CLINICAL ARTICLE

Vascular compression of the cochlear nerve and tinnitus: a pathophysiological investigation

**Dirk De Ridder · Sven Vanneste · Ine Adriaensens ·
Alison Po Kee Lee · Paul van de Heyning · Aage Möller**

Abstract

Objective Chronic microvascular compressions of the eighth nerve induce a slowing down of signal transmission in the auditory nerve, electrophysiologically characterized by IPL I-III prolongation.

Methods The authors hypothesize this is compensated by an active slowing down of signal transmission of the contralateral input at the level of the brainstem, characterized by contralateral IPL III-V prolongation.

Results Differences between ipsilateral and contralateral IPL I-III and IPL III-V are analyzed before and after microvascular decompression. ABR diagnostic criteria for microvascular compression are ipsilateral IPL I-III prolongation or ipsilateral peak II decrease + ipsilateral IPL I-III prolongation. With IPL I-III as diagnostic criterion, unlike preoperatively the difference between the ipsi- and contralateral IPL I-III is significant postoperatively. When using the stricter diagnostic criterion of IPL I-III + peak II, there is a preoperative significant difference between ipsi- and contralateral IPL I-III, but postoperatively the difference between the ipsi- and contralateral IPL I-III is not significant.

Conclusions Preoperatively, there is a marginal significant difference between the ipsi- and contralateral IPL III-V, which disappears postoperatively.

Abbreviations

ABR	Auditory brainstem response
dB HL	Decibel hearing loss
IPL	Interpeak latency
MVC	Microvascular compression
MVD	Microvascular decompression

D. De Ridder · S. Vanneste (✉) · I. Adriaensens · A. P. K. Lee
TRI Tinnitus Clinic, BRAI²N & Department of Neurosurgery,
University Hospital Antwerp,
Wilrijkstraat 10,
2650 Edegem, Belgium
e-mail: sven.vanneste@ua.ac.be
URL: http://www.brai2n.com

P. van de Heyning
TRI Tinnitus Clinic, BRAI²N & Department of ENT,
University Hospital Antwerp,
Wilrijkstraat 10,
2650 Edegem, Belgium

A. Möller
School of Behavior and Brain Sciences,
University of Texas at Dallas,
Richardson, TX, USA

Introduction

The success rate of microvascular decompression surgery of the eighth nerve for tinnitus reported in the literature is lower than that of trigeminal neuralgia, hemifacial spasm, and disabling positional vertigo, which in general is close to 85% [9]. Success rates for MVDs for tinnitus on the other hand vary from 40 to 77% [1, 16], and the criteria to evaluate such results have not received a full agreement. There is agreement that the longer the tinnitus exists before the decompression the worse the results of microvascular decompressions [1, 2, 4, 5, 8, 16, 19]. When a vertebral artery loop is the compressing blood vessel, 80% of good clinical results have been reported [7]. Hearing level at the moment of decompression seems to be important as well [19], as well as gender [16].

Some investigators used auditory brainstem response (ABR) in selection of patients for MVD operations for tinnitus [16]. A pathophysiological approach for interpreting changes has been proposed based on abnormalities in the amplitude of peak II and the interpeak latency (IPL) I-III of the ABR [2]. While no ABR changes could be detected during the first 2 years of tinnitus associated with a neurovascular conflict, after that period a decrease of the amplitude of peak II occurred, and a prolongation of the interpeak latency (IPL) of peak I-III occurred in patients whose peak II had disappeared. IPL I-III prolongation correlates with ipsilateral hearing loss at tinnitus frequency and worsens in time. Postoperative improvement of tinnitus correlated with postoperative improvement of peak II and postoperative improvement of hearing loss at the tinnitus frequency correlated with postoperative IPL I-III improvement [2].

Materials and methods

The study population was selected from a database consisting of tinnitus patients who presented at the multidisciplinary tinnitus clinic of the Antwerp University Hospital, Belgium.

The relevant associated symptoms such as optokinetic vertigo, ipsilateral cryptogenic hemifacial spasms, and ipsilateral paroxysmal short bouts of otalgia with pain stabs or feeling of pressure in the ear were documented. ABR parameters were assessed using Møller's criteria [15] (see Table 1) and considered abnormal in cases where at least one of the Møller's criteria was met. The patients' MRI was visually inspected for a vascular compression of the eighth cranial nerve. Based on these selection criteria (associated clinical symptoms, abnormal ABR, or abnormal MRI) and after undergoing a surgical microvascular decompression (MVD), 22 patients were classified in the certain CVCS group (see Table 2).

