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Cochlear Nerve Dimensions in Asymetrical Sensorineural Hearing Loss: A Morphometric Study

Asimetrik Sensörinöral İşitme Kaybında Koklear Sinir Boyutları: Morfometrik Çalışma

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ABSTRACT

Introduction: To investigate the relationship between morphometric variants of the cochlear nerve (CN) and the hearing level. To investigate the confounding effects of age, sex, and audiometric variables on the relationship between CN morphometrics and hearing loss, if present.

Methods: Audiological data and magnetic resonance imaging findings of 127 patients with asymmetrical sensorineural hearing loss (ASNHL) were reviewed retrospectively. According to pure tone average (PTA) frequencies of each ear, difference above 25 dB were accepted as ASNHL. The vertical (Vd) and horizontal diameters (Hd) and the cross-sectional area (CSA) of the CN were measured.

Results: The difference in CSA and Vd between ears showed a negative correlation with age. The mean CSA was 1.57 in AE and 1.60 in NE. Mean Hd was 1.00 in AE and 1.00 NE. Mean Vd was 1.40 in AE and 1.50 in NE. There was no correlation between the difference ratios of thresholds and CN diameter parameters. There was no significant correlation of CSA, Vd, and Hd with PTA thresholds at each frequency.

Conclusion: Aging is associated with losses in Vd diameter and CSA. The degree of hearing loss was not correlated with the morphometric features of the CN. The morphometry of the CN should be interpreted together with the etiology of hearing loss.

Keywords: Hearing loss, unilateral, deafness, ear, inner, cochlear nerve

ÖZ

Amaç: Koklear sinirin morfometrik özellikleri ile işitme seviyesi arasında ilişki varlığını araştırmaktır. Yaş, cinsiyet ve odyometrik özelliklerin, koklear sinir morfometrisi ve işitme kaybı ilişkisine etkisi olup olmadığını araştırmaktır.

Yöntemler: Asimetrik sensörinöral işitme kaybı (ASNİK) nedeniyle başvuran 127 olgunun odyolojik verileri ve manyetik rezonans görüntüleme bulguları retrospektif olarak tarandı. Saf ses ortalamasına göre kulaklar arasında 25 dB ve üzeri fark olması ASNİK olarak kabul edildi. Koklear sinirin vertikal çapı (Vd), horizontal çapı (Hd) ve kesitsel alanı (CSA) ölçüldü.

Bulgular: Kesit yüzey alanı ve Vd yaş ile negatif korelasyon gösterdi. Ortalama CSA etkilenen kulaklarda 1,57 iken etkilenmeyen kulaklarda 1,60 idi. Ortalama Hd'yi etkilenen ve etkilenmeyen kulakta aynı idi. Ortalama Vd etkilenen kulakta 1,40 etkilenmeyen kulakta 1,50 idi. İşitme eşiklerindeki değişim oranları ile koklear sinir çapları arasında ilişki gözlenmemiştir. CSA, Vd, Hd ile saf ses ortalaması arasında ilişki gözlenmemiştir.

Sonuç: Yaşlanma ile sinir Vd'den kaybeder ve toplam CSA azalır. İşitme kaybının derecesi ile sinirin morfometrik özellikleri arasında ilişki yoktur. Koklear sinir morfometrisi incelenirken işitme kaybının etiyolojisi göz önünde bulundurulmalıdır.

Anahtar Kelimeler: İşitme kaybı, tek taraflı, sağırlık, kulak, iç, koklear sinir

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Introduction

Asymmetrical sensorineural hearing loss (ASNHL) is defined as a difference in hearing loss greater than 15 decibels (dB) between ears at 0.5, 1, and 2 kHz, or greater than 20 dB at 3, 4, and 6 kHz on a bone conducted pure tone average (PTA) audiogram that interrupts binaural hearing (1-3). ASNHL demonstrates a wide spectrum of PTA threshold from mild sensorineural hearing loss to single-sided deafness (1). ASNHL is estimated to influence 7.9%-13.3% of the general population (4).

The causes of ASNHL can be listed as inner ear anomalies, cochlear nerve (CN) agenesis, mumps, congenital cytomegalovirus infection, meningitis, vestibular schwannoma, and idiopathic (2). ASNHL causes disruption of both temporal and spatial localization of sound in space. Patients experience difficulty understanding speech in the presence of noise (5). Rehabilitation of ASNHL is very important to provide balanced binaural hearing.

