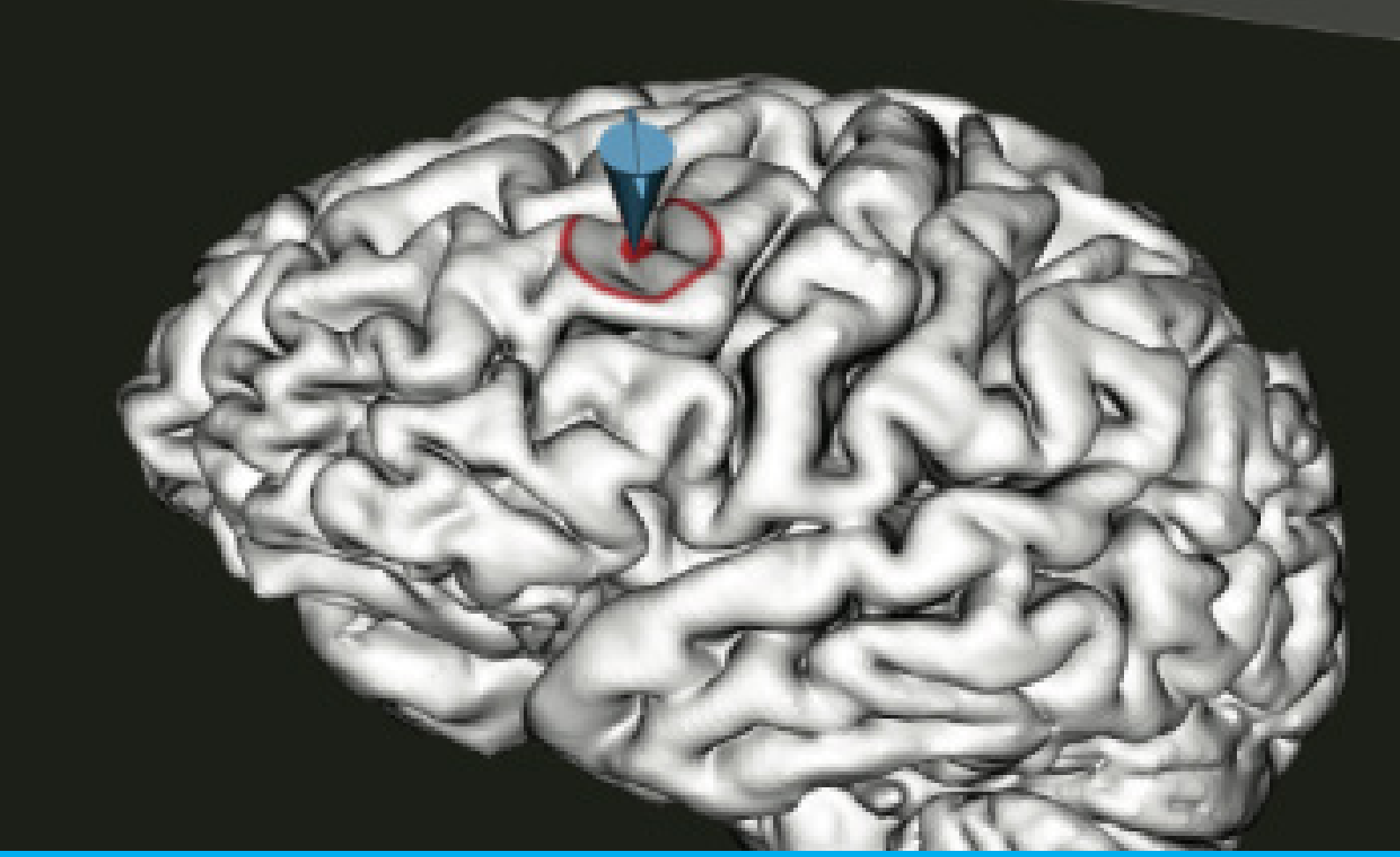


Transcranial stimulation rTMS

In reducing tinnitus caused by plasticity

Enhanced synchronization

Transcranial stimulation rTMS has become a well-recongized technology, commonly used in depression and schizophrenia treatment, and neuro-rehabilitation. More and more research is carried out on therapeutic effectiveness of this technology in tinnitus treatment. In our clinic, we choose transcranial stimulation rTMS to a tinnitus model caused by enhanced synchronization; plasticity model confirmed in research studies of J. Burger, E. Frank, P. Kreuzer, T. Kleinjung, V. Vielsmeier, M. Landgrebe, G. Hajak and B. Langguth (2011).

Therapeutic requirements

In transcranial stimulation we use two different devices: Neuronavigation and neurostimulator.

Transcranial neurostimulator rTMS

Is a device which sends an electromagnetic impulse to the inductor which is placed above the patient's head. More precisely, in the area which requires depolarization (reducing activity of neurons).