Audiological investigation consisted of pure tone and speech audiometry and tinnitus matching. Audiometry was conducted to determine hearing loss at tinnitus frequency, as well as maximal hearing loss and its frequency. Tinnitus matching investigated the frequency and intensity of the tinnitus by offering several sounds to the patient of

Table 1 Møller's ABR criteria for diagnosing a microvascular conflict of the eighth nerve [15]

Ipsilateral IPL I-III ≥2.3 ms
Contralateral IPL III-V ≥2.2 ms
IPL I-III difference ≥0.2 ms
IPL III-V difference ≥0.2 ms
IPL I-III difference ≥0.16 ms if low or absent peak II
IPL III-V difference ≥0.16 ms if low or absent peak II
Peak II amplitude <33%

Table 2 Demographic data (n=20)

Sex	11 women	9 men
Affected side	10 left	10 right
Age at MVD (years)	Age range: 35-67	Mean age: 49.5
Tinnitus duration at MVD (years)	Tinnitus duration range: 1–15	Tinnitus duration mean: 5.5

whom the patient had to indicate which sound resembled his tinnitus the best.

The ABRs elicited by clicks with alternating polarity were obtained with a Nicolet Viking IV D system. The stimuli were presented through headphones at a rate of 16 Hz. The stimulus intensity was 80 dB HL but a few were 90 dB or 100 dBHL, which was proportional to the participant's hearing loss. Noise was presented to the contralateral ear at a sound pressure level that was 40 dB below that of the ipsilateral presented clicks. The ABR potentials were recorded from electrodes placed on the vertex and the mastoid using filter settings at 150–1,500 Hz. At each stimulus condition, two runs of 2,000 responses were averaged and digitally filtered to enhance the peaks of the ABR. Computer programs were used to automatically identify the different peaks and to print the latencies of the peaks. Afterwards, these registrations were manually verified and corrected if necessary. As the used computer programs did not automatically identify the amplitude of peak II, these were distracted manually by measuring the distance from the top perpendicular to the baseline.

In these patients, microvascular compression was noted in all patients during surgery and successful surgical decompression was performed in all patients (Fig. 3), permitting a robust interpretation of the obtained data.

An exemplary case is detailed: A 67-year-old man presents with non-pulsatile tinnitus, initially intermittently present on the right side, associated with short-lasting bouts of optokinetically induced vertigo and an intermittent feeling of pressure in the right ear. The vertigo was associated with neither nausea nor vomiting. In time, the spells become more frequent, they last longer, and the tinnitus becomes constant, perceived as a high-pitched whistle. The vertigo spells later on can also be induced by rotation of the head. He scores his tinnitus 10/10 on a visual analogue scale. Still later, tinnitus also develops in the left ear. It scores 8/10. The tinnitus is perceived as disturbing and worsens on fatigue and stress.

He has no hemifacial spasms, and very rarely right-sided geniculate neuralgic pain (short-lasting spells of ear pain). Medication including betahistine is not beneficial.

Pure tone audiometry demonstrates normal hearing for low frequencies, 35 dB hearing loss for mid-frequencies and 55 dB for high frequencies on the right side, normal hearing for low frequencies, 25 dB hearing loss for mid-frequencies and 45 dB for high frequencies on the left side. Speech

audiometry shows 100% accuracy at 55 dB, 50% at 35 dB for both sides.

Tinnitus analysis matches it to 2,000 Hz 15 dBSL. The Tinnitus Questionnaire scores it as a grade III, i.e., severe without psychological decompensation (grading from I to IV- I: light, II: moderate, III: severe, IV: very severe with psychological decompensation).

Vestibular examination is normal, with a normal test of Romberg and Unterberger, absence of nystagmus, normal test of Dix-Hallpike, normal caloric testing and normal electronystagmography.

ABR demonstrates an absence of peak II (Fig. 4a), with still a normal IPL I-III and IPL I-III difference <0.2 ms, as well as a normal IPL I-V and normal IPL III-V contralaterally. Because his clinical picture is fitting with MVC as a cause for his tinnitus and his ABR only demonstrates an abnormal peak II, he is considered a good candidate for MVD [2].

Post MVD, the pure tone tinnitus disappears, but a noise-like sound remains. The optokinetically induced vertigo disappears as well, but not the rotationally induced vertigo.

