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MINISTRY OF HUMAN RESOURCES

NIOSH

The Preliminary Study of Elucidating Structural Integrity of Microstructural White Matter Tract of Auditory Cortex in Noise-Induced Hearing Loss: An MRI-based Diffusion Tensor Imaging Study

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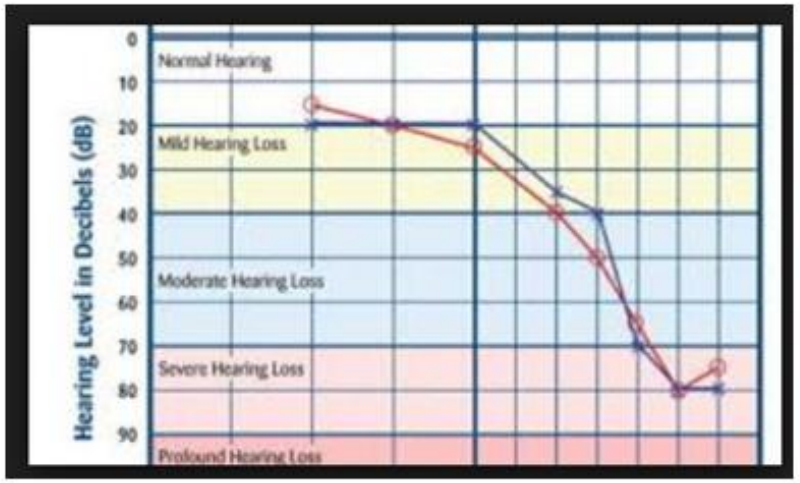
Research Background

Noise-induced hearing loss (NIHL) is considered the **most common occupational disease** ranked in Malaysia

Although counter measures have successfully reduced noise levels in many industries, **noise is still a major occupational hazard**.

How Do We Measure Hearing Impairment?

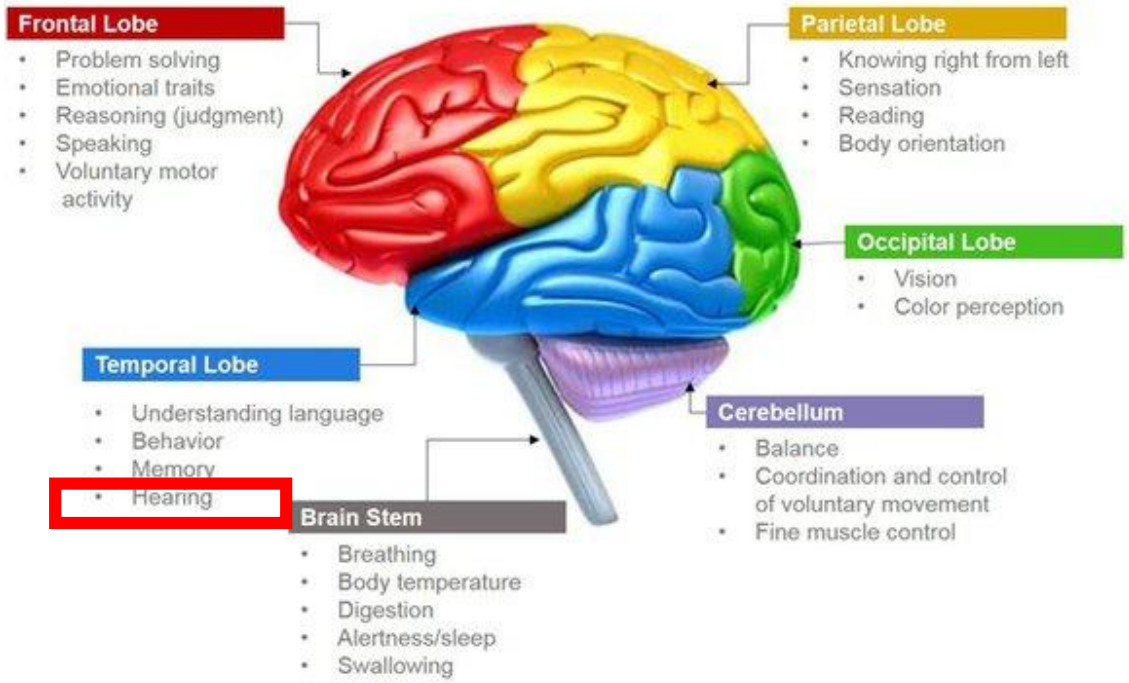
Pure Tone Audiometry (PTA) currently has been used as a method to assess hearing condition of workers

