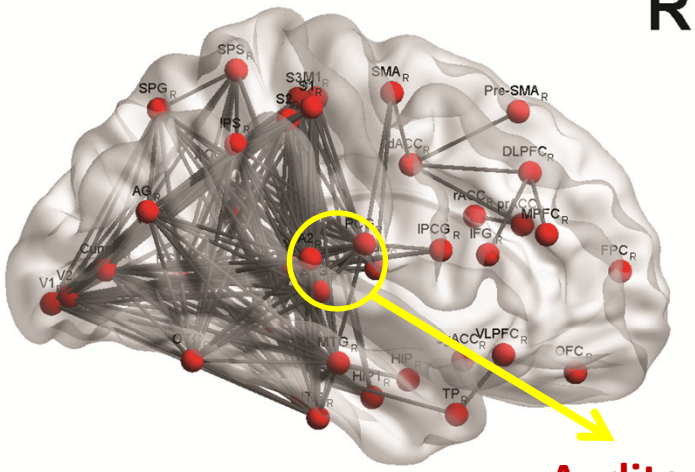
The brain involved in tinnitus

L

R

bottom-up

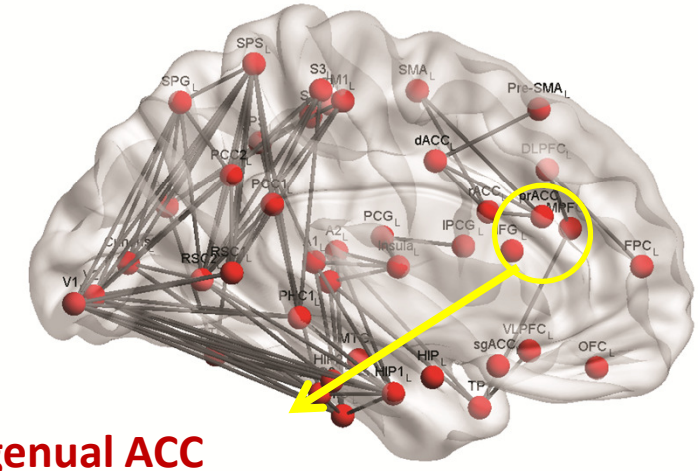


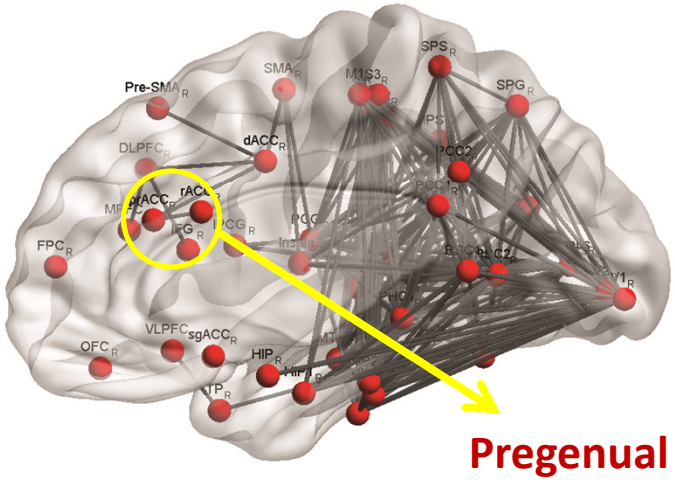


Auditory cortex

Auditory cortex

top-down





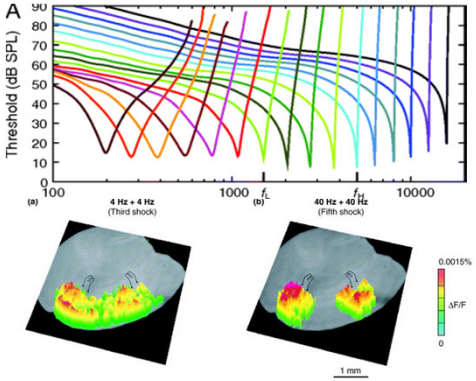
Pregenual ACC

Pregenual ACC

Mohan, De Ridder & Vanneste, submitted

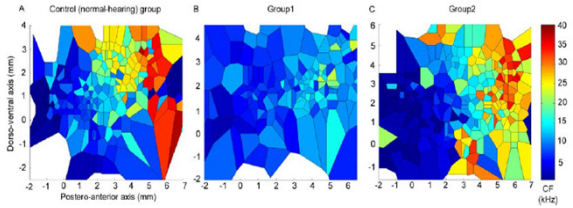
Hub: Auditory cortex

1. Little deafferentation



Spontaneous Hyperactivity

2. More deafferentation



Map plasticity

3. Very large deafferentation

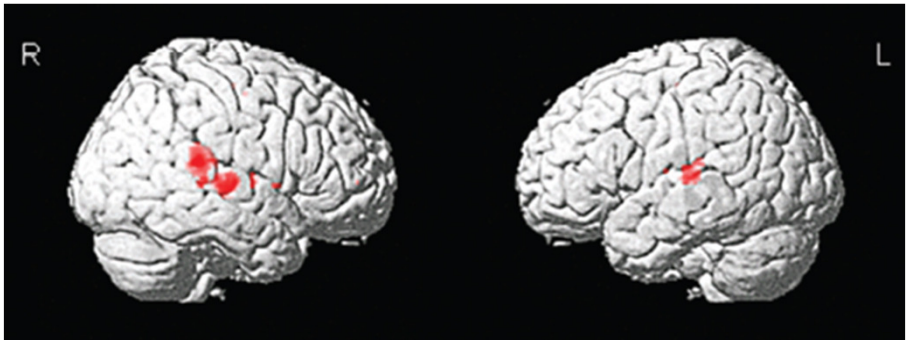
Memory

1. Hyperactivity within the auditory cortex

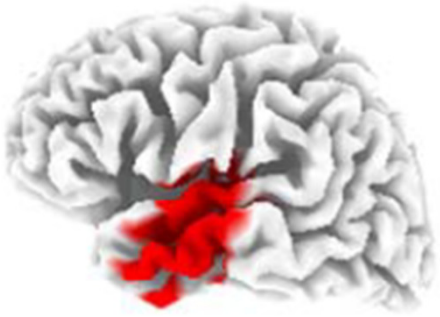
a. fMRI

Increased BOLD activity within the **auditory cortex**

De Ridder& Vanneste, JNS, 2011



b. Source localized EEG

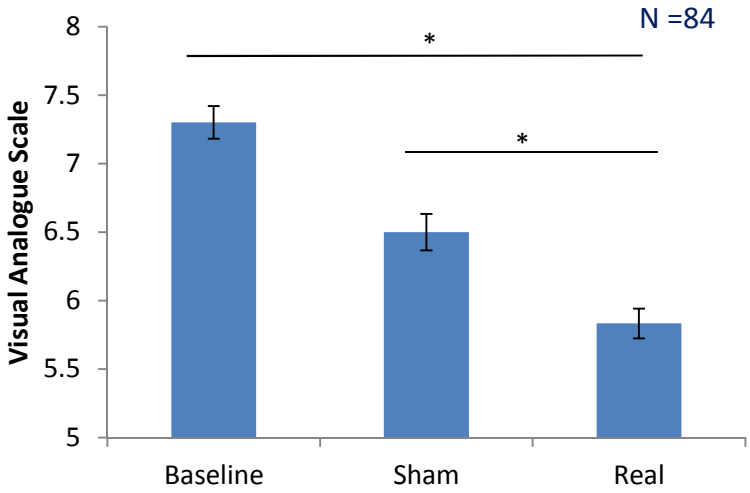


A **positive correlation** between **the tinnitus loudness** and the current density within the **auditory cortex** at the **gamma frequency band** (r = .65)

