# Micro-structural Auditory Pathway Changes in Patients with Sensorineural Hearing Loss with or without Tinnitus, could diffusion tensor imaging be valuable?

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**Abstract**

**Background:** Advanced magnetic resonance imaging (MRI) technique called diffusion tensor imaging (DTI) can assess tissue microstructure. It's challenging to identify sensorineural hearing loss (SNHL) cause suing CT or MRI without significant gross disruption.

**Objectives**: to assess microstructural integrity of auditory neural pathway SNHL patients with or without tinnitus by DTI.

**Patients and methods:** This prospective, case-control study included 55 subjects in three groups: 30 healthy volunteers in control group (GI), 12 patients in bilateral SNHL without tinnitus group (GII), and 13 patients in bilateral SNHL with tinnitus group (GIII) were MRI-assessed using 1.5 Tesla GE machine. Ordinary one-way ANOVA test was used to compare groups with normal distributions, Kroskal Wallis test: compares groups with abnormally distributed data; post-hoc test: determines significance between pairs.

**Results:** ANOVA test revealed statistically significant difference at Lateral lemniscus(LL), Inferior colliculus(IC), medial geniculate body (MGB), auditory radiation(AR), Superior temporal gyrus(STG), Hippocampus, amygdala, Superior longitudinal fasciculus(SLF), genu and splenium of corpus callosum (CC) with P value ≤0.05. Post-hoc test: group II had lower FA comparing to group I at LL, MGB, IC, AR, STG, genu and splenium of CC. In group III the forementioned regions were affected besides hippocampus and amygdala. Group III had statistically significant lower FA values compared to group II at LL, IC, MGB, hippocampus, amygdala, SLF, genu and splenium of CC.

**Conclusion:** Using DTI to assess microstructural integrity of auditory pathway, SNHL is associated with white matter microstructure affection as proved by the current study, and presence of tinnitus is associated with limbic system affection.

**Keywords:** Diffusion tensor imaging; Sensorineural Hearing Loss; Tinnitus; Fractional anisotropy; Mean diffusivity.

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## Introduction

Hearing loss is one of the widespread problems with high incidence and is classified into sensory neural hearing loss (SNHL), conductive hearing loss (CHL) or mixed **(Cunningham and Tucci, 2017)**. The cause of SNHL remains largely unclear **(Baird et al., 2019)** However, Degenerative ageing mechanisms, mutations in genes, exposure to noise, and therapeutic medication usage that has oto-toxic adverse reactions are among the leading causes of SNHL **(Cunningham and Tucci 2017)**.

The auditory nerve, thalamus, brain stem, and auditory cortex comprise the basic auditory circuit **(Zhang, 2013)**. The auditory cortex and limbic system are linked in the development and ongoing existence of tinnitus as well as to this conventional auditory circuit **(Chen et al., 2020)**.

The sensation of sound without an external acoustic stimulus is known as tinnitus **(Chari and Limb 2018)**. While non-pulsatile tinnitus is the most prevalent kind of tinnitus and nearly invariably subjective, pulsatile tinnitus is sometimes indicative of a vascular aetiology. Many times, tinnitus may develop without structure defects or other illnesses, but sometimes there is a structure defect (for example, an auditory neuroma) or pathological disorder (for example, Meniere's disease and multiple sclerosis) as the reason. Tinnitus may affect persons with good hearing, although it often affects those with hearing loss **(Naderinabi et al., 2018)**.

It may be challenging to identify the underlying aetiology of SNHL using diagnostic imaging modalities that include computed tomography (CT) or traditional magnetic resonance imaging (MRI) without significant structural disturbance **(Kim et al., 2020)**.

An improved magnetic resonance imaging (MRI) method called diffusion-tensor imaging (DTI) can quantitatively assess the microscopic structure of tissues **(Gunbey et al., 2017).** It uses the rate of diffusion of water molecules to make axonal bundles or tracts visible in the white matter **(Dhir et al.,2020).**

Through anisotropic tissue in the brain, water molecules diffuse variably in diverse directions. Instead of occurring uniformly in all directions, anisotropic diffusion happens predominantly in one direction. The walls of the cells that make up the brain prevent diffusion in various directions **(Razek and Sherif, 2019)**.

White matter integrity constitutes one of the most sensitive indications of axonal injury or demyelination, and DTI methodology is an efficient way for characterizing white matter organization **(Aung et al., 2013)**.

Fractional anisotropy (FA), which measures the degree of directional differences of water diffusion, and mean diffusivity (MD), which measures the average water diffusion rate, are two frequently mentioned DTI scalar metrics **(Soares et al., 2013)**. Many previous publications studied the white matter changes in either hearing loss or tinnitus. However, our present study analyzed patients with SNHL with/without tinnitus by analysis using DTI parameters as FA, MD on 12 regions of interest in the brain. This study aimed to assess quantitative analysis of microstructural integrity of the auditory neural pathway among individuals with SNHL with or without tinnitus by added value of diffusion tensor imaging.

## Patients and Methods

This prospective, case-controlled work was conducted after approval from the Ethical Committee of our institution. From 1st March 2022 till 1st March 2023. All the participants and the healthy volunteers who participated in this research provided written, informed consent.

This work was carried out on 55 subjects, 25 of them were patients diagnosed clinically with SNHL, with or without tinnitus, referred from audiology vestibular unit with normal conventional

MRI findings, with control group of healthy instances (N = 30) of nearly matched ages and sex. Full audiological assessment by pure tone audiometry in Audiology Department. The authors have no knowledge of the subject's name, age, or clinical data.

**Inclusion criteria:** All patients SNHL with/without tinnitus and had normal conventional MRI findings were included in this study.

**Exclusion criteria:** Patients who were clinically diagnosed as conductive hearing loss, or with organic brain lesions causing SNHL or tinnitus that were diagnosed by conventional MRI, patients had contraindications to MRI magnet as metallic devices placed in their body that are incompatible to MRI machine, such as (heart pacemaker and aneurysm clip and cochlear implants), refusal of patients or their guardians to undergo the examination, claustrophobic patients from MRI machine.

Participants were split into three groups: Control group involved thirty healthy volunteers (group I), Bilateral SNHL without tinnitus group included 12 patients (group II) and Bilateral SNHL with tinnitus group included 13 patients (group III).

MRI assessment by using 1.5 Tesla MRI GE (General Electric) machine. All the patients and volunteers removing any metallic objects, and entering the machine headfirst. Utilizing a head coil with the head maintained in a neutral position. Axial, coronal and sagittal planes taken. The slice thickness was 3 mm, the matrix was 256 x 256, and the field of view was 220-240 mm, with a standard circularly polarized head coil with a placed head support pillow to minimize patient's movement.

Magnetic resonance imaging: axial T1WI (TR/TE = 300–600/10–30 m/sec), axial T2WI(TR/TE = 700–2000/80–100 m/sec), axial, oblique coronal Fluid attenuated inversion recovery (FLAIR) (TR/TE/Inversion time(TI) = 6000–8000/140/1400), 3D FEISTA, 3D T1WI and Diffusion weighted images (B value; 0, 1000).

**Diffusion tensor imaging (DTI):** The following settings were used to collect the DTI data utilizing a single shot spin-echo-planar image: (TR= 8000-10000 m.sec, TE= 70-120 m.sec, matrix 256 x 220, Field of view :28 x 25, slice thickness 3 mm, (60) gradient encoding directions, Flip Angle: 35 degrees, b-value 1000 $mm^2/s$).