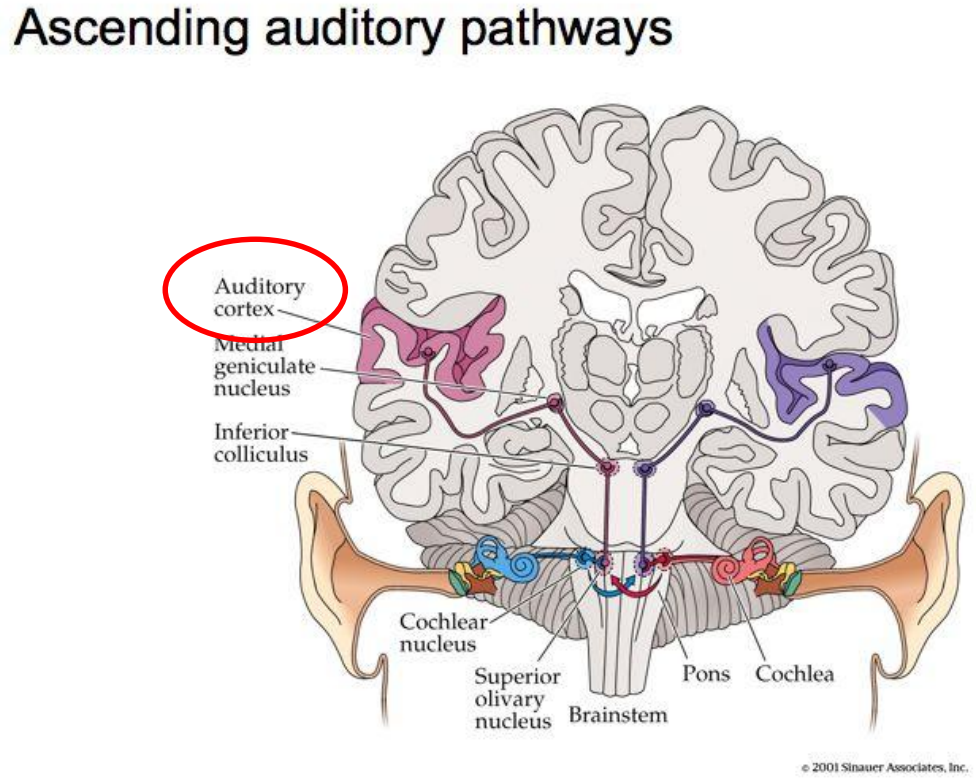


However, many factors can affect results, including **ambient noise, environmental distractions, tester competence, and subjective to patients' hearing perception.**

Therefore, **new biomarkers are needed to support** early and accurate diagnosis, prognosis of NIHL for early intervention and treatment

How Do We Perceive Sound ?





How Do We Measure Brain Changes ?

DTI (Diffusion Tensor Imaging) gives information of water diffusion in tissues - to **assess the microstructure of white matter** (as diffusion water is restricted or anisotropic in white matter) – thus can provide a **quantitative measurement** of degree of restricted water diffusion which called as **fractional anisotropy (FA)** (Moura et al., 2019)

A newly advanced magnetic resonance imaging (MRI) – based analysis technique such as **Diffusion Tensor Imaging (DTI)** has been used for the evaluation of sensorineural hearing loss such as congenital sensori-neural hearing loss (Mahmoud, Elshawaf et al. 2021)

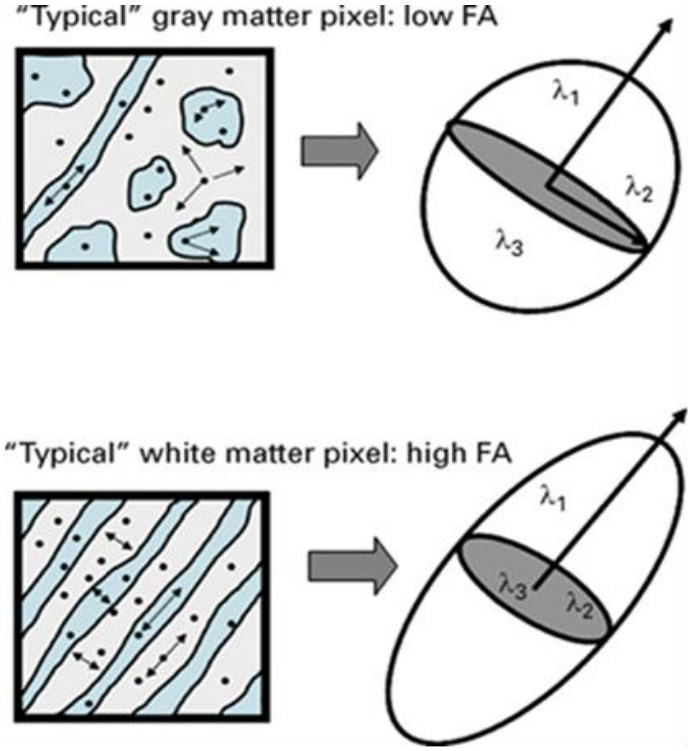
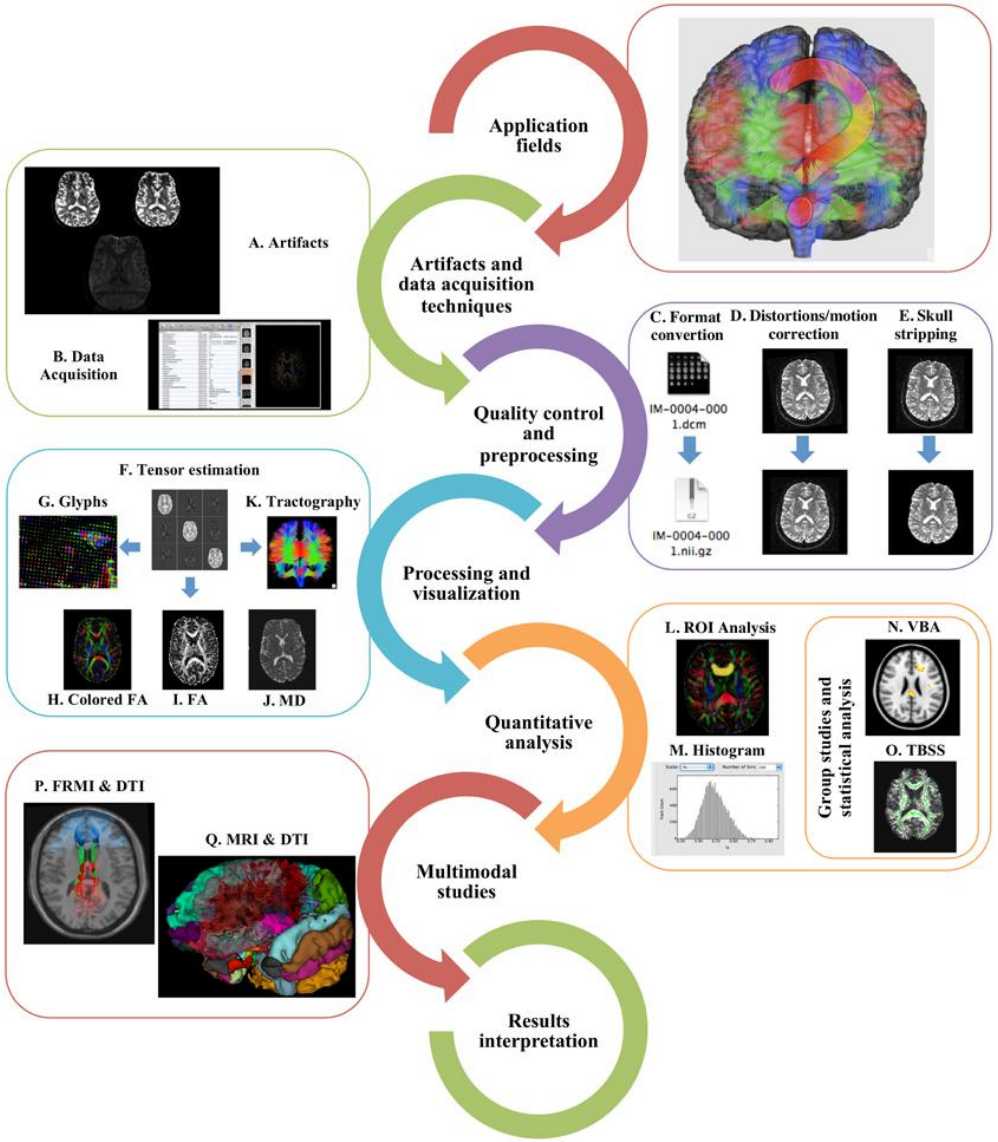


