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Relationship between auditory pathway fractional anisotropy and audibility in patients with cerebellopontine angle tumors on diffusion tensor imaging

Masahiko Kusaba[a], Toshinori Takagi[a], Yusuke Tomogane[a], Tomoko Iida[a], Daisuke Sakamoto[a], Reiichi Ishikura[b], Shinichi Yoshimura[a,*]

[a] Department of Neurosurgery, Hyogo College of Medicine, 1-1 Mukogawa, Nishinomiya, Hyogo, 663-8501, Japan
[b] Department of Radiology, Hyogo College of Medicine, 1-1 Mukogawa, Nishinomiya, Hyogo, 663-8501, Japan

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ABSTRACT

Objective: Recent reports demonstrated that acoustic nerve disorders affect the auditory pathway on diffusion tensor imaging (DTI). The aim was to investigate whether auditory pathway fractional anisotropy (FA) values are associated with audibility in patients with cerebellopontine angle tumors.

Patients and methods: Patients with cerebellopontine angle tumors were included in this retrospective study. Preoperatively, all patients underwent magnetic resonance imaging (MRI) including DTI. Two regions of interest on the lateral lemniscus (LL) and inferior colliculus (IC) were set bilaterally on DTI. FA values were calculated using software. Correlations between FA values and audibility were evaluated using Spearman's rank correlation coefficient. Statistical significance was defined as $p < 0.05$.

Results: Seventeen patients with cerebellopontine angle tumors were included in this study. FA values in the bilateral LL showed a significant negative correlation with hearing impairment severity ($r = -0.758, -0.600$, $p < 0.05$). FA values on the ipsilateral side of the IC showed a significant negative correlation with hearing impairment severity ($r = -0.477$, $p < 0.05$). FA values on the contralateral side of the IC did not correlate with hearing impairment severity ($r = -0.201$, $p > 0.05$). One patient with a low FA value on the contralateral side of the IC had postoperative hearing impairment despite good preoperative hearing ability.

Conclusions: FA values in the bilateral LL and on the ipsilateral side of the IC reflected hearing impairment severity. Decreased FA values on the contralateral side of the IC might predict hearing impairment postoperatively.

1. Introduction

Approximately 11% of all intracranial tumors occur at the cerebellopontine angle. Common tumors in this area include schwannoma (72%) and meningioma (20%) [1]. It is important to preserve audibility after surgery in the treatment of cerebellopontine angle tumor. Recent reports have shown that acoustic nerve disorders affect the auditory pathway on diffusion tensor imaging (DTI) [2–5]. Fractional anisotropy (FA) values from DTI can demonstrate the detailed structure of the white matter tracts objectively. Reductions in auditory pathway FA values were reported in patients with congenital cochlear nerve deficiency [2], sensorineural hearing loss (SNHL) [3], and acoustic schwannomas [4]. However, the relationship between auditory pathway FA values and audibility in patients with cerebellopontine angle tumors remains unclear. The purpose of our study was to evaluate FA values in the bilateral auditory pathway in patients with cerebellopontine angle tumors and to assess the relationship between auditory pathway FA values and audibility.

2. Material and methods

2.1. Patients

The study was reviewed and approved by the Hyogo College of Medicine Ethical Committee (No. 2729). Patients with cerebellopontine angle tumors were investigated comprehensively at the Hyogo College of Medicine between 2006 and 2015. The hearing acuity of all patients was assessed audiographically; audiometric testing consisted of pure-tone audiometry performed at octave frequencies from 125 Hz to 8 kHz. Pure-tone audiometry thresholds were recorded as the average of hearing thresholds through air conduction at 500 Hz, 1 kHz, and 2 kHz. Hearing was measured before and after surgery and graded using the

* Corresponding author at: Department of Neurosurgery, Hyogo College of Medicine, 1-1 Mukogawa, Nishinomiya, Hyogo, 663-8501, Japan.
E-mail address: hyogoneuro@yahoo.co.jp (S. Yoshimura).