Van der Loo, Vanneste et al., Plos one, 2009

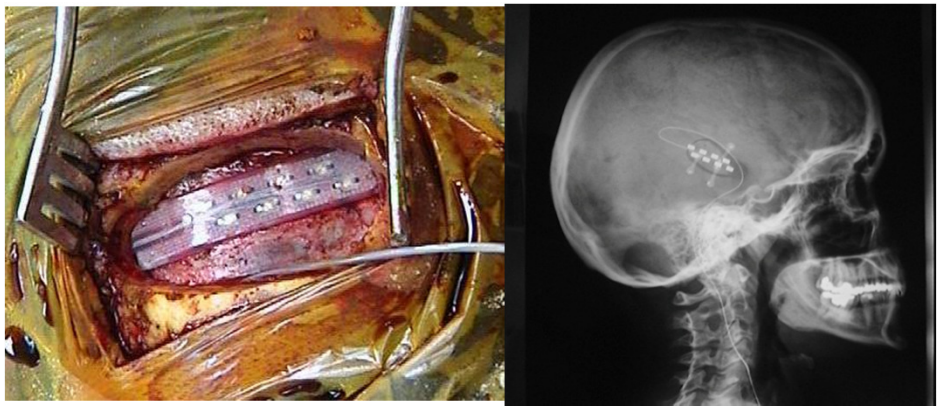
1. Hyperactivity within the auditory cortex

a. Transcranial magnetic stimulation (TMS)

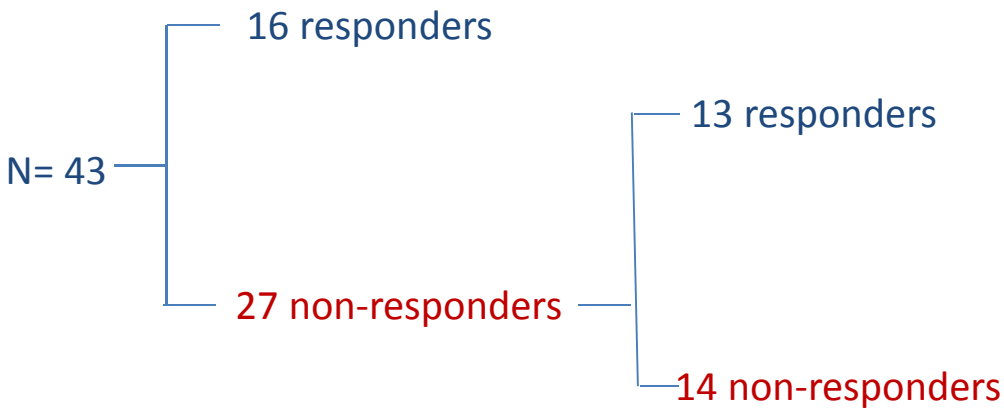


Vanneste et al., European Journal of Neurology, 2010

b. Auditory cortex implant



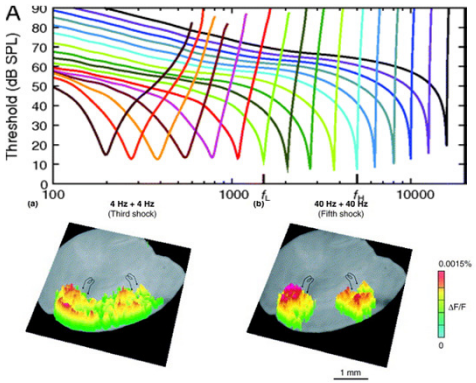
Tonic stimulation ***Burst stimulation***



De Ridder, Vanneste et al., JNS, 2011
De Ridder & Vanneste, WJN, 2014

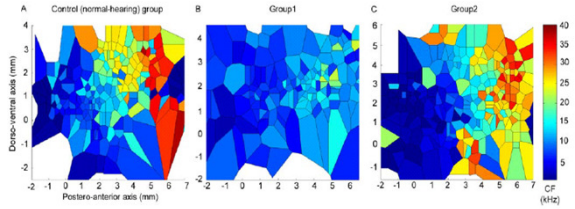
Hub: Auditory cortex

1. Little deafferentation



Spontaneous Hyperactivity

2. More deafferentation



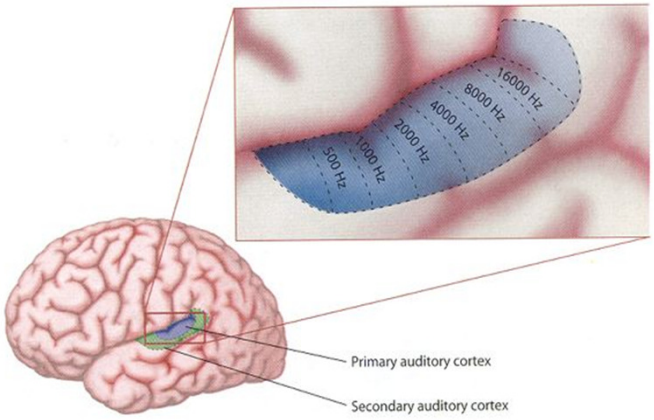
Map plasticity

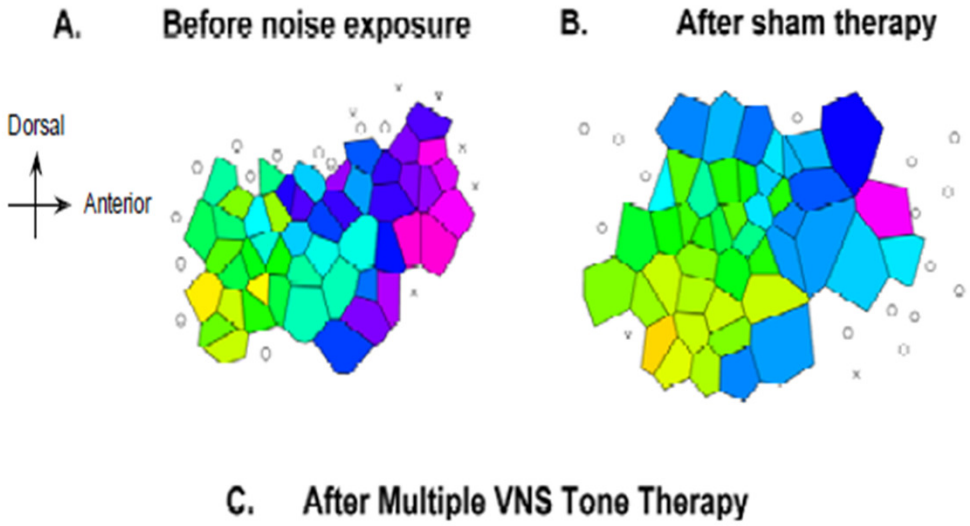
3. Very large deafferentation

Memory

2. Map plasticity

The tonotopic reorganization of the auditory cortex



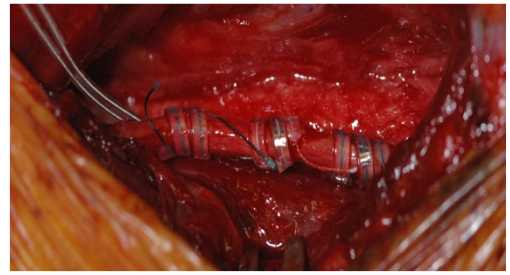


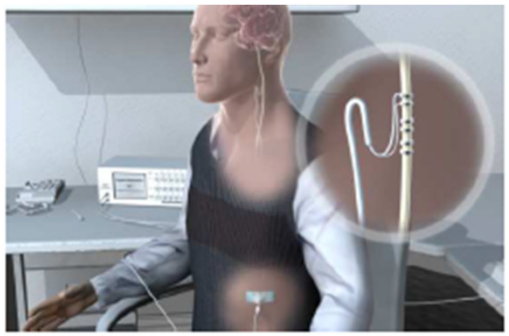
Cortical reorganization in the **auditory cortex** in after noise trauma has been associated with tinnitus