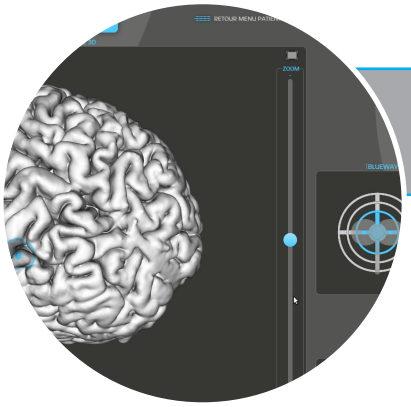
Neuronavigation rTMS

Is a device which illustrates 3D model of a patient's brain based on MRI or fMRI. During a therapy, the device follows and verifies inductor's position in a particular area which needs to be stimulated.

Necessary steps to start therapy:

Audiological diagnosis

MRI test



Beginning of a therapy

Audiological Diagnosis

Diagnosis of tinnitus model cause by enhanced synchronization. Required medical tests:

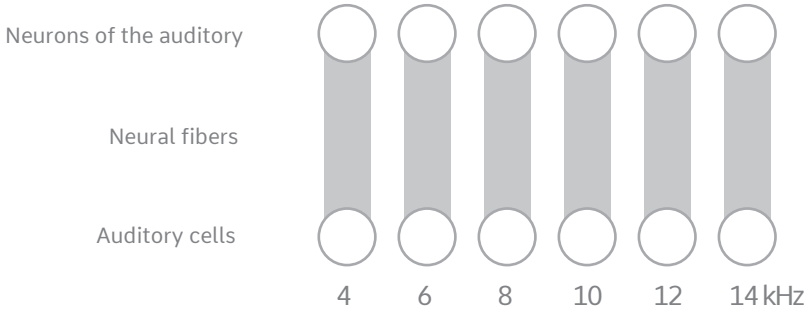
- High-frequency tonal audiometry
- Tinnitus characteristic
- Boundary frequencies test measuring its range

Enhanced synchronization is a model of tinnitus which constitutes around 40% of all tinnitus models. There are different plasticity kinds connected with enhanced synchronization, and not all of them concern an increase of neurons in the auditory cortex. However, in most cases neurons try to connect with a good-hearing structure due to a lack of acoustic stimulation in the range of auditory pathway affected by tinnitus. It emerges as generating tinnitus but not on the synaptic level of the peripheral auditory pathway, but on the neural level of the primary auditory cortex.

1

Normal hearing

Neurons are connected by neural fibers

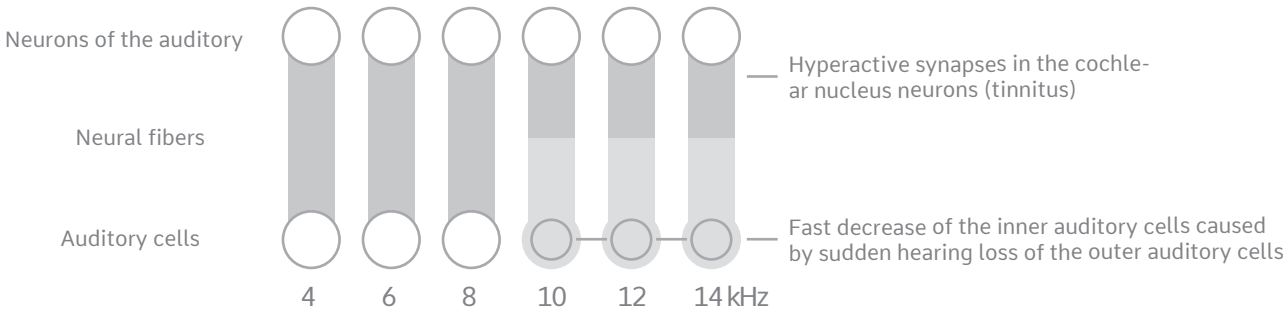


Every normal-hearing patient is characterized by tonopoty of the auditory pathaway (every cell, fiber and neuron analyze a certain pitch and frequency of sound). An auditory cell changes particular vibrations into electric potential and sends it through a joined neural fiber to certain neurons which receive this potential. In this way, information is sent as neurotransmitter between the inner ear and a neuron of the auditory cortex. This scheme functions regarding every normal-hearing patient.

2

Sudden hearing loss

Neurons of the auditory pathway are connected to each other, but the synapses are hyperactive in the range of sudden hearing loss, which appears as tinnitus.



