Structural asymmetry of the white matter language pathway in relation to functional hemispheric language lateralization in both right and left-handed healthy subjects: a combined functional MRI and DT-tractography study.

M. W. Vernooij[1,2], M. Smits[1], P. A. Wielopolski[1], G. C. Houston[3], G. P. Krestin[1], and A. van der Lugt[1]

[1]Radiology, Erasmus MC, Rotterdam, Netherlands, [2]Epidemiology & Biostatistics, Erasmus MC, Rotterdam, Netherlands, [3]ASL Europe, 's-Hertogenbosch, Netherlands

Background. A leftward asymmetry of the planum temporale and parietotemporal white matter have been reported previously [1] in right handed, presumed functionally left-lateralized subjects. The relation between structural asymmetry and functional lateralization in functionally non-left-lateralized subjects remains speculative.

Purpose. To investigate the relative fiber density (RFD) of the arcuate fasciculus (AF), using Diffusion Tensor (DT)-tractography, in relation to functional hemispheric language lateralization in both right and left-handed subjects.

Methods and Materials. Twenty healthy volunteers (7 male, mean age 32.9 years) were imaged at 1.5T (GE, Milwaukee, US). Thirteen subjects were left-handed (Edinburgh Handedness Inventory). Functional hemispheric language lateralization was established with functional MRI (T2*w-GRE-EPI sequence, acquisition time 5:15 mins). The stimulation paradigm was a blocked design, in which the subject either covertly produced verbs related to auditory presented nouns (active condition) or listened to tones (rest condition). A functional laterality index was calculated for each subject. DTI consisted of a single-shot SE-EPI sequence (*b*-max 1000 mm^2s-1, 25 non-collinear directions; 4:00 mins). DT-tractography was performed using the dTV software (Masutani, Tokyo, Japan) based on the FACT method [2]. DT-tractography of the AF was performed with placement of seed and target regions of interest (ROI) in the Superior Longitudinal Fasciculus (SLF) [3]. As a reference, DT-tractography was also performed of the corticospinal tract (CST), with seed ROI in the cerebral peduncle and target ROI in the internal capsule. A relative fiber density was calculated for the AF and CST in both hemispheres, by dividing the number of tracked lines by the number of seed points. Structural asymmetry index of the AF and CST was derived from the calculation $(RFD_{left}-RFD_{right})/(RFD_{left}+RFD_{right})$.

Results. In all subjects language-related cortical activation was seen, and the AF and CST could be tracked in both hemispheres. Hemispheric language lateralization was left-sided in all right and in 6 left-handed subjects. Two left-handers showed symmetrical activation and 5 had right-sided language lateralization. RFD of the AF was asymmetric in 16 subjects, which was leftward in all cases (figure 1). RFD of the CST showed no asymmetry. Mean RFD of the AF was significantly higher on the left than on the right side (paired t-test; $p < 0.001$), irrespective of handedness or functional language lateralization (figure 2). In right-handed subjects, the degree of structural asymmetry of the AF was significantly positively correlated to the degree of leftward functional lateralization.

Conclusion. Regardless of functional hemispheric language lateralization, the brain exhibits a predominant leftward asymmetry of the arcuate fasciculus, the main white matter fiber tract involved in language. Our findings have important implications for the understanding of structural and functional lateralization of brain regions as well as for the presurgical evaluation of language function.

References

1. Geschwind, N. and W. Levitsky, Science, 1968. **161**(837): p. 186-7.
2. Mori, S. and P.C. van Zijl, NMR Biomed, 2002. **15**(7-8): p. 468-80.
3. Nucifora, P.G., et al., Neuroreport, 2005. **16**(8): p. 791-4.

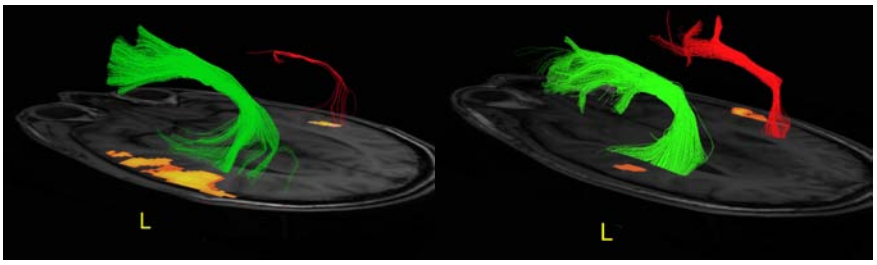

Figure 1.
Axial MR images showing fMRI activation (orange/yellow overlay) as well as DT-tractography results of the AF in a functionally left-lateralized subject (left panel) and a functionally right-lateralized subject (right panel). Fiber density of the AF was leftward asymmetric, regardless of functional lateralization.

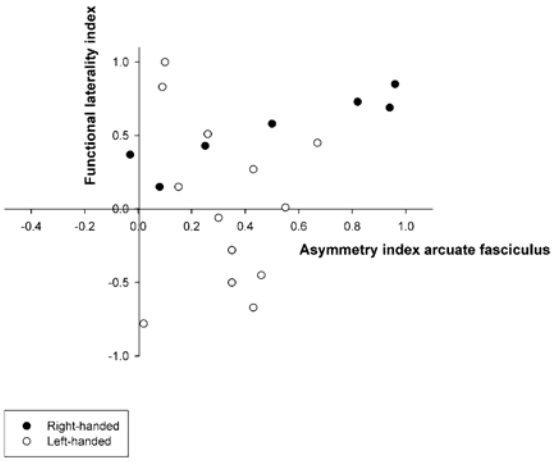

Figure 2.
Scatter plot of functional lateralization (y-axis) and structural asymmetry (x-axis) showing an overall leftward asymmetry in the AF, irrespective of functional lateralization.