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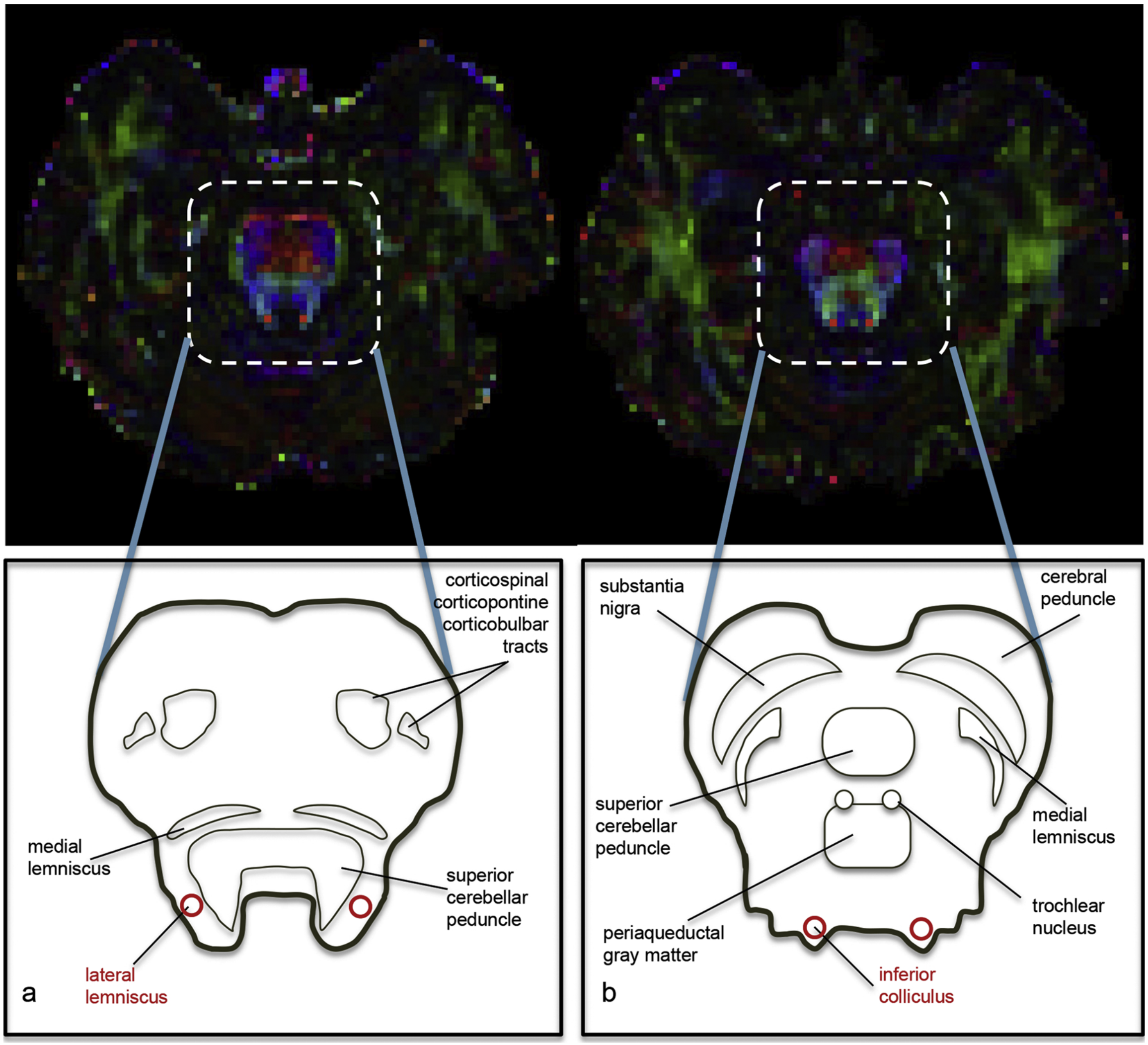

Fig. 1. Axial color-coded maps from patients with cerebellopontine angle tumors showing region of interest placement in the lateral lemniscus (a) and inferior colliculus (b). The figure below is scheme of nucleus and ROI.

Table 1
Clinical and imaging data.