Norena et al., Journal of Neuroscience, 2006
Mühlnickel et al., PNAS, 1998

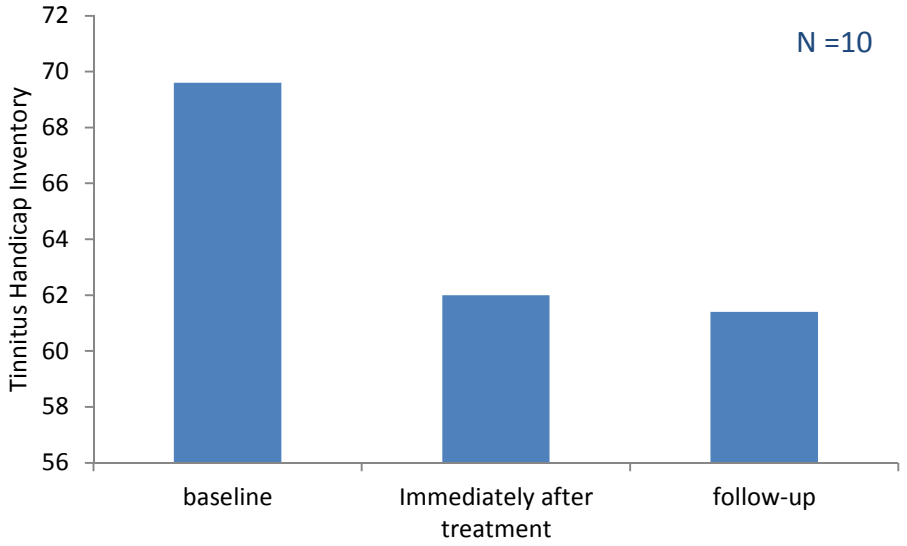
Engineer et al., Nature, 2011

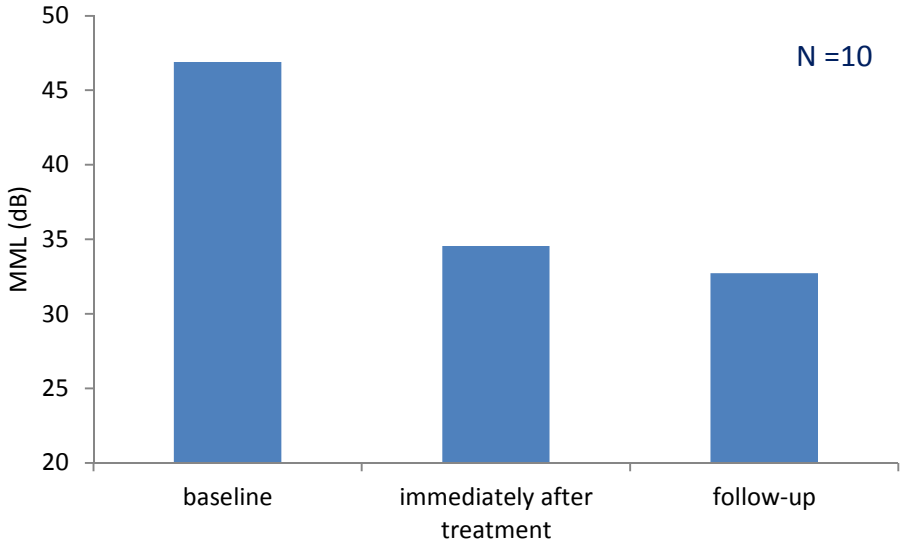
2. Map plasticity





4 week of treatment





De Ridder & Vanneste., Neuromodulation, 2014
De Ridder & Vanneste, Otology Neurotology, 2015

Hub: Auditory cortex

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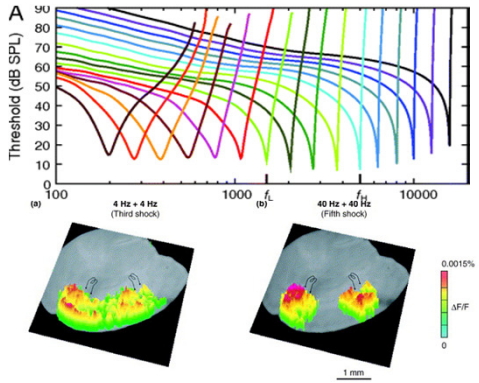

Spontaneous Hyperactivity

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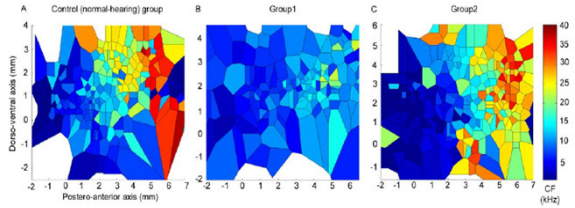
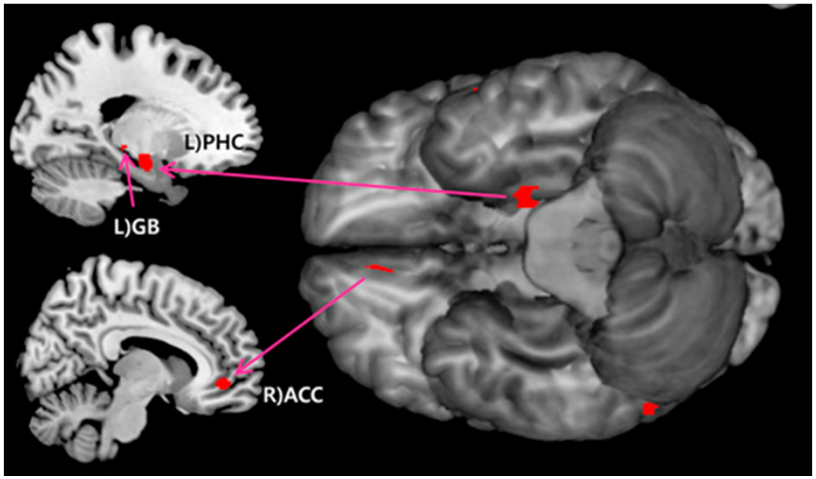