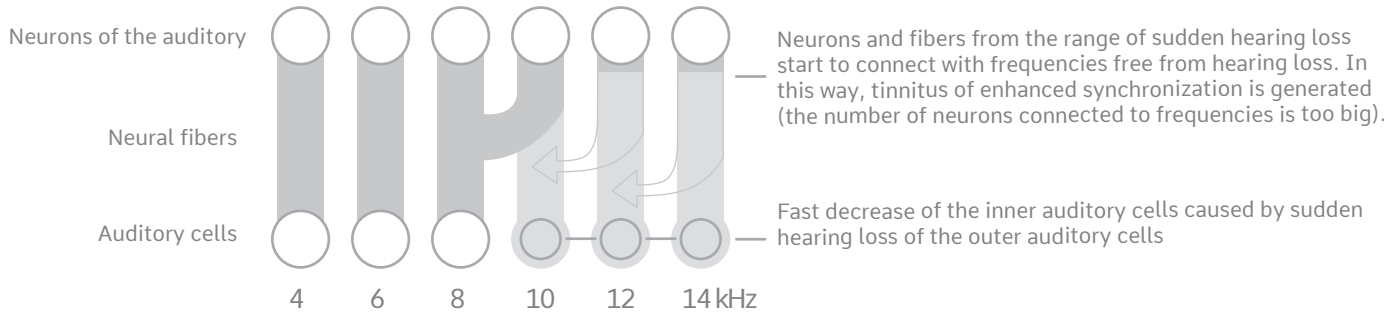
When sudden hearing loss appears, the very first symptom is tinnitus generated by the enhanced activity of synapses in the outlying part of the auditory pathway (cochlear nucleus is the first concentration of neurons from the auditory cortex). Synapses which mass and volume hasn't been changed due to lack of adaptation process (as a result of slow reduction of stimulation which lessens within time), they increase their sensitivity and send more of spontaneous activity as a neurotransmitter. If the synapses' activity level is high (100 Hz), therefore, electric potential from hyperactive synapses more often gets through to the neurons, which causes generating tinnitus (noise of too frequent release of synaptic activity). In this way, each patient's tinnitus is generated at the very beginning.

The nervous system sustains synapses in constant activity; therefore, it tries to increase its sensitivity by increasing axon segments in neurons, which generated greater synaptic sensitivity (Axon Initial Segment). In this process, the nervous system does not notice stimulation in cells where sudden death emerged.

3

Sudden hearing loss

Neurons of the auditory pathway are connected to each other, but the synapses are hyperactive in the range of sudden hearing loss, which appears as tinnitus.

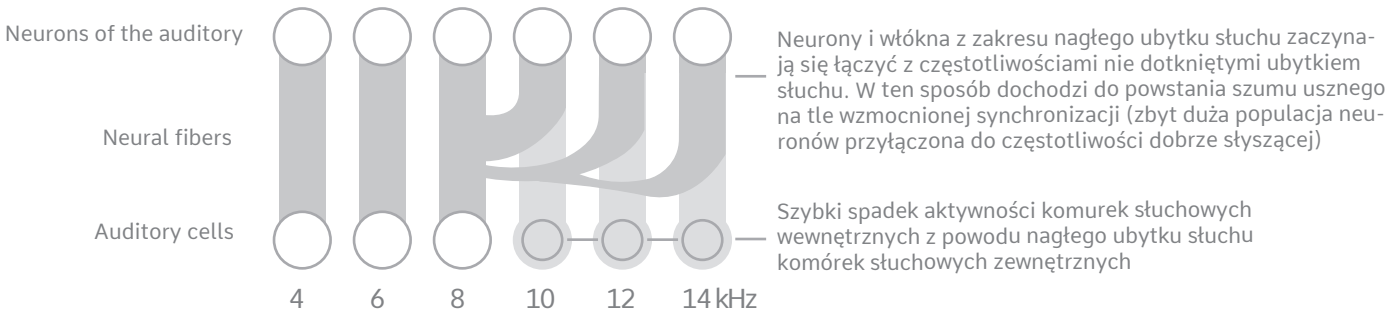


After a few years of not receiving appropriate stimulation, what's natural for the auditory cortex and the central nervous system is to join neurons without proper stimulation (from the range of sudden hearing loss) to neurons which receive stimulation (not affected by sudden hearing loss). The nervous system gradually joins more and more neurons from the range of sudden hearing loss to fibers and neurons with access to stimulation. This process begins within 3-4 years after tinnitus appeared. Duration of this process depends upon how many neurons of different intensity lacks stimulation. The number of neurons receiving stimulation is progressively increased.

4

Sudden hearing loss

After a few years of not receiving stimulation, tinnitus neurons and neurons of sudden hearing loss finished the process of incorporating to hearable regions. As a result, it created hyperactive structure of neurons and tinnitus model caused by enhanced synchronization.



At the end of the reorganization process, most of the neurons from the range of sudden hearing loss are rejoined with the range of fibers and neurons which receive stimulation from cells of lower frequencies than initially. In the range of sudden hearing loss, a cell is still connected to a neuron it was originally connected to, however, the representation of fibers is really weak. When the process of joining neurons is completed, a patient's tinnitus does not occur, but it changes its source. In the first stages, synapses from neurons of the cochlear nucleus used to be the source of generating tinnitus. Now, it is generated by too low stimulation level of a cell which has too many connected neurons and as a result of newly added neurons. They become active when there is a lack of sufficiently big stimulation level which results in hearing tinnitus. Enhanced synchronization process might emerge during acoustic trauma (4 % of cases) or chronic tinnitus (40 % of cases above 4-5 years since tinnitus occurrence). In both cases, a patient needs to be diagnosed. A characteristic trait of enhanced synchronization is auditory hypersensitivity connected with joining a certain intensity group in which additional neurons lack stimulation.