Case No.	Sex/Age (years)	Diagnosis	Location	Hearing level(dB)	Tumor size (mm)	Tumor volume (cm3)
1	M/51	schwannoma	L	58.3	19	3.9
2	F/63	schwannoma	L	106.7	14.7	1.7
3	F/49	schwannoma	R	38.3	36	18.2
4	M/64	schwannoma	R	38.3	18.6	4.6
5	F/53	schwannoma	R	35	15	1.8
6	F/64	schwannoma	R	48.8	35	14.4
7	F/60	schwannoma	R	91.7	14.5	0.5
8	F/65	schwannoma	R	100	18	0.7
9	F/53	schwannoma	R	111	41	22.6
10	F/67	schwannoma	R	115	2.5	5.7
11	F/63	meningioma	L	16.7	15.8	0.4
12	F/77	meningioma	L	16.7	31	5.4
13	F/48	meningioma	L	16.3	14.1	0.3
14	F/62	meningioma	R	16.7	17.9	2
15	F/52	meningioma	L	40	19.4	1.3
16	F/48	meningioma	L	100	2.5	1.1
17	F/59	meningioma	L	26.7	2.8	12.8

Gardner-Robertson (G–R) hearing classification [6]. The maximum tumor diameter and tumor volume were calculated using three-dimensional image analysis software (OsiriX v. 7.5.1; OsiriX Foundation, Geneva, Switzerland).

Table 2
FA values obtained from the ipsilateral and contralateral sides of patients with cerebellopontine angle tumors.

Locations	Lateral lemniscus	Inferior colliculus
Ipsilateral	0.80 ± 0.08	0.77 ± 0.06
Contralateral	0.81 ± 0.09	0.77 ± 0.07

2.2. MR imaging and images analysis

All studies were performed on an Achieva 3-T MRI scanner (Philips, Best, the Netherlands). The DTI protocol consisted of a single-shot, spin-echo, echo-planar sequence with fat suppression and the following parameters: repetition time/echo time (TR/TE) = 8,063/83 ms; matrix, 112 × 98; field-of-view, 240 mm; and slice thickness, 2 mm. Thirty-two diffusion-encoding directions were used at b = 0 s/mm^2 and b = 1000 s/mm^2. DTI data were analyzed using software (FMRIB Software Library [FSL] v. 5.0.7, http://www.fmrib.ox.ac.uk/fsl) [7]. All datasets were processed using the following steps: eddy current and head motion correction, estimation of the diffusion tensors, and calculation of the FA values. The DTI images first underwent corrections for eddy-current distortion and head motion using FMRIB's Diffusion

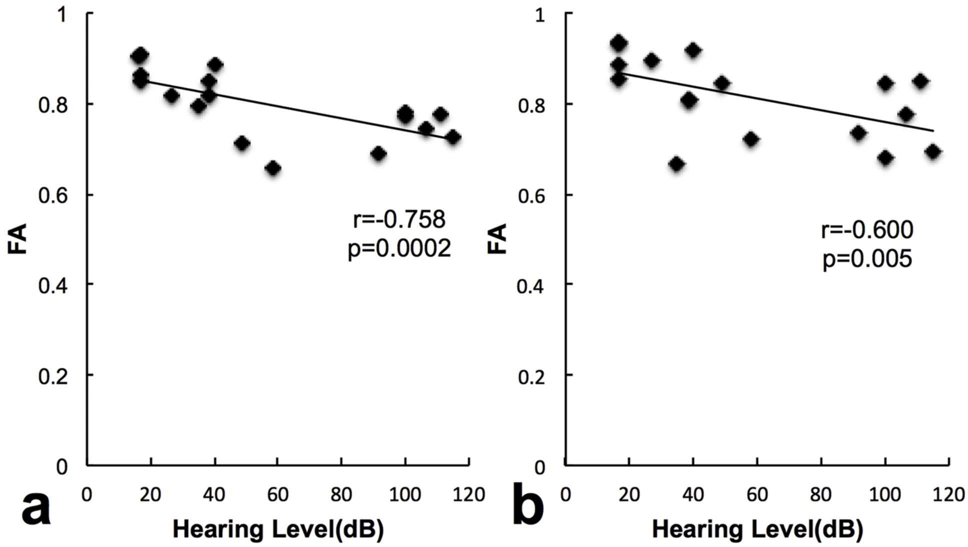

Fig. 2. A scatterplot of FA values in the LL and the audibility of patients with cerebellopontine angle tumors. FA values on both sides of the LL are inversely correlated with the measured audibility. (a) ipsilateral side; (b) contralateral side.

