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The role of gene DCDC2 in German dyslexics

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Abstract Dyslexia is a complex reading and writing disorder with a strong genetic component. In a German case-control cohort, we studied the influence of the suspected dyslexia-associated gene DCDC2. For the first time in a German cohort, we describe association of a 2445 basepair deletion, first identified in an American study. Evidence of association for three DCDC2 single nucleotide polymorphisms (rs807724, rs793862, rs807701), previously identified in German or American cohorts, was replicated. A haplotype of these polymorphisms showed evidence for association as well. Thus, our data further corroborate association of DCDC2 with dyslexia. Analysis of functional subgroups suggests association of investigated DCDC2 variants mainly with nondysphonetic, nonsevere, but probably dyseidetic (surface) dyslexia. Based on the presumed function of DCDC2, our findings point to a role of impaired neuronal migration in the etiology of the disease.

Keywords DCDC2 · Genetics · Genetics of dyslexia · Germans · Subgroups · Subgroup-specificity

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Introduction

Dyslexia is a complex disease, affecting at least 4% (Lewis, 1994) of all schoolchildren. It is characterized by extreme difficulties in acquiring skills in reading and writing, causing severe problems for children, parents, and teachers. Based on twin studies (Stevenson, 1991; Olson et al., 1994), genetic influence is estimated at 60–70%. Several genomic regions were identified which may contain genetic variants related to dyslexia (Grigorenko et al., 1997; Schulte-Körne et al., 1998). Therefore, further studies investigating specific genes within these regions appear to be a very promising approach leading to a better understanding of dyslexia. The aim of this study was to verify and refine recent findings from Anglo-Saxon studies in a German case-control cohort because it is crucial to regard the influence of different languages in dyslexia. Although both, English and German, belong to the Indo-Germanic languages, there are strong differences in the regularity of the grapheme-phoneme correspondence. So the same genes could have different consequences for dyslexia in both languages.

In genome scans, the best replicated regions concerning dyslexia are located on chromosomes 6 and 15 (overview in appendix I in the supplementary material) (Nöthen et al., 1999; Müller-Myhsok and Grimm, 1999; Schulte-Körne et al., 1998). From region 6p22.2, several genes have been studied previously (Cope et al., 2005; Schumacher et al., 2006; Harold et al., 2006; Brkanac et al., 2007; Luciano, 2007). Of these, we examined DCDC2 at the single nucleotide polymorphism (SNP) level. Additionally, a 2,445bp deletion in DCDC2, which was initially described in an American cohort (Meng et al., 2005), was included in our study.

Previous research showed association of the DCDC2 SNP rs807724 in an American cohort (Meng et al., 2005). Additionally, Meng et al. (2005) found a 2,445-bp stretch of DNA missing within DCDC2 (deletion) in about 17% of dyslexics. Two other DCDC2-SNPs, rs793862 and rs807701, showed association with dyslexia in a German study (Schumacher et al., 2006). Harold et al. (2006) examined all four markers in a British cohort, but only found the deletion associating and a weak trend for rs793862. Recently, Brkanac et al. (2007) could not replicate these findings for the SNPs in an American cohort, but also found evidence for association of the deletion.

The known role of DCDC2 in neuronal migration (Karl, 2004) provides an interesting hypothesis regarding the connection between DCDC2 and dyslexia. DCDC2 is expressed in neuronal precursor cells but not in adult neurons. It contains doublecortin domains whose function is known to be similar to the doublecortin-gene (DCX). DCX is expressed in the developing cortex and involved in stabilization and migration of neurons. The known function of doublecortin-domains is to bundle and stabilize microtubules, which are essential in neuronal migration (Moores et al., 2004). Doublecortin also participates by means of the Golgi apparatus in directed neuronal migration (Friocourt et al., 2003). A complete lack of doublecortin results in severe brain defects (Gleeson et al., 1998). Studies of the DCDC2-related DCX gene indicate that a deletion similar to that observed in DCDC2 is located in a regulatory region and influences the level of gene expression (Karl, 2004). Losses in this region induce decreased expression. Other data showed morphological differences in brains of dyslexics (Galaburda and Livingstone, 1993).

Dyslexia represents a phenotype comprising several subgroups according to various definitions. One definition defines the following subgroups (Boder, 1971).

Dysphonetic dyslexia This kind of dyslexia is also known as auditive-phonological type (Schulte-Körne et al., 1993), dysphonetic type (Reuter-Liehr, 1993), or phonologic dyslexia

(Coltheart, Masterson, Byng, Prior, & Riddoch 1983). It is characterized by problems in differentiation and synthesis of sounds. Children with the dysphonetic subtype have difficulties with reading (decoding) and/or writing (encoding), due to disturbed ability to segment phonetically regular words into their components (syllables, phonems). The affected children recognize words mostly due to their graphical appearance, which strongly limits the amount of vocabulary. Words are seen as a single unit. The semantic system immediately associates the meaning of the word. In case of unknown words, dysphonetic children guess (mostly on the basis of the initial letter) instead of using phonetic rules. The phonetical analysis of a word is slow and causes trouble. Accordingly, rhyme perception, rhyming, and reading of nonwords is difficult. (Coltheart et al., 1983). Spelling is nonphonetic; the visual word-memory is used. Other, nondysphonetic types of dyslexia include dyseidetic dyslexia.

