Lateralization of the Superior Longitudinal Fasciculus Across the Age Span and its Relation to Cognitive Abilities in Children

C. Lebel[1], and C. Beaulieu[1]

[1]Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada

INTRODUCTION: The superior longitudinal fasciculus (SLF) is a major white matter tract that is not only important in language function, but is also part of network that has been repeatedly implicated in reasoning and intelligence tasks[1]. Diffusion tensor imaging (DTI) tractography is a technique that allows for virtual reconstruction of white matter pathways such as the SLF *in vivo*. The SLF has demonstrated leftward asymmetry in most people for both structure[2] and diffusion parameters[3-5]. Also, a relationship between SLF asymmetry and language ability has been reported in 40 young adults[6]. However, this asymmetry is not yet fully understood, particularly across a wide age range. The purpose of this study was to use tractography to investigate SLF asymmetry over a wide age range (5-58 years) and explore the relationship between SLF asymmetry and cognitive ability in a subgroup of children (5-13 years).

METHODS: Subjects were 223 healthy, right-handed volunteers aged 5-58 years (120m/119f) with no history of neurological disease or injury. DTI was performed on a 1.5T Siemens Sonata scanner using dual spin echo EPI, 40 3mm slices (no gap), image matrix 96x128 zero-filled to 256x256, TE/TR=98ms/6400ms, b=1000s/mm^2, 8 averages, 6 directions, 6:06 min acquisition. We used a semi-automated tractography method, in which seeding, inclusion, and exclusion regions were drawn on a template FA map and automatically mapped to native space for each individual, to reconstruct three parts of the SLF: a direct, superior pathway between frontal and temporal brain regions (Fig.1), and two segments of an indirect pathway[7] (not shown). Tract volume, number of streamlines, and average fractional anisotropy (FA) were calculated per SLF in each hemisphere. A lateralization index, LI=(left-right)/(left+right), was calculated and subjects were classified based on LI: left-dominant, symmetric, and right-dominant (see Fig. 1 for examples of classification based on number of direct segment streamlines). Repetition of non-words, speeded naming and phonological processing (NEPSY), word ID and word attack (Woodcock Reading Mastery Test-Revised), Peabody Picture Vocabulary Test (PPVT-3), and Test of Nonverbal Intelligence (TONI) were performed on a subgroup of 59 children (30m/29f) aged 5-13 years. Raw scores were compared among lateralization groups using ANCOVA controlling for age and post-hoc tests with Bonferroni correction.

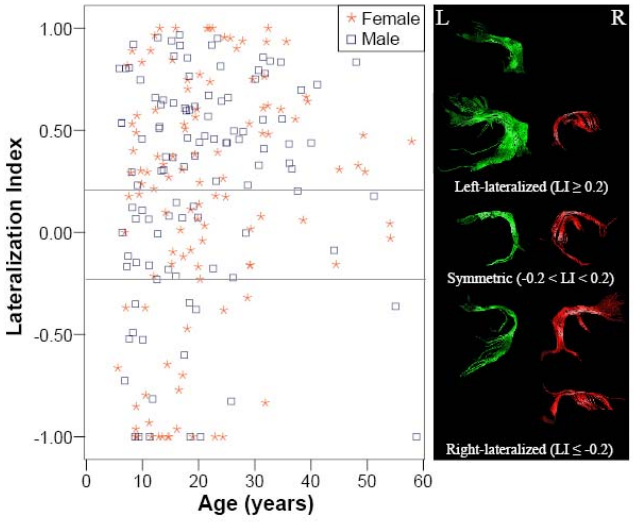

Figure 1: LI-age plot for number of streamlines in the direct superior longitudinal fasciculus (SLF) segment. Note that most right-lateralized individuals are young. Examples of left-lateralized, symmetric, and right-lateralized direct SLF in a 22 year old female (LI=1.0), 25 year old male (LI=0.66), 6 year old male (LI=0), 10 year old male (LI=-0.52), and 18 year old female (LI=-1.0). Indirect SLF segments are not shown.

RESULTS/DISCUSSION: In general, the direct segment of the SLF showed leftward asymmetry for volume, FA, and number of streamlines, although some individuals were right-lateralized. For number of streamlines, most right-lateralized individuals were young (see Fig.1), and LI was correlated with age (Spearman's rho=0.264, p<0.001). Subjects under 20 years (n=129) were 57% left-lateralized, 21% symmetric, and 22% right-lateralized. Of subjects 20 years and older (n=94), 70% were left-lateralized, 21% were symmetric, and 9% were right-lateralized. Among children who received cognitive assessment, lateralization of direct segment streamlines was significantly related to raw scores for five of seven tests (see Fig.2). The symmetric group significantly outperformed the left-lateralized group on five tests, and outperformed the right-lateralized group on three tests. There were no correlations between volume or FA lateralization and test scores, or between test scores and LI of the two indirect segments.

Previous studies have reported fewer right-lateralized individuals than we observed[5,6]; however, our larger sample includes children, and it was our younger group that showed the most right-lateralization. Lateralization was also significantly correlated with age. We also demonstrate a relationship between SLF lateralization and cognitive ability in children that is similar to previous findings in adults[6]. Although the majority of individuals are left-lateralized, there is clearly involvement of both hemispheres in advanced cognitive abilities, with more symmetric arrangements of the SLF offering a certain advantage.

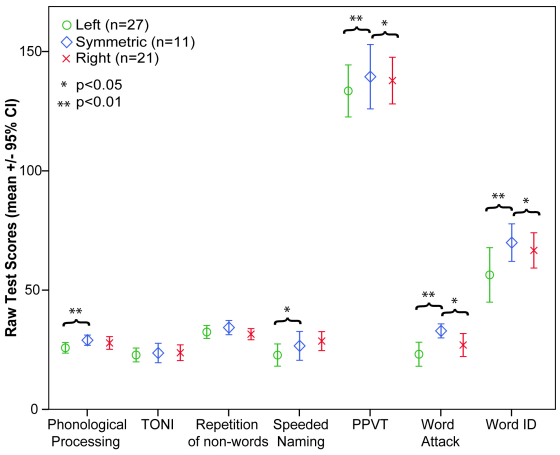

Figure 2: Raw scores for each group on cognitive tests in children aged 5-13 years (n=59). The symmetric group consistently outperformed the left-lateralized group, and in some cases also the right-lateralized group.

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