Map plasticity

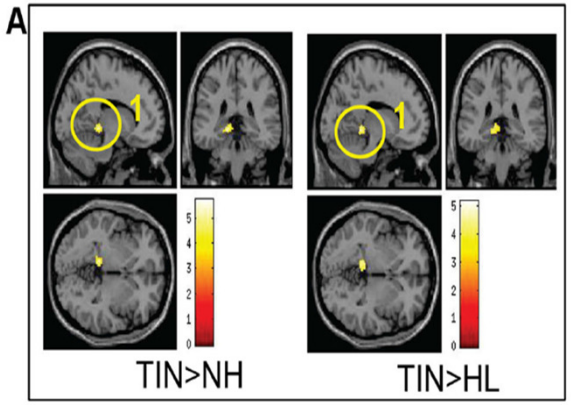
3. Very large deafferentation

Memory

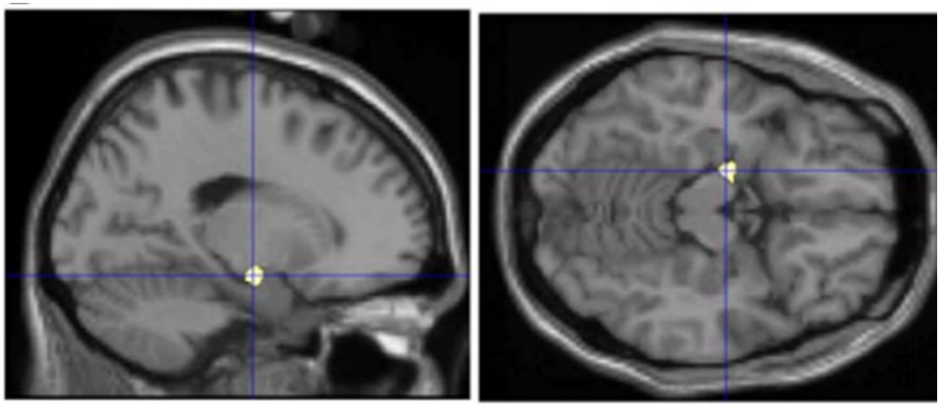
3. Memory



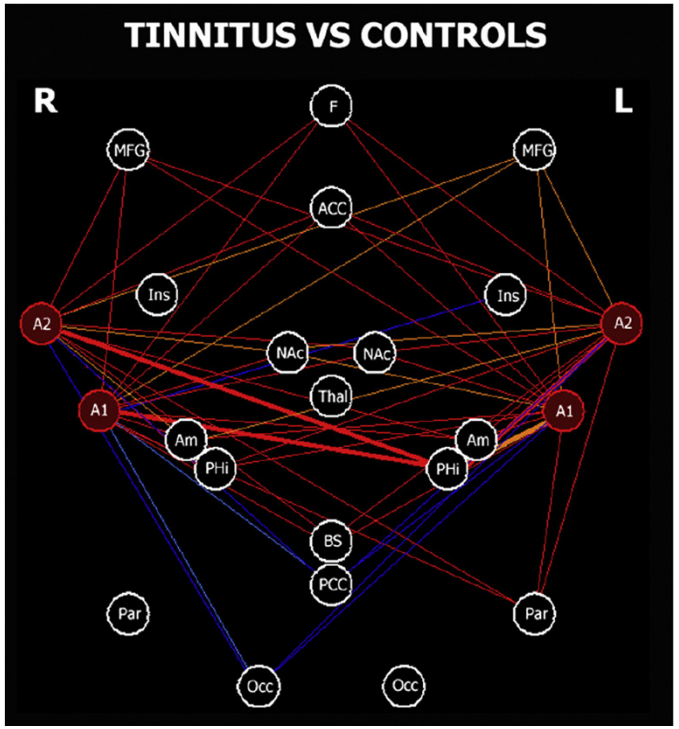
Song & Vanneste, Journal Nuclear Medicine, 2012



