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Right Hemispheric Homologous Language Pathways Negatively Predicts Post-Stroke Naming Recovery

Zafer Keser, MD[1], **Rajani Sebastian, PhD**[2], **Khader M. Hasan, PhD**[3], **Argye E. Hillis, MD**[4]

[1]Department of Neurology, The University of Texas Health Science Center, Houston TX,

[2]Departments of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine

[3]Departments of Diagnostic and Interventional Radiology, The University of Texas Health Science Center, Houston TX,

[4]Department of Neurology, Johns Hopkins University School of Medicine

Abstract

Background and Purpose—Stroke is the leading cause of disability in US, and aphasia is a common sequela after a left hemisphere stroke. Functional imaging and brain stimulation studies show that right hemisphere structures are detrimental to aphasia recovery but evidence from diffusion tensor imaging (DTI) is lacking. We investigated the role of homologous language pathways in naming recovery after left hemispheric stroke.

Methods—Patients with aphasia after a left hemispheric stroke underwent naming assessment using the Boston Naming Test (BNT) and DTI at the acute and chronic time points. We analyzed DTI of right arcuate fasciculus (AF) and frontal aslant tracts (FAT). We used Wilcoxon rank sum test to evaluate structural lateralization patterns and partial Spearman correlation/multivariate generalized linear model to determine the role of right AF and FAT in naming recovery after controlling for confounders. Results were corrected for multiple comparisons.

Results—On average, the structural integrity of left language pathways deteriorated more than their right homologues, such that there was rightward lateralization in the chronic stage. Regression/correlation analyses showed that greater preservation of tract integrity of right AF was associated with poorer naming recovery.

Conclusion—Our study provides preliminary evidence that preservation of right homologues of language pathways is associated with poor recovery of naming after a left hemispheric stroke, consistent with previous evidence that maintaining greater reliance on left hemisphere structures is associated with better language recovery.

Corresponding Author: Zafer Keser, MD, Department of Neurology, 6431 Fannin Street Suite 7.044, Houston, TX, 77030, Zafer.Keser@uth.tmc.edu, +1-409-434-8189.
Social Media: You can include Zafer Keser in the Facebook posts (https://www.facebook.com/zafer.keser.54)

Conflict of Interest
The authors report no conflict of interest.

Keywords

Post-Stroke Aphasia; Right Hemisphere; Naming; Recovery

Introduction

Stroke is the leading cause of the disability in US, and 19% of stroke survivors suffer from aphasia.[1] Predicting language recovery after a stroke remains difficult, although imaging markers have provided some predictive information.[2,3] The neural mechanisms that support aphasia recovery are not yet fully understood. Majority of the studies have investigated the role of left hemisphere regions in aphasia recovery; however, there are very few studies investigating the role of the right hemisphere in aphasia recovery. Prediction of aphasia recovery is crucial to individualize the treatment intensity and strategies early on, as many language deficits persist.[4] Determining the role of right hemisphere in aphasia recovery is crucial as many novel treatment modalities such as tDCS and TMS target right hemisphere regions for language recovery.[5]

Diffusion tensor imaging (DTI) is a reliable structural neuroimaging method for assessing the microstructural integrity of white matter pathways in the brain.[6] Most DTI studies of aphasia recovery have focused on left hemispheric pathways.[7] Only few studies[2,8,9] have investigated the role of right hemispheric homologous language pathways in post-stroke aphasia recovery. These studies showed that right hemisphere supplementary motor area extension of corpus callosum predicted a better verbal fluency task[2], an intensive intonation based therapy induced changes in underlying white matter of right homologous Broca's area correlated with improvements in speech production[8], and right arcuate fasciculus (AF) volume increased after intensive melodic intonation therapy.[9] Naming is the most common residual deficit in aphasia,[3] and there is a growing evidence that inhibitory stimulation of the Broca's homologue in the right hemisphere facilitates naming recovery after a stroke.[5] However, a DTI study investigating the role of right hemispheric homologous language pathways in naming recovery has been lacking.

