Magnetic and electrical stimulation of the auditory cortex for intractable tinnitus

Case report

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Tinnitus is a distressing symptom that affects up to 15% of the population for whom no satisfactory treatment exists. The authors present a novel surgical approach for the treatment of intractable tinnitus, based on cortical stimulation of the auditory cortex.

Tinnitus can be considered an auditory phantom phenomenon similar to deafferentation pain, which is observed in the somatosensory system. Tinnitus is accompanied by a change in the tonotopic map of the auditory cortex. Furthermore, there is a highly positive association between the subjective intensity of the tinnitus and the amount of shift in tinnitus frequency in the auditory cortex, that is, the amount of cortical reorganization. This cortical reorganization can be demonstrated by functional magnetic resonance (fMR) imaging.

Transcranial magnetic stimulation (TMS) is a noninvasive method of activating or deactivating focal areas of the human brain. Linked to a navigation system that is guided by fMR images of the auditory system, TMS can suppress areas of cortical plasticity. If it is successful in suppressing a patient’s tinnitus, this focal and temporary effect can be perpetuated by implanting a cortical electrode. A neuronavigation-based auditory fMR imaging-guided TMS session was performed in a patient who suffered from tinnitus due to a cochlear nerve lesion. Complete suppression of the tinnitus was obtained. At a later time an extradural electrode was implanted with the guidance of auditory fMR imaging navigation. Postoperatively, the patient’s tinnitus disappeared and remains absent 10 months later.

Focal extradural electrical stimulation of the primary auditory cortex at the area of cortical plasticity is capable of suppressing contralateral tinnitus completely. Transcranial magnetic stimulation may be an ideal method for noninvasive studies of surgical candidates in whom stimulating electrodes might be implanted for tinnitus suppression.

Key Words • tinnitus • auditory cortex • neurostimulation • cortical reorganization • functional magnetic resonance imaging • transcranial magnetic stimulation

Abbreviations used in this paper: fMR = functional magnetic resonance; IPG = internal pulse generator; pps = pulses per second; TMS = transcranial magnetic stimulation.
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Approval for both the TMS and the surgical implantation of the electrode was obtained from the ethics committee of the University Hospital of Antwerp, Belgium. The patient signed an informed consent form.

History. This 32-year-old woman presented at the neurosurgical clinic with a persistent left hemifacial spasm. She had undergone two unsuccessful microvascular decompression procedures at another institution 1 year earlier. The patient was offered a third microvascular decompression operation. Postoperatively, her hemifacial spasm disappeared, but she suffered a total loss of hearing in one ear. The loss of hearing was a result of injuries sustained by the auditory nerve due to a difficult dissection of scar tissue formed at the previous operations. Three weeks postoperatively the patient began to experience progressively worsening tinnitus. Three months postoperatively a constant, very disturbing, high-pitched nonpulsatile tinnitus developed and woke her up every night after 2 to 3 hours of sleep. The tinnitus was given a score of 8 to 9 of 10 on a visual analog scale. The loudness matching for the tinnitus was 80 dB and the frequency ranged from 3000 to 4000 Hz. In addition, the patient experienced a low-pitched tinnitus that was less disturbing and given a score of 6 to 7 of 10. Exposure to noise, especially high-frequency sounds, worsened the patient’s tinnitus. Clonazepam (0.5 mg administered three times each day) diminished the high-pitched tinnitus to a score of 6 to 7 of 10, but had no effect on the low-pitched noise. The patient exhibited no sign of an affective disorder.

Examination. Except for total loss of hearing in the left ear, the woman’s clinical examinations were unnoteworthy. The hearing deficit in her left ear was confirmed by pure tone audiometry. On the right side her hearing thresholds were within normal limits.

Acquisition of fMR Images. The patient underwent fMR imaging, which was performed using a 1.5-tesla imager with a paradigm consisting of 50 seconds of music (~1000–10,000 Hz delivered at 90 dB to both ears simultaneously) alternating with 50 seconds of nonstimulation. This was repeated six times. A T₁-weighted structural image was acquired using a three-dimensional turbo field echo sequence. Postprocessing was performed using Statistical Parameter Mapping software (SPM99; freely distributed by Wellcome Department of Cognitive Neurology, London, UK) and consisted of realignment (to correct for bulk head motion), coregistration of the functional and structural images, spatial smoothing, and statistical analysis to determine significantly activated brain regions (p < 0.05, corrected for multiple comparisons). Functional MR imaging of the auditory cortex (in the Heschl gyrus) demonstrated an asymmetry in activation strength and the size of area A1 (left side > right side); this indicates cortical reorganization because sudden unilateral deafness results in an initial absence of contralateral auditory cortex activity.