Image retrieved from Kim, D. (2009). Diffusion tensor imaging in developmental clinical neuroscience. In J. Rumsey & M. Ernst (Eds.), Neuroimaging in Developmental Clinical Neuroscience (pp. 314-325). Cambridge: Cambridge University Press. doi:10.1017/CBO9780511757402.025

Moura, L. M., Luccas, R., Paiva, J. P. Q. d., Amaro, E., Leemans, A., Leite, C. d. C., . . . Conforto, A. B. (2019). Diffusion Tensor Imaging Biomarkers to Predict Motor Outcomes in Stroke: A Narrative Review. Front Neurol, 10, 445.
Mahmoud, W., et al. (2021). "The role of diffusion tensor imaging in idiopathic sensorineural hearing loss: is it significant?" Pol J Radiol **86**: e474-e480.

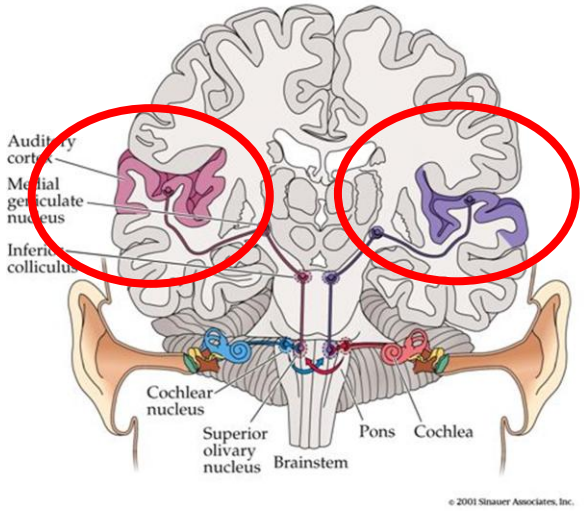
MR-DTI Acquisition Workflow

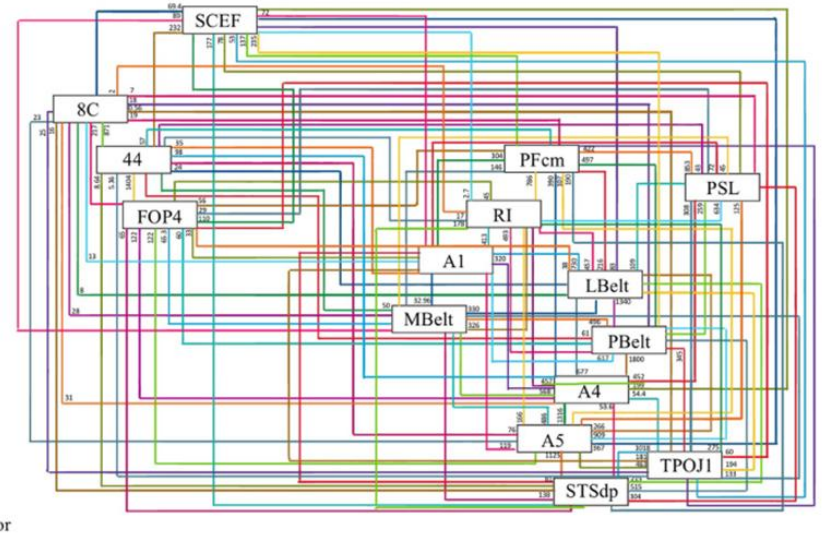


Soares JM, Marques P, Alves V, Sousa N. A hitchhiker's guide to diffusion tensor imaging. Front Neurosci. 2013 Mar 12;7:31. doi: 10.3389/fnins.2013.00031. PMID: 23486659; PMCID: PMC3594764.

