RESEARCH ARTICLE

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Raising the Voltage of Vagal Nerve Stimulation in Patients with Tinnitus

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ABSTRACT

Background: Aberrant neural activity within central auditory pathways can cause the symptoms of tinnitus. The dorsal cochlear nucleus (DCN) enhances auditory-somatosensory integration in tinnitus conditions, leading to increased spontaneous and sound-driven neural activity. Electric stimulation of the cranial nerves can stop this neural activity and make tinnitus less bothersome by stimulating the cochlear nucleus through somatosensory input.

Objectives: We wondered which voltage of PRF gave the best clinical results in tinnitus patients and want to observe the changes in pupillometric measures for the different voltages.

Methods: This study was conducted as a retrospective study in our center. Tinnitus patients treated with PRF of the vagal nerve in the period between October 2023 and November 2024 (n = 79) were the subjects. Patients could choose between 42, 55, or 70 Volt of PRF.

Results: PRF of the vagal nerve reduced the intensity of tinnitus in 45-58% of the patients with mild side-effects. Performing this technique with 70 V had a higher success-rate (58%) with no side-effects. We advise using 70 V PRF of the vagal nerve in order to reduce the intensity of tinnitus, especially if there is hearing loss at 250 Hz in the pre-operative audiogram. The difference in BPD caused by vagal nerve stimulation (VNS) correlated with the result of this therapy. In tinnitus patients who undergo PRF of the vagal nerve, the difference in BPD caused by therapy should be positive or slightly negative for a positive result of therapy, especially when patients are treated with 55 V.

Conclusion: Electrical stimulation of somatosensory input to the dorsal cochlear nucleus by pulsed radiofrequency of the vagal nerve can change the way the brain works in ways that are related to tinnitus and reducing the loudness of this sound. We advise using 70 volt during this technique for a better reduction of the intensity of tinnitus, especially if there is hearing loss at 250 Hz in the pre-operative audiogram. Vagal nerve stimulation caused a difference in basal pupil diameter, which correlated with the outcome of this therapy.

Keywords: Vagal nerve stimulation, Pupillometry, Tinnitus, Autonomic nervous system, Pulsed radiofrequency.

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INTRODUCTION

Aberrant neural activity within central auditory pathways can cause the symptoms of tinnitus[1]. The dorsal cochlear nucleus (DCN) enhances auditory-somatosensory integration in tinnitus conditions, leading to increased spontaneous and sound-driven neural activity[2,3]. Electric stimulation of the cranial nerves can stop this neural activity and make tinnitus less bothersome by stimulating the cochlear nucleus through somatosensory input[4].

Pulsed Radiofrequency (PRF) is widely used to manage chronic pain and tinnitus[5,6]. The duration and the level of the output voltage (V) of PRF are an object for discussion[7,8]. High-voltage PRF seems more effective than standard-voltage PRF. Therefore, in our clinic we offer tinnitus patients pulsed radiofrequency of the vagal nerve with 42 V, 55 V, or 70 V. We wondered which voltage of PRF gave the best clinical results in tinnitus patients and want to observe the changes in pupillometric measures for the different voltages.

METHODS

This study was conducted as a retrospective study in our center. The Ethics Committee United (Nieuwegein, the Netherlands) acknowledged this study (W25.019, February 2, 2025). Tinnitus patients treated with PRF of the vagal nerve in the period between October 2023 and November 2024 (n = 79) were the subjects. The information obtained included clinical information, the reduction in loudness at 7 weeks post treatment, side effects, data of the audiogram and of the quantitative pupillometry. Hidden hearing loss is defined as extra hearing loss with background noise.

Quantitative Pupillometry

We performed pupillometry using the NeuroLight Algiscan (ID-MED, Marseille, France) with one estimation before therapy, and one estimation after therapy for each eye of the patient. The ensuing parameters were obtained: baseline pupil diameter (BPD) (mm), maximum constriction amplitude (MCA) (mm), and maximal constriction velocity (MCV) (mm/sec).

PRF of the vagal nerve

Patients could choose between 42, 55, or 70 V of PRF. A 22-gauge, 60 mm-long needle with a 5 mm active tip was positioned percutaneously at the inner tragus. Next, we applied pulsed radiofrequency at 42, 55, or 70 V, 2 Hz, and ten milliseconds for 10 minutes.

Statistics

We used Minitab 18 (Minitab Inc., State College, PA, USA) to execute the statistical analysis. Student's t-test was handled for continuous variables and χ^2 test for dichotomous variables. Analysis of variance differentiated the differences between the patients who were treated with 42 V, 55 V, or 70 V. PRF of the vagal nerve. A value of P less than 0.05 was statistically significant.