Schmidt et al., Plos One, 2013

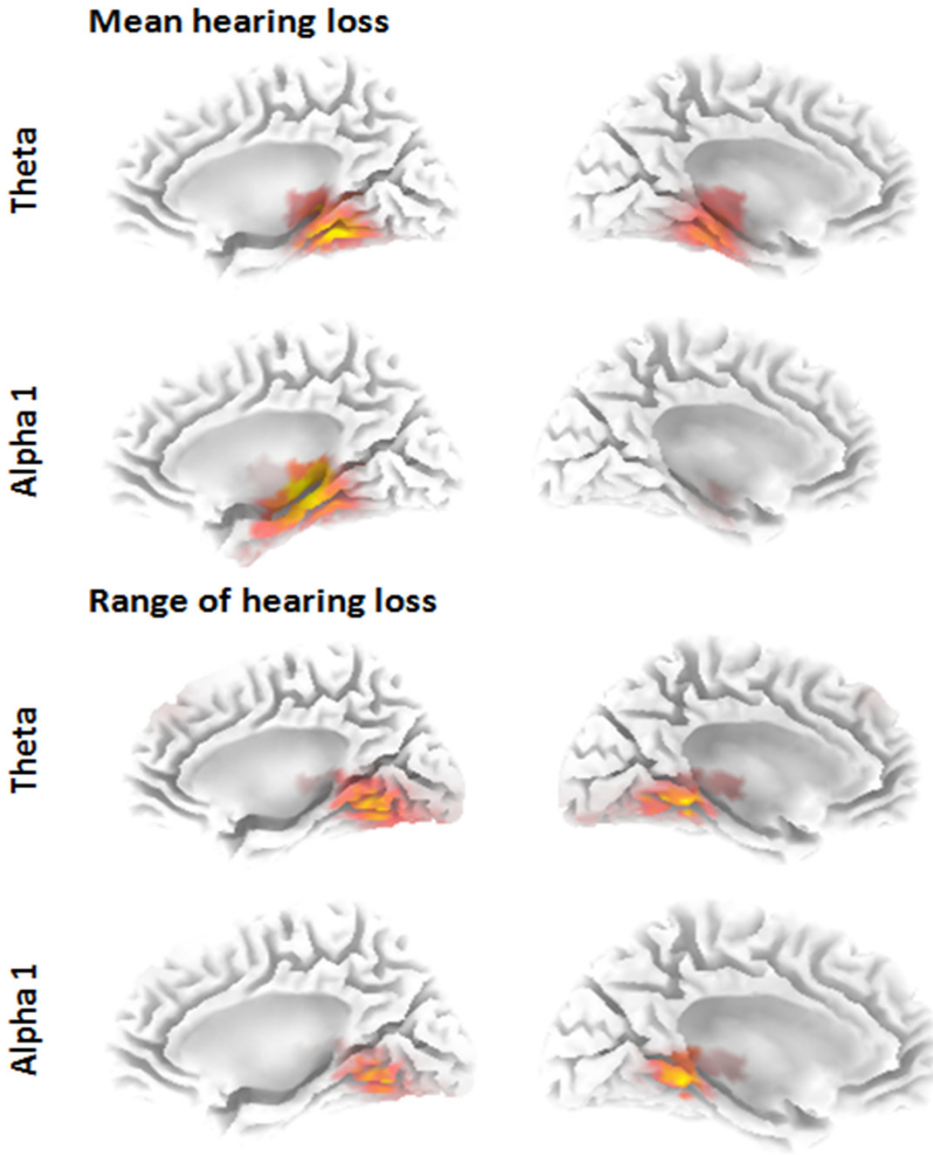


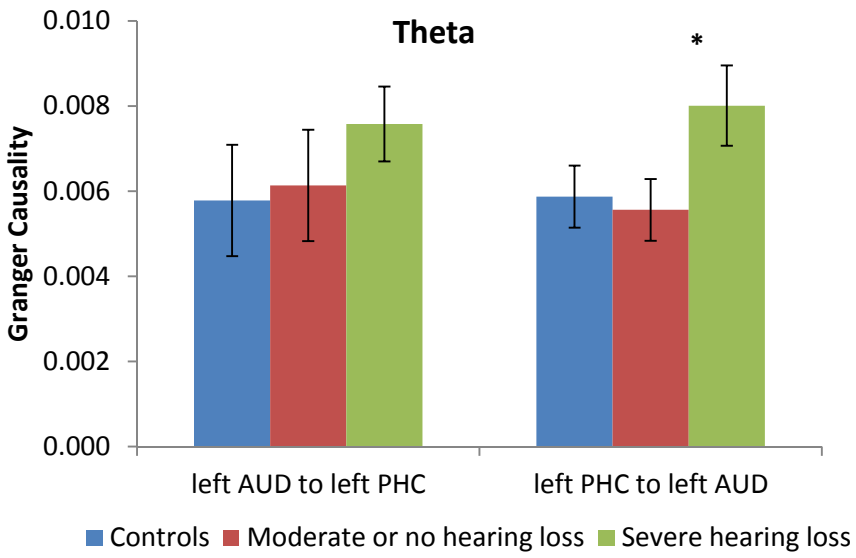
Landgrebe et al., Neuroimage, 2009

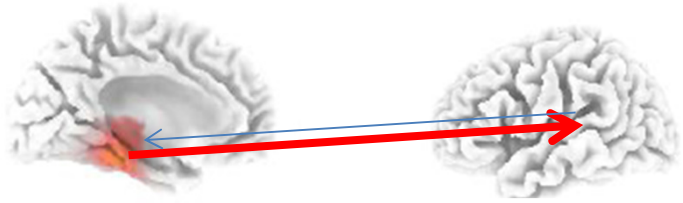


Maudoux et al., Plos One, 2012

3. Memory





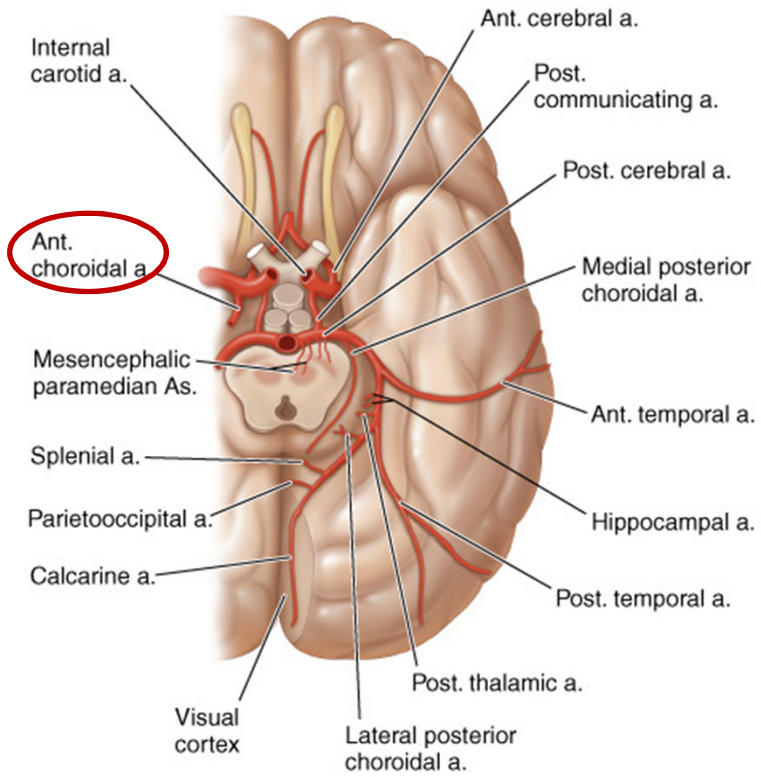


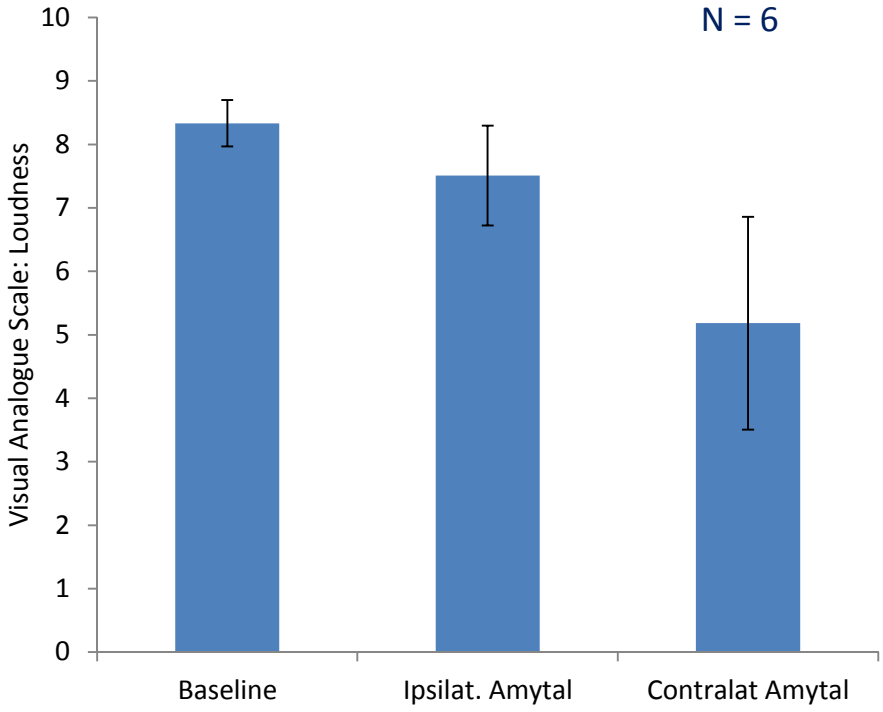
The more hearing loss…

…the more information goes from the parahippocampus to AC

