

Auditory Pathway Features Determined by DTI in Subjects with Unilateral Acoustic Neuroma

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Abstract

Purpose In the studies concerning the pathology of the auditory pathway in the vestibulocochlear system, few use advanced neuroimaging applications of magnetic resonance imaging (MRI) such as diffusion tensor imaging (DTI). Those who did use reported DTI changes only at the lateral lemniscus and inferior colliculus level. The aim of our study was to determine diffusion changes in the bilateral auditory pathways of subjects with unilateral acoustic neuroma (AN) and compare them with healthy controls.

Material and Methods A total of 15 subjects with unilateral AN along with 11 controls underwent routine MRI and DTI. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values obtained from the lateral lemniscus, inferior colliculus, corpus geniculatum mediale, and Heschl's gyrus of the auditory pathway were then compared.

Results The subjects' ADC values measured from the contralateral side were significantly higher at the lateral lemniscus, inferior colliculus, and corpus geniculatum mediale compared with those of the controls. Also, decreased FA values were noted at the inferior colliculus for both the contralateral and ipsilateral sides. The highest ADC values were detected in the inferior colliculus of the auditory pathway.

Conclusions In the auditory pathway of subjects with AN, the contralateral side is more affected than the ipsilateral side, the most affected region being the inferior colliculus. DTI is an advanced neuroimaging technique that can be used to determine the presence of microstructural damage to the auditory pathway in subjects with AN, whereas conventional MRI is not sensitive enough to detect damage.

Keywords Acoustic neuroma · DTI · Auditory pathway

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Introduction

Acoustic neuromas (AN), benign neoplasms arising from the eighth cranial nerve, mostly occur in the cerebellopontine angle [1]. The annual diagnosed incidence of AN is estimated to be 1 per 100,000, but in recent years, as a result of the increased use of magnetic resonance imaging (MRI), the ratio is two times greater [2, 3].

Patients with AN typically have nonspecific symptoms when their tumors are in the early stages. While the most common symptom with approximately 90% of these patients is slowly progressive unilateral hearing impairment, approximately 25% of AN patients experience sudden sensorineural hearing loss [4]. Day et al. [5] have reported that in approximately 11% of all AN patients, hearing could become completely normal.

Neural hearing loss may be caused by lesions in the cerebellopontine angle or in the intra-axial auditory pathway. Unilateral sensorineural hearing loss may be due to damage solely of the cochlear nerve or of the cochlear nuclei. Lesions in the proximal intra-axial auditory pathway of the midbrain, thalamus, and temporal lobe cause bilateral sensorineural hearing loss, which is greater on the contralateral side [6, 7].

The preferred method for the diagnosis and follow-up of AN is MRI [8]. Specifically, diffusion tensor imaging (DTI) is used to assess the auditory tract in the brainstem in those who have sensorineural hearing loss [9–11]. More comprehensively, our study used DTI to evaluate the auditory pathway of the lateral lemniscus, inferior colliculus, corpus geniculatum mediale, and Heschl's gyrus in subjects with unilateral AN. The purpose of our study was to determine any changes of diffusion in the bilateral auditory pathway in subjects with unilateral AN, to compare them with a control group, and to assess which areas in the auditory pathway are most affected.

Material and Methods

This prospective study included 15 subjects (6 male, 9 female; mean age: 49.8 ± 17 years; age range: 19–65 years) who had unilateral AN. The diagnosis of the patients was based on the findings from their MRIs performed on a 1.5-T system (Siemens, Avanto, Erlangen, Germany). The MRI protocol included T1-weighted (T1W; repetition time (TR)/echo time (TE)=460/14 ms) and T2W (TR/TE=2500/80 ms) sequences in the axial and coronal planes, and FLAIR images (TR/TE=8000/90 ms) in the axial plane with 5-mm-thick sections. After that, T1W 3D Magnetization prepared rapid gradient echo (MPRAGE) (TR/TE/TI=12.5/5/450 ms) sequences with and without contrast medium (Gadolinium-diethylenetriamine pentaacetic acid,

0.1 mmol/kg body weight, intravenously) were applied. The control group comprised 11 healthy volunteers with normal hearing (mean age: 48 ± 10 years; age range: 38–58 years) assessed by physical examination, hearing tests, and MRI. The procedures properly followed the guidelines of the Helsinki Declaration on human experimentation. Written informed consent was obtained from all participants, and the study was approved by the institutional ethical committee.