Pure tone audiometry improves by 10 dB at 4,000 Hz, and the other frequencies remain unchanged. His ABR with clicks at 80 dB, in identical settings as pre MVD improves as peak II returns (Fig. 4b).

Statistical analysis

Statistical analysis was performed using SPSS 15.0 for Windows. Since there was no relevance demonstrated of the ABR parameters with age, with the exception of inter peak latency (IPL) I-III, no age normalization has been implemented for any of the ABR parameters.

Following Møller's criteria [15] (Table 1), ABR parameters were analyzed as a function of the criterion IPL I-III ≥2.3 ms. In view of the proposed criterion, IPL I-III, IPL III-V, and IPL I-V were evaluated. Five patients fulfilled this criterion. However, for IPL III-V and IPL I-V, data were excluded for one patient because of an incomplete set of ABR parameters.

Based on the above-mentioned pathophysiology, it is estimated that adding a second diagnostic parameter, peak II amplitude decrease, might increase the certainty that the IPL I-III prolongation is related to the microvascular compression and not to any other cause. The same analyses are performed on the pre-and post-operative ABR data with peak II decrease as an extra selection parameter.

The Wilcoxon signed-rank test was used systematically to compare a specific ABR parameter with the proposed upper limit of what can be considered as normal. This statistical test in view of the small sample size. The following means are systematically compared: ipsilateral ABR parameters are compared with the contralateral ones both pre- and post-operatively. For IPL III-V, the differences between IPL III-V ipsilateral and contralateral preoperatively as well as the differences IPL III-V ipsilateral and contralateral postoperatively were calculated and compared using the Wilcoxon signed-rank test.

Results

IPL I-III ipsilateral versus contralateral

Analysis of the ABR parameters as a function of the Møller criterion IPL I-III ipsilateral ≥2.3 ms shows preoperatively no significant difference between IPL I-III ipsi- and contralateral $(Z(5)=-1.63, p=0.10$; see Table 3). There might be a trend to recuperation, shown by the shortening of the ipsilateral IPL I-III postoperatively while the contralateral IPL I-III is unchanged postoperatively. Unlike preoperatively, the difference between the ipsi- and contralateral IPL I-III is significant postoperatively $(Z(5)=2.02, p<0.04$; see Table 3).

IPL I-III plus Peak II, ipsilateral versus contralateral

When making the sum of IPL I-III + Peak II amplitude, i.e., when IPL I-III is measured in the presence of a

Table 3 Means and standard deviations for the different ABR parameter between Ipsilateral versus contralateral, preoperative, and post-operative

		Preoperative		Post-operative	
		Ipsilateral	*Contralateral*	*Ipsilateral*	*Contralateral*
IPL I-III	M	2.58	2.11	**2.47**	**2.11**
	SD	.32	.11	**.06**	**.13**
IPL I-III+PEAK II	M	**3.58**	**3.03**	3.13	3.35
	SD	**.31**	**.27**	.51	.34
IPL I-V	M	4.44	4.36	**4.39**	**4.07**
	SD	.15	.34	**.12**	**.09**
IPL III-V	M	**1.80**	**2.05**	1.91	1.90
	SD	**.18**	**.14**	.17	.09

Criterion: IPL I-III Ipsilateral ≥2.3 ms; *numbers in bold* indicate a significant effect between Ipsilateral and contralateral $(p<0.05)$, except for IPL III-V preoperative, which was marginally significant $(p=0.06)$

decreased peak II amplitude, preoperatively a significant difference between ipsi- and contralateral ($Z(5)=-2.02$, $p<0.05$; see Table 3) is noted. Postoperatively the difference between the ipsi- and contralateral IPL I-III is not significant ($Z(5)=-0.94$, $p=0.35$; see Table 3) anymore.

IPL I-V ipsilateral versus contralateral

Preoperatively there is no significant difference between the ipsi- and contralateral IPL I-V ($Z(4)=-0.73$, $p=0.47$; see Table 3). In contrast, the postoperative difference between the ipsi- and contralateral IPL I-V is significant ($Z(4)=-2.02$, $p<0.05$; see Table 3).

IPL III-V ipsilateral versus contralateral

Preoperatively, there is a marginal significant difference between the ipsi- and contralateral IPL III-V ($Z(4)=-1.83$, $p=0.06$; see Table 3) which disappears postoperatively ($Z(4)=-.14$, $p<0.89$; see Table 3). The differences between IPL III-V ipsilateral and contralateral preoperatively and the differences IPL III-V ipsilateral and contralateral postoperatively were compared and revealed a marginal significant effect ($Z(4)=2.82$, $p=0.08$).

