

Research report

Corpus callosum size in children with developmental language disorder

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Abstract

Using high-resolution in-vivo magnetic resonance morphometry of the midsagittal area of the corpus callosum (CC) and four callosal subareas in 21 children with developmental language disorder (DLD) of the phonologic–syntactic type we found no significant anatomical differences in comparison to an age- and gender-matched normal control group. There was also no significant between-group difference when the ~7% smaller forebrain volume among children with DLD was accounted for by relating CC measures to forebrain volume. Only a tendency towards a larger anterior and middle CC in relation to forebrain volume was found in DLD children. In our DLD children we found the same relationship between CC midsagittal size and forebrain volume as recently reported for normal adults, namely, that the CC area increases to the two-third power of forebrain volume. © 2000 Elsevier Science B.V. All rights reserved.

Theme: Neuronal basis of behavior

Topic: Cognition

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1. Introduction

Abnormalities that originate in the cerebral cortex may be reflected by abnormalities in the corpus callosum (CC) which connects the hemispheres. The CC seems to be important for the transfer and facilitation of associative information between the hemispheres [25]. It is topographically organized, with projections from specific cortical areas to specific regions of the CC, as shown in rhesus monkeys [30] and humans [6]. One hypothesis [12,13] has suggested that interhemispheric connections are negatively correlated with anatomical and functional asymmetries. This would imply that more symmetric brains have a stronger interhemispheric connectivity, which may be reflected by a larger size of the CC or its subregions [1,4,28,43,47,48,50]. Dyslexia is a developmental con-

dition with a presumed disturbance of normal asymmetry. Of four published papers comparing CC measures between dyslexics and controls [9,17,24,37] two found a larger CC in dyslexics, especially in the splenium [9,37]. This finding was explained by an increased perisylvian symmetry in this disorder [16,22,23].

The question of atypical cerebral asymmetry and accompanying abnormalities of the CC in dyslexia and developmental language disorder (DLD) is still under discussion. There are only two studies presenting CC data in developmental disorders of language (DLD) [11,27]. Gauger et al. [11] mentions normal total CC size as a result in passing in an MR morphometric study of children with DLD, and in the study of Njokiktjien et al. [27] the subgroup of children who exhibited both familial dysphasia and dyslexia had a larger CC than non-familial patients. Brain volume and subregions of the CC were not measured, and a distinct linguistic classification was not reported. An accepted definition and classification of DLD is that of Rapin et al. [34,35], where the subtype with

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predominant receptive–expressive deficits of phonology and grammar, the phonologic–syntactic subtype of DLD, is the most common. The present study was designed to further investigate whether there might be structural differences in CC morphology between DLD children and carefully selected control children. In order to account for possible between-group differences in brain size, we also related the CC area measures to forebrain volume (FBV).

2. Materials and methods

2.1. Study population

The 21 children with DLD of the phonologic–syntactic type (age range, 4 to 10 years; mean age \pm S.D., 100 ± 21 months) came from two schools for language-impaired children ($n=18$) located in Düsseldorf and Neuss/Germany, and from the Department of Pediatrics at the University of Düsseldorf, where they had been referred for examination ($n=3$). In 18 children a family history of language impairment, dyslexia or learning difficulties was reported. Family members were not examined. All children were normal upon clinical neurological examination, audiometry, and electroencephalography and had to fulfil several inclusion criteria. Their nonverbal IQ had to be above 85 according to Raven's Coloured Progressive Matrices [36] (mean IQ \pm S.D., 101.4 ± 10.2). One child aged 4.2 years (too young for the Raven test) had a score above 85 on the nonverbal scale of the Kaufman-Assessment Battery for Children [20] (German version: K-ABC [26]). All DLD children were self-reported right-handers which was corroborated by standardized hand preference and skill tests (11 tasks from the lateralization score of Denckla's neurological examination for subtle signs [8] and a paper-and-pencil hand-dominance test (HDT) [41]). Population characteristics are given in Table 1. Data on the normal intrasylvian anatomical asymmetry of the same study population have been published recently [33].

