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THE AUDITORY RADIATION IN TRAUMATIC BRAIN DAMAGE: DIFFUSION TENSOR IMAGING STUDY

by
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A thesis submitted to the faculty of the University of Mississippi in partial fulfillment of the requirements of the Sally McDonnell Barksdale Honors College

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ABSTRACT

Hearing loss is a known symptom among people who suffer from traumatic brain injuries. Studies have shown that sensorineural hearing loss is the most common type of hearing loss resulting from traumatic brain injury. However, it is not well understood whether the auditory pathway is affected by traumatic brain injury. In this study, we examined the auditory radiation, using diffusion tensor imaging data and probabilistic tractography. Fifty-three veterans with traumatic brain injury and forty-four veterans without traumatic brain injury are compared. There was no significant difference in fractional anisotropy of the auditory radiation between those with and without traumatic brain injury. It is suggested that the auditory radiation is not impacted by traumatic brain injury, while sensorineural hearing loss is commonly found in individuals with traumatic brain injury.

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List of Abbreviations

ANCOVA	One-way Analysis of Covariance
ASHA	American Speech Hearing Association
DoD	Department of Defense
DTI	Diffusion Tensor Imaging
FA	Fractional Anisotrophy
FSL	Functional Magnetic Resonance Imaging of the Brain Software Library
GCS	Glasgow Coma Scale
mTBI	Mild Traumatic Brain Injury
PTSD	Post Traumatic Stress Disorder
TBI	Traumatic Brain Injury

Introduction

Worldwide, approximately 10 million people sustain a Traumatic Brain Injury (TBI) (Humphreys et al., 2013). This means that 10 million people live with injuries to their brains. Compared to other traumatic injuries, TBI results in more deaths or disabilities (Werner & Engelhard 2007). A TBI involves brain dysfunctions as a result of a blow to the head. Blows to the head can happen in multiple ways. The most common causes include falls, vehicle accidents, struck by objects, or assaults (Faul et al., 2010).

Brain dysfunction resulting from TBI can lead to short-term and long-term cognition, motor, physiology, and psychology issues (Blennow et al., 2012). Those left with long-term or permanent deficits often experience a decrease in quality of life. Patients with TBI can experience a wide range of symptoms. Common symptoms include cluster headaches, dizziness, weakness, sensitivity to light and sound, nausea, and vomiting. Patients with TBI can experience cognitive symptoms, which include difficulties with attention, memory, and language (Marshall et al., 2012). Cognitive symptoms are nonuniform, whereby mild to severe cognitive symptoms are observed.

Symptoms of TBI associated with hearing loss include tinnitus, dizziness, and vertigo. Tinnitus is ringing or noise in the ears. Those with ear injury, circulatory system disorders, or presbycusis, age-related hearing loss, can experience tinnitus. 80% of people with tinnitus have a measurable hearing loss (Elgoyhen et al., 2015). Damage to the hair cells in the inner ear can cause both tinnitus and sensorineural hearing loss. These hair

cells are the most vulnerable part of the cochlea. Royce et al. (2019) reported that subjects of TBI have a tinnitus prevalence rate of 75.7%. Dizziness and vertigo are also common symptoms. According to the same study, up to 60% of people with TBI experience dizziness. The vestibular system shares fluid with the cochlea. It is not uncommon for those to have vestibular issues and sensorineural hearing loss. Swan et al. (2018) observed that veterans with blunt or bullet trauma on their comprehensive TBI evaluation were likely to have auditory or vestibular problems. Tinnitus and TBI are relevant in researching how TBI affects hearing.

TBI symptoms are commonly studied to better improve diagnostic procedures. Among conditions resulting from TBI, hearing loss is less investigated. Research on hearing loss and TBI have important implications and consequently lead physicians and audiologist to be prompt and precise with diagnoses. Shangkuan et al. (2017) found in a 10-year follow up that 1,334 out of 553,286 patients with brain injury developed hearing loss. Additionally, sensorineural hearing loss was higher. Multivariate analyses found that TBI increases the risk of hearing loss for an overall rate of 146.63 cases per 100,000 person-years. Sensorineural hearing loss results from improper function of the inner ear, auditory nerve, or the auditory cortex. Lew et al. (2007) and Bojana et al. (2019) both proposed that most post-TBI related auditory problems are sensorineural.