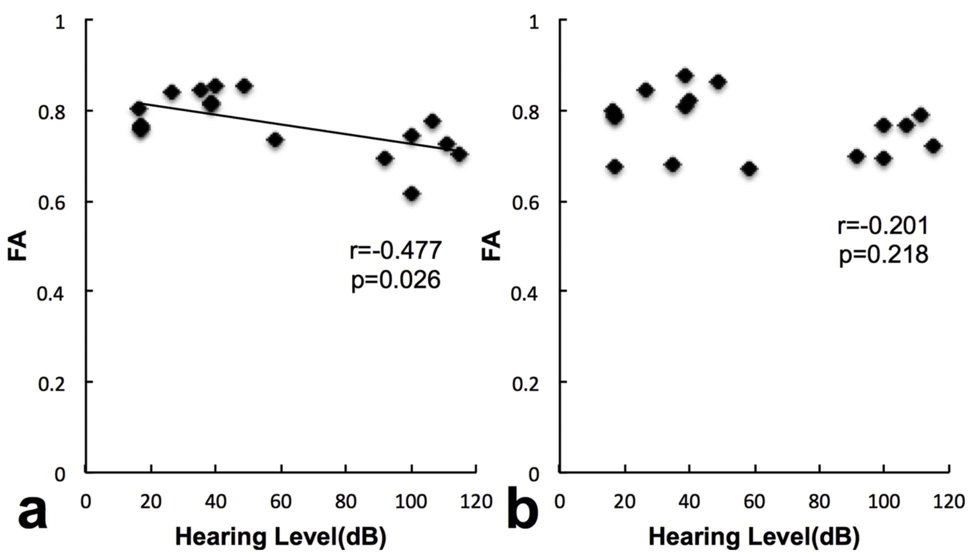

Fig. 3. Scatterplot of FA values in the IC versus the audibility of patients with cerebellopontine angle tumors. FA values on the ipsilateral side of the IC are inversely correlated with the measured audibility. (a) ipsilateral side; (b) contralateral side.

Toolbox. The brain image was extracted using the Brain Extraction Tool. FA values were extracted using FMRIB's Diffusion Toolbox. The adaptation of the sizes and placements of all regions of interest (ROIs) were evaluated by a neurosurgeon and a graduate student (Yusuke Tomogane and Masahiko Kusaba). ROIs were drawn manually with utmost care. Moreover, ROIs were drawn in the auditory pathways of the lateral lemniscus (LL) and inferior colliculus (IC) on color-coded maps of the ipsilateral and contralateral sides of the brain in patients with cerebellopontine angle tumors [3–5] (Fig. 1). All ROI sizes were set to single pixel.

2.3. Statistical analysis

For comparisons between FA values on the ipsilateral and contralateral sides, paired t-tests were performed separately for the LL and IC. Correlations between tumor volume, tumor diameter, FA values, and audibility were calculated using Spearman's rank correlation coefficient. Statistical significance was defined as $p < 0.05$. Data analysis was performed using statistical software (SPSS v. 20; IBM Corp, Armonk, New York).

3. Results

Patient demographics are shown in Table 1. Regarding the diagnosis of cerebellopontine angle tumor, there were 10 acoustic schwannomas and seven meningiomas in this study. The hearing thresholds ranged from 35 to 115 dB (median, 75 dB) and from 16.3 to 100 dB (median 16.7 dB) in patients with schwannomas and meningiomas, respectively. The maximum tumor diameter ranged from 2.5 to 36 mm (mean, 21.4 mm) for the 10 schwannomas and from 2.8 to 19.4 mm (mean, 14.8 mm) for the seven meningiomas. The tumor volumes ranged from 0.5–22.6 cm^3 (mean, 7.4 cm^3) for the schwannomas and from 0.3–5.4 cm^3 (mean, 3.3 cm^3) for the meningiomas.

Regarding the auditory pathway FA values, there was no difference statistically between the ipsilateral and contralateral sides (LL: $p = 0.28$; IC: $p = 0.82$) (Table 2). Moreover, there was no association between tumor volume or diameter and audibility ($r = 0.20$ and -0.05, respectively; $p > 0.05$).