**Data processing and analysis:** The DTI data was performed utilizing offline distinct work stations (Advantage Workstation 4.7, GE Medical Systems), where they are converted to different types of maps: a) Color coded FA map images that are directionally encoded, revealed the architecture and orientation of the tracts by assigning each of the three orthogonal planes a different color: red (for right-to-left tracts), blue (for craniocaudal tracts) and green (for anteroposterior tracts) mainly and sometimes a mixture between them. b) FA and MD maps: 3D T1WI image and / or color-coded images used for anatomical reference, ROIs drawn and cloned to FA, MD maps on: 1) Axial: Lateral Lemniscus, medial geniculate body, inferior colliculus, auditory radiation, amygdala, hippocampus, inferior longitudinal fasciculus and superior longitudinal fasciculus, 2) Coronal: Superior temporal gyrus and parahippocampus, 3) Sagittal: Genu and splenium of corpus callosum, illustrated in (**Fig.1**).

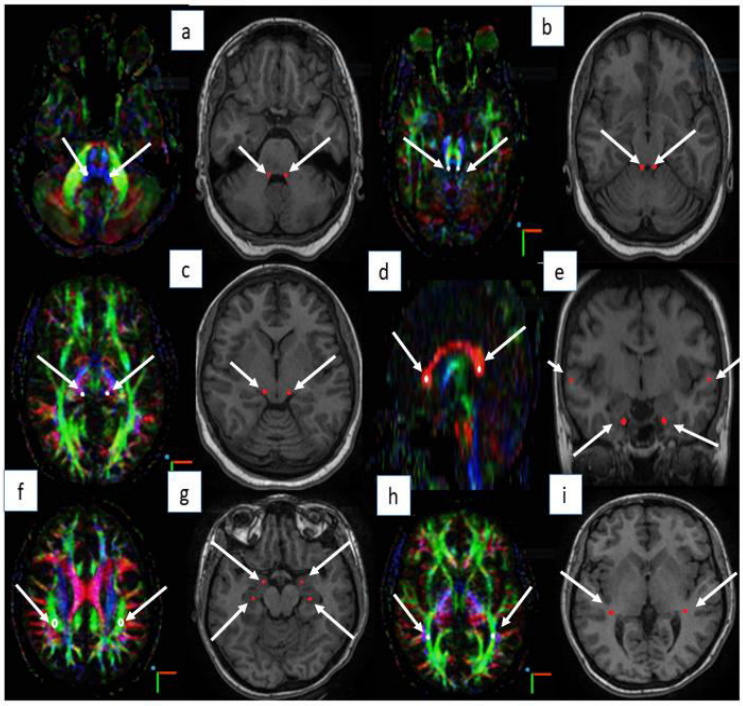


**Fig.1. Selected ROIs at a)** lateral lemniscus, **b)** inferior colliculus, **c)** medial geniculate body, **d)** genu and splenium of corpus callosum, **e)** Superior temporal gyrus (superior ROI), parahippocampus (inferior ROI), **f)** Superior longitudinal fasciculus, **g)** amygdala (anterior ROI), hippocampus (posterior ROI), **h)** inferior longitudinal fasciculus, **i)** auditory radiation at DTI color coded image and 3D T1-weighted MR image.

Each ROI's DTI values were calculated and compared to their corresponding ROIs in the other hemisphere. Fractional anisotropy (FA) and mean diffusivity (MD) were calculated quantitatively from the FA and MD maps for each ROI. Patients and the control group's data obtained from FA and MD maps and were compared. Additionally, the direction and the anatomy of the tracts are seen in the directionally color coded maps, where a specific color is assigned to tracts running in three orthogonal planes. Color coded DTI maps were analyzed, both subjectively by visual comparison and quantitively by comparing the FA and MD values with the contralateral normal side. Four radiologists with experience levels ranging from 3, 13, 25, and 28 years each reviewed and evaluated all the data. Each information about patients was blinded, and all of them received a unique ID number.

**Statistical analysis**

Statistical analysis was done by Graph-Pad prism version (8). Descriptive statistics e.g., was displayed in numbers (No), percentages (%) mean ($\bar{x}$) standard deviation (SD), Median, interquartile ranges (IQR). Paired t test was utilized to contrast matched pairs of normally distributed data and Wilcoxon rank test was applied for non-parametric data among control group. One-way ANOVA used to compare between groups with normal distributed data, Kruskal Wallis test: used to compare between groups with abnormal distributed data. Post-hoc test used as a second stage of analysis to find between which pairs the significance was found. With its sensitivity and specificity, the receiver operating characteristics curve (ROC) was utilized to evaluate the ideal cutoff point. AUC, and the area under the curve Sensitivity: - The likelihood that a test will provide a positive outcome when the illness is present (also known as the true positive rate, presented as a

percentages)., Specificity: - The likelihood that the test will provide a negative outcome in the absence of the condition (true negative rate, represented as a percentages); PPV stands for Positive Predictive Value and NPV for Negative Predictive Value, both of which indicate the likelihood of a disease when a test is positive or negative. Accuracy: The proportion of true positive to true negative results across all individuals, The standard academic point system determined by AUC (0.9-1 = excellent (A), 0.8-0.9 = good (B), 0.7-0.8 = fair (C), 0.6-0.7 = bad (D), and 0.5-0.6 = fail (F)) offers a basic reference for categorizing the test's accuracy. The Pearson's Chi-square test for independence was used to examine correlations among categorical parameters. Utilizing the Shapiro-Wilk test, the data's normality was evaluated. A two tailed P value ≤ 0.05 was considered significant.

## Results

This prospective case-controlled study involved 55 subjects divided into three groups: 30 normal hearing as control group (G I), 12 patients with bilateral SNHL without tinnitus group (group II) and 13 patients with bilateral SNHL with tinnitus (group III).

Patients' ages ranged from 17 to 63 years old, with a mean ±SD =43±13 years old, in bilateral group without tinnitus, ranged from 19 to 61 years old, with a mean ±SD =42±11 years old, in bilateral group with tinnitus, while in volunteers' ages varied from 17 to 63 years old, with a mean ±SD =36±12 years old. There were no statistically significant differences between groups as regards the patient's age (p-value=0.18) as in (**Table .1**).

**Table 1. Comparison between SNHL (with or without tinnitus) and control group regarding to fractional anisotropy (FA) at regions of interest:**