Discussion

Many investigators have presented hypotheses about the pathophysiology of microvascular conflict disorders that were based on demyelination of axons at the location of the vascular contact [6, 10, 11, 14]. Our previous ABR results in tinnitus patients in the setting of microvascular conflict [2] suggested that the tinnitus might not be the result of such suggested demyelination but rather to desynchronized signal transmission in the auditory nerve. The amplitude of sensory evoked potentials is a function of the temporal coherence of neural discharges and the number of nerve cells or fibers that are active [12]. The more synchronized the nerves fire, the higher the amplitude of the evoked potentials will become. The contact with a blood vessel may alter neural conduction (decrease conduction velocity in some fibers or inactivate some fibers) causing the temporal coherence of the firing in the central segment of the auditory nerve to decrease, resulting in a decrease of the amplitude of peak II, and clinically this may result in frequency specific tinnitus [2]. The desynchronized signal transmission within the auditory nerve from close contact with a blood vessel may lead to reorganization of auditory nuclei in the auditory brainstem through expression of neural plasticity [13]. This neural plasticity may affect the entire auditory pathways including the auditory cortex causing re-organization [17] and creating

hyperactivity in central structures of the auditory brain structures leading to clinically expressed as tinnitus [5].

It has been suggested that a vascular conflict, in order to become symptomatic, should be located at the CNS segment (and not just the root entry zone) [3], which is the neural generator of peak II [12]. Thus, peak II changes are expected to be the first abnormality to be noted in vascular conflicts of the auditory nerve. Vascular conflict of the eighth cranial nerve indeed seems to be accompanied by a sequential pattern of ABR changes resulting in a progressive pathology [2]. The finding that IPL I-III prolongs when peak II is absent suggests that over time the blood vessel may not only disrupt neural transmission or cause de-synchronization (peak II decrease) but over time may also induce a general slowing of neural conduction. It has been suggested that the slowing of conduction in the auditory nerve may be due to a focal demyelization [21]. Results of a previous ABR study in tinnitus patients harboring a MVC [2] showed that hearing loss (at the frequency of the tinnitus) is correlated with the prolongation of the ipsilateral IPL I-III but not so to the contralateral IPL I-III. IPL I-III reflects the velocity, actually the 1/velocity, of the signal transmission between the cochlea and the cochlear nucleus, thus, the longer the IPL I-III, the slower or the worse the transmission. IPL I-III prolongation is not directly correlated with tinnitus either. This suggests that hearing loss in this population is indeed most likely due to the vascular conflict and not to other factors such as age. Furthermore, as the auditory nerve is
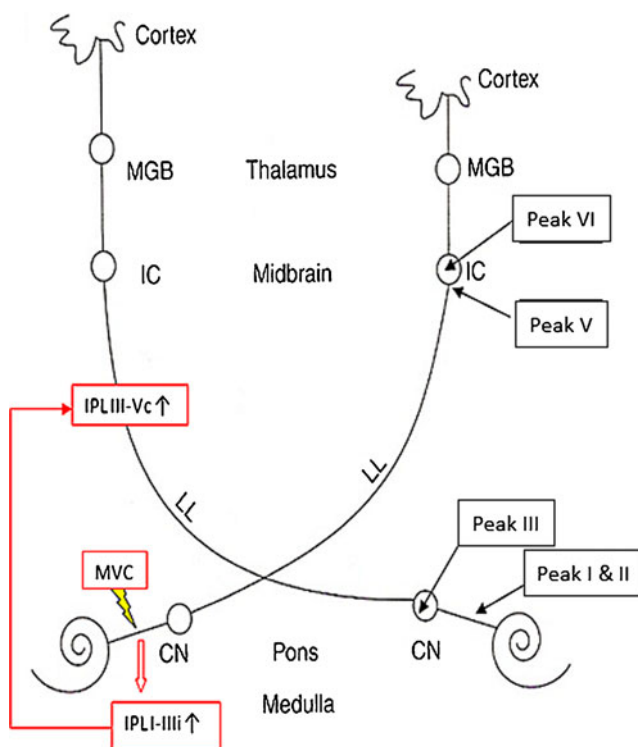
Fig. 1 Brainstem compensation mechanism involved in neurovascular conflict of the eighth nerve