The DTI protocol consisted of a single-shot, spin-echo, echo-planar sequence with the fat suppression technique: TR/TE=2700/89 ms; matrix, 128×128 ; field of view, 230 mm; and slice thickness, 5 mm. Thirty diffusion-encoding directions were used at $b=0$ s/mm² and $b=1000$ s/mm². The Leonardo console (software version 2.0; Siemens) was used for the postprocessing of DTI data sets, after which the apparent diffusion coefficient (ADC) and color-coded fractional anisotropy (FA) maps were reconstructed. T1W 3D-MPRAGE and T2W images were used as anatomic references for the placement and tracing of the regions of interest (ROIs) along the auditory pathway. These images were coupled with corresponding region of ADC and FA maps at the same section level. The adaptation of the sizes and placement of all ROIs were realized through simultaneous assessment by two experienced radiologists (Serpil Kurtcan and Alpay Alkan), and the ROIs were drawn manually with utmost care.

All ROI sizes were set to 4 pixels. ROIs in the auditory pathway of the lateral lemniscus, inferior colliculus, corpus geniculatum mediale, and Heschl's gyrus were drawn on color-encoded maps of the ipsilateral and contralateral sides of the subjects with AN and also on those of the controls (Figs. 1 and 2). The following ADC and FA values were obtained automatically. In the control group, the averaged values of the left and right sides were simply recorded. ADC and FA measurements of the patients' auditory pathways on the ipsilateral side were compared with those on the contralateral side. These values were then compared with those of the control group.

Fig. 1 The Axial color-coded maps from a subject with acoustic neuroma showing placement of region of interest on the lateral lemniscus (a) and inferior colliculus (b)

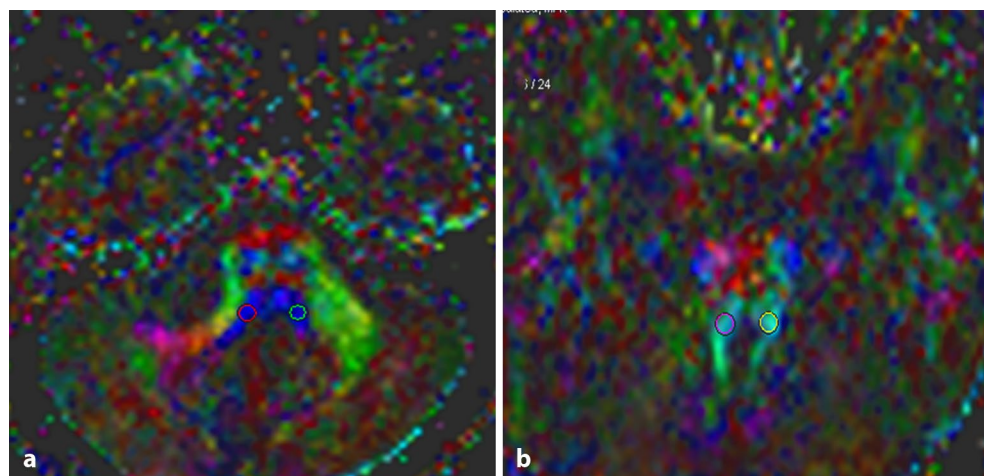
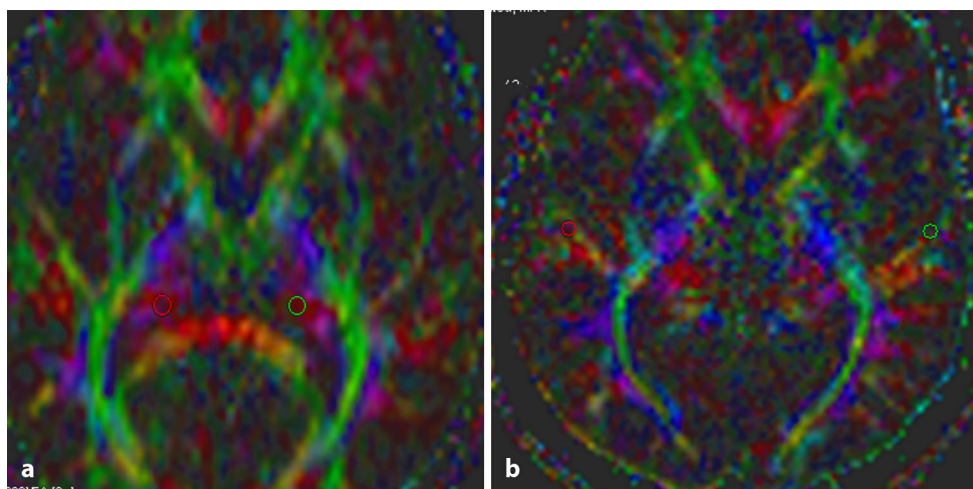


