

Relationship between the arcuate fasciculus and cortical structure in pediatric patients with polymicrogyria: a pilot study.

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Purpose: Polymicrogyria consists of abnormal cortical lamination, with most severe involvement of layer 5¹. This pathologic description predicts abnormal white matter connectivity primarily within projection pathways. In many cases, however, the location of cortical abnormality plus the involvement of projection pathways fails to explain the profound effect on higher-order functions, including language, that are mediated by cortico-cortical connections². The goal of this study was to characterize the arcuate fasciculus (AF), a major intra-hemispheric association pathway that connects key language areas in the inferior frontal (IFG) and superior temporal (STG) gyri, and its relationship to language development in a cohort of pediatric epilepsy patients with polymicrogyria.

Methods & Materials: IRB approval was obtained for this retrospective, HIPAA-compliant study. Patients were identified from a search of the medical record with the following inclusion criteria: 1. Epilepsy. 2. Polymicrogyria (PMG). 3. Imaging performed at 3Tesla including 30-direction diffusion tensor imaging (DTI). 4. Language characterized by a pediatric neurologist. Patients presenting for evaluation of headache without neurologic abnormality, language impairment, or MRI abnormality served as a comparative cohort; these subjects were imaged with identical MRI sequences. Diffusion Toolkit was used for deterministic tract reconstruction using a FACT algorithm (35 degree threshold); Trackvis (www.trackvis.org) was used for isolation of the AF and for fiber-track analysis. The AF in each subject was categorized as present on the left-only, on the right-only, or bilaterally. Mean ADC and mean FA were calculated within each identifiable AF. Patients were divided into three groups based on language: 1. Intact: appropriate for age. 2. Mild-to-moderate impairment: significant language development, but delayed by comparison to peers (either expressive or receptive). 3. Profound impairment: absence of verbal language. Based on standard anatomic images, the location of dysplastic cortex in PMG patients was evaluated by a pediatric neuroradiologist blinded to the DTI and language data. Proportions were compared using Fisher exact test; continuous variables between 2 groups with the Wilcoxon rank sum test.

Results: 11 PMG patients and 11 age-matched controls met the above criteria. There was no significant difference between diffusion characteristics of the AF (left, right, or combined) in patients versus controls. Regardless of age, when both AF are present, the diffusion characteristics are highly conserved in a given individual; PMG patients with unilateral dysplasia were not different in this respect from those with bilateral involvement. Trends toward higher FA in the left versus right AF in both PMG patients and controls did not meet statistical significance; however, FA was higher in the left AF in 5/5 PMG patients and 6/8 controls when both AF were present in an individual patient.

100% (3/3) of PMG patients with intact language had an identifiable left AF. 100% (6/6) of patients without a left AF had some degree of language impairment; 20% (1/5) of patients with a left AF were impaired. 100% of normatives had an identifiable left AF. The following differences were significant: 1. Frequency of impairment in PMG patients without a left AF versus normatives ($p<0.0001$). 2. Frequency of impairment in PMG patients with versus without a left AF ($p<0.015$). 3. Frequency of absence of the left AF in PMG patients versus normatives ($p<0.008$). Absence of the left AF had 100% specificity, 75% sensitivity, and 100% positive predictive value (PPV) for some degree of language impairment.

5/6 patients with dysplastic cortex within the IFG and/or STG had some degree of language impairment. Dysplastic involvement of one or both of these regions had 67% specificity, 63% sensitivity, and 83% PPV for some degree of language impairment.

5/6 PMG patients with dysplastic cortex within the left IFG and/or STG had no left AF; patients with no involvement of these gyri had a significantly lower frequency of absence of the left AF (1/5; $p<0.04$). The single patient who had dysplastic involvement of these regions of cortex and an identifiable left AF had normal language development; the FA and ADC for this left AF was not out of the 95% confidence interval for these parameters in either the normative group or in the sub-group consisting of PMG patients with no dysplastic involvement of the ipsilateral IFG or STG. Of the PMG patients with absent left AF, 5/6 had dysplastic cortex within the IFG and/or STG. The single patient who had no dysplastic involvement of the left IFG or STG and no identifiable left AF actually had no involvement of the left hemisphere by PMG; this patient was impaired with respect to language.

Discussion: In this pilot study, PMG within the expected anatomic locations of two key language areas had a significant impact on the presence/absence of the AF, but not on the diffusion characteristics of this pathway. These preliminary results suggest a greater impact on the establishment of cortico-cortical connections than on their microstructure and furthermore imply abnormal cortical structure beyond layer 5 in patients with PMG. These data promulgate the potential for tract-based approaches to probe cortical structure.

References:

1. JE Thompson et al., 1997. Radiologic-Pathologic correlation: polymicrogyria. *AJNR*; 18:307–312.
2. P Krsek et al., 2009. Incomplete resection of focal cortical dysplasia is the main predictor of poor postsurgical outcome. *Neurology*; 72: 217-223