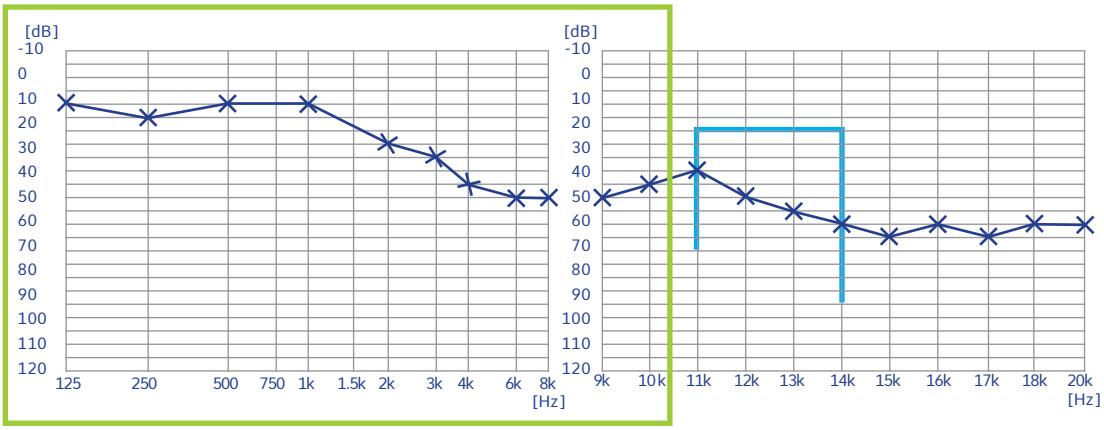
Qualificiation requirements for rTMS therapy

-Sudden hearing loss does not concern speech recognition from 125 Hz up to 10 kHZ, which means it is above this range

-A patient has auditory hypersensitivity

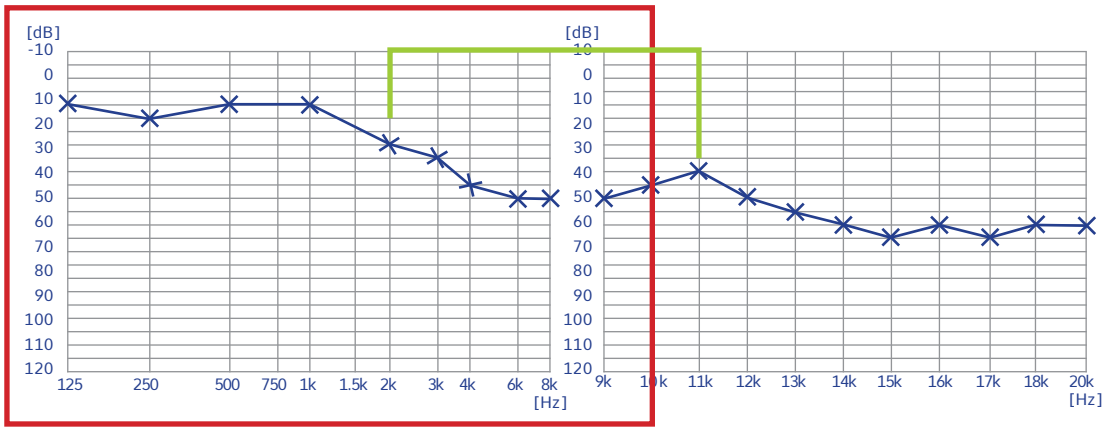
-Test of boundary frequencies shows that a patient is influenced by acoustic stimulation in the neighboring ranges, not in the range of hearing loss. Influence of acoustic stimulation in the range of sudden hearing loss does not reduce tinnitus; it coincides with it.

- An audiologist confirms consistency of the patient's results with the enhanced synchronization model (tinnitus model)



When a patient does not meet with the qualification requirements

A person struggling with hearing loss stepping into the range of speech recognition is qualified to tinnitus reduction in this model with a broadband hearing aid up to 14 kHz. Such a wide range of reinforcement will stimulate auditory cells and then it will reconstruct neurons of the spiral ganglion which were deprived during hearing loss. Thanks to this process, an appropriate organizing of the auditory pathway will take place and neurons from the boundary frequencies will be joined to the restimulated ranges. As an outcome, we should get better hearing range, tinnitus reduction and auditory hypersensitivity reduction.



Before the beginning of rTMS sessions, every patient is required to raise each level of neurotrophic proteins BDNF, NT -3 and cytoskeletal proteins Arc/arg 3.1; this will help achieve better results and shorten therapy duration.