Patients are commonly diagnosed with TBI through assessments such as the Glasgow Coma Scale (GCS), measurement levels of TBI, speech and language tests, cognition and neuropsychological tests, an imaging. The GCS assesses eye-opening response, verbal response, and motor response (Teasdale & Jennett, 1974). Measurement

of the TBI level labels patients' TBI either mild, moderate, or severe. Speech-language pathologists assess speech, language, and oral motor function (American Speech-Language-Hearing Association [ASHA], n.d.). Neuropsychological tests assess patients' cognitive, language, behavioral, and motor functions (Brain Injury Association of America, n.d.). Neuroimaging exams uses brain images to reveal possible bruising of brain tissue, swelling in the brain, bleeding in the brain, and other brain damage (Brain Injury Association of America, n.d.).

Diffusion Tensor Imaging (DTI), a magnetic resonance imaging (MRI) modalities, examines the white matter in the brain. Fractional Anisotropy (FA) obtained from DTI assess the integrity of the white matter (Basser & Pierpaoli, 2011). Poorer white matter integrity in those further removed from their brain injury is linked to reduced cerebral blood flow (Clark et al., 2017). A study comparing DTI images of veterans who had mild TBI (mTBI) to veterans with no TBI, found that the veterans with the mTBI had a significantly decreased FA (Jorge et al., 2012).

Examining the auditory radiation through DTI is possible. The medial geniculate nucleus of the thalamus and the primary cortex in the transverse temporal gyrus are connected through the auditory radiation. The sublenticular part of the internal capsule serves as the last connection in the auditory pathway way. This final connection is crucial in discerning sound. Researchers have localized subcortical auditory pathways using fMRI (Javad et al., 2014). Our study uses a similar approach.

Studies to determine if hearing loss is a common symptom of TBI are scarce in quantity. Penn et al. (2009) found in a sample of children who sustained a TBI between

birth and twelve years 6 months, 31% had hearing loss as a result of head injury. However, the authors of this meta-analysis suggest that hearing loss in those with traumatic injury might be higher than reported. In a case study, a 35-year old female patient was diagnosed with sensorinureal hearing loss following a diagnosis of mTBI by DTI (Jang et al., 2019). Munjal et al. case study found that the severity of TBI leads to an increase of ABR wave V absolute latency and I-V interpeak latency. The authors propose, on the basis of TBI severity, evaluation of patients for hearing problems. Despite that hearing loss has been a shown symptom of TBI, due to limited research the affects TBI has on the auditory radiation remain unclear. The purpose of this investigation is to study the impact TBI has on the auditory radiation.

The effects of TBI on the auditory pathway between the cochlea and the auditory cortex are not well researched. Knowledge is lacking in how different parts of the brain sustaining damage affect hearing. In this study, we examined whether the auditory radiation between the medial geniculate nucleus of the thalamus and auditory cortex is affected by TBI, using DTI data of Vietnam war veterans who did and did not suffer from TBI. DTI is commonly used to assess brain damages in TBI, but the affects of TBI on the auditory radiation are not yet determined. We hypothesized that traumatic damage to the brain affects the auditory radiation.

Methods

DTI data was obtained from the Department of Defense (DoD) Alzheimer's Disease Neuroimaging Initiative (ADNI, n.d.). The analyses in this study were approved by the Institutional Review Board of the University of Mississippi (14x-244). There were four groups in the study: a group of individuals with TBI, a group with Post-Traumatic Stress Disorder (PTSD), a group with TBI and PTSD, and a group with neither TBI nor PTSD. The PTSD group was excluded from the analysis.

The DTI series had 41 volumes of noncolinear directions as well as 5 volumes without diffusion weighting (TR = 7200ms, TE = 56ms, matrix = 232 x 232 x 160) with 2mm^3 isotropic resolution.

Functional Magnetic Resonance Imaging of the Brain Software Library (FSL) was the source used for imaging processing. Utilizing affine registration of 31 diffusion volumes to the first b0 volume using the Linear Registration Tool through FSL was utilized to correct eddy-current induced distortions and head-motion displacements. The Brain Extraction Tool through FSL removed non-brain tissue. Through fitting a diffusion tensor model to the raw diffusion data, FA was calculated at each voxel. Adjustments according to rotation parameters of linear correction were made to the b-vector table for each participant.