Transcranial magnetic stimulation was performed 9 months after the tinnitus first appeared by using a Super Rapid Stimulator (Magstim, Inc., Wales, UK), which is capable of repetitive pulse modes of up to 50 Hz. This magnetic stimulator was connected to a frameless stereotactic system (Brainsight; Magstim, Inc.), which permitted the exact localization of the target area that was chosen from the results of the fMR imaging study. The magnetic stimulation was directed toward the area identified by fMR imaging as having maximal activity, which was contralateral (right-sided auditory cortex) to the left-sided tinnitus. Different frequencies and intensities were applied at different sites and around the area displaying maximal activity.

The magnetic stimulation completely abolished the high-pitched tinnitus and reduced the less-annoying low-pitched noise by approximately 20%. The reduction in the tinnitus lasted beyond the duration of the stimulation (residual inhibition). The efficacy of the magnetic stimulation depended on the frequency and intensity of the magnetic impulses and on the exact site of stimulation. The degree of tinnitus suppression was directly related to the stimulation intensity and frequency (Fig. 2 upper). Magnetic stimulation at a rate of 5 pps had no effect, but stimulation at 10 and 20 pps had maximal effect (Fig. 2 upper). This maximal effect was obtained using a 500-msec burst at a pulse rate of 20 pps and an intensity of 90% of the threshold for evoking a motor response. This will induce a peak magnetic field strength of 1.2 tesla. Stimulation with 10 consecutive 500-msec bursts at 20 pps at 80% of motor threshold resulted in the absence of tinnitus for 20 seconds after the stimulation. Moving the coil 1 cm away from the target reduced the effect of the stimulation on the tinnitus. When the stimulating coil was...
moved farther away from the target, stimulation had little effect on the tinnitus. Sham stimulation also had no effect on the patient’s tinnitus (Fig. 2 lower), except for a site 1 cm posterior to the target. Sham stimulation consisted of delivering identical stimuli, but with the coil positioned orthogonal to the surface of the head, generating a magnetic pulse parallel to the surface of the brain. When this is performed, the clicking sound of the coil and the sensory contact are nearly identical to real stimulation.

Operation for Electrode Implantation. Three months later, that is, 1 year after the patient first experienced the tinnitus, an extradural octopolar electrode (Lamitrode 44; ANS, Inc., Plano, TX) was implanted for electrical stimulation of the auditory cortex. The Lamitrode 44 lead is made of eight electrodes with a 28-mm electrode span and a 60-cm lead length, configured with two offset rows of four electrodes, each measuring $4 \times 2.5$ mm with 3-mm spacing between the electrodes. A straight 6-cm-long incision was made overlying the auditory cortex, as determined by fMR imaging–guided neuronavigation. The $6 \times 2$-cm craniotomy and the location for electrode placement (Fig. 3) were determined using the same neuronavigation plan. The lead, which was extradurally placed, was sutured to the dura mater. It was then tunneled subcutaneously to the abdomen and connected to an IPG (Genesis; ANS, Inc.), which was im-

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**Fig. 2.** Bar graphs showing the results of TMS on tinnitus suppression as it relates to different stimulation parameters. **Upper:** Tinnitus suppression as influenced by stimulation frequency and intensity. **Lower:** Tinnitus suppression as influenced by the stimulation site and by sham stimulation. Note that stimulation 1 cm away from the target has no effect on subjective tinnitus.
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...planted into a subcutaneous pocket in the patient’s abdomen.