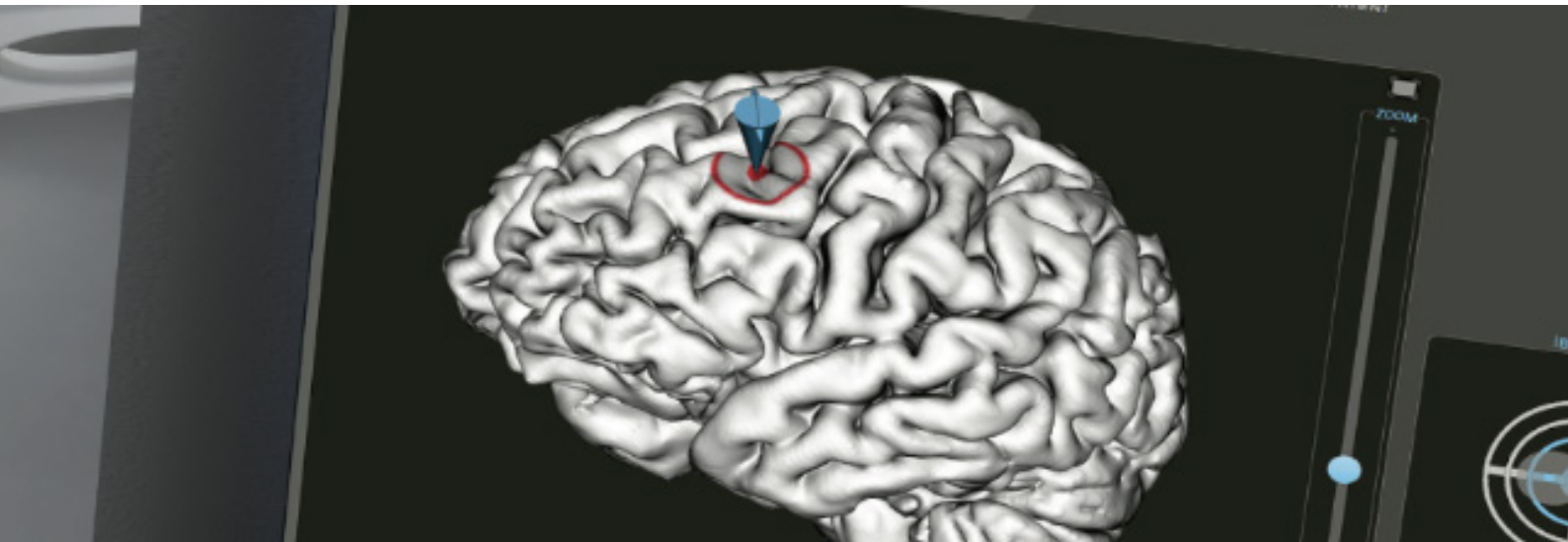
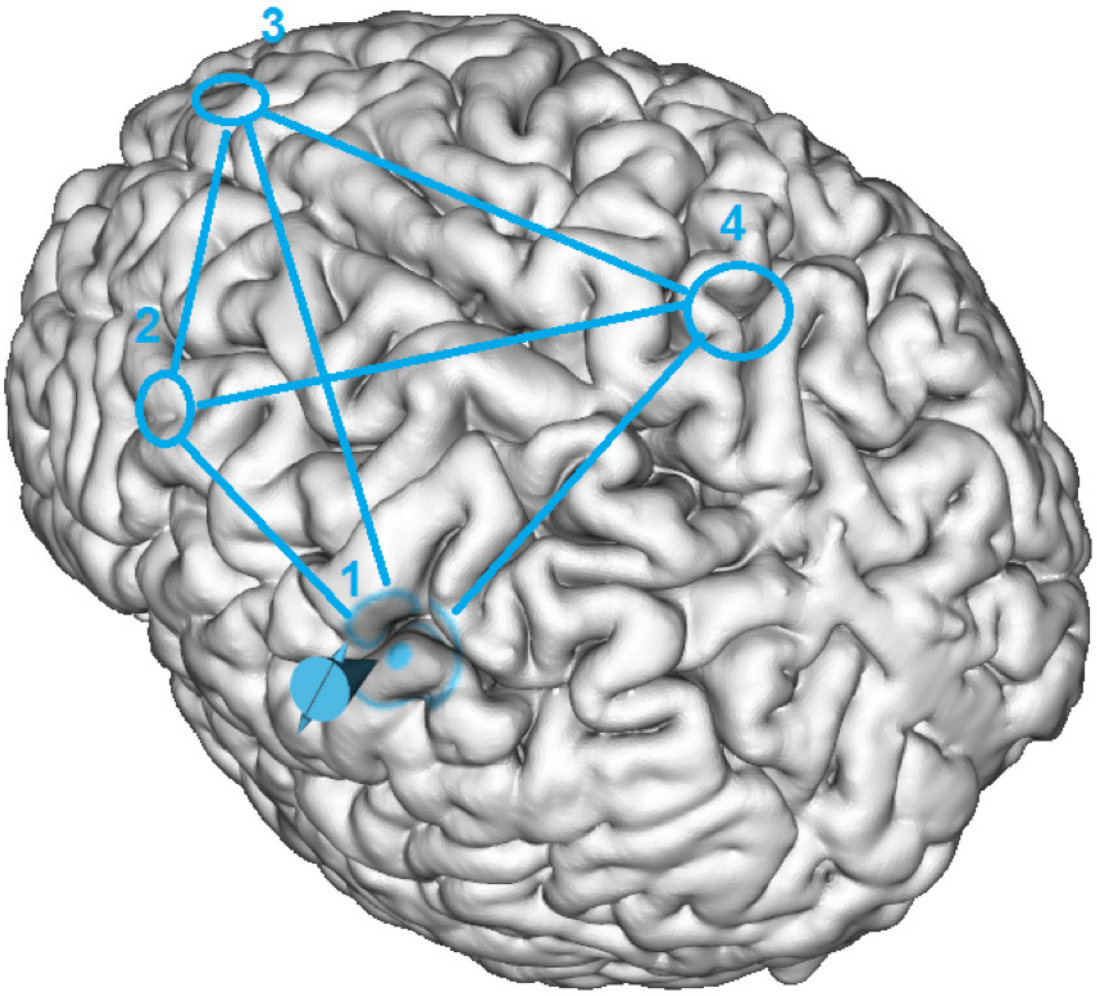