Management of ASNHL includes conventional hearing aids, cross devices, bone conduction hearing aids, and cochlear implantation. Cochlear implantation is indicated in ASNHL especially with down-sloping audiogram and single-sided deafness (6). Treatment success of ASNHL depends on several factors such as the age of the patient, duration of hearing loss, etiology of hearing loss, and cognitive capacity of the patient. However, the most important factor related to a satisfactory auditory outcome is a functioning CN (7). Sensorineural hearing loss can be caused by damage to either cochlear or retro- cochlear structures. If cochlear damage exists, retrograde axonal degeneration may cause neuronal degeneration, which eventually presents as a decrease in the cross-sectional area (CSA) of the CN (8-11).

The morphologic features of the CN have prognostic importance in determining the candidacy of a patient for cochlear implantation and for side preference. CN size is accepted as an important parameter in the estimation of postoperative auditory verbal abilities after CI (12). In the literature, some studies reveal a relationship between the function and size of the CN (13).

Magnetic resonance imaging (MRI) is a reliable method of measuring the diameter and CSA of the CN (14). The objective of our study is to investigate whether there is a relationship between the hearing level and the CN diameter.

Methods

This is a retrospective review of the audiological charts and MRI findings of the patients with ASNHL diagnosed between 2014 and 2017 at a tertiary referral center. Medical records of 127 patients were enrolled in this study. Informed consent was not taken because of its retrospective nature. Cases with acquired etiology such as trauma or labyrinthitis and those who display conductive components of hearing loss were excluded.

Patients' demographics, PTA averages at frequencies of 250, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, 8000 Hz were recorded. University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital by Institutional Ethics Committee approval was obtained (approval number: 2017/12).

Audiological Evaluation

PTA averages for frequencies of 250, 500, 1000, 2000, 4000, and 8000 Hz were evaluated. A difference in PTA average between the affected and unaffected ears of more than 25 dB HL (dB hearing level) was accepted as ASNHL. Patients with insufficient audiological documentation were not included in the study.

Temporal MRI Protocol and Measurement of Nerve Sizes

CN diameters of the affected and unaffected ear were measured and compared by using MRI. All MRI procedures were performed using a 3T MR unit (Verio; Siemens Medical Solutions, Erlangen, Germany) with an 8-channel head-array coil and parallel imaging techniques. All images were evaluated with an oblique-sagittal 3D-driven equilibrium sequence perpendicular to the internal auditory canal (IAC) (repetition time/echo time: 1000/132 msec; 3.48 min acquisition time; 20 cm field of view; 0.5 mm section thickness; 0.75 mm overlap; and number of acquisitions: 2) The sequences used for procedure were axial T2W, axial T1W, post-contrast axial and coronal T1W, and axial heavily T2W sequence [constructive interference in steady state, (CISS) sequence]. Oblique-sagittal images of the IAC were further evaluated, since the visualization of the CN is optimal at that section. Selected reconstructed images were then transferred to a specialized workstation where CSA measurements could be performed (Figure 1).

All MRI scans were reviewed by two independent observers (OY2 and EI2) who were blinded to patients' data (sensorineural deafness) as well as each other's measurements. The vertical, (Vd) horizontal diameters (Hd) and the cross-sectional area (CSA) of the CN was measured on the parasagittal image of the middle of the IAC.

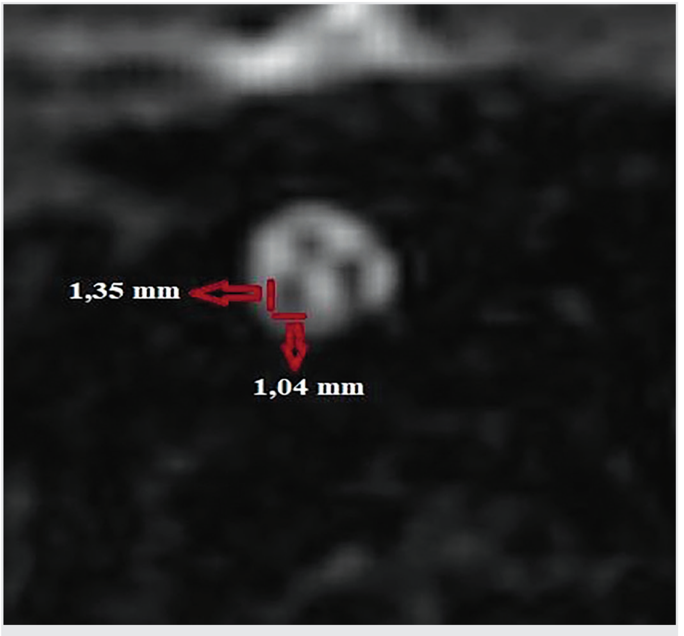

Figure 1. Parasagittal CISS MRI parasagittal images perpendicular to the nerve course at the internal auditory meatus. Measurement of the cochlear nerve (antero-inferior) diameter is demonstrated with the region of interest outlined, and cross-sectional area was calculated

CISS: Constructive interference in steady state, MRI: magnetic resonance imaging

Statistical Analysis

Mean, standard deviation, median, min and maximum, frequency and ratio values were used for descriptive statistics. The one-sample Kolmogorov-Smirnov test was used to test for the normal distribution.

