Language comprehension in young people with severe cerebral palsy in relation to language tracts: a diffusion tensor imaging study

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ABSTRACT

Abstract

Patients with severe cerebral palsy (CP) often have poor speech ability but potentially better language comprehension. The arcuate fasciculus and the extreme capsule are two important language tracts between Wernicke’s and Broca’s area. Using Diffusion Tensor Imaging, we visualized language tracts and pyramidal tracts in both hemispheres in 10 controls (10-18 years) and 5 patients (5-23 years) with severe CP. Language comprehension was assessed with a special instrument (C-BiLLT). The language tracts were visualised in all control children and in four CP patients. In one CP patient without any objective language comprehension skills, no language tract could be visualised. Both language and pyramidal tracts were smaller in patients than in controls. These preliminary data indicate a relation between language tracts and language skills. Further research is necessary to study the value of structural integrity of language tracts in predicting language comprehension in CP patients.

Keywords

cerebral palsy - language tracts - magnetic resonance imaging - diffusion tensor imaging

WHAT THIS PAPER ADDS

1. Language tracts are present, but have lower integrity in patients with severe CP who have capabilities for language comprehension.
INTRODUCTION
Cerebral palsy (CP) is a common motor disorder attributed to nonprogressive disturbances of the brain that originate from the fetal or early infancy period. Although some CP patients with severe impairments of gross and fine motor function cannot speak, development of language comprehension is possible in this group. Adequate assessment of language comprehension of non-speaking CP patients is important to estimate the developmental age and need of communication abilities.
However, the assessment of language comprehension in severely handicapped CP patients is difficult because language tests generally require speech or motor function.
A recently developed language test, the Computer-Based instrument for Low motor Language Testing (C-BiLLT), is a useful instrument to investigate language comprehension in severely handicapped CP patients (Gross Motor Function Classification System [GMFCS] classes IV and V). This instrument enabled us to evaluate the understanding of spoken language in severely handicapped CP patients. However, a few patients did not convincingly respond to the test questions; thus, no reliable statements on their level of language comprehension were possible.
Functional brain imaging would be ideal to search for specific language-associated cortical activation. Unfortunately, functional brain imaging cannot be performed in unsedated children with severe CP because of their impaired motor control and high levels of anxiety and arousal. However, even in sedated children, it is possible to visualize white matter tracts in the brain with diffusion tensor imaging (DTI). Therefore, as a first step, it is important to establish whether language-associated tracts are structurally intact. The arcuate fasciculus is an important language comprehension tract; it is a dorsally located connection between the Wernicke area and the Broca area. The extreme capsule is a ventrally located connection between the Wernicke and Broca areas and is also associated with language function.
The aim of this study was to visualize the language tracts in comparison with pyramidal tracts in typically developing children (controls) and in young patients with severe CP.

SUBJECTS AND METHODS
Subjects
Five CP patients (aged 5 to 23 years) diagnosed according to the criteria of Rosenbaum et al. and 10 controls (aged 5 to 18 years) were included. One CP patient could speak, whereas the remainder were anarthric or severely dysarthric. Additional characteristics are shown in Table 8.1. This imaging study is a small part of a larger development and validation study of the C-BiLLT instrument, which is a study with approval of the local ethical committee and for which study written informed consent was obtained. Six healthy controls were scanned with a routine imaging protocol including the short DTI sequence. All CP patients and four of the controls were scanned as part of routine clinical investigation, including the short DTI
sequence. The four controls had an unremarkable conventional magnetic resonance (MR) imaging and showed no neurological abnormalities (Table 8.1).

**Language Comprehension**

Language comprehension of the CP patients was investigated using C-BiLLT. In this instrument, patients are requested to select one image (out of two or four images) that corresponds to a spoken sentence (for example: “Where is the car?”). Subjects can select images using a touch screen, switch activators, or eye movement fixation (for details see Geytenbeek et al.). The C-BiLLT is norm referenced for children aged 1;6 to 6;6 years, and scores of patients are expressed as age equivalents (AEs), representing the same age range (in months) for a particular age-group.

**Magnetic Resonance Acquisition**

An MR examination of the head was performed on a 1.5-Tesla whole-body MRI scanner using a phased-array head coil (Siemens Sonata, Erlangen, Germany). Apart from anatomical images, DTI was obtained with an echo-planar imaging (EPI) sequence using one reference volume with $b=0$ s mm$^2$ and 12 diffusion-weighted directions with $b=750$ s mm$^2$. Two averages were obtained. Other acquisition parameters were TR/TE = 6,700/81 ms and 2.5-mm isotropic resolution for all 10 controls and 3 CP patients, and TR/TE = 10,000/90 ms and 2-mm isotropic resolution for two CP patients.