Fig. 2 The Axial color-coded maps from a subject with acoustic neuroma showing placement of region of interest on the corpus geniculatum mediale (a) and Heschl's gyrus (b)



Statistical Analysis

Statistical analysis was performed using SPSS 11.0 statistical software (SPSS Inc., Chicago, IL). The Kolmogorov–Smirnov test was used to determine whether the continuous variables were normally distributed. Parametric tests were applied with all parameters showing normal distribution, and variables were given as mean \pm standard deviation. The mean ADC and FA values with a 95% confidence interval among three groups were compared using one-way analysis of variance. To compare ADC and FA values obtained from the auditory pathways in the ipsilateral and contralateral sides of the subjects and controls, Dunnett *t*-test was used, in which one group is treated as a control, and all other groups were compared against it. A *p* value < 0.05 was accepted as statistically significant.

Results

The ADC and FA values obtained from the ipsilateral and contralateral sides of the subjects with AN and of the control group are presented in Table 1. Compared with the control group, the ADC values for the contralateral side of the subjects were, to a statistically significant degree, higher at

the lateral lemniscus, inferior colliculus, and corpus geniculatum mediale ($p=0.001$, 0.010 , and 0.005 , respectively). Conversely, the FA values were significantly lower at the inferior colliculus for both the contralateral and ipsilateral sides of the AN subjects when compared with the control group ($p=0.052$ and 0.05).

With regard to ADC and FA values obtained in the auditory pathway, the difference was not statistically significant between the ipsilateral and the contralateral side. On the other hand, the ADC values were significantly higher at the inferior colliculus for both the contralateral and the ipsilateral sides of the AN subjects according to the lateral lemniscus and corpus geniculatum mediale ($p=0.022$ and 0.04 ; Fig. 3).

Discussion

In approximately 95% of cases, AN can appear sporadically and are mostly unilateral. The hereditary form associated with type II neurofibromatosis occurs in 5% of AN cases and is usually bilateral [12]. Additionally, AN has been detected incidentally in approximately 0.02% of asymptomatic patients who were examined radiologically for other purposes [13]. Moreover, each ear provides impulses

Table 1 The ADC and FA values obtained from the ipsilateral and contralateral sides of the subjects with acoustic neuroma and of the control group

Locations	Lateral lemniscus		Inferior colliculus		Corpus geniculatum mediale		Heschl's gyrus	
	ADC	FA	ADC	FA	ADC	FA	ADC	FA
Ipsilateral	765.7 \pm 33.9	593.8 \pm 84.6	775.5 \pm 62.8 ^b	725.9 \pm 79 ^b	753.7 \pm 50.7	387.5 \pm 67.3	751.3 \pm 44	406.5 \pm 106
Contralateral	785.3 \pm 40.5 ^a	544.3 \pm 91.4	800.5 \pm 64.8 ^a	699.9 \pm 76.7 ^a	775.4 \pm 47.4 ^a	360.5 \pm 109	750.9 \pm 95.2	356.6 \pm 63.4
Control	731.4 \pm 21.9	657.6 \pm 103	734.4 \pm 51	751.3 \pm 36.4	719.7 \pm 43.1	401.2 \pm 68.3	724.4 \pm 37	301.4 \pm 81

ADC apparent diffusion coefficient, FA fractional anisotropy

^aStatistically significant differences between contralateral side and control group

^bStatistically significant differences between ipsilateral side and control group