Utilizing Markov Chain Monte Carlo sampling through the Bedpostx tool in FSL, the local probability density functions of the principal diffusion direction could be estimated (Behrens et al., 2007). Then, using the Probtrackx tool from FSL, an estimate of a spatial probability density function across voxels was made. For each input voxel with a 0.2 curvature threshold, 0.5 mm step length, and 2000 steps per sample, 5000 samples were made available. To make a DTI specific reference the FMRIB85_FA tool through FSL was utilized. This helped create a segmentation of the auditory radiation tracts and termination masks, which is based on the MNI152 T1 brain. To determine the primary auditory cortex seed, adjacent white matter regions to the Heschl's gyrus were taken through the HavardOxford cortical atlas (Desikan et al., 2006). R=3mm sphere centered at MNI ±18, -26,-6 were used as a definition for the primary auditory cortex seed. MNI x<-15 (left) and x>+15 (right) are used to define the termination masks excluding contralateral projections. A normalized probability value of 0.05 was each participants' bilateral auditory radiation threshold. For each individual, the mean FA within the bilateral auditory radiated was determined. To assess the group difference, a one-way analysis of covariance (ANCOVA) was tested between the group on the auditory radiation FA controlling for age and sex.

Results

There were 97 men whose auditory radiations were successfully segmented (Fig 1). The TBI group had 23 men (69.43 mean years old with a standard deviation of 5.71). The TBI&PTSD group had 30 men (68.15±2.95 years old). The control group had 44 men (69.78±4.93 years old). There was no significant effect on the FA of the auditory radiation between groups ($F(2,91)=0.00131$, $p=0.76$). Post-hoc analysis (t-tests between three groups) did not show any difference between groups.

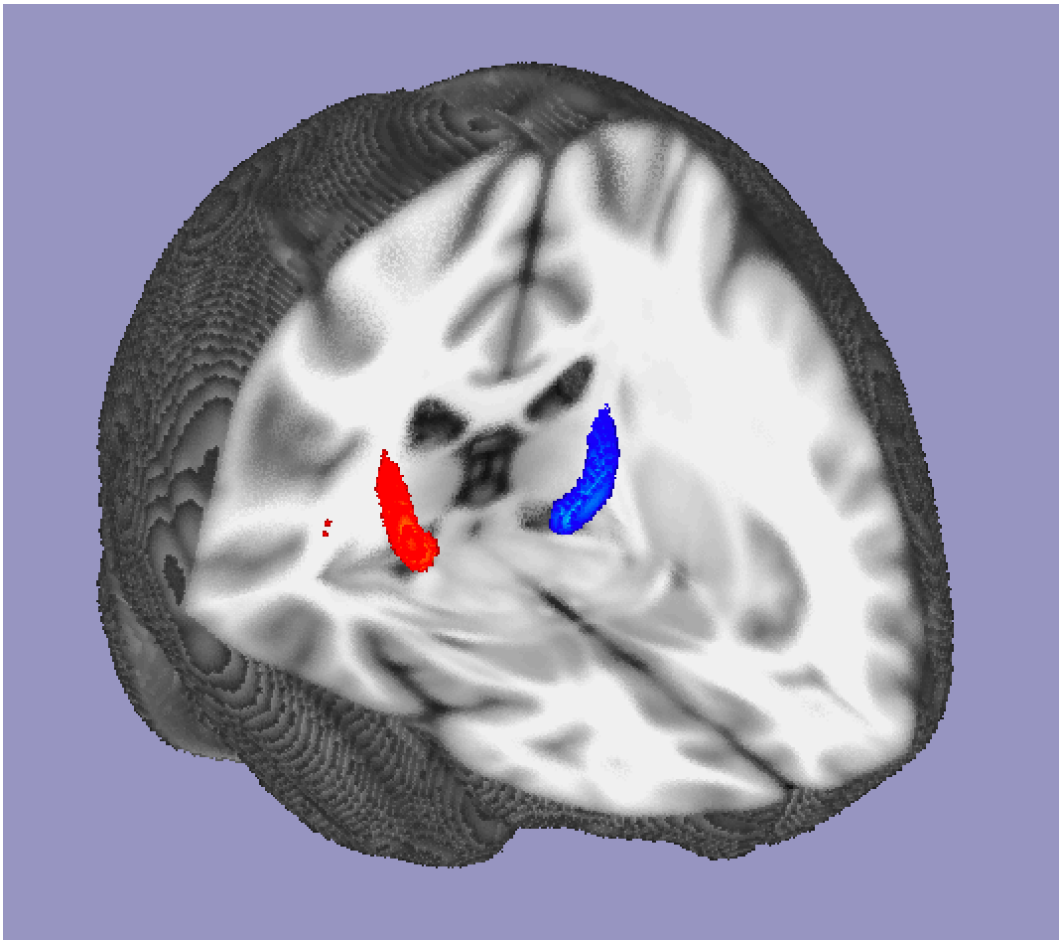

Figure 1: Probabilistic Tractography of the right (red) and left (blue) auditory radiations.