| ROIs | | G I (n = 30) | G II (n = 12) | | G III (n = 13) | | K/F | p |
|---|---|---|---|---|---|---|---|---|
| | | | **Rt** | **Lt** | **Rt** | **Lt** | | |
| **LL** | Mean | 0.57 | 0.47 | 0.48 | 0.25 | 0.25 | 65.50 | **<0.0001*** |
| | SD | 0.05 | 0.04 | 0.03 | 0.02 | 0.04 | | |
| | Median | 0.56 | 0.46 | 0.48 | 0.25 | 0.25 | | |
| | IQR | 0.54-0.59 | 0.42-0.51 | 0.44-0.50 | 0.23-0.27 | 0.23-0.28 | | |
| | Post hoc | **P1=0.02*** | **P2=0.04*** | **P3<0.0001*** | **P4<0.0001*** | **P5=0.04*** | **P6=0.02*** | |
| **IC** | Mean | 0.56 | 0.48 | 0.47 | 0.30 | 0.30 | 65.09 | **<0.0001*** |
| | SD | 0.04 | 0.04 | 0.04 | 0.03 | 0.03 | | |
| | Median | 0.54 | 0.49 | 0.49 | 0.308 | 0.306 | | |
| | IQR | 0.53-0.60 | 0.44-0.52 | 0.44-0.51 | 0.28-0.32 | 0.28-0.32 | | |
| | Post hoc | **P1=0.04*** | **P2=0.03*** | **P3<0.0001*** | **P4<0.0001*** | **P5=0.02*** | **P6=0.03*** | |
| **MGB** | Mean | 0.47 | 0.415 | 0.417 | 0.270 | 0.273 | 67.60 | **<0.0001*** |
| | SD | 0.027 | 0.022 | 0.023 | 0.023 | 0.025 | | |
| | Median | 0.47 | 0.410 | 0.415 | 0.25 | 0.27 | | |
| | IQR | 0.45-0.50 | 0.40- | 0.40- | 0.250- | 0.250- | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | 0.442 | 0.445 | 0.290 | 0.295 | | |
| | Post hoc | **P1=0.01*** | **P2=0.01*** | **P3<0.0001*** | **P4<0.0001*** | **P5=0.04*** | **P6=0.04*** | |
| **AR** | Mean | 0.39 | 0.33 | 0.32 | 0.31 | 0.30 | 49.37 | **<0.0001*** |
| | SD | 0.007 | 0.03 | 0.03 | 0.020 | 0.023 | | |
| | Median | 0.39 | 0.33 | 0.32 | 0.31 | 0.31 | | |
| | IQR | 0.39-0.40 | 0.29-0.36 | 0.31-0.34 | 0.30-0.33 | 0.28-0.33 | | |
| | Post hoc | **P1=0.001*** | **P2=0.1003*** | **P3<0.0001*** | **P4<0.0001*** | P5>0.9999 | P6>0.9999 | |
| **STG** | Mean | 0.35 | 0.26 | 0.27 | 0.25 | 0.26 | 57.99 | **<0.0001*** |
| | SD | 0.02 | 0.02 | 0.02 | 0.02 | 0.008 | | |
| | Median | 0.36 | 0.27 | 0.28 | 0.26 | 0.27 | | |
| | IQR | 0.34-0.37 | 0.24-0.28 | 0.25-0.29 | 0.25-0.26 | 0.26-0.27 | | |
| | Post hoc | **P1<0.0001*** | **P2=0.0003*** | **P3<0.0001*** | **P4<0.0001*** | P5>0.9999 | P6>0.9999 | |
| **Hippocampus** | Mean | 0.21 | 0.21 | 0.21 | 0.17 | 0.18 | 35.75 | **<0.0001*** |
| | SD | 0.01 | 0.01 | 0.01 | 0.02 | 0.01 | | |
| | Median | 0.22 | 0.22 | 0.22 | 0.18 | 0.18 | | |
| | IQR | 0.21-0.22 | 0.20-0.22 | 0.20-0.22 | 0.14-0.20 | 0.16-0.20 | | |
| | Post hoc | P1>0.9999 | P2>0.9999 | **P3<0.0001*** | **P4=0.0003*** | **P5=0.004*** | **P6=0.005*** | |
| **Amygdala** | Mean | 0.28 | 0.22 | 0.22 | 0.14 | 0.15 | 64.29 | **<0.0001*** |
| | SD | 0.03 | 0.02 | 0.01 | 0.02 | 0.02 | | |
| | Median | 0.29 | 0.22 | 0.22 | 0.15 | 0.15 | | |
| | IQR | 0.25-0.31 | 0.21-0.23 | 0.21-0.23 | 0.12-0.16 | 0.14-0.17 | | |
| | Post hoc | P1=0.06 | P2=0.06 | **P3<0.0001*** | **P4<0.0001*** | **P5=0.01*** | **P6=0.04*** | |
| **SLF** | Mean | 0.78 | 0.60 | 0.60 | 0.45 | 0.43 | 69.14 | <0.0001* |
| | SD | 0.06 | 0.04 | 0.05 | 0.04 | 0.03 | | |
| | Median | 0.79 | 0.58 | 0.59 | 0.42 | 0.41 | | |
| | IQR | 0.72-0.83 | 0.58-0.63 | 0.59-0.63 | 0.42-0.50 | 0.41-0.46 | | |
| | Post hoc | **P1=0.04*** | **P2=0.05*** | **P3<0.0001*** | **P4<0.0001*** | P5=0.19 | **P6=0.04*** | |

**LL:** Lateral Lemniscus , **IC :** inferior colliculus , **MGB** :medial geniculate body , **AR** :auditory radiation , **STG** :superior temporal gyrus **, SLF: Superior longitudinal fasciculus , FA:** Fractional Anisotropy, **K**: Kruskal Wallis Value, **F**: F value, **SD**: Standard Deviation**, IQR**: interquartile range, **p** value considered significant if ≤o.o5, **P1**: control versus Bi HL no Tinn Rt, **P2**: control versus Bi HL no Tinn Lt, **P3**: control versus Bi HL Tinn Rt, **P4**: control versus Bi HL Tinn Lt, **P5:** Bi HL no Tinn Rt versus Bi HL Tinn Rt, **P6**: Bi HL no Tinn lt versus Bi HL Tinn Lt

The sex distribution among the studied groups was as the following: (5 males, 7 females) with male to female ratio: 41% to 58 % in group II, (8 males and 5 females) with male to female ratio: 61 % to 38 % in group III, (17 males, 13 females) with male to female ratio 56% to 43 % in group I. No statistically significant relation could be detected with gender distribution in the studied participants, p-value=0.57.

On the audiological assessment, all cases showed bilateral type A tympanogram indicating bilateral normal middle ear pressure. Pure tone average of the hearing loss groups ranged from moderate to profound hearing loss in the frequency ranged from 250 to 8000 HZ.

The distribution of patients across the two subgroups according to the degree of hearing loss by pure tone average audiometry illustrated at (**Fig.2**).

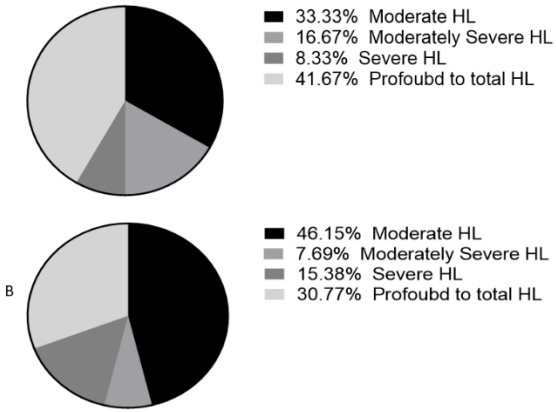


**Fig.2. Distribution of patients across the two subgroups according to the degree of hearing loss by pure tone average audiometry. A**: Bilateral HL group without tinnitus (G II) , **B**: Bilateral Group with tinnitus(G III).

All patients suffered from chronic progressive course. The duration of the disease among the studied groups that ranged from 2 to 25 years in bilateral group without tinnitus, from 2 to 19 years in bilateral group with tinnitus.

Regarding fractional anisotropy, as mentioned in (**Table. 1 & Fig.3 (a-f)**) ANOVA test revealed statistically significant differences between groups at all measured areas except for, parahippocampus and ILF ($p \leq 0.05$*)
Post hoc test was applied and revealed that group I was statistically significant from group II for both sides at LL, IC, MGB, AR, STG, SLF, G CC and SCC). Group I was statistically significant from group III for both sides at the same previous areas (LL, IC, MGB, AR, STG, SLF, G CC, S CC) plus (Hippocampus and Amygdala). While comparing the results of bilateral groups of hearing loss (with and without tinnitus); Group III showed statistically significant lower values from group II at the following areas (LL, IC, MGB, Hippocampus, amygdala, SLF, genu and splenium of CC).

Regarding mean diffusivity, as mentioned in (**Table.2 & Fig.4 (a-f)**): ANOVA test revealed no statistically significant differences between all different groups at all measured areas, $p \geq 0.05$.

