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

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• 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
In an adult population 10 to 15% perceives tinnitus continuously.
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• Increasing up to 33% in the elderly population
• 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 sets up a cascade of neurophysiologic changes in the central auditory system culminating to the perception of a phantom sound.
Loss of auditory input

Outside anechoic chamber

Healthy subjects

N = 17

0.00

94.12

Inside anechoic chamber

Gilles & Vanneste, submitted

Healthy subjects

N = 18

0.00

77.78

Before

Schaette et al., Plos One, 2012

After
The brain involved in tinnitus

Vanneste & De Ridder, Frontiers in System Neuroscience, 2012

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

Why a phantom sound?

De Ridder, Vanneste & Freeman, Neuroscience & Biobehavioral Reviews, 2014
Why does the brain generate 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

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

N = 84

1. Hyperactivity within the auditory cortex

b. Auditory cortex implant

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

N = 43

13 responders

27 non-responders

14 non-responders

Tonic stimulation

Burst stimulation

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

Vanneste et al., European Journal of Neurology, 2010
Hub: Auditory cortex

1. Little deafferentation

Spontaneous Hyperactivity

2. More deafferentation

Map plasticity

3. Very large deafferentation

Memory
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

De Ridder & Vanneste., Neuromodulation, 2014
De Ridder & Vanneste, Otology Neurotology, 2015
Hub: Auditory cortex

1. Little deafferentation

2. More deafferentation

3. Very large deafferentation

Spontaneous Hyperactivity

Map plasticity

Memory
3. Memory

Song & Vanneste, Journal Nuclear Medicine, 2012

Landgrebe et al., Neuroimage, 2009

Schmidt et al., Plos One, 2013

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
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

N = 1

De Ridder & Vanneste, JNS, 2015
The brain involved in tinnitus

Mohan, De Ridder & Vanneste, submitted

Auditory cortex

Pregenual ACC

bottom-up

top-down

Mohan, De Ridder & Vanneste, submitted
Hub: Pregenual ACC

Vanneste & De Ridder, J Neurosurg Sci 2013
Ascending 
Bottom up 
Noise-sensing

Descending 
Top down 
Noise-canceling

Hub: Pregenual ACC

Vanneste & De Ridder, J Neurosurg Sci 2013
Noise cancelation system

Hub: Pregenual ACC

Rauschecker, Neuron, 2010

Song & Vanneste, Plos One, 2015
Noise cancellation system

a. Transcranial magnetic stimulation (TMS)

b. AAC deep brain implant

Hub: Pregenual ACC

1 Hz TMS AC/DC TMS

N = 40

Permanent relief

Vanneste et al., Brain Stimulation, 2012

De Ridder & Vanneste, 2015, neurosurgery
Conclusion

• Different subtypes of tinnitus

• Depending on the underlying mechanism: different treatment?