RESULTS

The vagal nerve received PRF treatment for tinnitus in 79 patients. People with tinnitus patients had a high-frequency hearing loss on the audiogram, self-perceived hidden hearing loss (94%), and a hearing loss they thought they had (58%) **(Table 1)**.

PRF of the vagal nerve reduced the loudness of tinnitus in 45-58% of the patients with mild side-effects (0-14%) **(Table 2)**. Side-effects reported after therapies were an increase of tinnitus, pain, or fatigue. Although PRF of the vagal nerve with 70 V had a higher success rate (58%) with no side effects, it did not reach significance in the statistical analysis.

We compared the pupillometry measures before and after PRF of the vagal nerve with different voltages **(Table 3)**. The differences in BPD and MCV induced by PRF of the vagal nerve were statistically significant. When the vagal nerve's PRF was set to 70 V, BPD went down a little

Table 1: Clinical Characteristics of the patients with tinnitus.

	Prevalence	Median	Q1 – Q3
Age (year)		58	52 – 66
Gender (male)	50%		
Self-perceived hearing loss	58%		
Self-perceived hidden hearing loss	94%		
Hearing loss (dB) at:			
250 Hz		10	5 – 20
500 Hz		15	5 – 20
1 kHz		15	10 – 25
2 kHz		15	5 – 29
4 kHz		30	15 – 49
8 kHz		30	15 – 50
Pupillometry pre-operative			
BPD (mm)		3.9	3.3 – 4.4
MCA (mm)		1.1	0.8 – 1.4
MCV (mm/sec)		3.3	2.5 – 4.2

Q1 – Q3: Inter-Quartile Range; BPD: basal pupil diameter; MCA: maximum constriction amplitude; MCV: Maximum constriction velocity.

Table 2: Results and side-effects of PRF of the vagal nerve on tinnitus.

	PRF with 47V (n=24)	PRF with 55 V (n=29)	PRF with 70 V (n=26)	p-value
Positive effect of therapy	45%	45%	58%	0.617
Side-effects	4%	14%	0%	0.092
	Increase of tinnitus	Increase of tinnitus, pain or fatigue		

PRF: pulsed radiofrequency; V: volt

Table 3: The pupillometric effects of pulsed radiofrequency therapy of the vagal nerve.

	PRF with 47 V (n=47)		PRF with 55 V (n=58)		PRF with 70 V (n=52)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Preoperative							
BPD (mm)	3.9	0.83	4	0.82	3.8	0.73	0.262
MCA (mm)	1.2	0.66	1.2	0.53	1.1	0.45	0.544
MCV (mm/s)	3.5	1.77	3.5	1.75	3.4	1.22	0.824
Postoperative							
BPD (mm)	3.7	0.98	3.7	0.81	3.7	0.87	0.926
MCA (mm)	1	0.45	1	0.6	1.1	0.7	0.385
MCV(mm/s)	2.9	1.25	3	1.6	3.7	2.98	0.115
Difference							
BPD (mm)	-0.2	0.69	-0.5	0.91	-0.1	0.92	0.038
MCA (mm)	-0.2	0.64	-0.2	0.52	0	0.71	0.09
MCV (mm/s)	-0.5	1.57	-0.6	1.49	0.4	3.09	0.037

PRF: pulsed radiofrequency; V: volt; SD: standard deviation; BPD: basal pupil diameter; MCA: maximum constriction amplitude; MCV: Maximum constriction velocity.

Table 4: Tinnitus reduction following PRF of the vagal nerve compared with no effect of therapy.

	Tinnitus reduction (n=77)			No effect (n=80)			p-value
	Prev.	Mean	SD	Prev.	Mean	SD	
Gender (male)	48%			53%			0.577
Age (years)		57	10.2		58	13.1	0.647
Preoperative							
BPD (mm)		3.9	0.69		4	0.89	0.356
MCA (mm)		1.2	0.57		1.2	0.52	0.889
MCV (mm/s)		3.5	1.53		3.5	1.66	0.677
Postoperative							
BPD (mm)		3.8	0.67		3.6	1.05	0.325
MCA (mm)		1.1	0.47		1	0.7	0.175
MCV (mm/s)		3.3	1.21		3.2	2.73	0.892
Difference							
BPD (mm)		-0.1	0.55		-0.4	1.06	0.011
MCA (mm)		0	0.54		-0.2	0.71	0.098
MCV (mm/s)		-0.1	1.35		-0.4	2.8	0.506
Hearing loss (dB)							
at 250 Hz		19	17.4		12	9.7	0.013
at 500 Hz		19	17.4		14	11.4	0.046
at 1 kHz		21	15.2		16	11.9	0.05
at 2 kHz		21	17.8		16	12.1	0.048
at 4 kHz		35	21.2		30	21.6	0.241
at 8 kHz		37	26.1		32	24.1	0.273

PRF: pulsed radiofrequency; Prev.: prevalence; SD: standard deviation; BPD: basal pupil diameter; MCA: maximum constriction amplitude; MCV: Maximum constriction velocity; mm; millimetre; s: second; dB: decibel.

and MCV went up clearly compared to the other voltages. This pattern indicates a specific stimulation of the parasympathetic activity, along with some sympathetic stimulation.