Fig. 2 Proposed pathophysiological mechanism for tinnitus and hearing loss in neurovascular conflict of the eighth cranial nerve
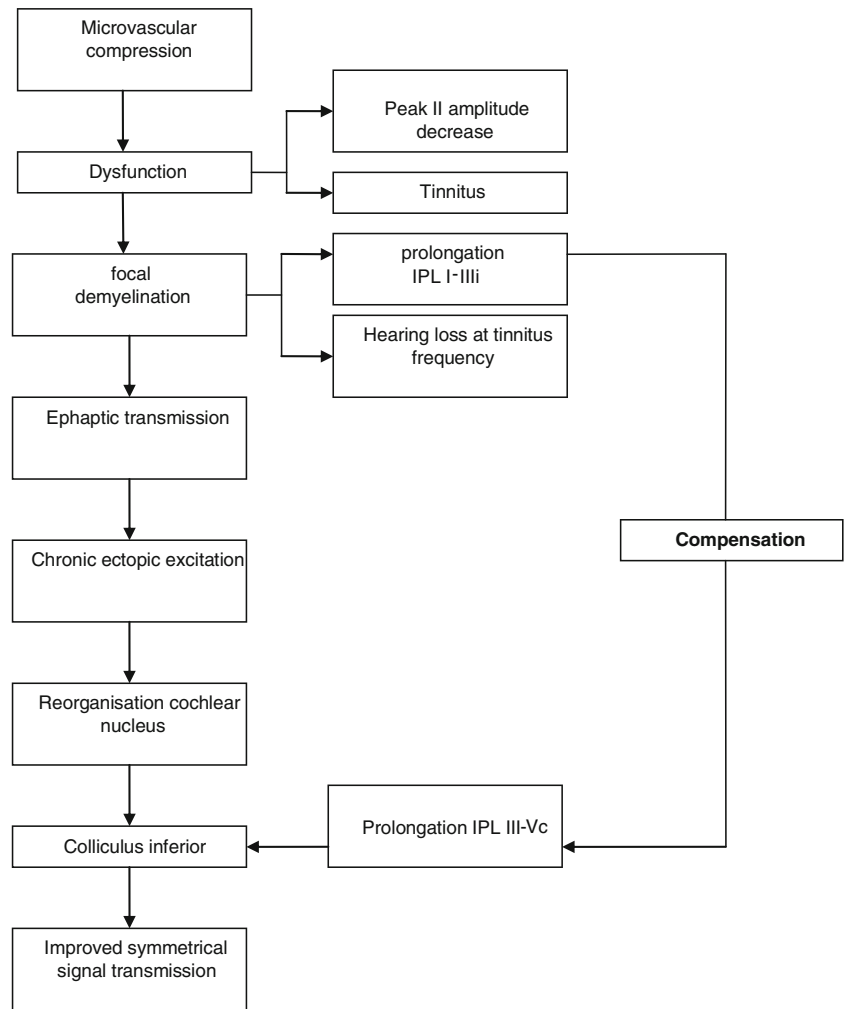

tonotopically organized [5, 20], the location of the conflict is therefore likely to cause frequency-specific hearing loss and a frequency-specific tinnitus [5, 18]. The hearing loss from MVC of the VIIIth cranial nerve is indeed frequency-specific and greatest at the frequency of the tinnitus [2].

That the frequency-specific hearing loss is associated with progressive increase in tinnitus and that the prolongation of IPL I-III that occurs over time is related to the severity of the

tinnitus suggests that the more the auditory nerve becomes damaged, the worse the tinnitus becomes [2].