Image diagnosis

MRI diagnosis is necessary to begin rTMS therapy and reduce tinnitus caused by enhanced synchronization. It will be used in creating patient's 3D brain map and in creating stimulus protocol, which will include regions that need stimulation.

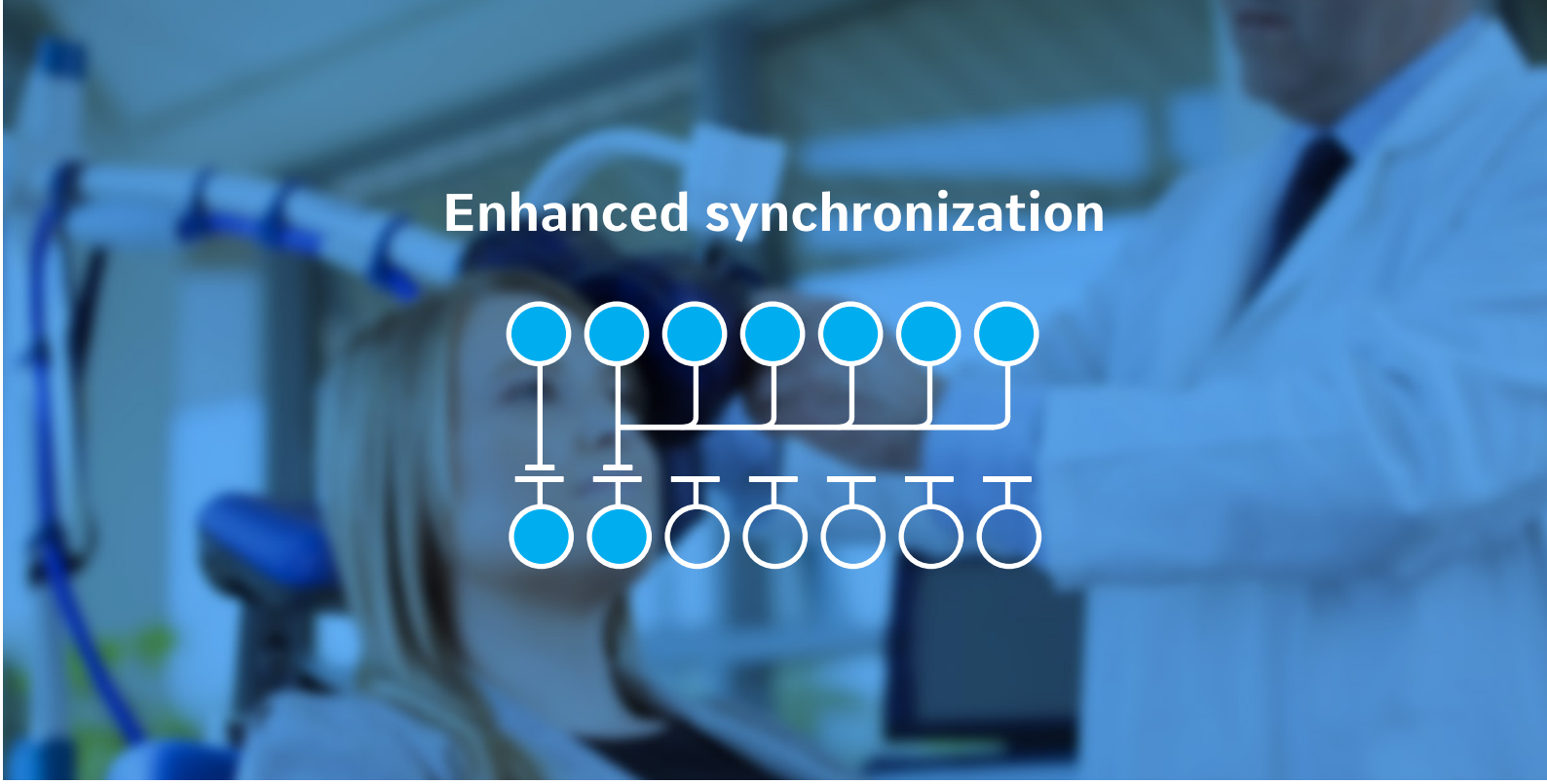


Requirements of MRI imaging

There are some recommended parameters in order to create a proper MRI image.