Vanneste et al., submitted

Selective anterior choriodal artery amytal injections

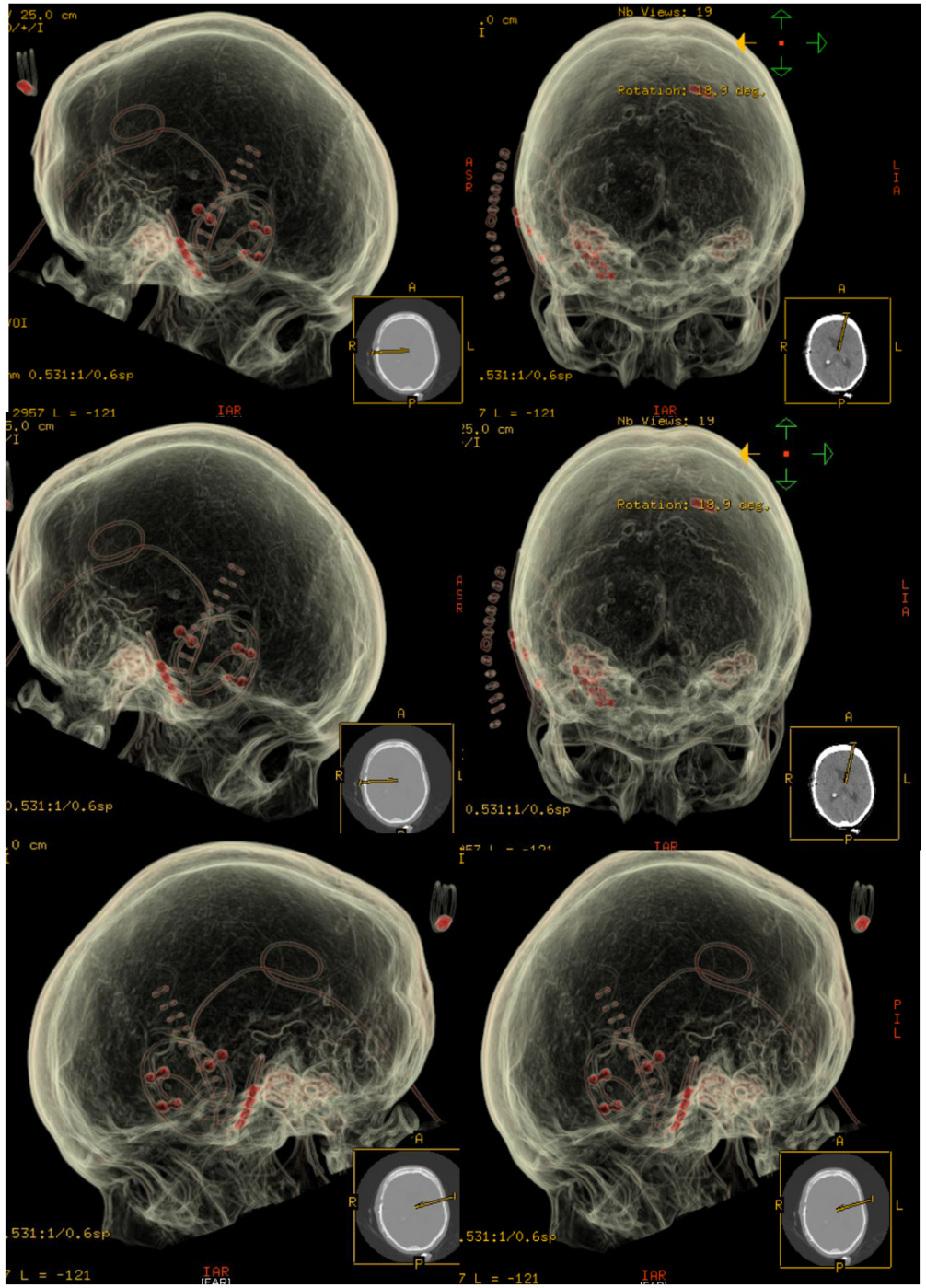


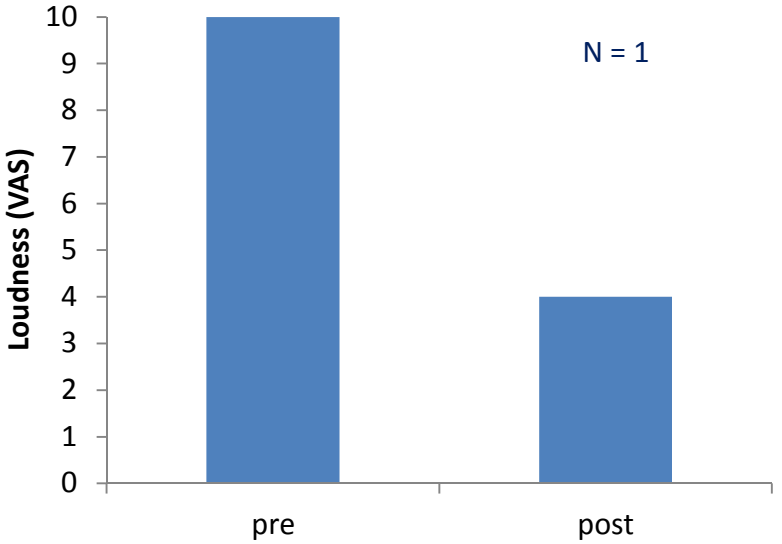


Amytal injection **ipsilaterally** resulted in **a maximal suppression of tinnitus of 30%,** and **contralaterally of 60-70%** in **three patients** with unilateral chronic tinnitus