Furthermore, our postoperative changes in the ABR suggested that IPLI-III is causally related to hearing loss at the tinnitus frequency, as the hearing loss at tinnitus frequency improves when the IPL I-III improves. Thus, when signal
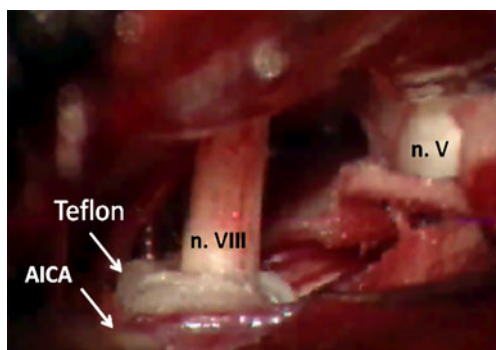
Fig. 3 Typical picture of microvascular decompression of vestibulocochlear nerve via retrosigmoid suboccipital approach
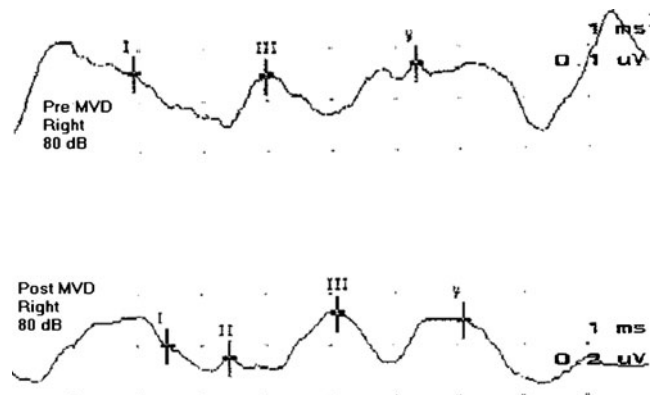
Fig. 4 Auditory brainstem responses (evoked potentials) from pre (**a**) and post (**b**) microvascular decompression: peak II returns after MVD and the IPL I-III normalizes. Clicks presented at 80 dB

transmission improves, i.e., when the auditory nerve recovers, hearing loss at the tinnitus frequency improves [2].

Thus, whereas tinnitus most likely develops as a result of irritation of the auditory nerve in an initial stage, corresponding to a decrease in the amplitude peak II, at a later stage it might be the result of a frequency-specific hearing loss, corresponding to IPL I-III prolongation, due to focal demyelination [6, 10, 11, 14]. At this stage, the tinnitus might be caused by auditory deprivation, rather than mere irritation or inducing desynchronized signal transmission. Analysis of the results of ABR recordings before and different times after the MVD indicates that before a microvascular decompression is performed the auditory input from both compressed and non-compressed sides arrives simultaneously in the inferior colliculus, as IPL I-V is symmetric. Preoperatively, there is a trend for slowed signal transmission in the compressed auditory nerve as demonstrated by the increased IPL I-III. This becomes significant when adding peak II abnormality as a criterion for diagnosis of CVCS and is in accordance with our previous study [2].

However, if the auditory information transmitted via the auditory nerve and auditory pathways in the brainstem arrives at the inferior colliculus at the same time, there has to be a compensation mechanism in the brainstem, either a speeding up of the affected auditory pathway or a slowing down of the information coming from the non-compressed side (see Fig. 1). Our data demonstrate that it is the information from contralaterally which slows down in its brainstem trajectory as shown by the prolongation of the contralateral IPL III-V. Thus, it seems as if the brainstem compensates for the slowed signal transmission in the central part (in its cisternal segment) of the auditory nerve related to the vascular conflict. Even after 1 year post-decompression, the auditory nerve and the brainstem transmission have not recovered completely as there is a difference in IPL I-V between the decompressed side and the other side. This could be an explanation why it can take up to 2 years to notice improvement after decompression (Möller, unpublished results). The brainstem has however already begun to functionally recompensate as postoperatively the significant difference in IPL III-V has normalized. The incomplete compensation is probably secondary to the incomplete normalization of the auditory nerve signal transmission as IPL I-III is not normalized yet after 1 year. This could be due to a slow recovery of the structural damage (demyelination) associated with the pulsatile 'hammering' vascular compression. This in contrast to what is noted when IPL I-III plus peak II are used as criteria, as we note a normalization of signal transmission in the cisternal part of the auditory nerve.

Conclusions

In summary, the following pathophysiological mechanism can be suggested for tinnitus (see Fig. 2): when a blood vessel comes into contact with the auditory part of the eighth nerve, a disorganized signal transmission arises (peak II decreases), resulting in tinnitus [2]. In time, the contact/compression induces a focal demyelination, resulting in slowing down of the signal transmission, and hearing loss at the tinnitus frequency develops (IPL I-III prolongs) [2]. As a compensation mechanism, the signal transmission of the auditory input from the non-compressed side slows down between the cochlear nucleus and the inferior colliculus so that both signals arrive in the inferior colliculus at the same time (this study) (Figs. 3, 4).

After a microvascular decompression, signal transmission does not normalize after 1 year at the level of the auditory nerve (IPL I-III), hypothetically due to structural damage, but functional brainstem compensation already sets in, normalizing the slowed compensated signal transmission in the brainstem (IPL III-V). This could explain the prolonged clinical improvement with microvascular decompressions of the eighth nerve performed for tinnitus.

Conflicts of interest None.

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