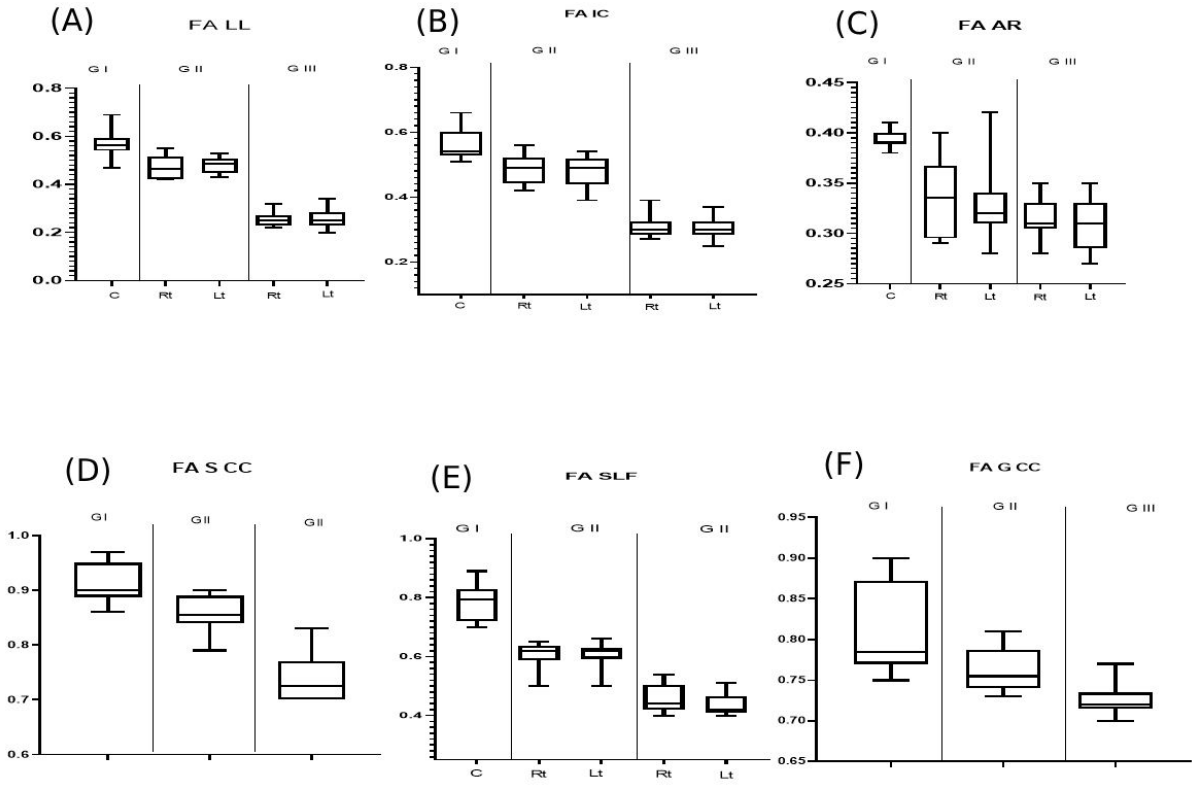


**Fig.3. a)** Fractional anisotropy values of lateral lemniscus between different subgroup, **b)** Fractional anisotropy values of Inferior Colliculus between different subgroups ,**c)** Fractional anisotropy values of auditory radiation between different subgroups , **d)** Fractional anisotropy values of splenium of carpus callosum between different subgroups , **e)** Fractional anisotropy values of superior longitudinal fasciculus between different subgroups, **f)** Fractional anisotropy values of genu of corpus callosum between different subgroups

**Table 2. Comparison between SNHL (with or without tinnitus) and control group regarding mean diffusivity (MD) at regions of interests**

| ROIs | | | G I (n = 30) | G II (n = 12) | | G III (n = 13) | | K/F | p |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Rt | Lt | Rt | Lt | | |
| LL | MD (-03mm 2/s) | Mean | 0.65 | 0.67 | 0.66 | 0.64 | 0.66 | 3.693 | 0.4492 |
| | | SD | 0.015 | 0.021 | 0.017 | 0.022 | 0.024 | | |
| | | Median | 0.65 | 0.67 | 0.68 | 0.66 | 0.66 | | |
| | | IQR | 0.64-0.67 | 0.65-0.68 | 0.65-0.69 | 0.62-0.67 | 0.64-0.68 | | |
| IC | MD (-03mm 2/s) | Mean | 0.63 | 0.65 | 0.64 | 0.63 | 0.65 | 2.105 | 0.7165 |
| | | SD | 0.02 | 0.02 | 0.03 | 0.02 | 0.03 | | |
| | | Median | 0.65 | 0.65 | 0.64 | 0.66 | 0.66 | | |
| | | IQR | 0.63-0.67 | 0.64-0.66 | 0.62-0.67 | 0.63-0.69 | 0.64-0.68 | | |
| MGB | MD (-03mm 2/s) | Mean | 0.83 | 0.86 | 0.85 | 0.82 | 0.83 | 1.496 | 0.2120 |
| | | SD | 0.03 | 0.04 | 0.04 | 0.05 | 0.06 | | |
| | | Median | 0.83 | 0.86 | 0.84 | 0.83 | 0.87 | | |
| | | IQR | 0.82-0.86 | 0.83-0.90 | 0.81-0.89 | 0.78-0.87 | 0.79-0.87 | | |
| AR | MD | Mean | 0.88 | 0.87 | 0.85 | 0.88 | 0.86 | 1.150 | 0.3399 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | SD | 0.02 | 0.02 | 0.01 | 0.02 | 0.03 | | |
| | | Median | 0.86 | 0.89 | 0.85 | 0.88 | 0.87 | | |
| | | IQR | 0.86-0.90 | 0.85-0.90 | 0.87-0.89 | 0.87-0.91 | 0.84-0.89 | | |
| **STG** | (-03mm MD 2/6) | Mean | 0.96 | 0.94 | 0.98 | 0.97 | 0.98 | 4.713 | 0.3180 |
| | | SD | 0.04 | 0.03 | 0.05 | 0.05 | 0.04 | | |
| | | Median | 0.97 | 0.96 | 1.01 | 0.97 | 0.99 | | |
| | | IQR | 0.93-1.00 | 0.94-0.99 | 0.94-1.03 | 0.91-0.98 | 0.96-0.02 | | |
| **Hippocampu** | (-03mm MD 2/6) | Mean | 0.70 | 0.68 | 0.67 | 0.68 | 0.70 | 3.519 | 0.4750 |
| | | SD | 0.03 | 0.03 | 0.04 | 0.04 | 0.03 | | |
| | | Median | 0.71 | 0.69 | 0.66 | 0.69 | 0.70 | | |
| | | IQR | 0.67-0.73 | 0.66-0.71 | 0.64-0.73 | 0.65-0.70 | 0.66-0.74 | | |
| **Parahippo** | (-03mm MD 2/6) | Mean | 0.68 | 0.70 | 0.67 | 0.69 | 0.68 | 2.371 | 0.667 |
| | | SD | 0.02 | 0.02 | 0.02 | 0.02 | 0.03 | | |
| | | Median | 0.71 | 0.72 | 0.72 | 0.70 | 0.69 | | |
| | | IQR | 0.67-0.70 | 0.69-0.71 | 0.68-0.72 | 0.68-0.71 | 0.66-0.71 | | |
| **Amygdala** | (-03mm MD 2/6) | Mean | 0.65 | 0.67 | 0.65 | 0.68 | 0.69 | 1.098 | 0.363 |
| | | SD | 0.02 | 0.02 | 0.02 | 0.01 | 0.02 | | |
| | | Median | 0.66 | 0.67 | 0.68 | 0.69 | 0.70 | | |
| | | IQR | 0.65-0.68 | 0.65-0.70 | 0.66-0.71 | 0.66-0.69 | 0.65-0.69 | | |
| **Genu CC** | (-03mm MD 2/6) | Mean | 0.81 | 0.79 | | 0.80 | | 1.674 | 0.1974 |
| | | SD | 0.03 | 0.04 | | 0.02 | | | |
| | | Median | 0.81 | 0.79 | | 0.80 | | | |
| | | IQR | 0.79-0.83 | 0.76-0.82 | | 0.78-0.82 | | | |
| **S CC** | (-03mm MD 2/6) | Mean | 0.75 | 0.72 | | 0.71 | | 3.858 | 0.1453 |
| | | SD | 0.05 | 0.01 | | 0.03 | | | |
| | | Median | 0.75 | 0.72 | | 0.71 | | | |
| | | IQR | 0.72-0.79 | 0.71-0.72 | | 0.67-0.74 | | | |
| **SLF** | (-03mm MD 2/6) | Mean | 0.77 | 0.74 | 0.76 | 0.75 | 0.76 | 8.701 | 0.0690 * |
| | | SD | 0.01 | 0.01 | 0.01 | 0.02 | 0.02 | | |
| | | Median | 0.73 | 0.76 | 0.74 | 0.75 | 0.76 | | |
| | | IQR | 0.75-0.78 | 0.73-0.76 | 0.73-0.76 | 0.72-0.75 | 0.74-0.79 | | |
| **ILF** | (-03mm MD 2/6) | Mean | 0.67 | 0.69 | 0.70 | 0.69 | 0.66 | 7.044 | 0.1336 |
| | | SD | 0.008 | 0.04 | 0.04 | 0.02 | 0.03 | | |
| | | Median | 0.67 | 0.69 | 0.70 | 0.67 | 0.66 | | |
| | | IQR | 0.67-0.68 | 0.66-0.72 | 0.65-0.75 | 0.68-0.70 | 0.66-0.69 | | |