A persisting phonological and grammatical deficit was confirmed by a series of standardized linguistic tests (see Table 2): six grammatical subtests from the Heidelberger Sprachentwicklungstest [14] (Heidelberger test of language development), three subtests ('Grammatical closure', 'Auditory closure', 'Sound blending') from the Illinois Test of Psycholinguistic Abilities [21] (German version: Psycholinguistischer Entwicklungstest [2]) and Fried's expressive phonological test [10] of single-word articulation skill. Inclusion criteria were a value >1.5 S.D. below the normal age-adjusted mean value in at least one of the seven grammatical tests listed in Table 2, and, in addition, for children below the age of 8 years, a value >1.5 S.D. below the normal age-adjusted mean value in the expressive phonological test. The five children belonging to this age group showed a mean \pm S.D. percentile rank of $0.6 \pm 1.3\%$ in this test.

Table 1
Population characteristics^a

	DLD children	Control
Number of subjects	21	21
Gender: male (female)	14 (7)	14 (7)
Age (months, mean \pm S.D.)	100 ± 21	99 ± 21
Handedness score (HDT, mean \pm S.D.)	42.13 ± 18.38	50.65 ± 26.98
Raven IQ (mean \pm S.D.)	$101.35 \pm 10.19^*$	111.20 ± 2.15
K-ABC (means \pm S.D.)		
Sequential scale	$81.9 \pm 11.4^*$	100.3 ± 9.6
Simultaneous scale	$95.7 \pm 11.7^*$	107.7 ± 10.7
Nonverbal scale	$93.7 \pm 13.7^*$	108.1 ± 11.9
Achievement scale	$75.2 \pm 9.5^*$	107.8 ± 9.4
Subtest: reading/decoding (%)	$40.8 \pm 37.3^*$	78.9 ± 26.8
Subtest: reading/understanding	$77.6 \pm 12.6^*$	106.9 ± 8.1

^a HDT, paper-pencil hand-dominance test; Raven, Coloured Progressive Matrices; K-ABC, Kaufman-Assessment Battery for Children; S.D., standard deviation. Note: the standardized means of all psychometric tests are 100 with 1 S.D.=15, except the results of the subtest reading/decoding which are given as percentage rank (mean 50%).

* Significant difference compared to control group ($P < 0.01$).

The 21 age-, handedness- and gender-matched children of the control group came mainly from families of medical staff members of the University of Düsseldorf, or from their close friends. They had no neuropsychiatric disorders, no history of language impairment, no dyslexia, and no phonological or grammatical deficits according to the same tests that were conducted with the DLD children. All parents of all 42 children gave informed consent to the present study which had previously been approved by the Ethics Committee of the University of Düsseldorf.

2.2. In vivo MR morphometry

As in previous studies, we used a Siemens 1.5T magnet, and a 22-min fast-low-angle-shot MR sequence yielding 128 contiguous sagittal slices with $1.00 \times 1.00 \times 1.17$ mm image voxel size [42]. The midsagittal image (Fig. 1) was selected for segmentation of the CC as in previous studies [18,43,44]. The total midsagittal callosal area was divided into four subareas, according to Fig. 2. This subdivision refers to that of Witelson [46,47], except for the definition of the maximum CC length. To increase reliability we used an external reference axis, namely the line between anterior and posterior commissures (AC–PC line) (Fig. 1). Parallel to this line the maximum CC length was defined. The measurement of forebrain volume (FBV) was achieved by means of image segmentation, a computerized, stepwise procedure removing all tissue and fluid not corresponding to brain gray or white matter from each of the 128 slices of each dataset. The hindbrain was removed by a cut-off line between the base of the mamillary bodies and the upper margin of the posterior commissure. All measurements were performed by a blinded investigator (S.P.).

Table 2

Linguistic test battery and corresponding results for 21 children with DLD of the phonologic–syntactic type and the control group^a

	DLD children*		Control group	
	T-value		T-value	
	Mean	S.D.	Mean	S.D.
Subtests of the Heidelberger Sprachentwicklungstest				
Understanding of grammatical structures	35.8	7.4	54.7	5.4
Production of plural and singular	34.5	12.4	60.3	7.6
Imitation of grammatical structures	22.5	8.0	56.2	3.6
Derivation morphology	39.2	6.8	61.4	5.8
Adjective derivation	38.2	8.7	59.3	5.0
Sentence production	27.0	10.8	66.5	6.2
Subtests of the Illinois Test of Psycholinguistic Abilities (German version)				
Grammatical closure	37.4	9.3	62.1	5.9
Auditory closure	35.6	13.8	60.5	5.0
Sound blending	37.8	10.9	58.9	6.2

^a Note: normal mean *T*-value is 50 and 1 S.D. is 10.* Significant difference compared to control group for each subtest ($P < 0.001$, respectively).