FA values in the ipsilateral and contralateral LL showed a significant negative correlation with the severity of hearing impairment (ipsilateral side: $r = -0.758$ [Fig. 2a], contralateral side: $r = -0.600$

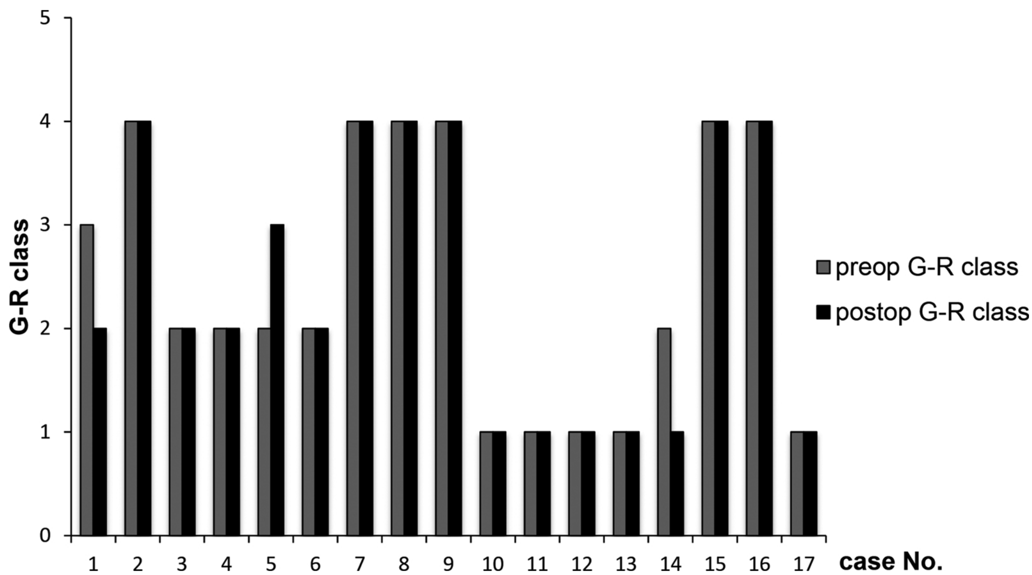

Fig. 4. Preoperative (preop) and postoperative (postop) hearing grades according to the Gardner-Robertson (G–R) hearing classification system for all patients.

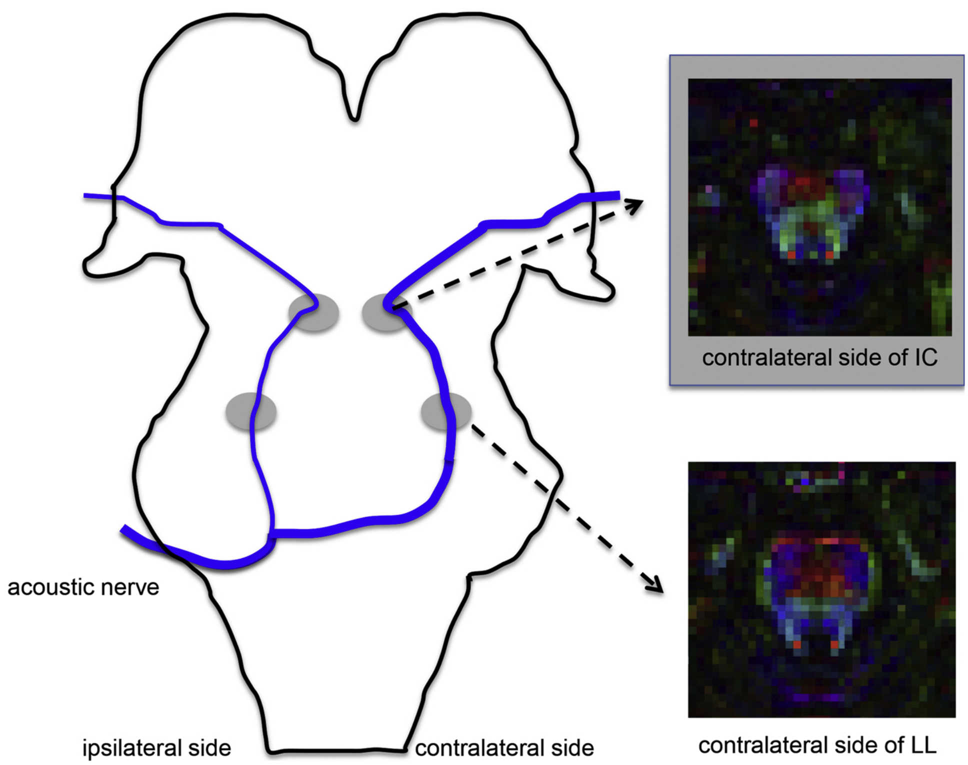

Fig. 5. Schematic representation of the auditory pathway evaluated using DTI.