**LL:** Lateral Lemniscus, **IC:** inferior colliculus, **MGB**: medial geniculate body, **AR** :auditory radiation, **STG** :superior temporal gyrus ,Parahippo:parahippocampus, **CC** :corpus callosum , **SLF** :superior longitudinal fasciculus , **ILF** :inferior longitudinal fasciculus **FA:** Fractional Anisotropy, **K**: Kruskal Wallis Value, **F**: F value, **SD**: Standard Deviation**, IQR**: interquartile range, **p** value considered significant if ≤o.o5.

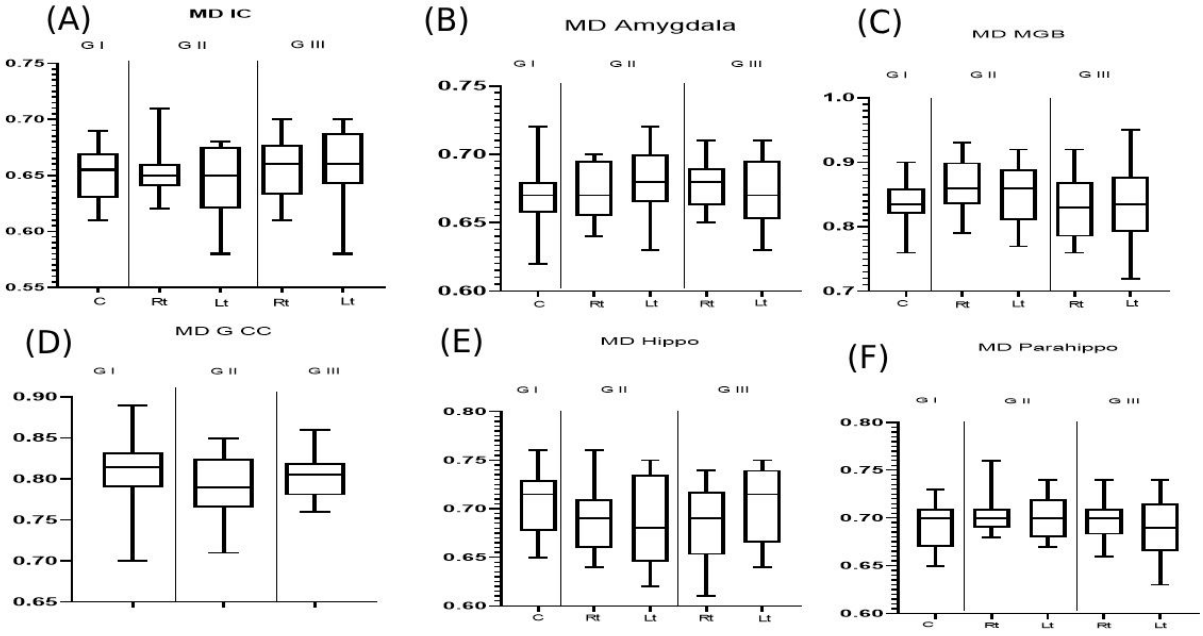


**Fig.4. a)** Mean diffusivity values of inferior colliculus between different subgroup, **b)** Mean diffusivity values of amygdala between different subgroups, **c)** Mean diffusivity values of medial geniculate body between different subgroups, **d)** Mean diffusivity values of genu of carpus callosum between different subgroups, **e)** Mean diffusivity values of hippocampus between different subgroups, **f)** Mean diffusivity values of parahippocampus between different subgroups

***Receiver operating characteristic (ROC) curve***

In the current study, a ROC curve was plotted for the fractional anisotropy in different areas predict bilateral SNHL patients with or without tinnitus as illustrated in (**Table .3**) and **Fig.5 (a-d)**

**Table 3. Features of Receiver operating characteristic (ROC) curves of fractional anisotropy in different tracts of bilateral SNHL patients (with or without tinnitus)**

| FA | | Groups | AUC | p | 95% CI | Cut off | Sens | Spec | PPV | NPV |
|---|---|---|---|---|---|---|---|---|---|---|
| LL | G II | Rt | 0.997 | <0.001* | 0.988 -1.006 | ≤0.51 | 91.67 | 96.67 | 91.7 | 0.997 |
| | | Lt | 0.999 | <0.001* | 0.993 –1.004 | ≤0.51# | 100.0 | 96.67 | 100.0 | 0.999 |
| | G III | Rt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.32# | 100.0 | 100.0 | 100.0 | 1.000 |
| | | Lt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.32# | 100.0 | 100.0 | 100.0 | 1.000 |
| IC | G II | Rt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.5# | 100.0 | 100.0 | 100.0 | 1.000 |
| | | Lt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.49# | 100.0 | 100.0 | 100.0 | 1.000 |
| | G III | Rt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.41# | 100.0 | 100.0 | 100.0 | 1.000 |
| | | Lt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.39# | 100.0 | 100.0 | 100.0 | 1.000 |
| MGB | G II | Rt | 0.981 | <0.001* | 0.939 – 1.022 | ≤0.43# | 91.67 | 100.0 | 100.0 | 0.981 |
| | | Lt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.42# | 100.0 | 100.0 | 100.0 | 1.000 |
| | G III | Rt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.33# | 100.0 | 100.0 | 100.0 | 1.000 |
| | | Lt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.32# | 100.0 | 100.0 | 100.0 | 1.000 |
| AR | G II | Rt | 0.906 | <0.001* | 0.770 – 1.041 | ≤0.38 | 83.33 | 90.0 | 76.9 | 93.1 |
| | | Lt | 0.913 | <0.001* | 0.756 – 1.069 | ≤0.38 | 91.67 | 90.0 | 78.6 | 96.4 |
| | I I | Rt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.35# | 100.0 | 100.0 | 100.0 | 100.0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Lt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.35# | 100.0 | 100.0 | 100.0 | 100.0 |
| STG | G II | Rt | 1.000 | 0.001* | 1.000 – 1.000 | ≤0.29# | 100.0 | 100.0 | 100.0 | 100.0 |
| | | Lt | 0.999 | 0.003* | 0.993 – 1.004 | ≤0.31# | 100.0 | 96.67 | 92.3 | 100.0 |
| | G III | Rt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.3# | 100.0 | 100.0 | 100.0 | 100.0 |
| | | Lt | 1.000 | <0.001* | 1.000 – 1.000 | ≤0.28# | 100.0 | 100.0 | 100.0 | 100.0 |
| Hippo | G III | Rt | 0.914 | <0.001* | 0.828 – 1.000 | ≤0.22# | 76.92 | 83.33 | 66.7 | 89.3 |
| | | Lt | 0.908 | <0.001* | 0.819 – 0.996 | ≤0.20# | 76.92 | 83.33 | 66.7 | 89.3 |
| Am | G III | Rt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.18# | 100.0 | 100.0 | 100.0 | 100.0 |
| | | Lt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.19# | 100.0 | 100.0 | 100.0 | 100.0 |
| SLF | G II | Rt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.66# | 100.0 | 100.0 | 100.0 | 100.0 |
| | | Lt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.65# | 100.0 | 100.0 | 100.0 | 100.0 |
| | G III | Rt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.54# | 100.0 | 100.0 | 100.0 | 100.0 |
| | | Lt | 1.000 | <0.001* | 1.000 –1.000 | ≤0.54# | 100.0 | 100.0 | 100.0 | 100.0 |
| G CC | G II | | 0.756 | 0.010* | 0.583 –0.928 | ≤0.77 | 66.67 | 60.0 | 40.0 | 81.8 |
| | G III | | 0.974 | <0.001* | 0.926 –1.000 | ≤0.75# | 92.31 | 93.33 | 85.7 | 96.6 |
| S CC | G II | | 0.878 | <0.001* | 0.767 –0.989 | ≤0.89 | 91.67 | 63.33 | 50.0 | 95.0 |
| | G III | | 1.000 | <0.001* | 1.000 –1.000 | ≤0.83# | 100.0 | 100.0 | 100.0 | 100.0 |

