Do the language deficit in autism and specific language impairment (SLI) have a common neuro-anatomical substrate?

J. S. Verhoeven1, E. Prodi2, S. Deprez3, N. Rommel3, A. Leemans4, W. Van Hecke5, R. Peeters5, P. De Cock1, L. Lagae1, and S. Sunaert1
1Pediatrics, University Hospitals of the Catholic University of Leuven, Leuven, Belgium. 2Radiology, Istituto Neurologico Besta, University of Milan, Milan, Italy. 3Radiology, University Hospitals of the Catholic University of Leuven, Leuven, Belgium. 4Neurosciences, Exp ORL, University Hospitals of the Catholic University of Leuven, Leuven, Belgium. 5Image Sciences Institute, University Medical Center Utrecht, Utrecht, Netherlands

Introduction
Speech and language problems are frequently reported in early childhood. They often occur in an otherwise normal developmental trajectory with no discernible cause and are referred to as Specific Language Impairments (SLI). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) a clear distinction can be made between primary speech and language disorders, such as SLI and, speech and language problems that occur as a part of a more global developmental problem. Autism is one of those developmental disorders in which communication deficits can be considered to be of crucial importance, but that can be clearly distinguished from SLI by the DSM-IV. The clinical criteria for autism describe besides impairments in the domains of communication, the presence of problems with social interaction and of repetitive or restrictive behaviours and interests. Despite this clear theoretical differentiation, in everyday practice, the diagnostic boundaries between autism and SLI are not always that clear. The discussion of an overlap between these two conditions exists for multiple decades and some recent studies are outlining that they may indeed represent a spectrum of the same disorder. One of the intriguing overlaps is the similarity of their language deficits (1,2).

In this study, we examined the neuro-structural basis of language impairment in SLI and autism spectrum disorder (ASD) using diffusion tensor imaging (DTI). Since the superior longitudinal fasciculus (SLF) is a major intrahemispheric fiber tract involved in language processing we analyzed the white matter characteristics of the SLF in these groups of patients and in control subjects.

Materials and Methods
We studied 19 subjects with ASD (mean age 13.8±1.5 y) and 21 age-matched controls. We compared them to 13 children with SLI (mean age 10.1±0.3 y) and 10 age-matched controls. Patients and controls were screened for the presence of ASD symptoms using standardized parental questionnaires. Two SLI patients were excluded for further analysis due to the presence of substantial ASD symptoms. All patients and controls underwent extensive language testing as well as a short intelligence test (short form of WISC-III). DTI data were acquired with a 3T scanner using a spin-echo echo-planar-imaging pulse sequence with 45 diffusion directions (b=800 s/mm²) and with an isotropic resolution of 2 mm. This sequence was repeated twice and data were concatenated to improve the reliability of the estimated diffusion measures. Analysis was performed using ExploreDTI (3). Pre-processing steps included motion and distortion correction as well as a correction for the rotational component of the motion. Subsequently, deterministic fiber tractography of the superior longitudinal fasciculus (SLF) was performed, using the robust ROI definition protocol of Wakana (4) on a whole brain fiber tractography data set. SLF mean fractional anisotropy (FA) and mean diffusivity (MD) values were extracted. Differences in FA or MD between groups were evaluated using a MANOVA test. The statistical threshold for significance was set at p<0.05 and Bonferroni correction was applied to account for multiple testing.

Results
Both control groups did not show a difference in SLF mean FA and MD values (p= 0.6; p= 0.8). Consequently, both groups were treated as one for further comparison to the ASD and SLI patients. No significant difference was found in SLF mean FA and MD when comparing the control subjects and the ASD patients (p=1.00). However SLF mean FA was significantly reduced (p= 0.004) and MD was significantly increased (p= 0.008) in SLI children compared to controls. (figure 1). A significant difference was also found between SLI patients and ASD patients in SLF mean FA (p= 0.005) and SLF mean MD (p= 0.0045).

![Estimated Marginal Means of FA](image)

Figure 1: At the left: Graphic representation of the FA values in SLI patients (SLI), aged-matched controls for SLI (CO_SLI), ASS patients (ASS) and aged-matched controls for ASS.
At the right: table showing the results of MANOVA testing with FA and ADC as dependent variables. CO_SLI and CO_ASS were taken together, after showing no significant difference between both. Mean difference, standard error and p values for significance are shown. Bonferroni correction was performed to account for multiple testing.

Conclusion
Although SLI and ASD have a similar phenotypic presentation of the language deficit, the presence of structural differences in the superior longitudinal fasciculus demonstrated in our study indicates a different substrate in the development of the language impairment in these two conditions.

References
1 Lefever et al (2008), Autism Research 1, 284-296
2 Bishop et al (2010), Behav Genet 40, 618-629
4 Wakana et al (2007), Neuroimage 36, 630-644