In this study, we investigated the longitudinal changes in the white matter integrity of the right hemispheric homologous language pathways – AF (Figure 1A) and frontal aslant tract (FAT) (Figure 1B) - and their association with naming recovery in patients with aphasia due to left hemispheric ischemic strokes.

Methods

The datasets analyzed during the current study are available from the corresponding author on reasonable request. 24 patients with aphasia due to left hemispheric ischemic stroke (11 women, age range 36–86; see supplementary for detailed demographics) with no history of previous neurological or psychiatric disease were enrolled within 48 hours after symptom onset.

Patients underwent detailed language testing including the short version of the Boston Naming Test (BNT)[10] as well as neuroimaging evaluation at the acute (<2week) and chronic

(6–12 months) time points and proportional recovery rate was calculated as detailed in supplementary. This study was approved by Institutional Review Board of Johns Hopkins University School of Medicine. All patients provided written informed consent according to the Human Subjects Protocol for Johns Hopkins University School of Medicine. The patients only received standard of care speech therapy during the study.

The patients underwent high resolution T1weighted, T2weighted, FLAIR and Diffusion weighted imaging (DWI). FAT and AF tracts were reconstructed and quantified as well as white matter lesions and infarct volumes as detailed in supplementary.

Statistical Analyses

We compared means of DTI metrics of AF and FAT between right and left hemisphere in the acute and chronic time points by using non-parametric tests. For the 10 out of 24 patients who had DTI at both acute and chronic time points we evaluated proportional changes in DTI metrics. Regression and correlation analyses adjusted for age, education, lesion load, were used determine the predictor of naming recovery rate. False discovery rate was conducted for multiple comparison analyses. Please see supplementary for more details in the analyses.

Results

In the acute time point, no lateralization was observed between the left and right AF (FA; p=0.05 and RD; p=0.07) and FAT (FA; p=0.2 and RD; p=0.05), whereas in the chronic time point there was rightward lateralization in AF (FA; p=0.00004, RD; p=0.00004) and FAT (FA; p=0.007, RD; p=0.001) (Figure 1C). Longitudinal data shows that both hemispheres show a trend of diminished FA with time but the trend was more pronounced for the left FAT than right FAT (p=0.01) (Figure 1D). After FDR correction, the chronic right AF FA/RD and right FAT RD values remained significantly higher than the left. Regression and correlation analyses were conducted to determine right hemispheric correlates and predictors of naming recovery rate. The recovery rate was not found to be significantly correlated with acute right and left sided AF FAT DTI values ($p>0.05$). Longitudinal changes in right AF showed a significant inverse correlation ($r=-0.74$, $p=0.004$) with recovery rate (Figure 2A). Recovery rate did not show a significant correlation with longitudinal changes of right FAT FA/RD or chronic right/left AF/FAT FA/RD values ($p>0.05$) (Figure 2B–D). After FDR correction, longitudinal right AF FA remained significant predictor of naming recovery.

Discussion

In this study, patients with post-stroke aphasia were, on average, found to evolve to a right lateralization of AF in the chronic time point. Additionally, regression and correlation analyses showed that patients who had preserve tract integrity of the right AF showed poorer naming recovery. This correlation was not observed for FAT possibly due to higher specialization of AF in picture naming. Our findings are in line with a previous fMRI study showing that incorrect naming responses were selectively associated with right hemisphere

activation[11] and a meta-analysis study of randomized clinical trials revealing that inhibitory brain stimulations to the right hemisphere regions improved naming recovery after stroke.[5]

Our cohort consisted of subjects with heterogenous clinical severity and white matter pathway integrity at baseline. Despite this variability at baseline, the tract integrity of language pathways was diminished longitudinally both in the right and left hemispheres but this decrease was more accentuated in the left hemisphere. Although we corrected our analyses for other confounders such as lesion load, education and age, more pronounced loss of tract coherence on the left was possibly related to Wallerian degeneration.