,**CI**:Confidence,Intervals,**NPV**: Negative predictive value ,**PPV:** Positive predictive value*:Statistically significant at p ≤ 0.05 ,#Cut off was choose according to Youden index, **FA**:fractional anisotropy, **LL**:Lateral leminiscus, **IC**:inferior colliculous, **MGB**:Medial geniculate body, **AR** :auditory radiation ,**STG**:superior temporal gyrus,Hippo:hippocampus, Amy:amygdala, **SLF**:superior longitudinal fasciculus,S **CC**:splenium corpus callosum,G **CC**:genu corpus callosum **.**

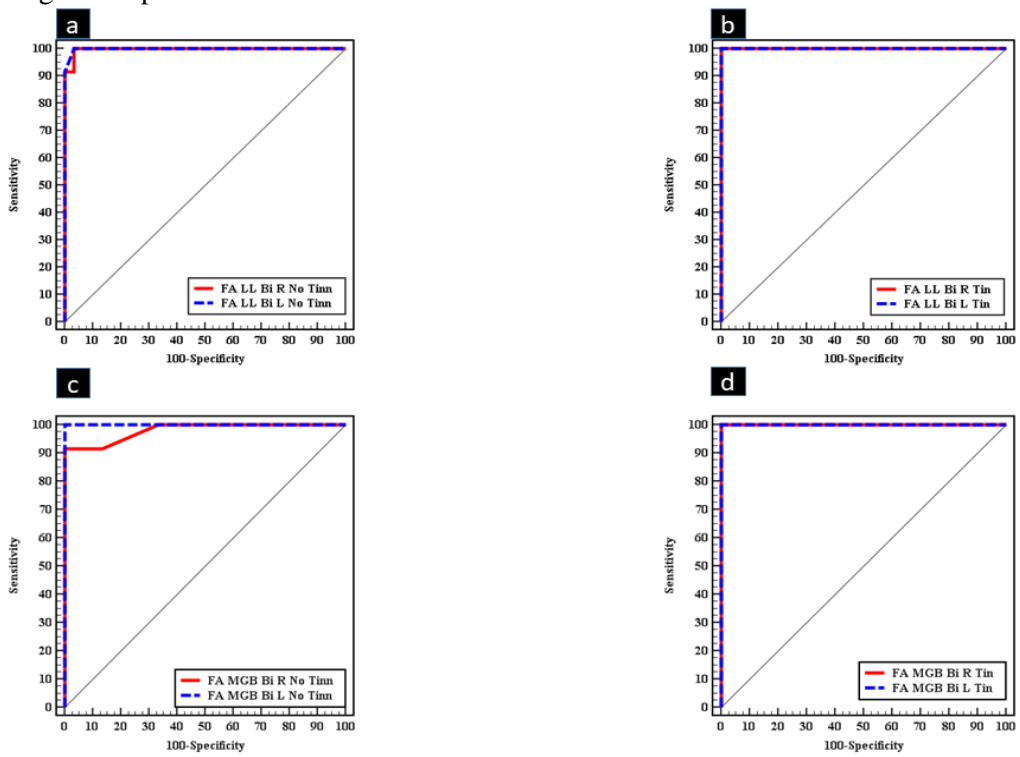


**Fig.5. a)** ROC curve for FA LL to discriminate group II (R and L) (n = 12) from control (n = 30)**, b**) ROC curve for FA LL to discriminate group III (R and L) patients (n = 13) from control (n = 30), **c)** ROC curve for FA MGB to discriminate group II (R and L) (n = 12) from control (n = 30), **d)** ROC curve for FA MGB to discriminate group III (R and L) patients (n = 13) from control (n = 30).

**Cases**

**Case 1:** A 47-year-old female patient presented by bilateral gradual diminution of hearing in both ears (right = left), with progressive course of 5 years' duration, no comorbidities regarding any systemic disease (as DM, previous viral infection, meningitis), psychiatric, previous neurological diseases, no past history of skull base trauma, on examination: otoscopic examination of both ears was normal. Basic Audiological Evaluation; immittancemetry revealed bilateral type A tympanogram (suggesting bilateral normal middle ear pressure) and pure tone audiometry revealed bilateral symmetrical severe SNHL, underwent conventional MRI scan that revealed no gross pathological abnormalities of inner ear , while on advanced MRI imaging (DTI) revealed the following changes (**Fig 6 ( a- f)**).

