# Differences in white matter microstructure between children with right and left unilateral sensorineural hearing loss

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## Introduction

Children with unilateral sensorineural hearing loss (USNHL) have shown deficits in central auditory processing and academic performance relative to normal-hearing children [1, 2]. In addition, children with right USNHL show greater deficits in academic performance as compared to children with left USNHL [3]. The neural basis for this "right-ear advantage" has been previously investigated using functional MRI [4]. Here, we investigate possible differences in white matter microstructure between the two groups using diffusion tensor MRI (DTI).

## Materials and Methods

DTI data was acquired using a Siemens 3T Trio system using a double spin-echo EPI sequence. Scan parameters were: TR/TE = 6000/87 ms, FOV = 25.6 X 25.6 cm, matrix = 128 X 128, slice thickness = 2 mm, NEX = 3. One scan without diffusion weighting and twelve scans with diffusion weighting (b = 1000 s/mm$^2$) were acquired. Data was acquired from 9 subjects; data from 1 subject was discarded due to subject motion between the whole-brain and the DTI sequence. Of the remaining 8 subjects (6M, 2F), 4 had left USNHL and 4 had right USNHL. Age range was 7.2 – 11.8 years; there was no significant difference in age between the two groups ($p > 0.75$, student's T-test). Severe-to-profound USNHL was verified via standard audiometry.

The data was analyzed using SPM5 (Wellcome Dept. of Cognitive Neurology, London, UK) and in-house routines in IDL (Research Systems Inc., Boulder, CO). The whole-brain datasets were segmented into gray matter, white matter, and CSF, using pediatric templates [5]. The white matter maps were normalized into standardized space, using the white matter pediatric template. Fractional anisotropy (FA) and mean diffusivity (MD) maps were calculated from the DTI data, and the FA maps were normalized using the same registration parameters. The spatially normalized FA maps were then co-registered to the spatially normalized white matter maps for further accuracy. The FA maps were analyzed using a General Linear Model (GLM) on a voxelwise basis. To account for possible confounds resulting from imperfect spatial normalization or morphometric differences, the data was masked using the criteria of WM probability of 0.9 or greater and an FA value of 0.25 or greater. Only voxels which met these criteria in at least 7 subjects were retained for analysis, and for each voxel only those datapoints which met those criteria were included in the GLM. The T-scores were converted to Z-scores, filtered with a Gaussian filter of width 4 mm, and thresholded to $Z > 6$ with a spatial extent threshold of 200 voxels, resulting in a corrected $p < 0.01$, determined via Monte Carlo simulation [6].

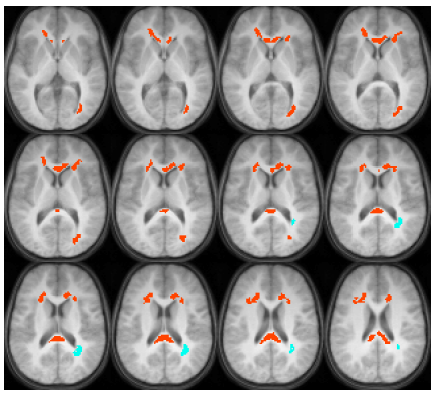

**Figure 1.** Regions with larger (red) and smaller (blue) FA in children with right USNHL compared to children with left USNHL. All regions significant with $p < 0.01$ (corrected). Images in radiologic orientation.

## Results

Children with right USNHL displayed greater FA in the genu and splenium of the corpus callosum, in frontal regions bilaterally, and in the left occipital lobe (Figure 1, red). Children with left USNHL displayed greater FA in temporo-parietal white matter in the left hemisphere (Figure 1, blue). A chart of the differences is displayed in Figure 2.

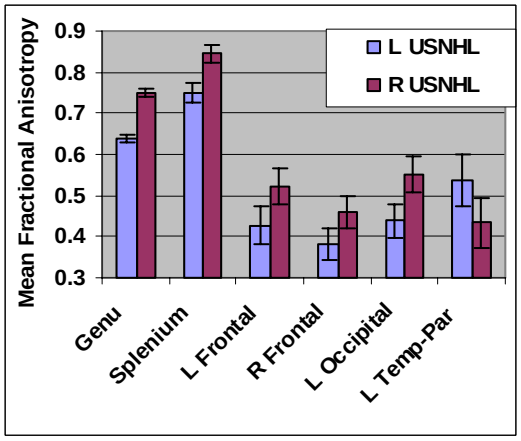


**Figure 2.** Comparison of FA values (error bars = +/- σ) for the regions shown in Figure 1.

## Discussion

Our data shows a very large effect size (Table 1), with statistically significant differences detectable despite the small sample size, unlike studies involving intelligence [7] or gender [8]. This may indicate the usefulness of DTI for the investigation of neuroanatomical bases for various types of audiologic pathologies even when large sample sizes are unavailable.

The brain is known to cortically reorganize in response to USNHL [9]. Part of this involves a shift toward bilateral cortical representation in the primary auditory cortex; however, reorganization may occur in higher-order processing centers as well, which may differ between children with right USNHL and children with left USNHL [4]. Children with left USNHL perform better on auditory processing tasks and academic performance, as auditory input from the right ear directly enters the language processing centers in the left hemisphere.

Here we show preliminary evidence of differences in development of anatomical connections between children with right and left USNHL. Our data suggests that compensatory reorganization occurring in children with right USNHL involves development of interhemispheric pathways, especially in the corpus callosum and in frontal regions. As more subjects with USNHL are recruited, we will able to investigate whether this effect represents a "speeding-up" of normal developmental processes via comparison with normal controls, controlling for age. In addition, our data may indicate retarded development of intra-hemispheric pathways in the left hemisphere, as demonstrated by the greater FA found in children with left USNHL in temporo-parietal white matter adjoining posterior language processing regions ("Geschwind's territory"; BA 39).

Future studies will also incorporate functional connectivity or effective connectivity analyses from fMRI studies, in children with USNHL, in order to further elucidate the development of functional pathways, differences between normal children, and relation to side of hearing loss.

| REGION | Effect Size |
|---|---|
| Genu | > 10 |
| Splenium | 4.1 |
| L. Frontal | 2.1 |
| R. Frontal | 2.0 |
| L. Occipital | 2.6 |
| L. Temporo-Parietal | 1.7 |

**Table 1.** Effect sizes (Cohen's d) for the FA differences shown in Figure 2.

## Conclusion

A preliminary DTI study was performed investigating possible changes in white matter microstructure between children with right and left USNHL. Results indicate preferential formation of inter-hemispheric pathways in children with right USNHL, and intra-hemispheric pathways in the left hemisphere in children with USNHL, and provide a possible neurobiological basis for the behavioral and audiological "right-ear advantage" shown in children with left USNHL.

## References

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