MRI specyfication for Syneika One navigator	
Input storage	CD-ROM/USB memory stick
Format	DICOM Standard
Modality	3D anatomical MRI
Signal weighting	T1
Spatial resolution	At least 1mm/voxel
The full patient head should be scanned included: -scalp -nose -ear	

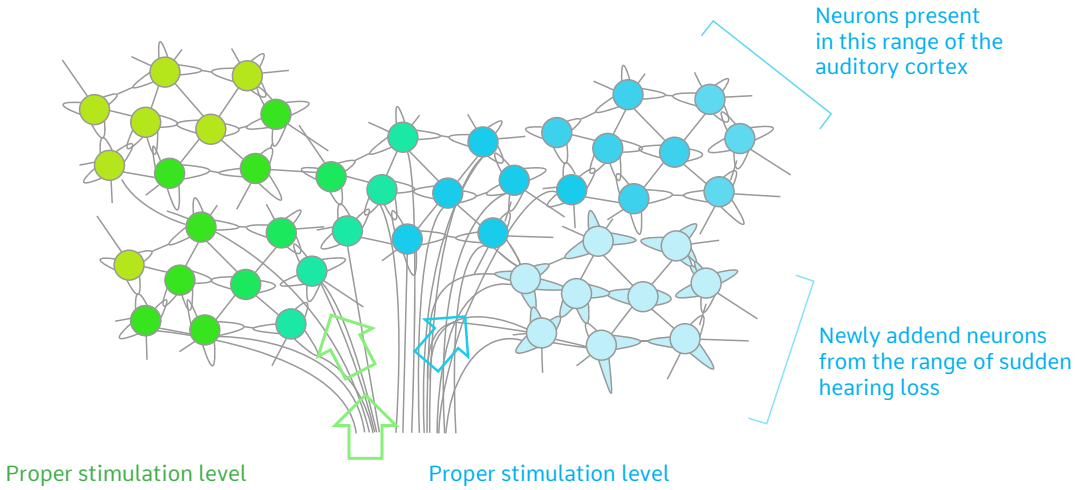
Proper MRI settings are necessary to create a legitimate 3D brain map by the neuronavigation system. It's necessary in following patient's results and effects of rTMS stimulation.



Stimulus protocol and use of rTMS

Transcranial stimulation rTMS is recommended for tinnitus caused by enhanced synchronization between neurons of the auditory cortex from the healthy, good-hearing range and those which lack stimulation.

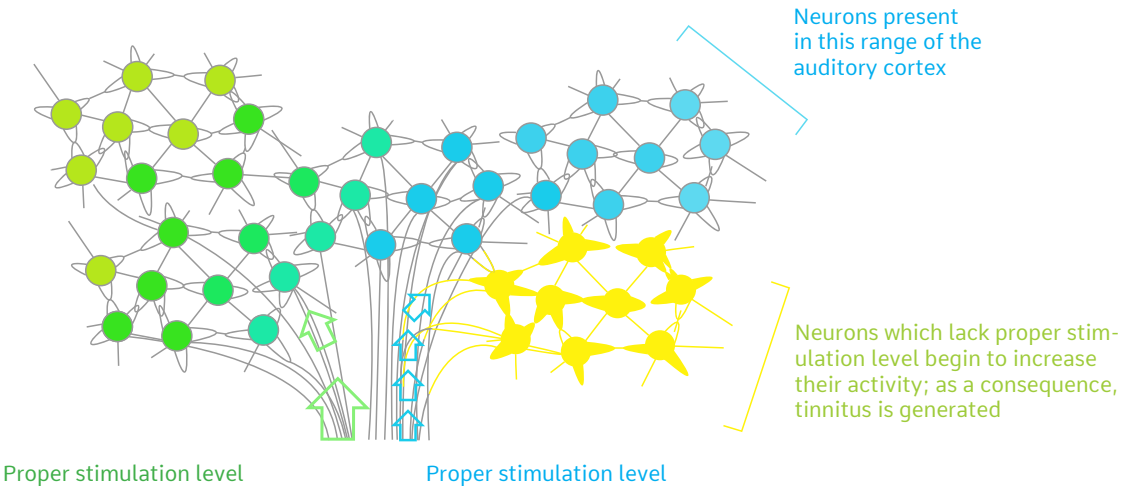
1 Neurons of the auditory cortex are divided into medium and high frequencies



The picture above shows a scheme of neurons from the auditory cortex. In green we have neurons which analyze ranges of medium frequencies, in blue neurons which analyze high frequencies. Some groups of these neurons constitute initial neurons of high ranges, since the beginning of organizing in the auditory cortex. Light blue indicates neurons which were added from the hearing loss range and tinnitus part of the auditory cortex.