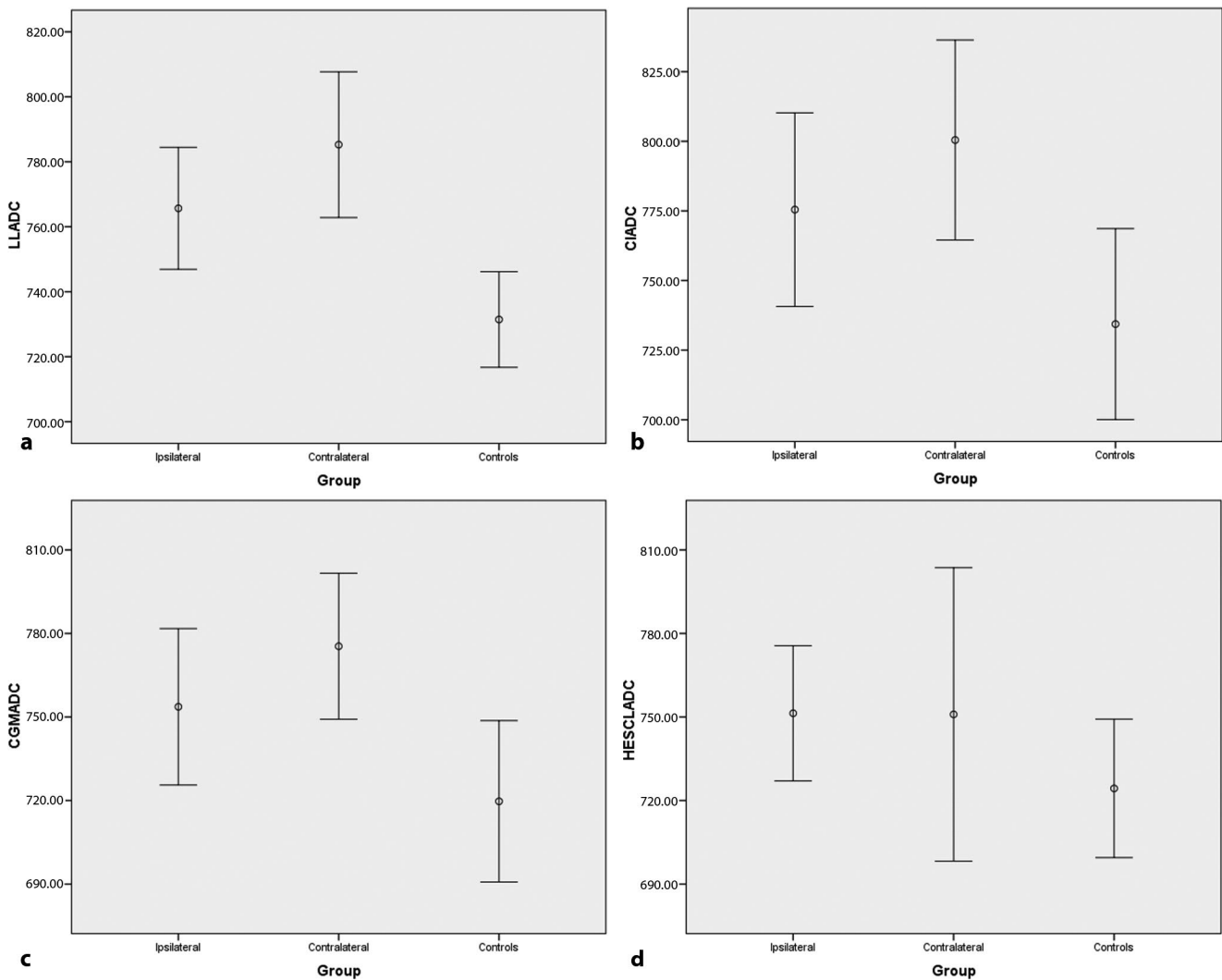


Fig. 3 The apparent diffusion coefficient (*ADC*) values at the lateral lemniscus (**a**), inferior colliculus (**b**), corpus geniculatum mediale (**c**), and Heschl's gyrus (**d**) for the ipsilateral and contralateral sides of the subjects with acoustic neuroma compared with those of the control

group (plots with error bars representing 95% confidence interval). *LL* lateral lemniscus, *CI* inferior colliculus, *CGM* corpus geniculatum mediale

by crossing at the brainstem level to the auditory cortices in both hemispheres. It is believed that unilateral AN have no effect on hearing in the ipsilateral side of the ear, but may cause minor and transient hearing loss in the contralateral side of the ear [14].

Auditory impulses come through the cochlear branch of the eighth cranial nerve. These impulse synapses first occur inside the cochlear nucleus in the medulla oblongata, then fibers project into the ipsilateral superior olivary nucleus or cross into the contralateral superior olivary nucleus, continuing into the inferior colliculus through the lateral lemniscus in the midbrain. From the inferior colliculus, efferent fibers project to the medial geniculate body in the thalamus and end at the auditory cortex in the superior temporal Heschl's gyrus [15]. Contribution from contralateral pathways is more important than from the ipsilateral pathway for the

processing of the auditory stimuli [16]. In intact auditory systems, neuroimaging studies show that monaural stimulation induces strong contralateral activity and weak ipsilateral activity, while on the other hand, binaural stimulation induces balanced cortical activity in both hemispheres [17–19].