Speech and language functions consist of various components, and the recruitment of right hemisphere homologous language pathways is not always unfavorable in the recovery of some of the components. For example, a DTI study showed that right hemispheric white matter integrity positively predicted speech fluency in chronic post stroke aphasic patients[2]. Thus, we believe the role of right hemispheric white matter pathways in post-stroke aphasia is heterogenous and highly related to the specific function and anatomical structure.

To the best of our knowledge, our study is the first DTI study providing preliminary evidence that greater reliance on the right AF may have deleterious effect on naming recovery after stroke. Our findings should be interpreted with caution due to possible type I errors as the study is statistically underpowered due to significant subjects' variability and small sample size. Another limitation of the study is that our analyses might have not captured rapid and dynamic changes in language networks after stroke due to lack of more imaging time points.[12] Larger clinical studies with greater statistical power are needed to confirm our findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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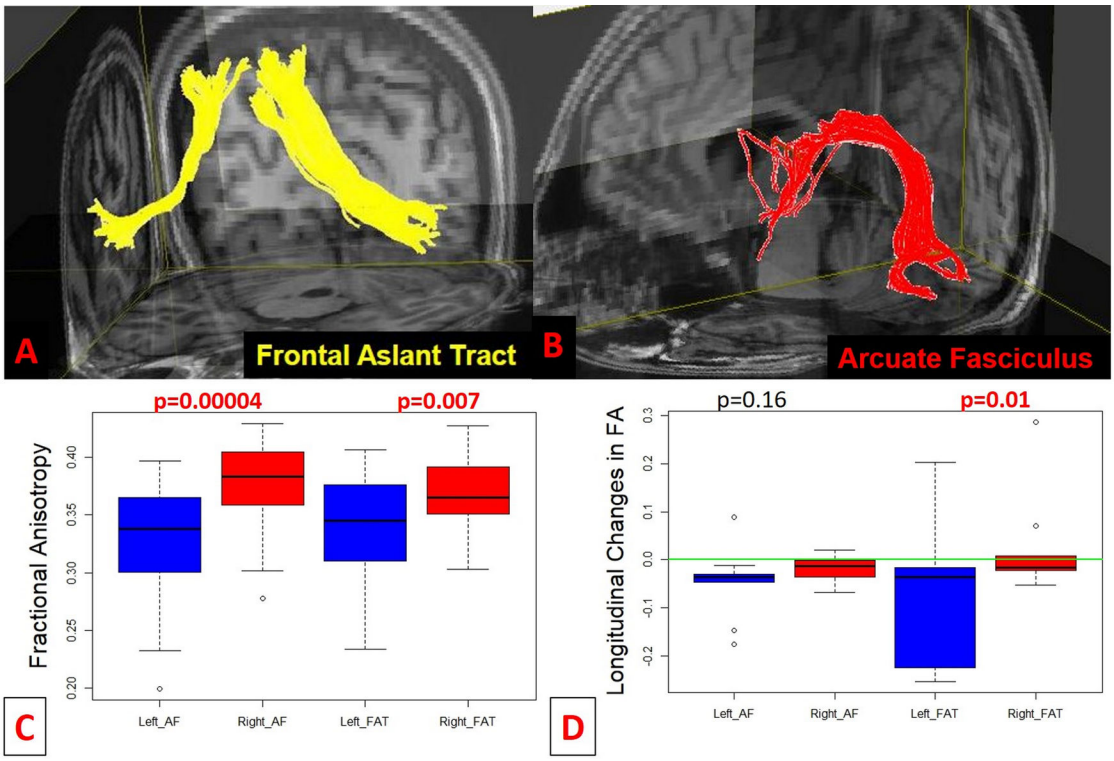

Figure 1.