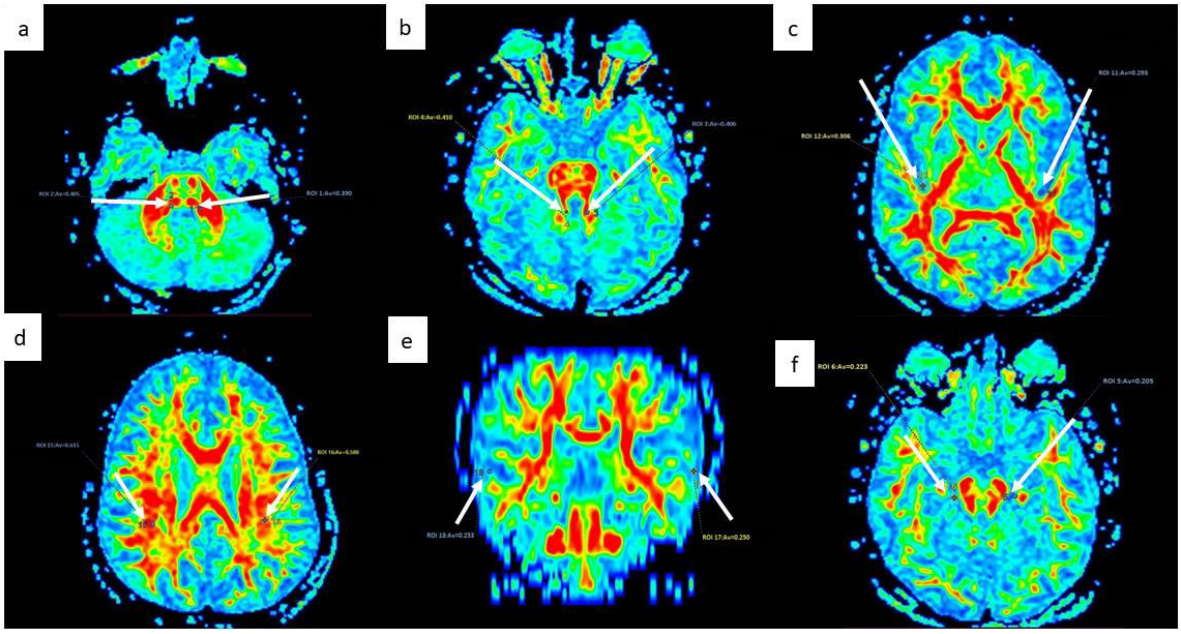


**Fig.6. a)** Axial fractional anisotropy map image at lateral lemniscus showing bilateral decrease FA value, measuring 0.405 at right side and 0.390 at left side,**b)** Axial fractional anisotropy map image at inferior colliculus showing showing bilateral decrease FA value, measuring 0.410 at right side and 0.406 at left side,**c)**Axial fractional anisotropy map image at auditory radiation showing bilateral decrease FA value, measuring 0.306 at right side and 0.293 at left side,**d)**Axial fractional anisotropy map image at superior longitudinal fasciculus showing bilateral decrease FA value, measuring 0.615 at right side and 0.580 at left side,**e)** Coronal fractional anisotropy map image at superior temporal gyrus showing bilateral decrease FA value, measuring 0.253 at right side and 0.250 at left side,**f)** Axial fractional anisotropy map image at hippocampus showing no significant changes regarding FA value, measuring 0.223 at right side and 0.205 at left side.

**Case 2:** A 40-year-old female patient presented by bilateral gradual progressive diminution of hearing (right = left) of 4 years' duration, and bilateral high pitched intermittent tinnitus of 3 years' duration .no comorbidities regarding any systemic disease (as DM, previous viral infection, meningitis), psychiatric, previous neurological diseases, no past history of skull base trauma, on examination: otoscopic examination of both ears was normal. Basic Audiological Evaluation; immittancemetry revealed bilateral type A tympanogram (suggesting bilateral normal middle ear pressure) and pure tone audiometry revealed bilateral symmetrical moderate SNHL, underwent conventional MRI scan that revealed no gross pathological abnormalities of inner ear, while on advanced MRI imaging (DTI) revealed the following changes, **Fig 7(a-g).**

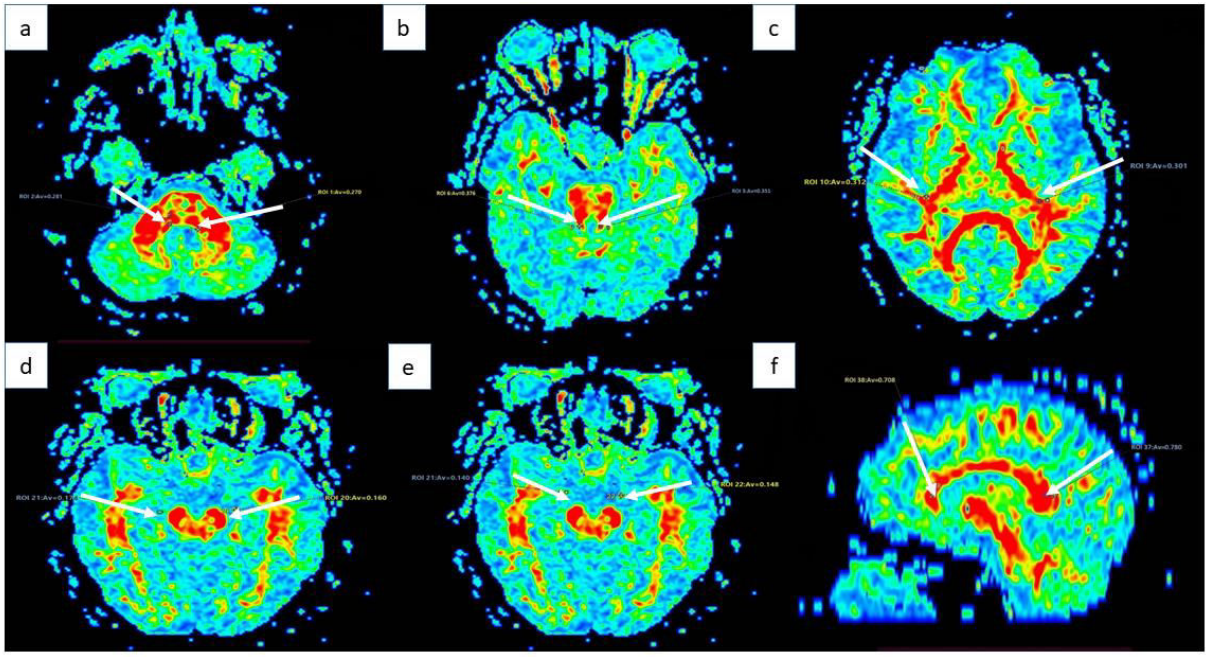


**Fig.7. a)**Axial fractional anisotropy map image at lateral lemniscus showing bilateral decrease FA value, measuring 0.281 at right side and 0.270 at left side, **b)**Axial fractional anisotropy map image at inferior colliculus showing bilateral decrease FA value, measuring 0.376 at right side and 0.351 at left side , **c)**Axial fractional anisotropy map image at auditory radiation showing bilateral decrease FA value, measuring 0.312 at right side and 0.301 at left side,**d)**Axial fractional anisotropy map image at hippocampus showing bilateral decrease FA value, measuring 0.174 at right side and 0.160 at left side **e)**Axial fractional anisotropy map image at amygdala showing bilateral decrease FA value, measuring 0.140 at right side and 0.148 at left side. **f)** Sagittal fractional anisotropy map image at genu and splenium of corpus callosum, showing decrease FA value, measuring 0.708 at genu and 0.780 at splenium.

## Discussion

Various aetiologies may lead to loss of hearing, manifest itself at all ages, and can either be acquired or inherited **(Alford et al.,2014).** CHL, SNHL, and mixed hearing-loss are the three types of loss of hearing **(Baird et al.,2019).** This prospective case control work was performed on 55 subjects were split in to three groups: Control group included 30 healthy volunteers (group I), Bilateral SNHL without tinnitus group included 12 patients (group II) and Bilateral SNHL with tinnitus group included 13 patients (group III), with matched age and sex (P ≥0.05). All patients suffered idiopathic SNHL with no anatomical abnormality of inner ear, no history of any systematic disease, psychiatric, previous neurological diseases, no noise exposure, no ototoxic drugs. This is consistent with **(Mahmoud et al.,2021)** who carried out their studies on patients with idiopathic SNHL hearing loss. While disagreed with our study, **(Wu et al., 2009)** who studied SNHL groups with congenital aetiology of hearing loss.

Patients' ages ranged from 17 to 63 years old, in bilateral group without tinnitus, and 19 to 61 years old in bilateral group with tinnitus, while in volunteers' ages varied from 17 to 63 years old. The sex distribution among the studied groups were (5 males, 7 females) with (8 males and 5 females) in bilateral group without tinnitus, and (17 males, 13 females) in bilateral groups with tinnitus, and with male to female ratio 56% to 43 % in the control group. Twelve areas of interest were chosen for this research, analysed, and divided into 2 categories. The lateral lemniscus, medial geniculate body, inferior colliculus, auditory radiation, and superior temporal gyrus are among those initially recognised to be

linked to the processing of auditory information. The second set of regions includes non-auditory regions such the hippocampus, amygdala, para-hippocampus, genu and splenium of the corpus callosum, inferior longitudinal fasciculus, and superior longitudinal fasciculus, which are often sampled in DTI investigations of the brain.