Aim of Study

Ascending auditory pathways

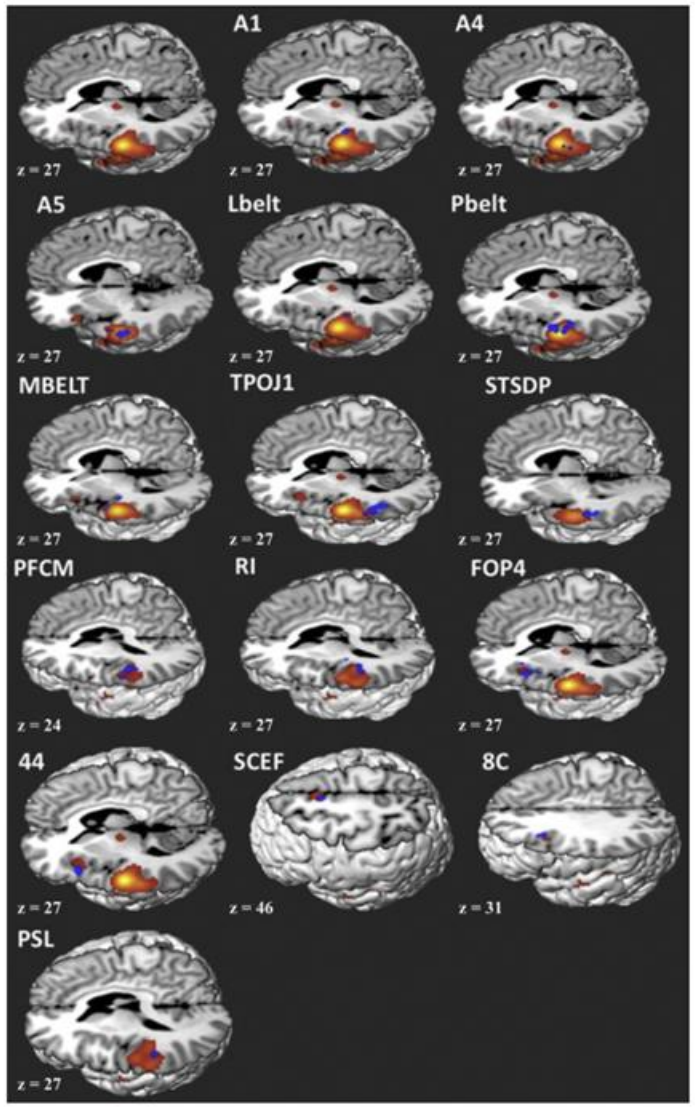




- DTI suggests that hearing loss may be **associated with uniform micro-sensitive changes in central auditory tract of white matter brain orientation**. The microstructural brain changes thus can provide **information in detection of sensorineural hearing loss.**
- Nevertheless, no studies have been conducted to **assess the microstructural brain changes in auditory cortex and its correlations to NIHL among workers.**

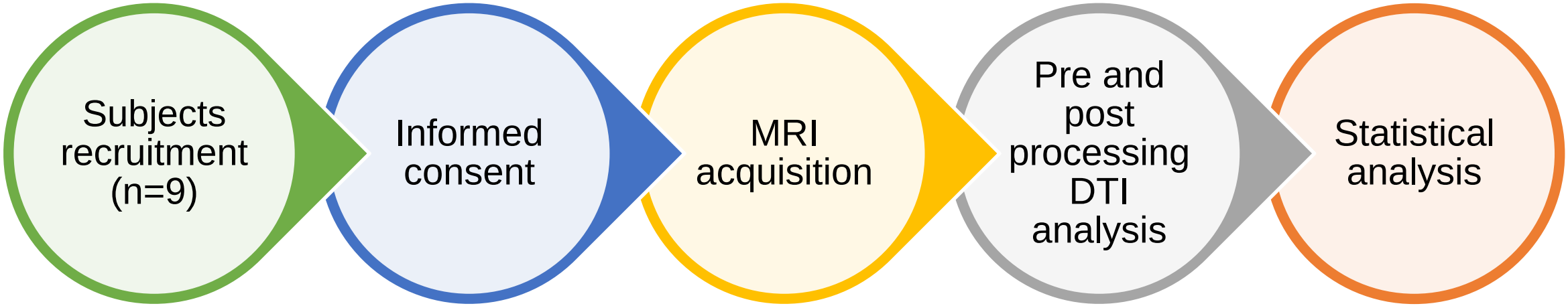
Cortical of the auditory network included area **A1, A4, A5, LBelt, MBelt, PBelt**, and **RI** of the superior temporal gyrus and adjacent insula; **PFcm, PSL, STSdp,** and **TPOJ1** of the posterior temporal lobe; regions **44** and **FOP4** of the inferior frontal gyrus; and regions **8C** and **SCEF** of the middle frontal gyrus

Mahmoud, W., et al. (2021). "The role of diffusion tensor imaging in idiopathic sensorineural hearing loss: is it significant?" Pol J Radiol **86**: e474-e480.