Diffusion tensor imaging reconstructions of Frontal Aslant Tract (FAT) (A) and Arcuate Fasciculus (AF) (B) are illustrated on background T1w images. For AF, rightward asymmetry of fractional anisotropy (FA) was noted at the chronic stage of stroke (C). Longitudinal data shows that both hemispheres show a trend of diminished FA with time but the trend was more pronounced for left hemisphere (D). Green line represents no change in FA.

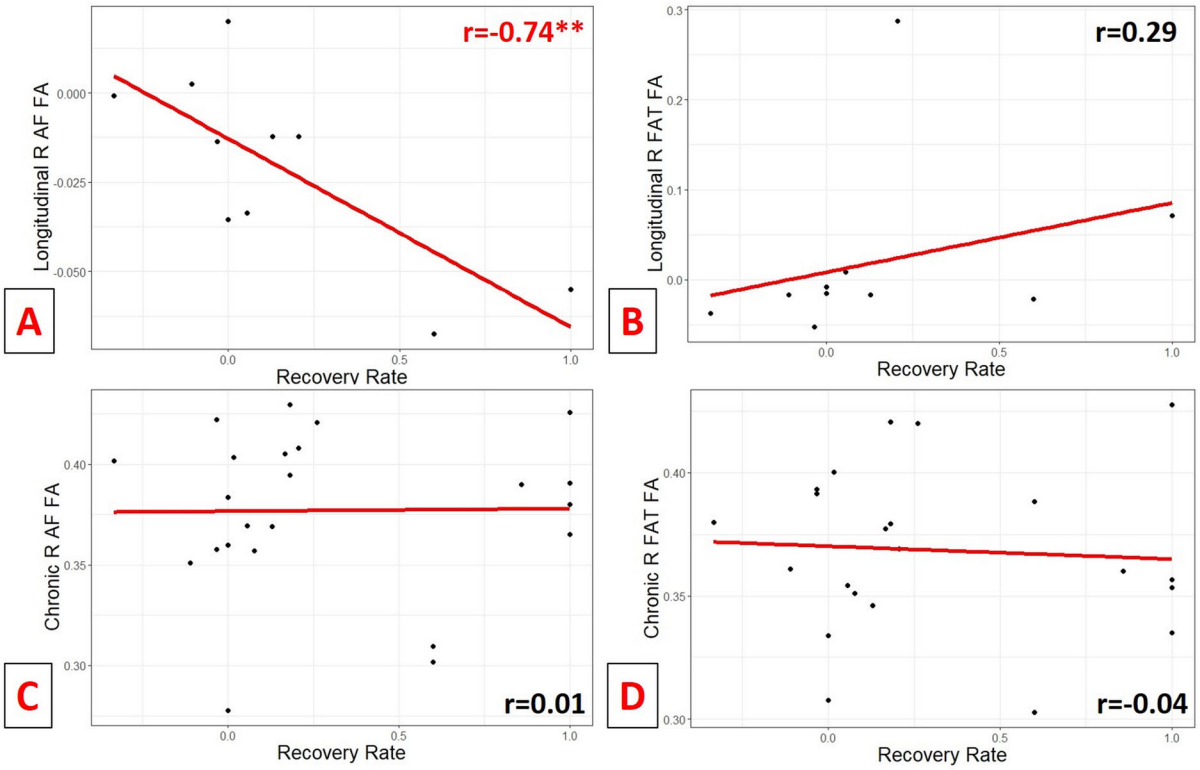

Figure 2.

Longitudinal changes in fractional anisotropy (FA) of right Arcuate Fasciculus (AF) negatively correlated with picture naming recovery rate after correcting for age, education and lesion load, whereas right Frontal Aslant Tract (FAT) did not show a similar finding. In the chronic setting, FA values of AF and FAT did not show a significant correlation with Recovery Rate. **means $p<0.01$. For patients with recovery rate >1 is shown as equal to 1 for illustrative purposes.