**Analysis**

Tractography was performed using FMRIB Software Library (FSL). Regions of interest, which were used as masks for tractography, were defined in two anatomical atlases: the Harvard–Oxford cortical and subcortical structural atlases (http://www.cma.mgh.harvard.edu/fsl_atlas.html) and the Johns Hopkins University (JHU) white-matter atlas (http://cmrm.med.jhmi.edu/).

Language tracts were measured in both hemispheres. The Wernicke area was defined in the superior temporal gyrus: posterior division (10) and planum temporale (46) from the Harvard–Oxford atlas. The Broca area was defined in the inferior frontal gyrus: pars triangularis (5) and pars opercularis (6) from the Harvard–Oxford atlas. Bilateral pyramidal tracts were measured as the control tract. Masks for this tract were motor cortex (precentral gyrus (7) from the Harvard–Oxford atlas) and cerebral peduncle (15 and 16 in the JHU atlas).

All masks, which were defined in the Montreal Neurological Institute (MNI) standard space, were nonlinerly transformed to individual subject space using FNIRT from FSL. Connectivity distributions between masks were calculated with probtrackX in FSL. Pixels were included in a tract when at least 5% of the total number of estimated tracts passed through that pixel.
Table 8.1
Characteristics of the subjects and results from tractography.

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<th>Patients</th>
<th>Age</th>
<th>M/F</th>
<th>Type</th>
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<th>Speaking</th>
<th>C-BiLLT&lt;sup&gt;a&lt;/sup&gt; AE score</th>
<th>Volume (cm&lt;sup&gt;3&lt;/sup&gt;)</th>
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<td>V</td>
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<th>C-BiLLT&lt;sup&gt;a&lt;/sup&gt; AE score</th>
<th>Volume (cm&lt;sup&gt;3&lt;/sup&gt;)</th>
<th>Mean FA</th>
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<td>0.4 0.6 0.8 0.5</td>
<td>0.03 0.03 0.02 0.03</td>
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</table>

Abbreviations: F, female; M, male; FA, Fractional anisotropy; GMFCS, Gross Motor Function Classification Scale; C-BiLLT, Computer-based instrument for low motor language testing; AE, age-equivalent score (in months); Pyr, Pyramidal tract; R, Right; L, Left; Lan, Language tract; m, month; y, year; p<0.05 vs controls.
For each tract, the size was obtained as well as the mean fractional anisotropy (FA). Values were expressed as mean with standard deviation. All methods following selection of masks in standard space are independent of an investigator. Because of potential problems with transformation of masks from standard space to individual subject space, especially for the CP children, the position of the masks was carefully checked.

Differences between controls and CP patients were analyzed with the nonparametric Mann–Whitney test (IBM SPSS version 20.0, Armonk, New York).

RESULTS

The patients’ characteristics and results are shown in Table 8.1. Two patients did not respond to C-BiLL T (patients 2 and 3), and the scores of the three other CP patients were not appropriate for age (Table 8.1). On the conventional MR images of the CP patients, we observed abnormalities in the following brain areas: central cortex, putamen, and thalamus (patient 1); white matter (severe loss) putamen, caudate nucleus, and thalamus (Patient 2); ventricles (abnormal wide) (patient 3); putamen and thalamus (patient 4); and thalamus (patient 5).

Language Tracts

In all controls, the language tracts could be visualized in both hemispheres (Figure 8.1A). The tract size was $5.4 \pm 0.8 \text{ cm}^3$ in the left hemisphere and $5.1 \pm 0.5 \text{ cm}^3$ in the right hemisphere. Mean FA was $0.42 \pm 0.02$ and $0.40 \pm 0.03$, respectively.

In four CP patients, the left language tract could be visualized (Figure 8.1B). The mean tract size was $3.9 \pm 1.3 \text{ cm}^3 \ (p = 0.054 \ vs. \ controls)$ and mean FA was $0.39 \pm 0.08 \ (\text{nonsignificant} \ [\text{NS}] \ vs. \ controls)$. The right language tract could be visualized in all CP patients (mean tract size $3.1 \pm 1.7 \text{ cm}^3$, $p < 0.05 \ vs. \ controls$, mean FA $0.31 \pm 0.14$, NS vs. controls). In Patient 2 the left language tract could not be visualized at all (Figure 8.1C), and the right tract was small with a very low FA value, causing a low group average.