Postoperative Course. The postoperative course was uneventful. One hour after completion of the operation (with the IPG still in off mode), the patient awoke with the same tinnitus she had experienced before the operation. When the IPG was activated 4 hours later while the patient was in the prone position, the patient’s high-pitched tinnitus disappeared completely and her low-pitched tinnitus was reduced by approximately 60%. The IPG was set to deliver impulses with a duration of 0.5 msec and a rate of 40 pps and 2.7 mA. The stimulation was turned off for 10 seconds and turned on for 10 seconds. During her hospital stay the parameter settings were modified to allow better tinnitus suppression while the patient was in the upright position as well, because changing to an upright position resulted in recurrence of the tinnitus, although it was less intense. A similar effect was noted in noisy environments (40 Hz, 507 μsec, and 1.6 mA at night; 40 Hz, 507 μsec, 3.5 mA when standing or in noisy surroundings). A postoperative x-ray film demonstrated the placement of the electrodes (Fig. 3). The patient was discharged home on the 5th postoperative day and was completely free from tinnitus, both at low and high frequencies. Nevertheless, 3 weeks postimplantation the high-pitched tinnitus reappeared. With maximal stimulation parameters only the low-pitched tinnitus could be abolished. We hypothesized that this was the result of cortical plasticity in response to constant stimulation at the high-frequency area and we thus started using two alternating but different stimulation programs, stimulating in between different poles of the electrode (80 Hz, 390 μsec, and 2.5 mA; and 80 Hz, 390 μsec, and 2 mA) in an attempt to prevent plasticity as a reaction to the stimulation. Since then the patient has remained tinnitus free for 10 months. She is also able to increase or decrease the amplitude of the stimulation as wanted by using a remote control unit, an option she has only used twice.

Discussion

Any lesion along the auditory tract that influences the normal function of that tract can generate tinnitus, and an alteration in the normal sensory input or, especially, deprivation of input can lead to the plasticity of nuclei of the auditory pathways, including the contralateral cerebral cortex, through the expression of neural plasticity. Neural plasticity is regarded as a means to restore functions after injury and to change functions in accordance with altered demands; however, neural plasticity can also cause symptoms and signs of diseases.

Functional changes that are caused by the expression of neural plasticity are best known in the somatosensory system, where the role of neural plasticity in the cause of central neuropathic pain has been studied extensively. For example, phantom limb pain is associated with a reorganization of the somatosensory cortex, the degree of which correlates with the amount of pain. This reorganization is reversed in patients who are successfully treated with spinal cord stimulation for deafferentation pain, as demonstrated by magnetoencephalography studies. Tinnitus is accompanied by a change in the tonotopic map of the contralateral auditory cortex. Deprivation of input is a strong promoter of neural plasticity and that may explain why injuries to the auditory nerve, such as those that may occur during operations in the cerebellopontine angle, often are accompanied by severe tinnitus. The subjective intensity of the tinnitus is correlated with the size of the shift in the tinnitus frequency in the auditory cortex. Tinnitus can be treated with electrical stimulation and patients with cochlear implants sometimes experience elimination of their tinnitus. In one report 60% of patients reported that their tinnitus had been suppressed or abolished, and tinnitus was also suppressed in the contralateral ear.

It is not known why electrical stimulation of the cerebral cortex eliminates tinnitus. The mechanism of auditory cortex stimulation in the treatment of tinnitus may be similar to that of motor cortex stimulation in the treatment of deafferentation pain. Stimulation of the cerebral cortex may act directly on cortical neurons or it may act on descending pathways.

Transcranial magnetic stimulation is a noninvasive tool used to study the human brain. Depending on the stimulation parameters, TMS can excite or inhibit the brain and is, therefore, an ideal tool to study and to interfere with cortical reorganization. Only very recently has TMS been used in the clinical setting of tinnitus. In more than 40 TMS sessions performed in patients with unilateral tinnitus, we only encountered one patient in whom the tinnitus could be suppressed by stimulation of the ipsilateral auditory cortex (unpublished data). This confirms data obtained from positron emission tomography scans, which demonstrate that in unilateral tinnitus a site of hyperactivity is noted contralateral to the tinnitus, as well as data from magnetoencephalography studies, which demonstrate identical results. It seems that acute unilateral tinnitus is the result of a site of hyperactivity in the contralateral auditory cortex.

Extensive testing in our patient demonstrated that the high-pitched tinnitus could be completely abolished using TMS. Sham stimulation did not abolish the tinnitus and stimulation that was administered progressively farther away from the target led to a consistent decrease in tinnitus suppression, which reached zero suppression when the stimulation was more than 1 cm distant from the target. It therefore seems of utmost importance to use an fMR imaging navigation-based stimulator as a means for noninvasive testing of tinnitus sufferers.
Conclusions
Focal extradural electrical stimulation of the primary auditory cortex at the area of cortical reorganization is capable of suppressing contralateral tinnitus completely. Transcranial magnetic stimulation seems to be an ideal method for noninvasive studies of surgical candidates for implantation of stimulating electrodes for tinnitus suppression.

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References