We analyzed the relationship between dependent variables on a frequency basis, and for 250 Hz, speech frequencies and 8000 Hz. We used the intra-class correlation coefficient to determine the inter-observer reliability.

For independent quantitative variables a Mann-Whitney U test and for dependent quantitative variables a Wilcoxon signed-rank test was performed. Correlation was tested with a Spearman correlation test. The interclass correlation coefficient (ICC) was performed to examine inter-rater reliability (15). Results were considered statistically significant at $p<0.05$, and all statistical analyses were performed using SPSS Statistics for Windows, Version 22.0 (IBM Inc., Armonk, NY).

Results

Thirty-six female and 31 male participants were enrolled in the study. Their mean age was 16.9 (minimum: 13; maximum: 84) years. Two cases with higher displacement of non-dehiscent jugular bulbus but neither inner ear nor intracranial anomaly, including the intracranial path of the CN, were diagnosed.

We studied the difference between the PTA thresholds of the two ears. The mean PTA threshold was 58.14 dB for AE and 26.16 for NE. The median difference between the affected and non-affected ear [ΔAE-NE (%)] in the PTA averages of each frequency were 31%, 38%, 29%, 34%, 31%, and 32% for 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz, respectively. The AE has significantly worse thresholds than the NE. Correlations between variations of Vd, Hd, CSA, and ΔAE-NE (%) were calculated. The ICC was calculated as 78%, which indicates good reliability.

There was no significant association of CSA, Vd, and Hd with PTA thresholds at each frequency (Spearman's correlation p for Vd: 0.828, p for horizontal: 0.947, p for CSA: 0.930) (Table 1).

The difference in CSA and Vd between affected and non-affected ears showed a negative correlation with age for speech frequencies. As age increased, the difference in the Vd and CSA of the affected ear decreased by more than that of the non-affected ear at speech frequencies ($p=0.008$ Vd; $p=0.006$ for CSA) (Table 2). The difference in CSA, Vd, and Hd between the affected and non-affected ears did not demonstrate any significant relationship with gender (p for Vd: 0.229, p for horizontal diameter: 0 885, p for CSA: 0.274) (Table 3).

The differences in frequency between the affected and non-affected ears were analyzed for a relationship with the difference ratio of CSA, Vd, and Hd. Mean CSA was 1.57 (±0.62) in AE and 1.60 (±0.50) in NE. Mean Hd was 1.00 (±0.99) in AE and 1.00 (±0.17) in NE. Mean Vd was 1.40 (±0.24) in AE and 1.50 (±0.21) in NE. There was no correlation between the difference ratios of thresholds and CN diameter parameters (p-values for 250, 500, 1000, 4000, 8000 Hz = 0.623; 0.305; 0.361; 0.056; 0.065; 0.176, respectively).

Table 1. There was no correlation between age and the difference in pure tone average averages with cross-sectional area, vertical diameter, and horizontal diameter at each frequency

		AE-NE Difference dB		
		Vertical	**Horizontal**	**CSA**
250 Hz	r	-0.041	-0.107	0.046
	p	0.743	0.389	0.714
500 Hz	r	0.049	-0.101	-0.001
	p	0.691	0.416	0.992
1 kHz	r	0.023	-0.075	0.060
	p	0.856	0.547	0.628
2 kHz	r	0.146	-0.069	0.140
	p	0.237	0.579	0.259
4 kHz	r	-0.006	-0.064	-0.033
	p	0.961	0.605	0.793
8 kHz	r	-0.010	-0.083	0.033
	p	0.938	0.506	0.788

Spearman correlation.
PTA: Pure tone average, CSA: cross-sectional area, AE: affected ear, NE: non-affected ear

Table 2. Negative correlation between age and cross-sectional area, vertical diameter, and horizontal diameter at speech frequencies

		AE-NE Difference		
		Vertical	**Horizontal**	**CSA**
Age	r	-0.320	-0.120	-0.329
	p	0.008	0.332	**0.006**

Spearman Correlation.
AE: affected ear, NE: non-affected ear, CSA: cross-sectional area

Table 3. There was no correlation between the difference between the affected ear and non-affected earaccording to pure tone average averages of 500-4000 Hz and sex

	Female		Male		p	
	Mean ± SD	Median	Mean ± SD	Median		
Difference AE-NE						
Vertical	-3.8±14.7	-7.1	-0.4±17.9	0.0	0.229	m
Horizontal	-1.5±16.6	0.0	1.1±23.2	0.0	0.885	m
CSA	-5.2±24.6	-7.8	0.1±31.2	4.0	0.274	m

m: Mann-Whitney U test, SD: standard deviation, AE: affected ear, NE: non-affected ear, CSA: cross-sectional area