Cortical parcellation assessed for inclusion in the auditory network included area **A1, A4, A5, LBelt, MBelt, PBelt, and RI** of the superior temporal gyrus and adjacent insula; **PFcm, PSL, STSdp, and TPOJ1** of the posterior temporal lobe; regions **44 and FOP4** of the inferior frontal gyrus; and **regions 8C and SCEF** of the middle frontal gyrus

Methodology



Subjects Recruitment

Comprised of 9 bilateral NIHL gender-matched male patients

Approved by the Research Ethics Committee of International Islamic University Malaysia (IIUM), and informed consent was obtained from each of the patients prior to the examination

Had normal anatomy of peripheral and central auditory circuits in conventional MRI study

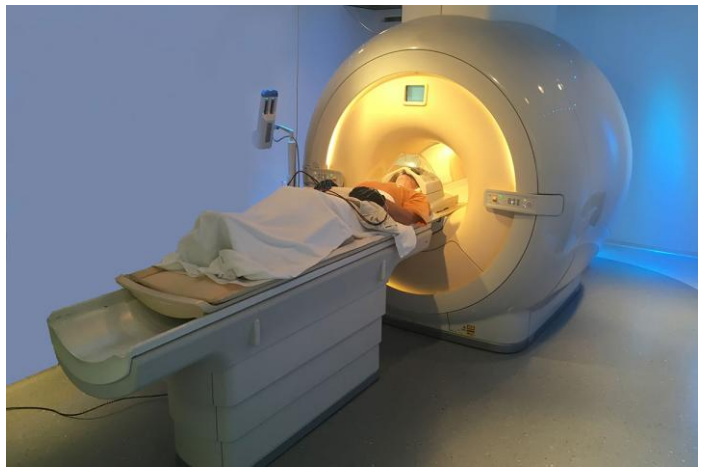
Had no history of brain surgery, trauma, infection, or ototoxic medication intake

All patients were submitted to full audiological history and otoscopic examination and pure tone average data of each patient was obtained

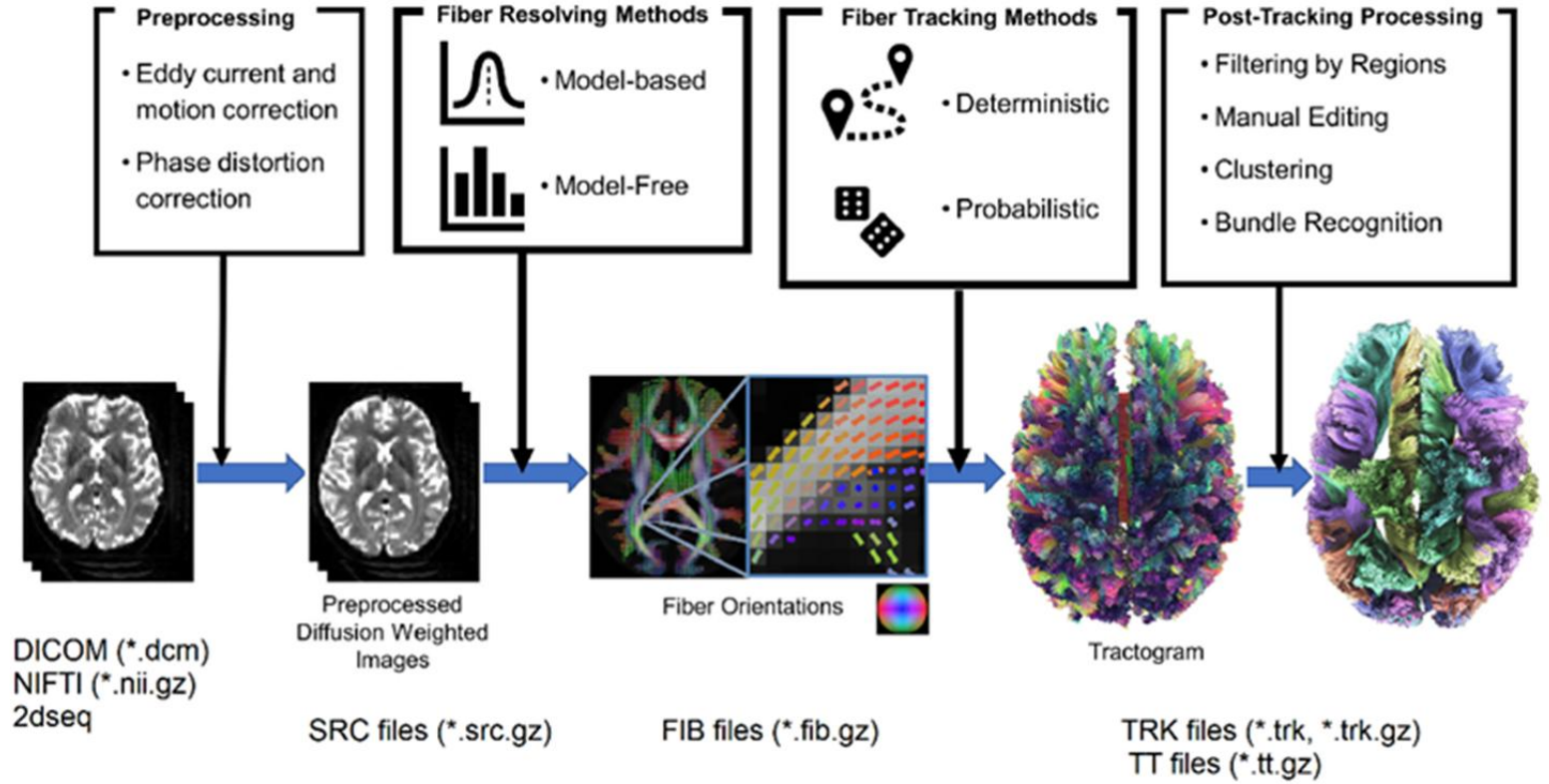
Hearing loss ranged from mild to severe (from 30 to 90 db).