2.3. Statistical analysis

Four different CC measurements were used as dependent variables in the present study: (i) absolute CC area and subareas, (ii) CC subareas related to total CC, (iii) CC ratios (CC area and subareas relative to FBV), and (iv) adjusted CC ratios (CC area and subareas relative to $FBV^{0.67}$). These measurements (i)–(iii) were also used in a recent study on the relationship between CC size and

FBV in adults [18]. In the study presented here we further added the transformed brain size measurement $FBV^{0.67}$ as done by Holloway et al. [15]. Because there was no unique relationship between CC measurements and FBV for both groups, it was impossible to calculate analysis of covariance with FBV as covariate. To further analyse possible allometric covariations, power functions were calculated to explain the relationships between forebrain volume and callosal size as

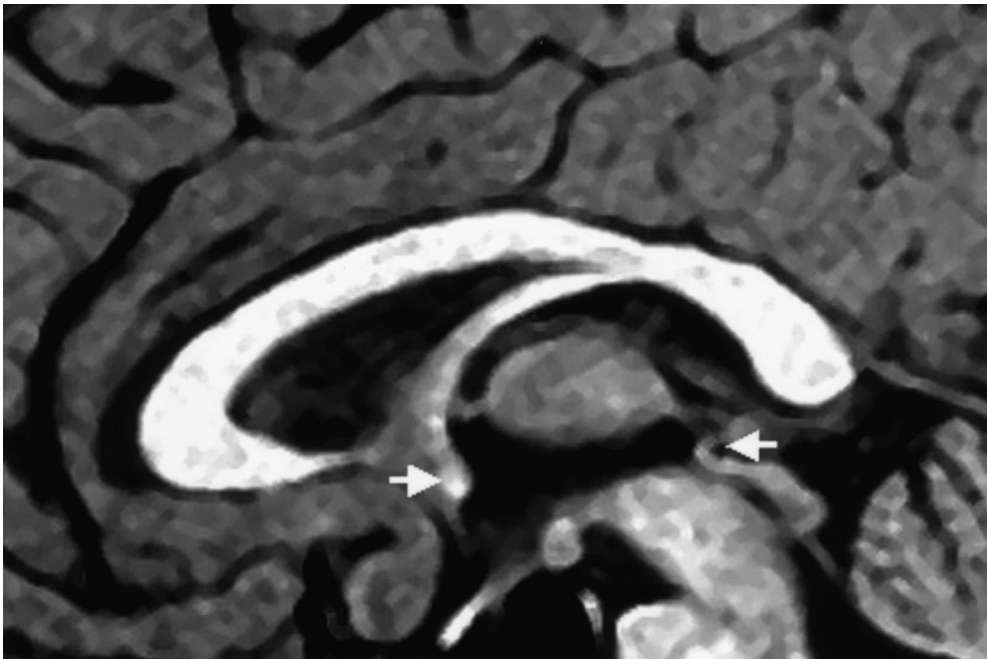


Fig. 1. Detail of a midsagittal MRI of the corpus callosum (CC). White arrows indicate the anterior and posterior commissures.

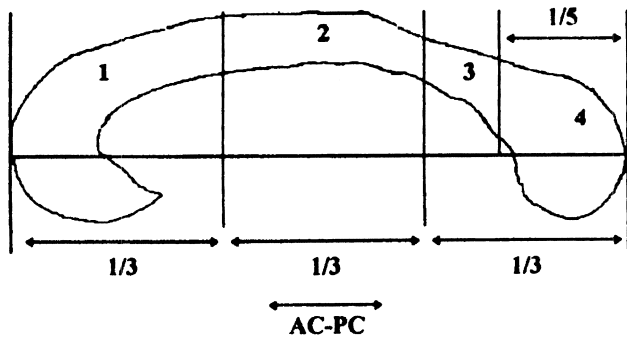


Fig. 2. Anatomical subdivision of the corpus callosum (CC) used in the present study. The maximum anterior–posterior length of the CC is determined parallel to the bicommissural line (AC–PC). The CC is divided into four subareas as delineated in the figure (1, anterior third; 2, middle third; 3, isthmus; 4, splenium).