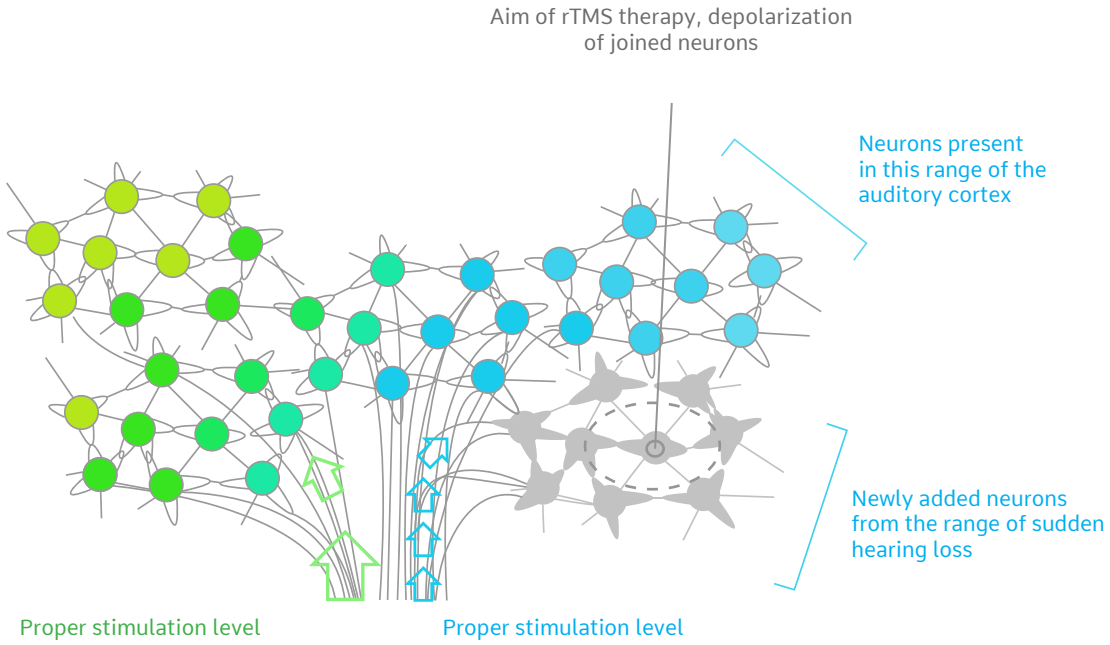
In time, a big population of neurons with hearing loss joins a population of good-hearing neurons; a bigger population of neurons of the same frequency is created (bigger than other segments of the auditory cortex).

2



Initially joined neurons' stimulation level is normal and neurons are engaged in signal analysis, whereas newly joined neurons lack a proper stimulation level, namely, it's too low. In this case, neurons of the auditory cortex which lack a proper stimulation level begin to increase their activity which results in enhanced synchronization (reinforced work eurhythmics). A patient hears it as tinnitus.

3



The main goal of this stimulation is to decrease activity of neurons in the auditory cortex with depolarization rTMS. Stimulation of neurons in the range of 1Hz causes decline and suppression of hyperactivity of synapses between those neurons; it reduces the opportunity of future excitement and enhanced synchronization. Due to weaker representation of neurons joined to a new population, acoustic stimulation might be of low effectiveness in a short period of time. Thus, transcranial stimulation rTMS should be chosen to this particular tinnitus model caused by enhanced synchronization. In a situation in which a patient cannot use electromagnetic stimulation, it is recommended to use a protocol of the synaptic adaptation therapy Arc in the first stages to reconstruct fibers and representation of connections between a cell and disconnected neurons, and then, adaptation protocol to reduce tinnitus.

References and research studies on effectiveness of rTMS treatment in tinnitus reduction

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Dornhoffer 2010 Using repetitive transcranial magnetic stimulation for the treatment of tinnitus

Garin 2011 Short and long lasting tinnitus relief induced by transcranial direct current stimulation

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Laterality, frequency and replication of rTMS treatment for chronic tinnitus - pilot studies and review of maintenence treatment

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Lehner 2013 Comparing single-site with multisite rTMS for the treatment of chronic tinnitus

Lehner 2013 Multisite rTMS for the treatment of chronic tinnitus - stimulation of the cortical tinnitus network

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Londero 2006 Magnetic stimulation of the auditory cortex for disabling tinnitus

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Marcondes 2006 Tinnitus and brain activation - insights from transcranial magnetic stimulation

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Mennemeier 2011 Variable changes in PET activity before and after rTMS treatment for tinnitus

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Phillips 2012 What is the evidence that 1 Hz rtTMS positively affects chronic tinnitus Plewnia 2003 Transient suppression of tinnitus by transcranial magnetic stimulation

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Vanneste 2012 Noninvasive and invasive neuromodulation for the treatment of tinnitus - an overview

Wang 2011 Repetitive transcranial magnetic stimulation enhances BDNF - TrkB signaling in both brain and lymphocyte

Yang 2013 The characteristic and changes of the event-related potentials and brain topographic maps before and after treatment with rTMS in subjective tinnitus patients