

# Exploring deep brain stimulation as a treatment for tinnitus

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## Valorisation

Tinnitus can pose a great burden on patients, their families and society. The impact on patients varies from a not-bothersome form (in 24% of the cases) to a form in which tinnitus plagues a patient all day long (17%) (Axelsson and Ringdahl, 1989). This can lead to a series of psychological symptoms ranging from tension, frustration, sleep disturbance and loss of concentration, to depression and in severe cases even suicide (Andersson et al., 2005; Pridmore et al., 2012; Sullivan et al., 1988). It is not surprising that there is an impact on friends and family; 41% of the patients report negative effects on personal relationships (Holmes and Padgham, 2009).

Tinnitus-related societal costs in The Netherlands are estimated to add up to 6.8 billion euro per year. From these costs, health care costs of tinnitus were 1.9 billion euro, the rest is mainly related to productivity losses. The tinnitus-related health care costs account for 2.3% of the total Dutch health care expenditure (Maes et al., 2013).

At this moment, patients are not satisfied with the current tinnitus care; in The Netherlands a mean grade of 5.6 is given by patients. This grade is highest for patients with moderate symptoms (6.1) and is worse for patients with more severe symptoms (4.6). After the first outpatient visit, almost 75% of the patients consult a second doctor or other caregiver. Only 30% of the patients reported to be benefited from this second visit (Schenk-Sandbergen, 2012). Outpatient visits mainly focuses on explanation, reassurance and education. Absence of a thorough treatment of tinnitus is likely to contribute to the struggle in tinnitus care.

The high impact of tinnitus on patients, society and economics on the one hand and the absence of an effective treatment on the other hand stresses the importance of developing new treatments for this condition.

Here, we investigated the effect of deep brain stimulation (DBS) on tinnitus to find a treatment for severe tinnitus sufferers. As DBS is an invasive procedure, finding patients willing to accept this treatment could be a first challenge. Therefore, we assessed the willingness of acceptance by means of a questionnaire study. Approximately 40% of the patients expressed that they were willing to undergo invasive neuromodulatory treatments such as DBS. Given the high prevalence of tinnitus, this figure can be considered substantial. Patients wish to undergo invasive neuromodulatory treatment despite a risk of sometimes severe side-effects, such as deafness or complications leading to death. For example, the risk of deafness and death were accepted as side effects by respectively 33% and 19% of the patients, when only a 50% tinnitus remission is expected. Based on these results and taken the high prevalence of tinnitus into account, a large group of patients could be treated by DBS. Regarding to ethical considerations in DBS, the risks and benefits have to be balanced thoroughly without hampering the patient's autonomy (Schermer, 2011).

A quarter of the patients is willing to pay more than 20 times their monthly income for treatment if complete tinnitus elimination is given in prospect. In The Netherlands, this means a mean outlay of €38,900. At the moment, there is no reimbursement of outlay for these forms of invasive treatments for tinnitus since these treatments are still in state of development.

The outcomes of preclinical experiments in this thesis are in line with initial reports which have shown a positive effect of DBS on tinnitus. With preclinical studies valuable information regarding the optimal target for DBS in tinnitus can be extracted, which could lead to maximum therapeutic effects and cause minimal side effects. One of the targets to further be studied is the medial geniculate body of the thalamus. This target is also involved in the auditory pathway and is stereotactically easily reached in human DBS surgery.

Until now DBS has not been performed in auditory structures. A clinical study will provide a unique opportunity to record neuronal activity in central auditory structures. With the implanted DBS electrodes, local field potentials can be measured and can be combined with electroencephalography and auditory brainstem responses. These measurements lead to more insight in the auditory function such as central auditory crossing, tonotopic organization and allocation of attention to sound. This information is crucial to get a better understanding of altered activity in the auditory network. Finally, these recordings may establish a neurophysiological marker which could serve as an input parameter for a (closed-loop) neuromodulation device for individualized treatment.

In case of a future clinical study, multidisciplinary collaboration is essential for a successful project. Disciplines that need to be involved are departments of ear, nose and throat, neurosurgery, neurology, clinical neurophysiology, clinical psychology, neuropsychology and psychiatry. Because of the overlapping facets of tinnitus in these areas, future collaboration of disciplines is crucial. Therefore, this project could be a start in a more interdisciplinary approach in clinical tinnitus care. This may result in higher quality tinnitus care, with more satisfied patients.

Overall, this thesis is a step forward in finding an evidence-based treatment for tinnitus, which substantially diminishes the tinnitus without hampering physiological processes such as hearing. This therapy might not replace existing therapies but could serve as a treatment for therapy-resistant patients who highly suffer from tinnitus. The translational aspect of this thesis and the multidisciplinary environment paves the way for a clinical trial to assess tinnitus outcome during DBS. Secondary important, new information of central auditory processing will be gained.

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