We compared patients with a reduced intensity of their tinnitus following PRF of the vagal nerve to those who had no effect **(Table 4)**. Patients with a successful effect of vagal nerve stimulation had a statistically significant difference in BPD and hearing loss at 250, 500, and 2 kHz compared to the non-responders. The non-responders had a lower difference in BPD, in MCA, and in MCV. This could suggest a decrease in parasympathetic and

Table 5: Pulsed radiofrequency of the vagal nerve with different voltages and the relation to hearing loss at 250 Hz and to a successful result of therapy in patients with tinnitus.

			Beneficial result of PRF		No effect of PRF		p-value
	HL at 250 Hz (dB)		HL at 250 Hz (dB)		HL at 250 Hz (dB)		
	Mean	SD	Mean	SD	Mean	SD	
PRF with 42 V	15	15	17	13.4	13	8.6	0.284
PRF with 55 V	16	15.4	19	20.3	14	10.1	0.29
PRF with 70 V	15	11.4	22	18.5	11	10.1	0.039
p-value	0.956						

PRF: pulsed radiofrequency; HL: hearing loss; dB: decibel; SD: standard deviation; V: volt.

Table 6: Pulsed radiofrequency of the vagal nerve with different voltages and the relation to the difference in basal pupil diameter between before and after therapy and to a successful result of therapy in patients with tinnitus.

			Beneficial result of PRF		No effect of PRF		p-value
	Difference BPD (mm)		Difference BPD (mm)		Difference BPD (mm)		
	Mean	SD	Mean	SD	Mean	SD	
PRF with 42 V	-0.2	0.69	-0.1	0.39	-0.2	0.87	0.678
PRF with 55 V	-0.5	0.91	-0.2	0.52	-0.7	1.09	0.014
PRF with 70 V	-0.1	0.91	0	0.66	-0.3	1.18	0.304
p-value	0.038						

PRF: pulsed radiofrequency; BPD: basal pupil diameter; mm; millimetre; SD: standard deviation; V: volt.

sympathetic activity due to vagal nerve stimulation. Hearing loss at 250 Hz in the pre-surgery audiogram was statistically significantly higher in people who got better after 70 V PRF of the vagal nerve **(Table 5)**. PRF of the vagal nerve with 70 Volt is advocated for tinnitus patients with a hearing loss at 250 Hz.

An important difference in BPD caused by PRF of the vagal nerve was seen between the groups that were given 42 V, 55 V, or 70 V **(Table 6)**. The difference in BPD caused by therapy was statistically significantly higher in patient who did well with a 55 V PRF of the vagal nerve in the group that was treated. For this reason, the difference in BPD caused by PRF of the vagal nerve therapy should be positive or slightly negative for the therapy to work for people with tinnitus, especially when they are treated with 55 V.

DISCUSSION

PRF of the vagal nerve reduced the intensity of tinnitus in 45-58% of the patients with mild side-effects. Performing this technique with 70 V had a higher success-rate (58%) with no side-effects. We advise using 70 V PRF of the vagal nerve in order to reduce the intensity of tinnitus, especially if there is hearing loss at 250 Hz in the pre-operative audiogram. The difference in BPD caused by vagal nerve stimulation (VNS) correlated with the result of this therapy. In tinnitus patients who undergo PRF of the vagal nerve, the difference in BPD caused by therapy should be positive or slightly negative for a positive result of therapy, especially when patients are treated with 55 V.

Tinnitus patients were characterized with the presence of self-perceived hidden hearing loss (94%). Defects in the cochlea can cause hidden hearing loss, which in turn can lead to the development of tinnitus 9. Tinnitus is a symptom of aberrant neural activity within central auditory pathways 1. The increased spontaneous activity in tinnitus could be due to alterations in fusiform-cell plasticity[10,11]. However, only dorsal cochlear nucleus cells with connections to the somatosensory system show increased spontaneous rates after noise damage. It seems that in patients with tinnitus, hidden hearing loss can induce both hyperactivity and a lack of inhibition in the auditory pathway connected to the somatosensory system.