$$CC = \text{constant} \times \text{FBV}^{\text{exponent}} \quad (1)$$

The exponents of power functions are the main messages (allometric signals) carried by the power functions. They are used to detect proportionality or deviations from proportionality. As demonstrated in earlier papers [15,18], the exponents are useful to evaluate whether the CC to FBV relationship follows a simple geometric rule. According to this rule, the geometric size of a cross-sectional area of a three-dimensional object does not increase proportionally to the volume of this object, but only to the two-thirds power of the volume. If the surface to volume relationship follows this geometrical rule the exponents are 0.67. In this case smaller brains have, relative to their brain volumes, larger cross-sectional CC surfaces than larger brains. In order to test whether the CC to FBV relationship deviates from proportionality in the children examined here, the exponents were tested for deviation from 1 because an exponent of 1 indicates exact proportionality. Because of this, CC area measurements and FBV were logarithmically transformed and the allometric equation was expressed as

$$\log CC = \log \text{constant} + b \times \log \text{FBV} \quad (2)$$

where b is the slope of the regression line and equals the exponent of formula 1. Applying the b and the appropriate S.D. of b ($S.D._b$) tests for deviation of proportionality were

carried out using the formula $(b - 1)/S.D._b$ according to Sachs [38].

Additionally, the effect size was computed, because it is not only important how probable an effect is, but also how large. Effect size was calculated in terms of variance accounted for [31]. For instance, an effect size of 0.10 (conventionally termed η^2) for the between-groups difference would state that 10% of observed variance in the dependent variable is due to the between-groups variable. According to the Bonferroni correction a significance level of $P < 0.0025$ ($0.05/20$) was chosen, since 20 tests were performed (six absolute measures, four measures of CC subareas related to total CC, five CC measures related to FBV, and five CC measures related to $\text{FBV}^{0.67}$). All statistical analyses were performed using the SPSS for Windows software package, version 8.0.

3. Results

As shown in Table 3 the FBV was 1058 ml for DLD children and 1138 ml for controls, thus, slightly larger for controls than for DLD children ($P = 0.017$). Neither group differed in absolute total CC area and CC subarea measures, although the DLD children tended to have a smaller splenium. Furthermore, CC subareas related to total CC showed no group differences, except for the relative isthmus which tended to be smaller in DLD children (Table 4).

Because there was a between-group difference in fore-brain volume (FBV), the CC measures were also adjusted for FBV. Subjecting these CC ratios to the statistical analyses a trend emerged towards a between-group difference for the anterior CC/FBV ratio ($P = 0.03$) and middle CC/FBV ratio ($P = 0.05$) (Table 5).

As already mentioned, the relationship between CC and FBV might not be proportional. Thus, we calculated an allometric equation, which revealed significant relationships between all CC measurements and FBV (except for the relatively small isthmus). The mean slope (or exponents) for the allometric relations was 0.5 for the total sample and each slope differed significantly from proportionality. However, they did not differ significantly

Table 3
Absolute morphometric data for 21 DLD children and the control group

	DLD children		Control group		T^a	P^a (two-tailed)	η^2
	Mean	S.D.	Mean	S.D.			
Forebrain volume (ml)	1058	116	1138	92	2.490	0.017	0.130
Total corpus callosum (mm^2)	674.6	95.2	682.4	80.0	0.288	0.775	0.002
Anterior third (mm^2)	283.3	40.4	278.7	39.9	0.373	0.711	0.003
Middle third (mm^2)	165.3	28.0	162.6	18.5	0.371	0.713	0.003
Isthmus (mm^2)	65.0	11.8	65.4	11.7	0.118	0.907	0.000
Splenium (mm^2)	161.0	25.7	175.8	29.7	1.710	0.094	0.069

^a T , T -value from t -test for independent samples; P , two-sided P -value.

Table 4

Midsagittal corpus callosum (CC) area and subareas relative to total CC for 21 DLD children and the control group

	DLD children		Control group		T^a	P^a (two-tailed)	ETA ²
	Mean	S.D.	Mean	S.D.			
Anterior third/CC	0.42	0.02	0.41	0.03	1.64	0.11	0.063
Middle third/CC	0.24	0.02	0.24	0.02	1.02	0.31	0.026
Isthmus/CC	0.24	0.02	0.26	0.02	2.65	0.01	0.149
Splenium/CC	0.10	0.01	0.10	0.02	0.05	0.96	0.000

^a T , T -value from t -test for independent samples; P , two-sided P -value.