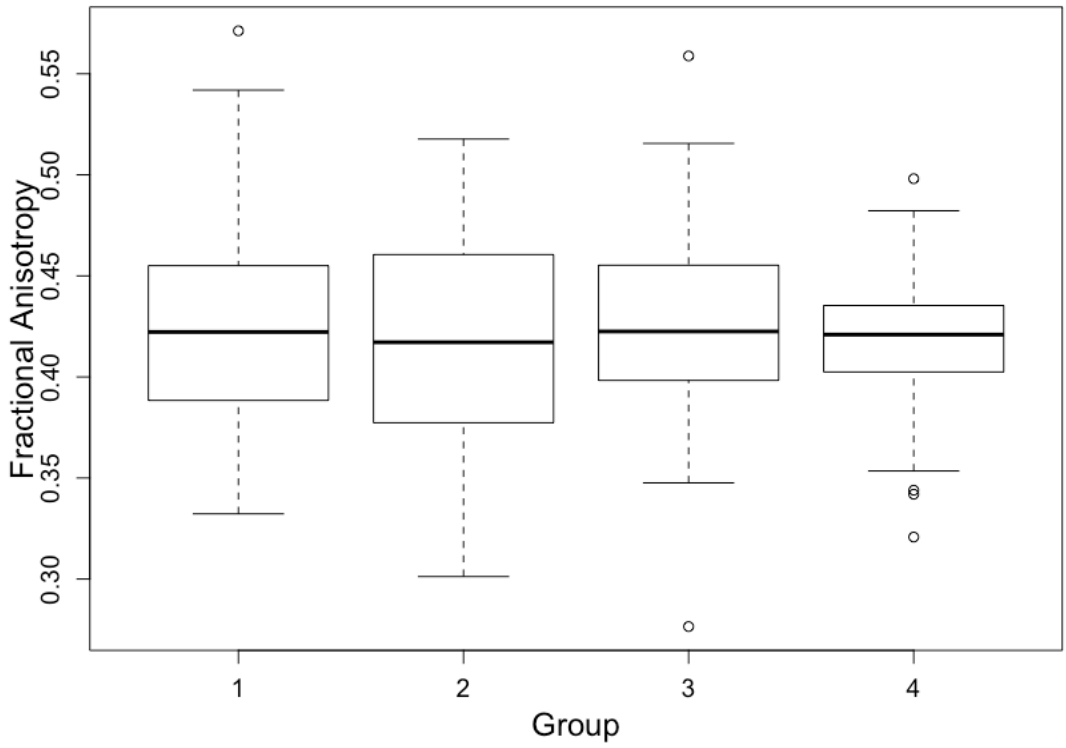

Figure 2: Fractional Anisotropy of the auditory radiation. Group 1: PTSD group (Not Included in the analysis); Group 2: TBI group; Group 3: Control group; Group 4: TBI&PTSD Group

Discussion

In this study, we examined the effect TBI had on the auditory radiation. We hypothesized that traumatic damage to the brain affects the integrity of the auditory radiation. In our sample, 49 individuals had PTSD, 23 individuals had TBI, and 30 individuals had PTSD and TBI. 44 subjects make up the control group. The participants' mean age was 68.72 years old. Our results did not support such a difference in the auditory radiation between groups.

Our analysis using probabilistic tractography of the auditory radiations was successful in isolating the auditory radiation of our participants. This allowed us to compare auditory radiations between those with and without TBI. We placed each participant in a category that we later were able to analyze to find our results. Many studies have used DTI as an appropriate way to observe those with TBI. However, there are considerations why we did not find differences in the auditory radiation associated with TBI.

TBI tends to affect the periphery of the brain. These periphery areas are against the ridged and rough skull making them common places susceptible to brain damage. One study found that direct traumatic injury to the temporal lobe, which can affect the auditory cortex due to the impact against the temporal lobe bony ridges (Werff & Vander, 2016). A common area in the brain affected by TBI is the frontal lobe. The frontal lobe is

responsible for cognitive skills, problem-solving, memory, and decision making (Collins & Koechlin, 2012). Specifically, the majority of brain damage from TBI happens in the prefrontal cortex. Located in the front of the frontal lobe, the prefrontal cortex is responsible for decision making, memory, and reasoning. Cognitive problems might be commonly found in TBI patients due to most damage from TBI happening in the frontal lobe. While, the auditory radiation is in the middle of the brain, which tends to be less affected in TBI. This is one possibility, which may account for, why we found no difference between the groups.