The cochlear nucleus is subjected to multisensory integration[12,13]. These include input of the auditory nerve and somatosensory projections from the trigeminal ganglia, cervical dorsal root ganglia, trigeminal nucleus, dorsal column nuclei and the lateral reticular formation. The somatosensory projections end in the granule cell domain of the cochlear nucleus as mossy fibres and en passant endings. Through the mossy fibre-parallel fiber-fusiform cell pathway, the secondary somatic sensory neurons affect the output of the DCN in a roundabout way. The apical dendrites of fusiform cells are activated through stimulation of somatosensory nuclei while the basal dendritic synapses are activated with sound[10]. Somatosensory stimulation can directly influence the auditory pathway in the cochlear nucleus.

VNS showed clinically meaningful long-term reductions of the loudness of tinnitus[14]. Adverse effects were mild and well-tolerated. A previous study found that 48% of people with tinnitus who had PRF of the vagal nerve said their tinnitus got softer[15]. In 87% of these cases, the improvement was considered moderate to good. This reduction mostly exceeded a year. Also, this study found that PRF of the vagal nerve reduced the intensity of tinnitus in 45-58% of the patients with mild side-effects.

Stimulation of afferent cranial nerve axons activates specific brain circuits linked to tinnitus. The nucleus tractus solitarius (NTS), the locus coeruleus (LC), the

trigeminal brainstem nuclei, and the nucleus cuneatus are all part of the activated VNS network[16]. To reach granule cells and unipolar brush cels in the DCN, the trigeminal nuclei and the nucleus cuneatus are important[17]. Trigeminal pathways that connect to the cochlear nucleus can change how neurons in the ventral and dorsal cochlear nucleus naturally work[18]. Besides the effects of VNS on the cochlear nucleus, there is also an effect on the brain stem. Neurons within the NTS project to the noradrenergic LC, the amygdala, and the cholinergic basal forebrain[19-21]. Two paths connect the NTS to the LC: one is an excitatory pathway that goes through the nucleus Paragigantocellularis (PGi)), and the other is an inhibitory pathway that goes through the nucleus prepositus hypoglossi. The activation of the PGi during LC discharge primarily involves excitation but, in a minority of cells, it also involves inhibition. Peripheral stimulation of vagal afferents elicits an inhibition-excitation sequence in the LC[22].

You can use BPD to index LC activity. The LC controls the Edinger-Westphal nucleus, which mediate the pupillary light reflex[23]. The MCV and MCA parameters are markers of parasympathetic cholinergic activity[24]. Sympathetic activity primarily controls the BPD. BPD, MCA, and MCV were significantly reduced in tinnitus patients[25]. This suggests that patients with tinnitus have impaired parasympathetic and sympathetic nervous systems.

In our study, we discovered that VNS lowers the BPD and that the difference in BPD caused by PRF of the vagal nerve is connected to the therapy outcome and the vagal nerve's voltages. Non-responders to PRF of the vagal nerve had a lower difference in BPD, in MCA, and in MCV. The PRF of the vagal nerve may have induced a reduction in parasympathetic and sympathetic activity. Raising the voltage of PRF to 70 V gave an increased difference in MCV and BPD, indicating a specific stimulation of the parasympathetic activity with also some sympathetic stimulation. We've come to the conclusion that the difference in BPD caused by PRF of the vagal nerve should be positive or slightly negative for therapy to work well for people with tinnitus, especially when 55 V is used.

Electric stimulation of the cranial nerves can make tinnitus less bothersome by stimulating the cochlear nucleus through somatosensory input. It is thought that stronger stimulation parameters cause LC firing rate to rise more, and they are linked to better clinical effectiveness[26]. In our study, PRF of the vagal nerve with 70 V worked better and had fewer side effects than PRF of the vagal nerve with 42 and 55 V, but the differences were not statistically significant. The therapeutic effect of VNS seems to be associated with less activity at the LC. These results suggest that the PGi inhibitory pathway may be a key part of how VNS helps treat tinnitus.

Hearing loss at 250 Hz in tinnitus patients was associated with a beneficial result following PRF of the vagal nerve. When somatosensory areas are electrically activated in the DCN, they change the timing and rates of pyramidal cell spikes that respond to sound stimuli[27]. The increased sensitivity of DCN neurons to somatosensory stimuli in patients with hearing loss might explain the better response following PRF of the vagal nerve.

We should interpret our findings in the context of several inherent study limitations, such as the retrospective study concept and the number of patients. A prospective study with a larger patient cohort can solve this issue.

CONCLUSION

Electrical stimulation of somatosensory input to the dorsal cochlear nucleus by pulsed radiofrequency of the vagal nerve can change the way the brain works in ways that are related to tinnitus and reducing the loudness of this sound. We advise using 70 volt during this technique for a better reduction of the intensity of tinnitus, especially if there is hearing loss at 250 Hz in the pre-operative audiogram. Vagal nerve stimulation caused a difference in basal pupil diameter, which correlated with the outcome of this therapy.

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