MR-DTI Acquisition

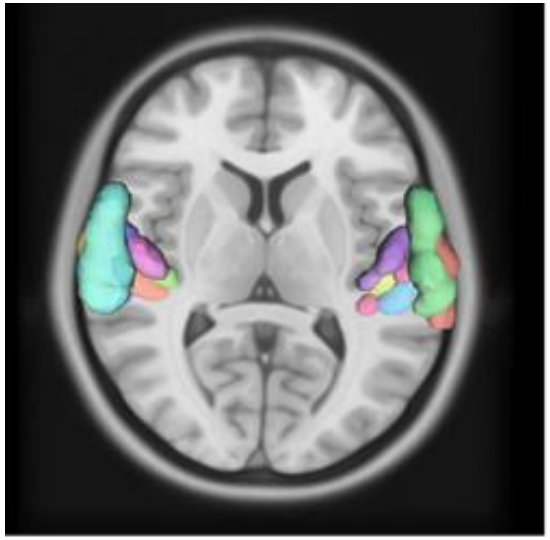
Brain MRI scan



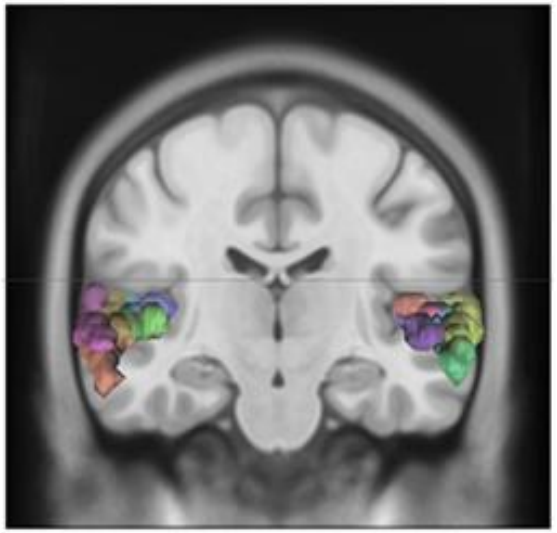
DTI Analysis



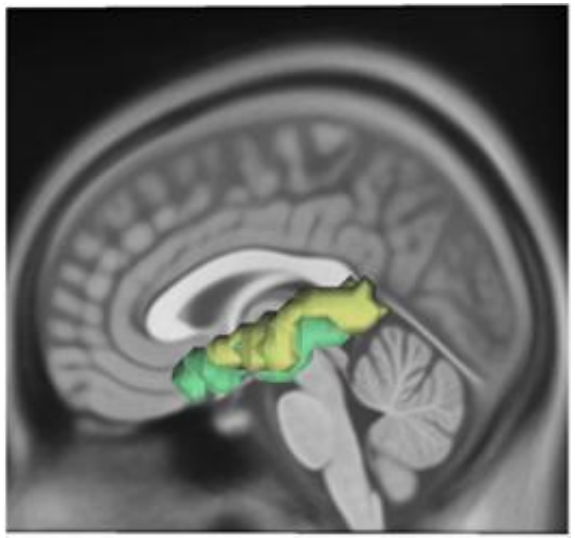
Data acquisition from ROIs



A



B



C

We have localised ROI for several regions in the cortical parcellation of the auditory network; left and right **A1, A4, A5, LBelt, MBelt, PBelt**. Data was extracted as fractional anisotropy (FA) parameter from each region.

Results and Discussion

Table 1 Mean And Standard Deviation Of Age Of Partcipants, Right And Left Pure Tone Average Dataa And FA Values Measured In Six Regions; A1, A4, A5, LBelt, MBelt, And PBelt

Variables	Mean ± SD values (n=9)
Age	45 ± 6.1
Right pure tone average (dB)	38.5 ± 13.5
Left pure tone average (dB)	41.5 ± 13.3
MR-DTI FA values measured in different regions of auditory cortex	
Right side	
A1	0.174 ± 0.022
A4	0.096 ± 0.015
A5	0.106 ± 0.015
LBelt	0.180 ± 0.033
MBelt	0.211 ± 0.027
PBelt	0.179 ± 0.031
Left side	
A1	0.171 ± 0.031
A4	0.091 ± 0.017
A5	0.103 ± 0.008
LBelt	0.192 ± 0.029
MBelt	0.218 ± 0.023
PBelt	0.166 ± 0.023

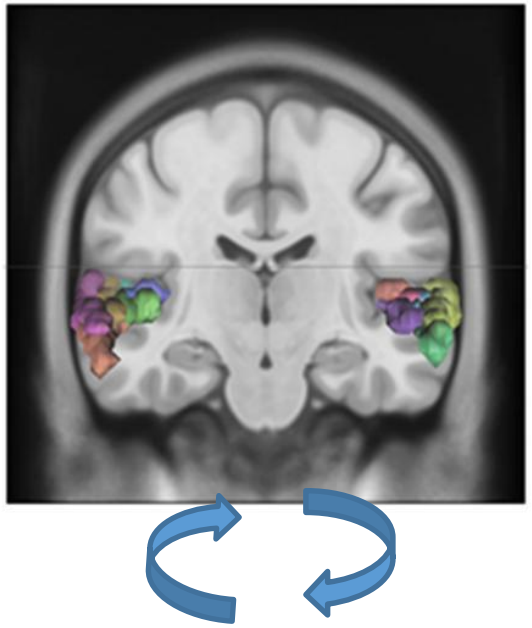
Pure Tone Average = (0.5 Khz + 1 Khz + 2 Khz + 4khz)/4.