Discussion

The dimensions of inner ear structures are valuable prognostic parameters for beneficial estimation of future interventions in patients with sensorineural hearing loss. According to Kang et al. (7), in normal-hearing ears, there is no relation between CN size and age. The CN is ovoid rather than round, i.e., its vertical and horizontal diameters are not equal (16,17). CN morphometry is well measured by MRI with CISS sequence) on parasagittal images of the IAC, in which the CN is optimally visualized (18-20). In the present study, two-dimensional measurements were performed for the vertical and horizontal diameters. Nadol et al. (23) reported that the diameter of the CN was smaller in the deaf population, compared with that of normal-hearing controls, but wide variability of diameters of the CN in hearing and deaf subjects complicates its usefulness (21,22). In our study, the difference ratios between the affected and non-affected ear for each frequency threshold were analyzed for a relationship with the difference ratio of CSA, Vd, and Hd of the affected and non-affected ear, and no correlation was found ($p>0.05$).

Aging is an important parameter in the volume decrease of neuronal structures either due to cell death or atrophy. Age-related cell loss in the spiral ganglion was studied many times (21). Nadol et al. (23) demonstrated that spiral ganglion cell count is lower in older deaf individuals (22). In our study, Vd and CSA of the affected ear decreased with age more than non-affected ear did ($p=0.008$ for vertical, $p=0.006$ for CSA). Kim et al. (12) stated such relevance although they did not observe statistical significance. It is known that development and regeneration of both neural structures and their supporting cells have receptors of sex hormones. Kempster et al. (25) reported the presence of sexual dimorphism in favor of females exhibiting more abundant electrosensory axons, especially via ERβ receptors (24). In the present study, difference ratio of CSA, Vd, and horizontal diameter between the affected and non-affected ear did not show a correlation with sex ($p>0.05$). Russo et al. (19) reported on a genetic study in which they compared a Connexin 26 (Cx26)-mutated sensorineural hearing loss group and a non-mutated sensorineural hearing loss group with a normal-hearing control group. Although there was no difference in nerve size between the Cx26 mutated group and non-mutated group, both groups with profound hearing loss had smaller CNs, in comparison with the normal-hearing group (19).

In an analysis of the correlation between CN dimensions and the degree of hearing loss, patients were divided in to five groups: mild, moderate, severe, and profound hearing loss and normal hearing. There was no correlation between the severity of hearing loss and CN size for 250 Hz, speech frequencies, and 8000 Hz. For the affected ear, no relationship was observed between the level of hearing loss and CN size for 250 Hz, speech frequencies, and 8000 Hz.

Etiological evaluation of SNHL is of great importance. Henneberger et al. (26) reported that if the etiology of SNHL is Meniere's disease, a swelling may be observed in the cranial nerves, especially in the CN. A major limitation of our study is the lack of etiological analysis of hearing losses and the duration of hearing loss, which both may affect the size of the CN (12). However, absent correlation of CN size between affected and non-affected ears may be due to the confusing effect of such swelling of CNs in SNHL with Meniere's disease (26).

The literature provides data about how CN sizes differ between the hearing and non-hearing population. However, this is the first study that compares the CN sizes of the good hearing ear with the bad hearing ear in the same person. If a hazardous insult is present on a patient this will affect the CNs of both ears. Therefore, each patient should be evaluated in their own.

Study Limitations

The lack of previous audiologic history, including the etiology of hearing loss and follow-up, were the major limitations of the study.

Conclusion

There is a negative correlation between Vd and CSA with aging. However, because the severity of hearing loss lacks correlation with nerve size, we concluded that the more affected ear does not necessarily have the smaller nerve. A smaller nerve might be more vulnerable to hazardous effects, which results in hearing loss. Prospective studies should be performed to identify the relationship between size and function in detail. The morphometry of the CN should be interpreted together with the etiology of hearing loss.

Ethics Committee Approval: University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital by Institutional Ethics Committee approval was obtained (approval number: 2017/12).

Informed Consent: Informed consent was not taken because of its retrospective nature.

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Design - A.P.Y., Ö.Y., L.K., H.A., F.T.K., E.İ.; Data Collection or Processing - A.P.Y., Ö.Y., L.K., H.E.K., E.İ.; Analysis or Interpretation - A.P.Y., Ö.Y., H.E.K., F.T.K., E.İ.; Literature Search - A.P.Y., Ö.Y., L.K., H.A.; Writing - A.P.Y., Ö.Y., L.K., H.E.K., H.A., F.T.K., E.İ.

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