[Fig. 2b], $p < 0.05$, respectively). FA values on the ipsilateral side of the IC showed a significant negative correlation with the severity of hearing impairment ($r = -0.477$ [Fig. 3a], $p < 0.05$). In contrast, FA values on the contralateral side of the IC did not correlate with the severity of hearing impairment ($r = -0.201$ [Fig. 3b], $p > 0.05$).

Next, the contralateral side of the IC was evaluated in detail. We focused on two cases (numbers 5 and 13) in which preoperative hearing ability was maintained but FA values on the contralateral side of the IC were decreased (0.68 and 0.68, respectively). In one of these two cases, there was preoperative audibility, while postoperative audibility was impaired by 35 dB–61.7 dB (case 5). In addition, postoperative hearing loss was observed in only one case in this series in which the FA value on the contralateral side of the IC was decreased. In summary, FA values in the bilateral LL and on the ipsilateral side of the IC showed significant negative correlations with the severity of hearing impairment, and FA values on the contralateral side of the IC did not show a statistically significant relationship with audibility (Fig. 4). FA values in the contralateral IC were decreased in two cases despite good hearing ability preoperatively.

4. Discussion

It remains unclear whether auditory pathway FA values correlate between the ipsilateral and contralateral sides. Recent reports have shown that in patients with SNHL and cochlear nerve deficiency on one side, FA values on the contralateral side were significantly lower than those on the ipsilateral side [2,3,5]. In contrast, another study suggested that FA values were not statistically significantly different between the ipsilateral and contralateral sides [4]. Our data agreed with those in the latter study. In previous reports on patients with acoustic schwannomas, tumor size did not correlate with audibility [8]. Hearing loss in patients with acoustic schwannomas is believed to be caused by compression of the cochlear nerve. Moffat et al reported that hearing loss was associated with the position of the tumor [9]. There is a possibility that the presence or absence of tumor progression to the bottom of the internal auditory meatus is involved in hearing loss. For the reasons stated above, tumor diameter and volume might not correlate with audibility in this study. Other studies have concluded that in non-profound hearing loss (25–90 dB) in patients with SNHL, FA values in the LL and IC showed significant negative correlations with the severity of hearing impairment [3]. In our study, FA values in the bilateral LL showed a significant negative correlation with the severity of hearing impairment ($r = -0.758$ [Fig. 2a] and -0.600 [Fig. 2b], respectively; $p < 0.05$). FA values on the ipsilateral side of the IC showed a significant negative correlation with the severity of hearing impairment ($r = -0.477$ [Fig. 3a], $p < 0.05$). Therefore, in patients with decreased FA values, the auditory nerve is injured by compression of tumor, resulting in hearing loss. The injured auditory nerve was associated with microstructural changes including demyelination. For the above reasons, the FA value of the auditory nerve could be a valuable biomarker of hearing impairment.

On the other hand, FA values on the contralateral side of the IC did not show a significant negative correlation with the severity of hearing impairment ($r = -0.343$ [Fig. 3b], $p < 0.05$). Cases 5 and 13 showed low FA values on the contralateral side of the IC regardless of their good hearing abilities before surgery. After surgery, only case 5 showed a decline in G–R class from II to III (Fig. 4). In a previous study on the processing of auditory stimuli, the contralateral pathway was more important than the ipsilateral pathway [10]. Additionally, the IC is likely to receive multiple impulses from the lower auditory pathway on both sides of the brain [11]. For these reasons, the contralateral side of the IC was most affected by the tumor and may have contributed to the results of this study. Fig. 5 is a schematic of impairment of the auditory pathway on DTI imaging.

A limitation of the present study is the small number of cases. Moreover, a second limitation is that we could not compare the results with those from healthy volunteers. Additional study is needed to elucidate the association between hearing disability and auditory pathway FA values.

5. Conclusion

FA values in the ipsilateral and contralateral LL and on the ipsilateral side of the IC showed significant negative correlations with the severity of hearing impairment. FA values on the contralateral side of the IC were decreased in two cases despite having good hearing ability before surgery; one case showed hearing loss after surgery. Surgery is invasive and thus conclusions cannot be stated unconditionally; however, if the FA value is decreased on the contralateral side of the IC, there may be a cause for concern regarding hearing loss after surgery.

Declarations of interest

None.

Acknowledgments

None.

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