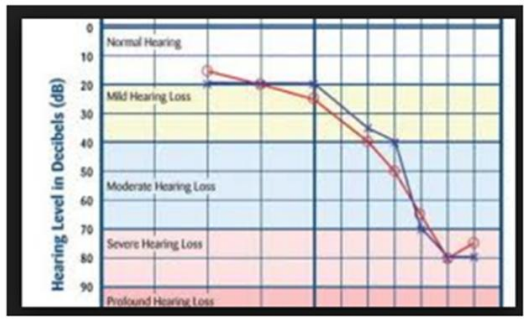
Table 2 Correlation Analysis Between Mean Fractional Anisotropy (FA) and Severity of Sensorineural Hearing Impairment (Pure Tone Average)

Regions in auditory cortex	Right pure tone average		Left pure tone average	
	p-value	r-value	p-value	r-value
Right side (FA value)				
A1	0.796	0.101	0.932	0.033
A4	0.456	0.286	0.244	0.433
A5	0.983	0.008	0.865	0.067
LBelt	0.682	-0.160	0.732	-0.133
MBelt	0.332	-0.367	0.557	-0.227
PBelt	0.406	-0.317	0.260	-0.420
Left side (FA value)				
A1	**0.009****	**-0.807**	**0.030***	**-0.717**
A4	0.364	-0.345	0.286	-0.400
A5	0.079	-0.613	0.088	-0.600
LBelt	0.949	0.025	0.688	0.167
MBelt	0.415	0.311	0.356	0.350
PBelt	0.250	-0.429	0.308	-0.383

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

Relationship Between Mean FA Value of Left A1 Region With The Left and Right Pure Tone Average Data





Hearing loss with **dominant affection on the contralateral side may impact both ipsilateral and contralateral auditory neural pathways** due to the early and numerous decussations of the auditory nerve system beginning at the level of the cochlear nucleus (CN) (Tae, Yakunina, Kim, Kim, & Nam, 2014).

These asymmetries in humans is either **hard to identify or extremely difficult to deal with because of the widespread corticofugal effects on the auditory system**.

Adult males typically have somewhat better audiometric hearing thresholds in the right ear than the left, but females are known to have more symmetric hearing sensitivity. Better hearing in the right ear of adults may be related to another asymmetry, the fact that **the left ear is more susceptible to noise-induced hearing loss** (Pirilä, Jounio-Ervasti, & Sorri, 1992)

Tae, W. S., Yakunina, N., Kim, T. S., Kim, S. S., & Nam, E. C. (2014). Activation of auditory white matter tracts as revealed by functional magnetic resonance imaging. Neuroradiology, 56(7), 597-605. doi:10.1007/s00234-014-1362-y

Pirilä, T., Jounio-Ervasti, K., & Sorri, M. (1992). Left-right asymmetries in hearing threshold levels in three age groups of a random population. Audiology, 31(3), 150-161. doi:10.3109/00206099209072910

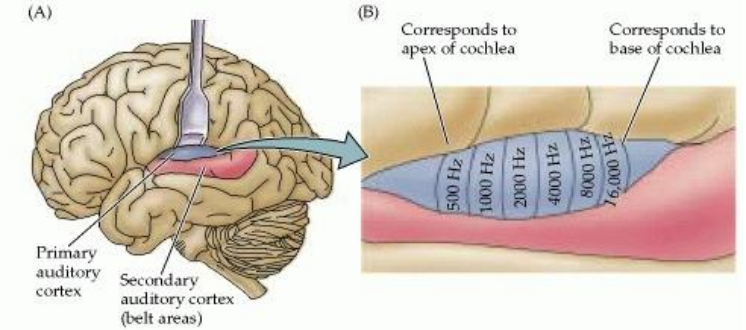
Association Between A1 Region With Pure Tone Average Data

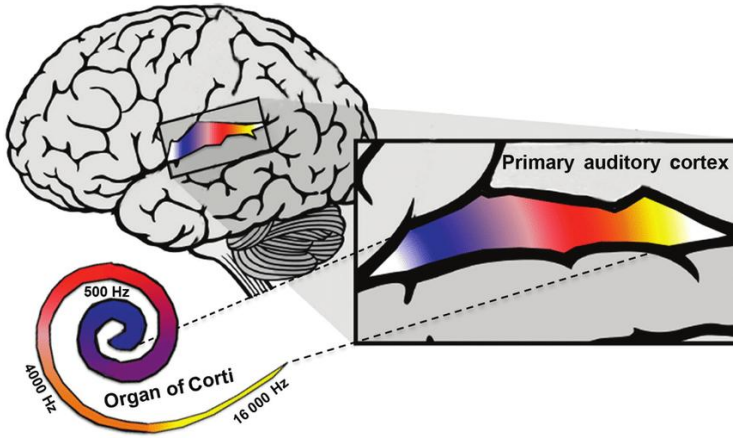
The primary auditory cortex (A1), which is situated on the superior temporal gyrus in the temporal lobe has an **accurate tonotopic map that spans a large range of sound frequencies; similar to topographical map of the cochlea** (Alloway, 2001).

In NIHL, the **cochlea has already decomposed the acoustical stimulus so that it is arrayed tonotopically along the length of the basilar membrane**.

A1 and the majority of the ascending auditory structures between **the cochlea and the cortex are thought to include a tonotopic map, which explains their close association with pure tone average values** that are computed from various sound frequency ranges.