Table 5

Corpus callosum (CC) ratios for 21 DLD children and the control group (=midsagittal CC area and subareas relative to forebrain volume FBV)

	DLD children		Control group		T^a	P^a (two-tailed)	ETA ²
	Mean	S.D.	Mean	S.D.			
Total CC/FBV	640.64	82.07	601.41	69.05	1.67	0.10	0.066
Anterior CC/FBV	268.86	33.80	245.37	32.79	2.28	0.03	0.116
Middle CC/FBV	156.97	25.10	143.47	17.88	2.01	0.05	0.092
Isthmus/FBV	61.65	10.57	57.91	11.85	1.08	0.29	0.028
Splenium/FBV	153.16	23.32	154.66	24.06	0.20	0.84	0.001

^a T , T -value from t -test for independent samples; P , two-sided P -value.

from the geometrical rule that the size of a cross-sectional area of a three-dimensional object increases to the two third power of the volume [39], expressed by the exponent $FBV^{0.67}$. Analysing each group separately there were non-significant relations between CC measurements and FBV for the control subjects. Although this relationship was non-significant, the slopes for the allometric relation of the control group were in principle similar to those of the DLD group, because they differed significantly from proportionality, thus indicating that this relationship also follows the geometrical rule. The DLD children exhibited slightly steeper slopes than the controls (see equations in Fig. 3).

The relationship between CC and FBV was not proportional. It was less than proportional following the previously mentioned geometrical rule with an exponent of 0.67, as we found no significant difference between the exponents calculated for our sample and the exponent 0.67. Thus, we also calculated the midsagittal CC area and subareas relative to $FBV^{0.67}$. These data are presented in Table 6. Again, there were no significant between-group differences. However, the DLD children tended to have higher $CC/FBV^{0.67}$ values for total CC and subareas than the control group, except for the splenium. In particular the anterior and middle third of the $CC/FBV^{0.67}$ again tended

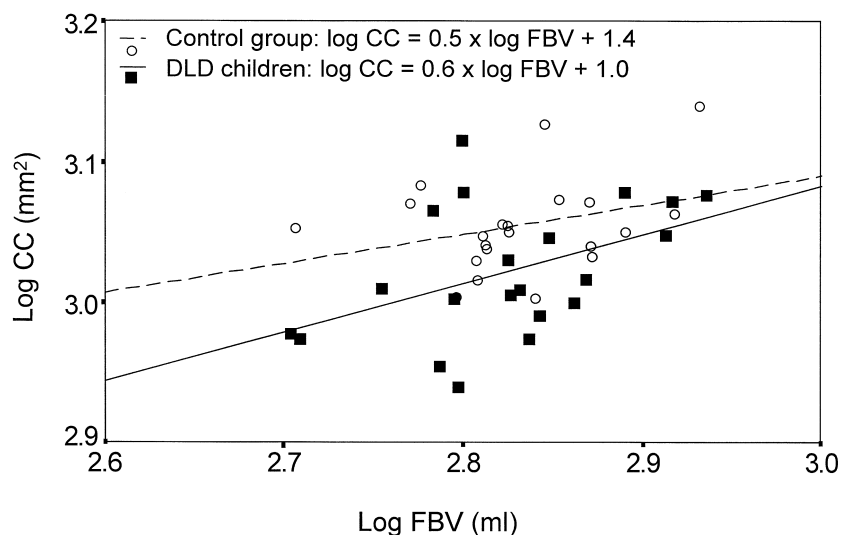


Fig. 3. Total corpus callosum (CC in $\log \text{mm}^2$) and forebrain volume (FBV in $\log \text{ml}$) in children with developmental language disorder (filled squares) and control group (unfilled circles). The regression slope for the control group is the dashed line.

Table 6

Adjusted corpus callosum (CC) ratios for 21 DLD children and the control group (=midsagittal CC area and subareas relative to forebrain volume $FBV^{0.67}$)

	DLD children		Control group		T^a	P^a (two-tailed)	ETA ²
	Mean	S.D.	Mean	S.D.			
Total CC/ $FBV^{0.67}$	650.86	80.048	626.60	68.40	1.01	0.32	0.027
Anterior CC/ $FBV^{0.67}$	273.21	33.408	255.72	33.46	1.69	0.10	0.067
Middle CC/ $FBV^{0.67}$	159.47	24.661	149.41	17.24	1.51	0.13	0.055
Isthmus/ $FBV^{0.67}$	62.65	10.508	60.24	11.72	0.69	0.49	0.012
Splenium/ $FBV^{0.67}$	155.54	22.852	161.22	25.00	0.99	0.45	0.015

^a T , T -value from t -test for independent samples; P , two-sided P -value.

to be larger in DLD children than in control children (see Fig. 4).