The superior temporal-gyrus and the auditory radiating were the areas that were most often imaged **(Profant et al., 2014)** whereas the inferior colliculus and lateral lemniscus were less often studied **(Trabichi et al.,2018).**

**(Wu et al., 2009)** restricted their DTI measures to the lateral lemniscus and inferior colliculus, **(Mahmoud et al.,2021)** concentrated on DTI measures in the lateral lemniscus, inferior colliculus and superior olivary nucleus. Trapezoid body, superior olivary nucleus, medial geniculate body, inferior-colliculus, auditory radiating, and white matter of Heschel's gyrus were the main subjects of (**Hunag et al.,2015)** In their investigation, **(Wu et al.,2014)** concentrated on STG and auditory radiating. The auditory cortex, lateral-lemniscus, inferior-colliculus, medial geniculate body, amygdala, thalamic reticular nucleus, hippocampus, para-hippocampus, and prefrontal cortex were the subjects of **(Gunbey et al.,2021)** study.

The findings of the current study revealed that bilateral hearing loss without tinnitus had statistically significant lower FA comparing to the control group in the following regions: lateral-lemniscus, medial geniculate body, inferior-colliculus, auditory radiating, superior temporal gyrus, superior longitudinal fasciculus, genu and splenium of corpus callosum. In the bilateral group with tinnitus the forementioned regions were affected besides hippocampus and amygdala. This is in agreement with (**Mahmoud et al., 2021)** who found significant reduction of FA bilaterally in patients with SNHL compared to healthy control at region of lateral lemniscus and inferior colliculus. **(Hussein et al.,2011)** studied three distinct groups: One is a mild to moderate loss of hearing along with tinnitus, and two is a mild to moderate loss of hearing alone. 3) hearing normal accompanied with tinnitus, the authors found reduction of FA in superior longitudinal fasciculus in group 1 and 2 compared to control group.

A systematic review and meta-analysis done by **Trabichi et al (2018)** reported that previous studies found decrease FA in inferior colliculus, medial geniculate body, auditory radiation, superior longitudinal fasciculus, genu of corpus callosum, superior temporal gyrus **( Miao et al.,2013)** reported that decrease of FA in the superior temporal gyrus and splenium of the corpus callosum. also **(Huang et al., 2015)** stated that FA decreased inferior colliculus, medial geniculate body and auditory radiation, Moreover **(Wu et al., 2014)** found that reduction of FA bilaterally in patients with SNHL compared to healthy control along auditory radiation and superior temporal gyrus however, the latter three researches performed their study on congenital hearing loss. Most recently **(Gunbey et al., 2017)** reported decrease in FA values in lateral lemniscus, inferior colliculus, amygdala, medial geniculate body, hippocampus in the bilateral loss of hearing with tinnitus contrasted to control normal hearing.

In line with our findings, **(Husain et al.,2011)** revealed significant decrease of FA in patients with bilateral loss of hearing combined with tinnitus at the level of superior longitudinal fasciculus compared to control group.

Furthermore, subgroup analysis revealed that the group of bilateral hearing loss with tinnitus had statistically significant lower FA values compared with those without tinnitus at the following regions: lateral lemniscus, medial geniculate body, inferior colliculus, hippocampus, amygdala, genu and splenium of corpus callosum, superior longitudinal fasciculus.

Disagreed with the current findings, **(Husain et al.,2011)** reported that individuals without tinnitus had greater decrease in FA compared to those with tinnitus at auditory radiation, inferior longitudinal fasciculus and superior longitudinal fasciculus.

Concerning the mean diffusivity; no significant statistically variation was existed among the different groups at different regions of interest, this is in line with **(Mahmoud et al., 2021),** who stated that no difference between bilateral hearing loss groups and control at lateral lemniscus and inferior colliculus. Also **(Huang et al.,2015)** reported that MD remained unchanged at inferior colliculus, medial geniculate body and auditory radiation between patient and control group, However, this study carried out their work on congenital hearing loss.

Regarding this heterogeneity of the results in MD may be influenced by factors that have not been taken into consideration, including loss of hearing (cause, degree and duration), age, or emotional disturbance **(Khan et al., 2021).** In the current research, the finding of MD remained unchanged, denoting the absence of axonal injury or inflammation and good integrity of axonal fibbers tracts **(Huang et al.,2015)**

To predict SNHL patients (with or without tinnitus) in this study, receiver operating characteristic curve was plotted for all the measured fractional anisotropy in different areas.

The best results obtained at lateral lemniscus, inferior colliculus, medial geniculate body and superior temporal gyrus in auditory areas while at amygdala and superior longitudinal fasciculus in non-auditory areas.

The best results obtained at lateral lemniscus with area under the curve (AUC) of FA was 0.997 and 91.76 sensitivity in group II and 1000 and 100% sensitivity in group III, (AUC) of FA, with a cutoff point ≤ 0.51, ≤ 0.32 respectively in both groups, while the best results obtained at inferior colliculus with area under the curve (AUC) of FA was 1000 and 100% sensitivity in both groups (II, III) with a cutoff point ≤ 0.50 at group II, ≤ 0.41in group III.

The best results obtained at medial geniculate body with area under the curve (AUC) of FA was 0.981 and 91.67 % sensitivity in group II and 1000 and 100% sensitivity in group III, with a cutoff point ≤ 0.43 at group II, ≤ 0.33 in group III, also the best results obtained at superior temporal gyrus with area under the curve (AUC) of FA was 1000 and 100% sensitivity in both groups (II, III), with a cutoff point ≤ 0.31 in group II, ≤ 0.28 in group III.

The best results obtained at amygdala with area under the curve (AUC) of FA was 1000 and 100% sensitivity in group III, with a cutoff point ≤ 0.19, also the best results obtained at superior longitudinal fasciculus with area under the curve (AUC) of FA was 1000 and 100% sensitivity in both groups (II, III), with a cutoff point ≤ 0.65 at group II, ≤ 0.54 in group III.

**Mahmoud et al (2021)** reported that The area under curve (AUC) of FA at the inferior colliculus yielded the best outcome, which was 0.987; a cut-off point of 0.763 was chosen to distinguish across the groups of patients and the control group, revealed a sensitivity of 95.0% **(Mahmoud et al.,2014).**

The sample size for the current study was relatively small with few patients in each subgroup. It was impossible to obtain the entire auditory nerve from the cochlear nerve to the cerebral cortex, a high-resolution focussed DTI approach, with 1.2 mm slice thickness, was employed for imaging the auditory nerve. This technique limited the number of brain slices and their area of coverage.

## Conclusion

DTI, is a novel non-invasive MRI tool for evaluation of micro-structural integrity of the auditory pathway SNHL patients with or without tinnitus especially fractional anisotropy. SNHL associated with white matter microstructure involvement as proved with the current Study, presence of tinnitus is associated with involvement of limbic system.

**Abbreviations: CT:** Computed tomography**. MRI**: Magnetic resonance imaging. **SNHL**: sensorineural hearing loss.**CHL**: conductive hearing loss. **FIESTA:** Fast imaging using steady state acquisition. **FLAIR:** Fluid-attenuated inversion recovery. **T1WI**: T1-weighted image. **T2WI**: T2-weighted image. **ANOVA**: analysis of variance. **SD:** Standard deviation. **DTI**: Diffusion tensor imaging. **A**: Fractional anisotropy. **MD:** Mean diffusivity, **LL:** lateral **lemniscus, IC:** inferior colliculus, **MGB: medial** geniculate body**, AR:** auditory radiation**, STG:** superior temporal gyrus**, CC:** corpus callosum, **SLF:** superior longitudinal fasciculus**, ILF: inferior** longitudinal fasciculus**.**

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