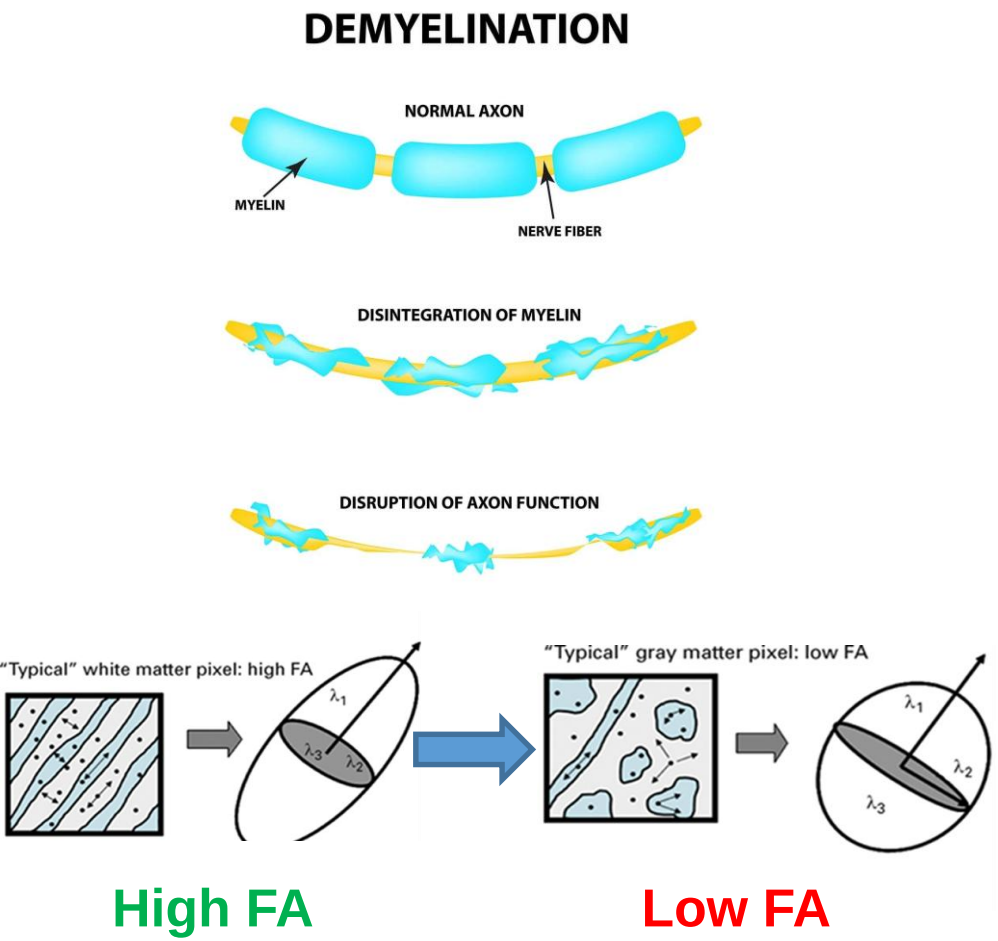
Since belt sections of the medial geniculate complex get more diffuse input, the auditory cortex's belt areas are less accurate in their tonotopic organisation (Brewer & Barton, 2016)





Alloway, K. (2001). Neuroscience Dale Purves George J. Augustine David Fitzpatrick Lawrence C. Katz Anthony-Samuel LaMantia James O. McNamara S. Mark Williams. Quarterly Review of Biology - QUART REV BIOL, 76. doi:10.1086/420640
Brewer, A. A., & Barton, B. (2016). Maps of the Auditory Cortex. Annu Rev Neurosci, 39, 385-407. doi:10.1146/annurev-neuro-070815-014045

Reduction In Mean FA Value With Hearing Loss



Auditory deprivation resulted in inadequate myelination. Hearing loss can produce cortical and subcortical microstructural alterations in numerous auditory neurological systems (Kim et al., 2018)

Due to decreased functional activity in the auditory pathway, there may be a demyelinating process present. This could be **caused by increased water diffusivity across neural fibre tracts.**

The **FA may be regarded as a useful biological indicator of the degree of hearing impairment due to earlier findings that showed an apparently linear association between decreased FA values and audiometrically demonstrated hearing loss** (Kim et al., 2018).

Kim, S. Y., Heo, H., Kim, D. H., Kim, H. J., & Oh, S. H. (2018). Neural Plastic Changes in the Subcortical Auditory Neural Pathway after Single-Sided Deafness in Adult Mice: A MEMRI Study. Biomed Res Int, 2018, 8624745. doi:10.1155/2018/8624745

Limitations of The Study

- Small population in the NIHL group
- Only 6 regions in the auditory network were investigated in this study
- The ages of subjects were not restricted and thus results may have included age-related brain degeneration
- Did not measure long-term effects of NIHL on the brain; longitudinal studies
- Absence of reproducibility of FA correlations with repeated pure tone average data in longitudinal study

Conclusion

We conclude that a decline in **FA values can be used to reflecting microstructural abnormalities of the central auditory tract in patients with NIHL** and well correlated with degree of hearing impairment in auditory cortex.

The primary auditory cortex (A1), which is situated on the superior temporal gyrus in the temporal lobe has an accurate tonotopic map that spans a large range of sound frequencies; similar to topographical map of the cochlea

We propose that using the **current state of the art technology of MR-DTI, the information about central auditory pathway integrity should be included as potential novel neurological biomarker** in earlier detection, diagnosis, and assessing the severity progress of a NIHL in future.

Acknowledgement

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THANK YOU

Q&A