De Ridder et al., Acta Oto-Laryngologica, 2006

3. Memory





Temporal relief of 3 weeks

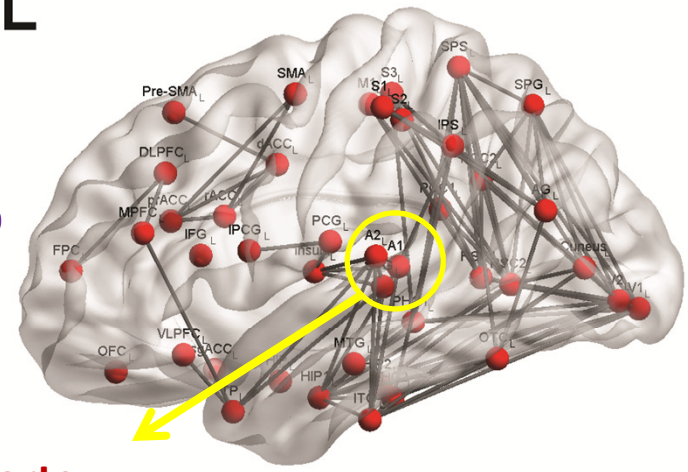
De Ridder & Vanneste, JNS, 2015

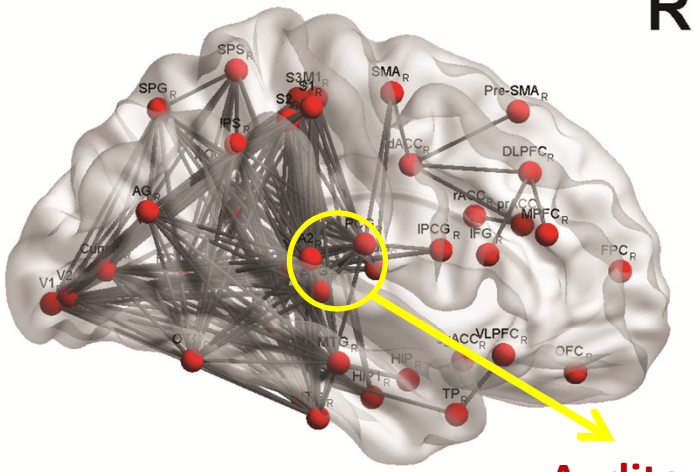
The brain involved in tinnitus

L

R

bottom-up

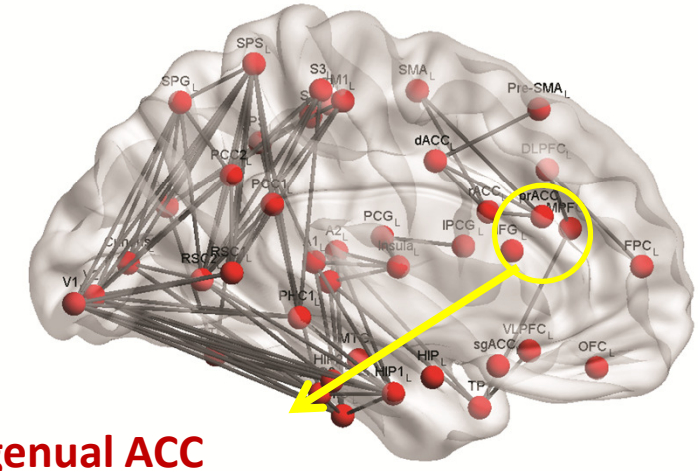


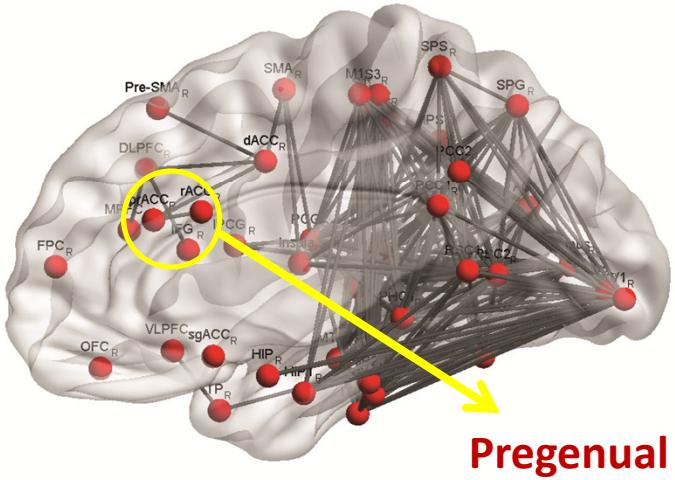


Auditory cortex

Auditory cortex

top-down



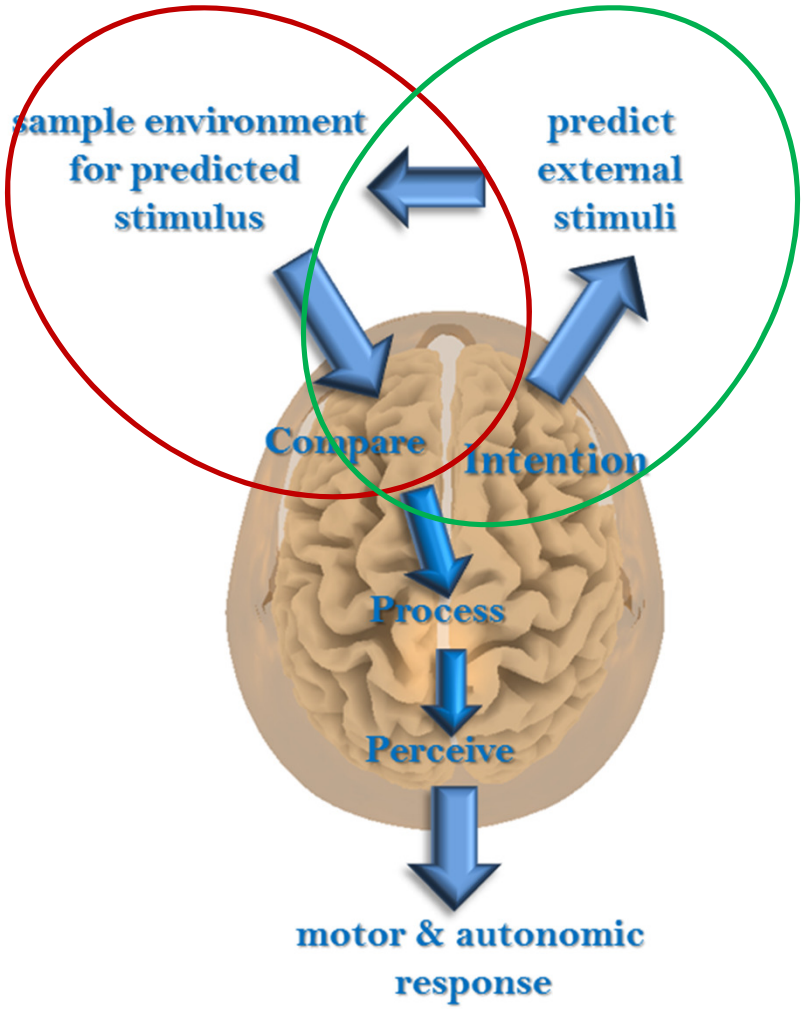


Pregenual ACC

Pregenual ACC

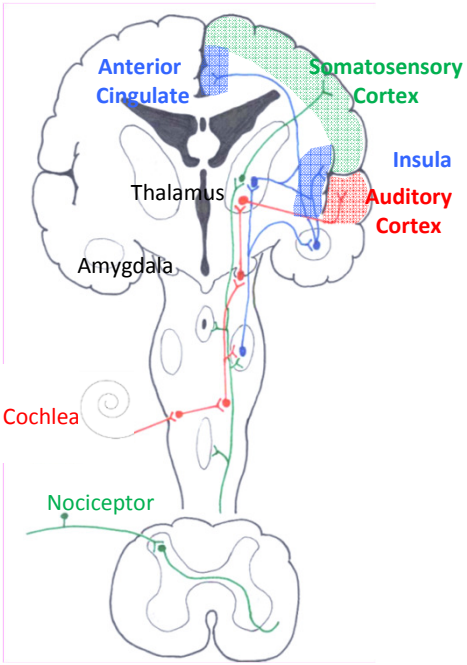
Mohan, De Ridder & Vanneste, submitted

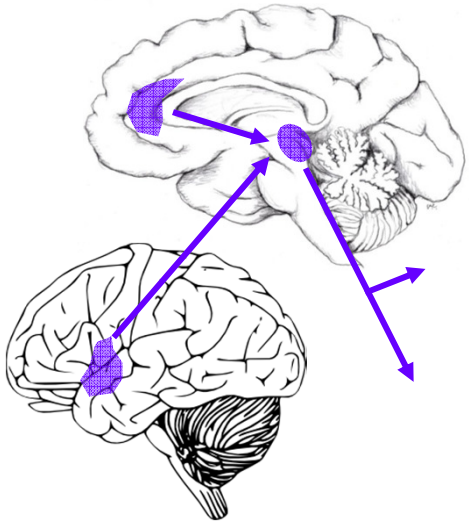
Hub: Pregenual ACC



Vanneste & De Ridder, J Neurosurg Sci 2013

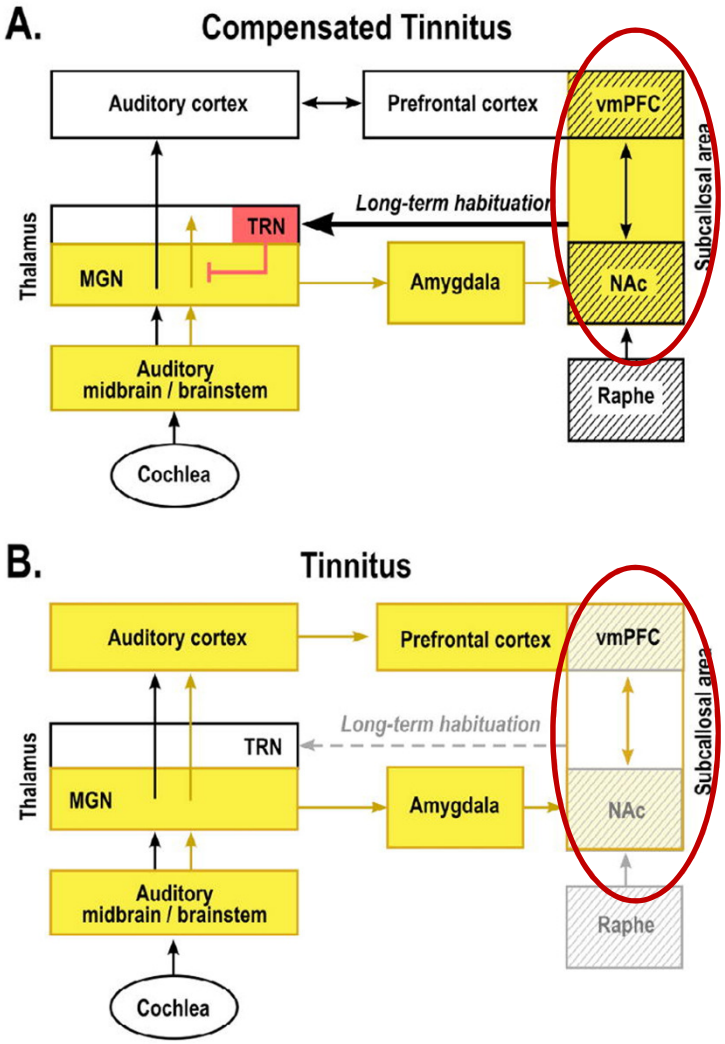
Hub: Pregenual ACC





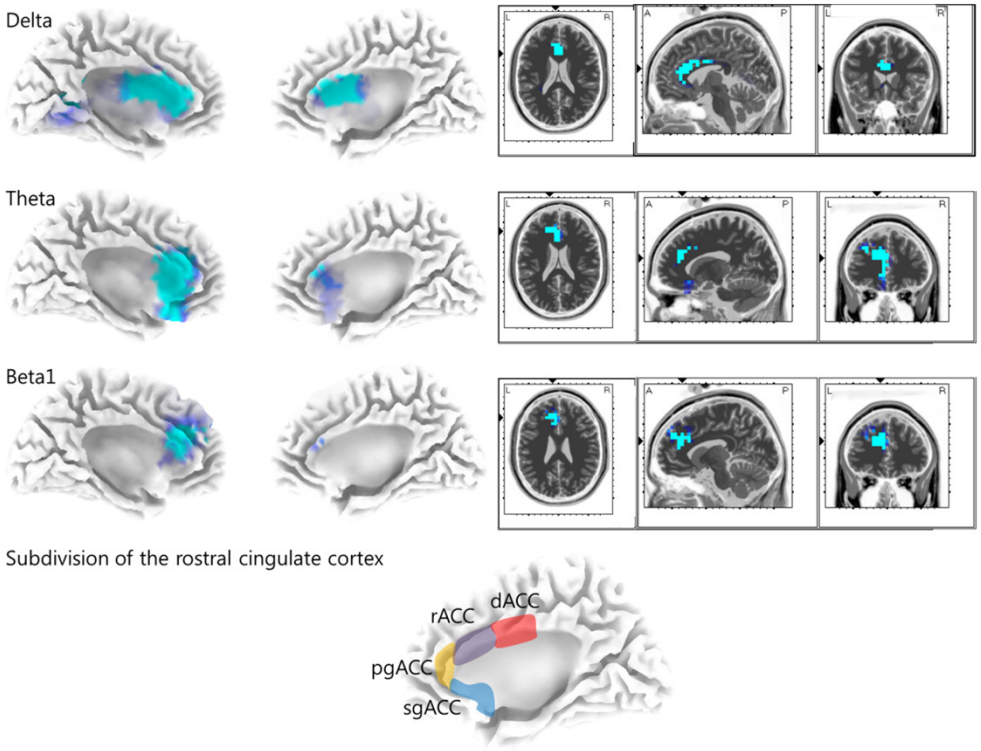
Vanneste & De Ridder, J Neurosurg Sci 2013