4. Discussion

We found no significant difference between DLD children and an age- and gender-matched control group for the absolute CC and CC subareas as well as for CC ratios (Tables 3–6). We included forebrain volume (FBV) into our analysis (Tables 5 and 6). This has not been done by most previous studies, although some measured the supratentorial [17] or the total midsagittal brain area [9,37]. However, DeLacoste et al. [7] have demonstrated that such measures are unreliable for estimating total brain size. Measurement of FBV is of further interest because there is no simple proportionality between CC and brain volume. The relationship between both measures follows the geometrical rule that smaller bodies have, relative to their

volume, larger cross-sectional surfaces than larger bodies of the same shape [18,19,39]. In this study the relationship between CC and FBV did not differ from the well-known relationship that the size of a cross-sectional area of a three-dimensional object increases to the two third power of the volume, expressed by the exponent $FBV^{0.67}$ (Fig. 3).

It was not possible for us to match for nonverbal IQ and socio-economic background because it is difficult to perform MR scans with healthy young children when they and their parents are not interested in such scientific investigations. Thus, the control children came mainly from families of medical staff members or their friends, whereas most of the DLD children were from public schools for language-impaired children. We are aware of speculations concerning a possible relationship between socio-economic status, birthweight, brain size, and intellectual function [29] (for a summary see Refs. [32,49]). However, we argue for caution in drawing conclusions regarding the significance of this interpretation. Neverthe-

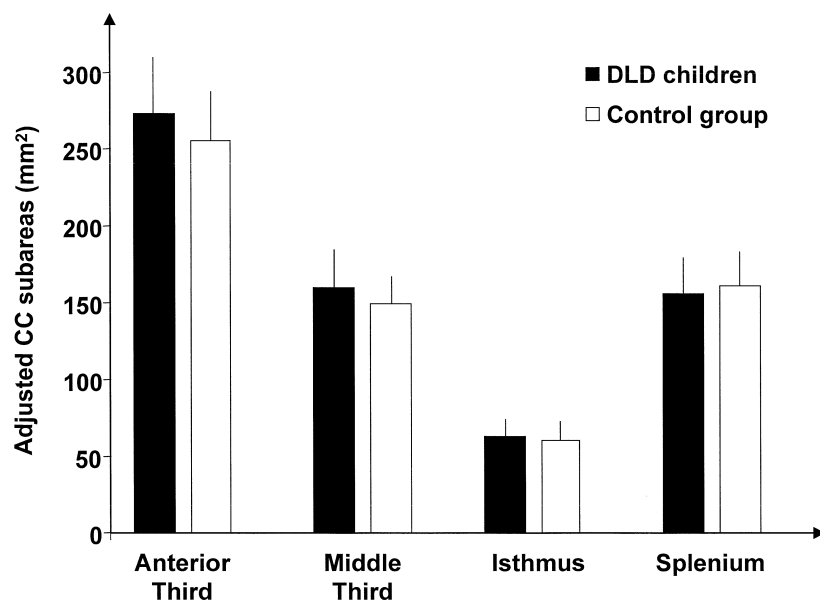


Fig. 4. Adjusted corpus callosum (CC) subareas (mm^2) of children with developmental language disorder (filled columns) and control group. CC subareas are adjusted to the corrected forebrain volume ($FBV^{0.67}$).

less, it is unlikely that a social gradient is responsible for the observed lack of a significant difference in CC and its subareas.

Most studies of the CC in learning disabilities have been performed with dyslexic people and reported a larger CC and a larger splenium in affected persons compared to controls [9,37,40]. Our investigation has focused on DLD children. Although some experimental data in children with DLD and dyslexia suggest that both disorders may be due to a basic temporal processing impairment [45], dyslexia seems to be characterized by a more severe deficit in reading decoding than reading comprehension [5], whereas a contrary pattern is found in DLD [3]. In our DLD children this pattern can be seen in the subtests 'reading/decoding' and 'reading/comprehension' (see Table 1). Thus, it cannot be excluded that developmental dyslexia represents a separate diagnostic entity with differences in anatomical and physiological substrates.

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