Pyramidal Tracts

Averaged over hemispheres, in controls the pyramidal tracts measured $6.0 \pm 0.5 \text{ cm}^3$ and had a mean FA of $0.48 \pm 0.03$. In CP patients the pyramidal tracts were smaller and more variable with a size of $4.0 \pm 1.5 \text{ cm}^3 \ (p < 0.05 \ vs. \ controls)$ and mean FA of $0.43 \pm 0.14 \ (\text{NS} \ vs. \ controls)$.

DISCUSSION

In the present study, visualization of the language tracts with DTI was possible in controls and in young CP patients. In all controls, the language tracts were visualized in both hemispheres. In CP patients, tract sizes were smaller and FA values more variable than in controls. Language comprehension scores (measured as C-BiLLT scores) of three patients were not appropriate for age and two patients did not respond to the C-BiLLT questions at all. In one of these latter patients the language tract could not be visualized. The other patient showed normal tract sizes in both hemispheres.
In four CP patients, the tract size was smaller and/or the FA of the pyramidal tracts was lower than in controls. This is in line with another study showing smaller tract size (lower number of fibers) and lower FA values of the pyramidal tract (at the level of the posterior limb of the internal capsule) in spastic CP patients. However, our patient 3 displayed a normal tract volume and FA of the corticospinal tract despite severe limited mobility. A possible explanation for this might be the selective damage to the basal ganglia in this patient, which caused pure dystonia without spasticity.

This preliminary study has a small sample size and used a simple DTI sequence with 12 directions and a short acquisition time of 3 minutes. In addition, analysis of the results may be influenced by the use of smaller voxel sizes in the DTI protocol of patients 4 and 5, possibly yielding higher FA values due to a lower signal-to-noise ratio. Some of the controls had comorbidity as epilepsy, mild mental retardation, and pervasive developmental disorder (PDD). This might have influenced the data for the controls as previously suggested. However, the reported effects on mean diffusivity and general network connectivity were relatively small, ranging from a 1 to 2% decrease to a 10% increase. The authors of one study showed similar FA values in the arcuate fasciculus for controls and children with autism spectrum disorders. Therefore, inclusion of the children with PDD cannot explain the found difference between “controls” and CP patients in our study. We performed additional analyses excluding these three subjects and we found a similar effect on the tract size (i.e., decrease in CP patients). Therefore, in our opinion the results indicate differences between patients and controls with regard to tract integrity. It should be noted that the CP patients had severe anatomical brain damage, which influenced the definition of brain masks for tractography. The use of anatomical atlases defined in standard space, (nonlinearly) transformed into individual subject space, allows a comparison to be made between subjects. The tractography masks that were selected in the brain atlas in MNI space are large and, therefore, the position of the masks transformed to subject space was quite robust to the potential problems mentioned above. For all subjects the position of the masks was checked in subject space. For larger groups, definition of brain masks could even be improved using a combination of brain atlases and structural three-dimensional (3D)-MRI data of CP patients.

CONCLUSION
DTI is a promising method to visualize language tracts. In the present study, most patients with severe CP had detectable language tracts, though smaller and with lower FA than controls, suggesting a lower integrity. This disturbed integrity of language pathways coincided with severely hampered language comprehension. Structural identification of the language tracts using DTI could be important in understanding language impairment in CP, justifying further research in this field.
Figure 8.1
Bilateral pyramidal tracts are visualized on a high-resolution T1-weighted coronal image (left column). The pyramidal tracts are shown in red/yellow and the corresponding masks in green (precentral gyrus) and blue (cerebral peduncle). Yellow indicates high probability, based on probabilistic tractography. Left and right language tracts are visualized on high-resolution T1-weighted sagittal images (middle and right column). The language tracts are shown in blue/light blue and the corresponding masks in red (Broca) and yellow (Wernicke). Light blue indicates high probability. (A) In Control 4, all tracts are well visualized. (B) In Patient 1, all tracts are well visualized. (C) In Patient 2, the pyramidal tracts are visualized, whereas a possibly language-related tract is only marginally visible in the right hemisphere, with a low mean fractional anisotropy (FA = 0.10); this patient did not respond to the computer-based instrument for low motor language testing.
References