Commonly, hearing loss resulting from TBI is sensorineural (Bojana et al., 2019). This means that hearing loss is due to the improper function of either the inner ear, auditory nerve, or the auditory cortex. Trauma to the brain, the eighth nerve, cochlear concussion, or perilymphatic fistulas are all outcomes of traumatic injury that can lead to sensorineural hearing loss (Penn et al., 2009). The auditory cortex is in the temporal lobe which is located in the periphery of the brain. The temporal lobe is another area where people frequently experience brain damage due to TBI. However, the auditory cortex is more internal/medial from the temporal lobe's lateral surface. (Kiernan, 2012). This may account for why we did not find a difference in auditory radiation, which is connecting the thalamus and temporal lobe.

A case study observed a woman who suffered from head trauma in her occipital area. On her 1.5-year DTI, the auditory radiations in both brain hemispheres were narrowed. Following an mTBI, this patient was diagnosed with sensorineural hearing loss

(Jang et. al., 2019). Though we did not find auditory radiation was affected in our study, this study found different. The severity and location of her injury could account for why our results do not align. It is suggested that damages to the auditory radiation are possible in TBI but are not common.

Cortical deafness is a relatively rare disorder that can result from damage to the gray matter of the auditory cortex. It possibly can result in damage to the auditory radiation, white matter adjacent to the auditory cortex. Patients diagnosed with cortical deafness are unable to hear sounds but have no damage outer, middle, or inner ear. In a study, a patient with vascular lesions of bilateral auditory cortices, completely loss his hearing and was diagnosed with cortical deafness. This patient had normal distortion product otoacoustic emissions and auditory brain responses. However, they had 0% speech discrimination and perception (Kaga et al., 2015). Narayanan et al. (2017) observed a patient who had abrupt onset hearing loss after a seizure. Acute infarcts in bilateral Heschl's gyri were discovered through neuroimaging. This patient was also diagnosed with cortical deafness. These two patients suffered damage to their auditory radiation, the axonal fiber between the thalamus and auditory cortex. Auditory radiation tends to be affected by non-traumatic brain damage such as strokes, lesions, seizures, or birth defects. This can explain why we did not find that TBI affects auditory radiation.

Another possibility is that the group difference was eliminated through probabilistic tractography and the quality control process, where subjects with failed segmentation were excluded. It could be the case that those with traumatic damage that

would affect the auditory radiation were excluded from the analysis. However, the results suggest that the TBI, in general, does not affect the auditory radiation as we are able to trace them. The TBI tends to happen in the anterior and posterior periphery of the brain (Lew et al., 2010). It is unlikely that TBI would always affect the auditory radiation to cause injury. Our results suggest that it is uncommon for the auditory radiation is affected in TBI.

Our study suggests that it is unlikely that TBI induces hearing loss through damages to the auditory radiation. Conversely, hearing loss remains a problem that patients face after a TBI. Those with TBI are at an increased risk of both having immediate hearing loss or later developing hearing loss. According to a study, patients with TBI have a 2.1 times higher risk of developing hearing loss than the overall population (Shangkuan et al., 2017). Furthermore, they found that the highest percentage of patients had sensorineural hearing loss.

The limitation of our study is the smaller sample size. Only 53 individuals had TBI. However, the lack of difference is evident in this restricted sample and it is not likely that a greater sample size would yield difference between groups. Another limitation of this study is that we do not have access to the subjects' hearing status. This extends to the fact that we do not have access to the subjects' hearing status prior to their TBI. Our study examined the auditory radiation without current and prior hearing status knowledge. That is, some are likely to have hearing loss. However, our findings suggest that the auditory radiation is not affected by the history of TBI, even if some individuals

with TBI may have hearing loss. It is also possible that the control group has some hearing loss. In this study, we could not detect the difference in auditory radiation. This could be due to some unknown hearing issues in the control group side.

In conclusion, we conducted probabilistic tractography of the auditory radiation and found that there is no significant difference in the auditory radiation in those with or without TBI. While auditory radiation serves as a crucial part of sound perception, we found that TBI does not affect it. However, it has to be mentioned that sensorineural hearing loss can result from TBI. Further research on how TBI affects the auditory radiation might not be necessary. Nonetheless, research on hearing loss after TBI is not sufficient. Hearing loss can dramatically affect the quality of life. Studying and conducting research on where in the brain TBI affects hearing has important clinical implications. Further research can help audiologists and other clinicians to better diagnose the type of hearing loss and better manage patients' treatments. It is strongly hoped that more research is done concerning the connection between hearing loss and TBI.

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