In the studies concerning the pathology of the auditory pathway in the vestibulocochlear system, few use advanced neuroimaging applications of MRI such as DTI [20, 21]. Those who did use reported DTI changes only at the lateral lemniscus and inferior colliculus level. To our knowledge, no study has used DTI to evaluate the entire auditory pathway (from the lateral lemniscus, inferior colliculus, and medial geniculate body to the Heschl's gyrus) in subjects who have unilateral AN.

DTI is one of the most popular MRI modalities because it provides a noninvasive measure of structural integrity of white matter tracts and also evaluates anatomical connectivity between regions of the brain. DTI enables the assessment and quantification of the diffusion properties of white matter, and has been used in detecting the subtle changes in the structure of tissues associated with brain development, degeneration, and injury [22]. ADC and FA are DTI parameters that have been found to be sensitive to white matter damage and thus have been used in medical studies [23].

Lin et al. [24] have reported reduced FA values and increased radial diffusivity bilaterally at the lateral lemniscus and inferior colliculus of patients with sensorineural hearing loss. Additionally, they also detected reduced FA values and increased radial diffusivity at the lateral lemniscus and inferior colliculus on the contralateral side of their patients who had profound unilateral hearing loss according to the ipsilateral side, which suggests the presence of a dysmyelinating process. In another study, Wu et al. [21] reported reduced FA values with increased radial diffusivity on both the ipsilateral and contralateral sides of patients with cochlear nerve deficiency, which could have been attributed to axonal loss and/or demyelination of the subcortical auditory tract.

Our study determined changes in the diffusion characteristics of the auditory pathway for the ipsilateral and contralateral sides of the subjects with AN. Their ADC values were significantly higher than those of the control group at the contralateral side of the lateral lemniscus, inferior colliculus, and corpus geniculatum mediale. Also, the average ADC values of the lateral lemniscus, inferior colliculus, corpus geniculatum mediale, and Heschl gyrus on the ipsilateral side of the patients were higher than in those of the control group, although the differences were not statistically significant. We thought that higher ADC values might be related to microstructural changes such as loss of myelin or demyelination. On the other hand, the average ADC values of the lateral lemniscus, inferior colliculus, and corpus geniculatum mediale on the contralateral side were higher than those on the ipsilateral side, but again, the differences were not statistically significant. Previous studies reported that of the fibers of the nerve bundles to the auditory cortices, 20–30% come from the ipsilateral side and 70–80% from the contralateral side [21]. This situation may explain our higher ADC values at the contralateral side in subjects with unilateral AN.

This study determined that compared with the controls, FA values of the AN patients were significantly lower at the inferior colliculus on the contralateral and ipsilateral sides. In addition, we determined significantly increased ADC values at the inferior colliculus of the contralateral and ipsilateral sides according to the lateral lemniscus and

corpus geniculatum mediale. It may be that the inferior colliculus receives multiple impulses from the lower auditory pathway on both sides of the brain, such that acoustic information reaches each inferior colliculus either directly by projections from the cochlear nucleus, or indirectly via cochlear nucleus projections to the superior olivary nucleus and nuclei of the lateral lemniscus [25]. Also, single-unit recordings from the inferior colliculus show strong excitatory responses to stimulation of the contralateral side of the ear, and excitatory or inhibitory responses to stimulation of the ipsilateral side of the ear [26]. The findings identified on a DTI show microstructural changes causing axonal loss and/or demyelination, and that the inferior colliculus is where injuries most often occur.

The most important limitation of our study is the relatively small number of patients. This situation may explain the lack of statistically significant differences with regard to patient-control group ADC values of the auditory pathway on the ipsilateral side, or when comparing the contralateral and ipsilateral sides. Such differences may arise in further studies with large series.

Conclusion

The present study demonstrates that in the auditory pathway of patients with AN, the contralateral side is more affected than the ipsilateral side, and the most affected center in the auditory pathway is the inferior colliculus. DTI is an advanced neuroimaging technique that can be used to determine the presence of microstructural damage to the auditory pathway in subjects with acoustic neuroma, whereas conventional MRI is not sensitive enough to detect damage.

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Conflict of Interest The authors declare that they have no conflict of interest.

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