Noise cancelation system



Rauschecker, Neuron, 2010

Hub: Pregenual ACC

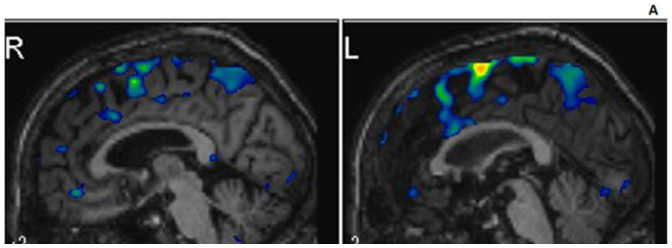


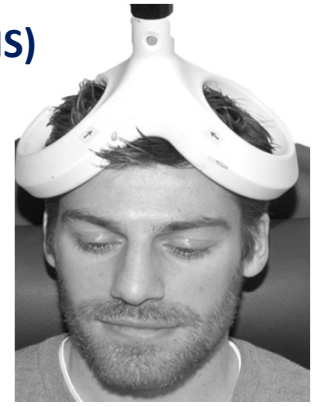
Song & Vanneste, Plos One, 2015

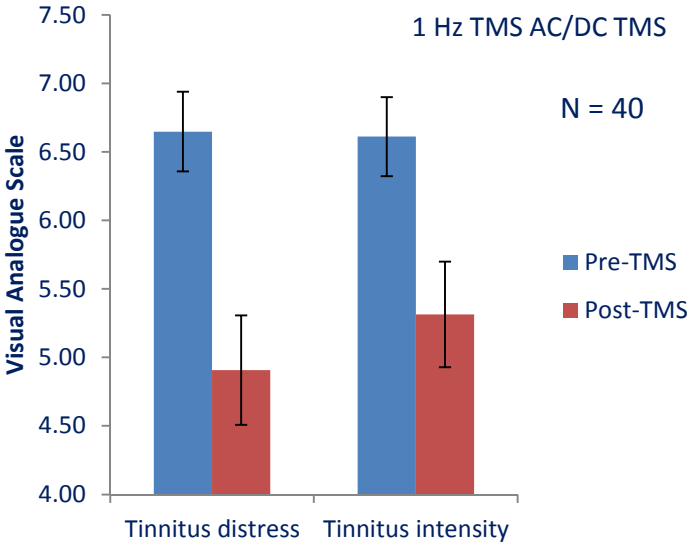
Noise cancellation system

Hub: Pregenual ACC

a. Transcranial magnetic stimulation (TMS)

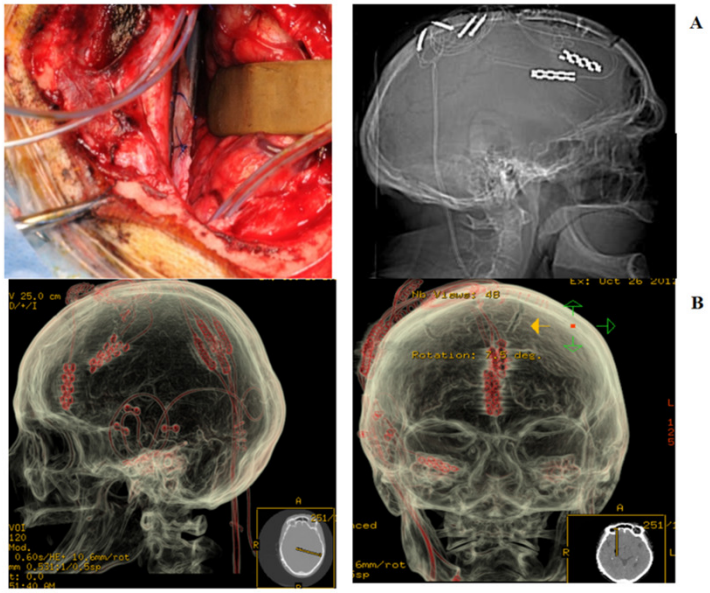


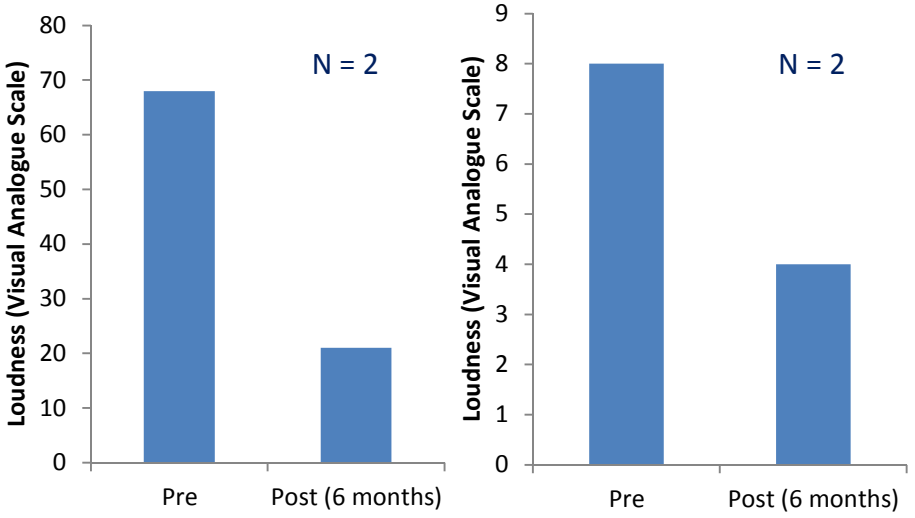




Vanneste et al., Brain Stimulation, 2012

b. AAC deep brain implant





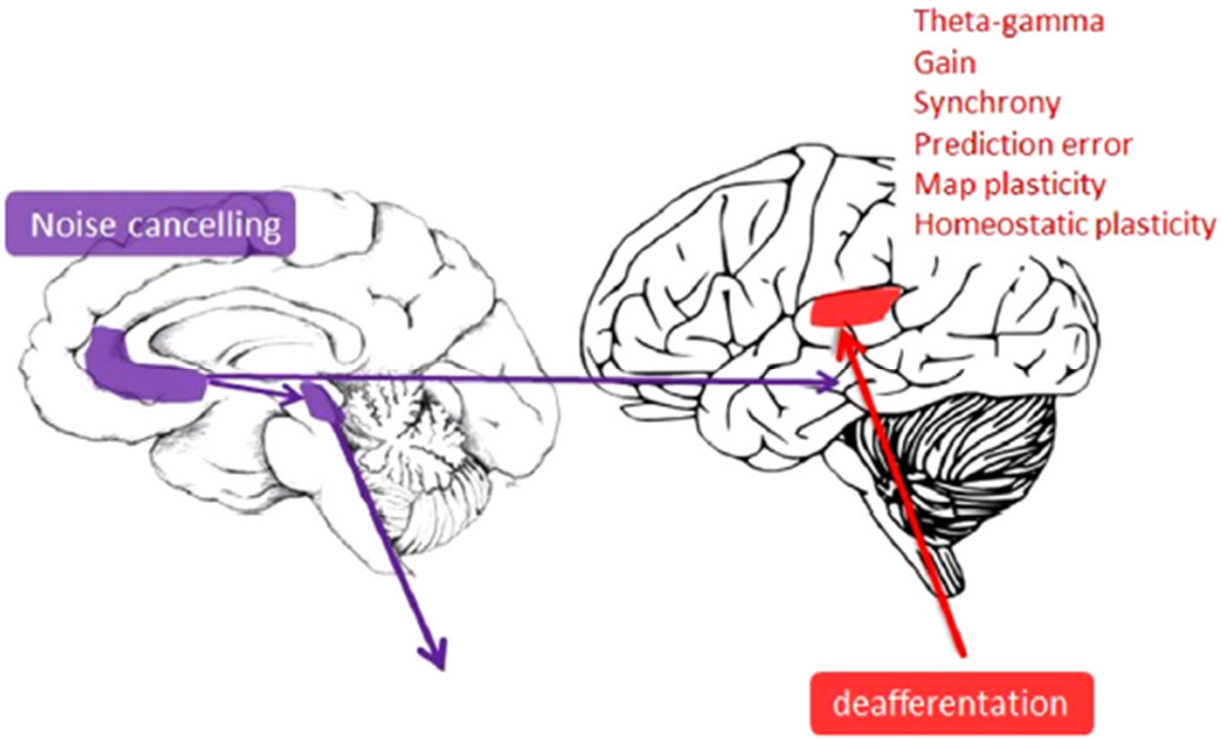
Permanent relief

De Ridder & Vanneste, 2015, neurosurgery

Conclusion

- Different **subtypes of tinnitus**

Top-down **Bottom-up**



- Dependening on the underlying mechanism: **different treatment?**