Dyseidetic dyslexia This kind of dyslexia is also known as visual-receptive type (Schulte-Körne et al., 1993) or surface dyslexia (Coltheart et al., 1983). Dyseidetics have problems with visual perception concerning the discrimination of written words. Due to a hampered ability to graphemically remember irregular word forms, difficulties in decoding and encoding arise. The affected children focus on phonem- and not graphem-structure, i.e., irregular words are spelled phonetically correct but orthographically wrong. When a word is graphemically analyzed, similar letters or letters differing only in their spacial orientation (e.g., bd, pq, sz) cause problems. Even "mirror" reading or writing appears (e.g., mood| doom). Due to the deficits in visual word and letter recognition, omission of letters or whole words is common. Furthermore, children of the dyseidetic subtype often lose line or word position during reading (Coltheart et al., 1983).

Addtionally, mixed forms of the different dyslexia subtypes are common. For example, dysphoneidetics have problems with language processing in the visual, as well as in the auditive, system. The dysphoneidetic type is also considered to be the most severe form of dyslexia.

The phenotype "dyslexia" appears to be a common name for a condition with potentially different causes. Therefore, phenotype definition and subgroup analysis are crucial aspects of phenotype–genotype association studies of dyslexia.

We performed a case-control study on several SNPs and a deletion, as well as haplotype analysis for the dyslexia-associated gene DCDC2. Additionally, cases were further phenotyped to identify dyslexia subgroups and to enable subgroup-specific analyses. Our results suggest a subgroup-specific association of DCDC2 variants with dyslexia.

Materials and methods

Ethical approval

Ethical approval was obtained from the Ethics Committee of the University of Leipzig and the regional school council Leipzig. Informed and written consent was obtained from subjects' parents.

Study group

The study group consisted of 72 dyslexics of German origin, of which 68 could be assigned to subgroups [severe cases (25) and nonsevere cases (43), respectively, dysphonetics (34) and nondysphonetics (34)]. Controls were 184 healthy blood donors of German origin.

We ascertained children with dyslexia in two stages: First, we contacted schools with special dyslexia classes, specializing in the education of children with reading difficulties. All children were diagnosed thoroughly by the local school board before entering these classes. Tests included letter knowledge, word reading, phoneme mergence, and reading comprehension. Additional tests in mathematics and poem recitation made sure that the children had no general learning or memory problems. Only children without math and memory problems are included in these classes.

In a second step, we did detailed intelligence and concentration tests and another reading and writing test specifically for subgroup classification. Inclusion criteria for probands were an IQ ≥85, no attention-deficit hyperactivity disorder (ADHD), and the verified diagnosis of dyslexia. IQ was tested with the nonlanguage based Culture Fair Test 20 (CFT-20) (Weiß, 1998), ADHD with the concentration test d2 (Brickenkamp and Zillmer, 2002). For the later analysis of dyslexia, we performed the reading and writing test KNUSPEL-L (Marx, 1998). Since KNUSPEL-L is a test specific for the German language, it will be described here in more detail: The test is suitable for children from second to fourth grade. Items are not staggered in difficulty because it is a moderate speed test. The test is based on a theoretical model of reading development and measures in four subtests the basic reading skills of recoding and decoding at word level, reading–understanding at sentence level, and the corresponding auditive understanding. Retest reliability is between r=0.83 (1–3 weeks) and r=0.85 (12 months). Ecological validity, i.e., correlation between teacher rating and test is between r=0.61 and r=0.67. Test interpretation is based on standardized scales compared to a normative sample, which also can be used to estimate severity by comparison. These scales were standardized with a test sample of n=4746 children (Marx, 2000).

All dyslexics in our study were from either the third or fourth grade and were subtyped for severity and the dysphonetic form of dyslexia (Boder, 1971). For classification, we applied a regression model for IQ-discrepancy scores with a standard deviation (SD) of 1.5, described in detail in Schulte-Körne et al. (2001). Severity was classified as results more than 1.5 SD below the average score for reading performance in the test sample. Additionally, we used 1.5 SD discrepancy scores between IQ and subtest 3 (decoding of misspelled, but phonetically regular words) of KNUSPEL-L to classify the dysphonetic subtype. Where the above mentioned criteria were not applicable, no assignment was given. Sixty eight of 72 children could be assigned to subtypes.

Genotyping

DNA was extracted from 8 ml venous EDTA blood with chemagen Magnetic Separation Module I (Chemagen, Germany) and from mouth-wash with Qiagen Blood&Tissue kit using standard procedures. PCR-primer design was implemented by use of the NCBI *dbSNP* and Ensembl databases and the computer programs muPlex (Rachlin et al., 2005), ePCR (Schuler, 1997), HumanBlat (Kent, 2002), and Netprimer (PREMIER Biosoft International, Palo Alto, CA). PCR-primers for the observed deletion in DCDC2 were used as published in Meng et al. (2005). All PCR-primers were obtained from MWG-Biotech (Ebersberg, Germany).

SNP genotyping was done using the GenoSNIP method with slight modifications (Wenzel, 2003; Kirsten et al., 2007). PCR reactions were performed under the following conditions: 10 μl reaction volume, initial denaturation at 95°C for 15 min, 40 cycles with denaturation at 95°C for 45 s, primer hybridization at 58°C for 45 s, and elongation at 72°C for 45 s. A final extension step was 72°C for 5 min. Reaction volumes consisted of 1 μl buffer B 10×, 1 μl $MgCl_2$ 25 mM, 0.16 μl HotFirePolTaq 5 U/μl (all from Solis Biodyne,

Tartu, Estonia), 0.08 µl dNTP 25 mM (Carl Roth GmbH, Karlsruhe, Germany), completed to 10 µl with primers and aqua bidest. Template was added as 1 µl DNA at 15 ng/µl.

The resulting PCR product was digested at 37°C for 1 h in the same tube by adding 2 µl of a mix containing exonuclease I (0.2 U) and shrimp alkaline phosphatase (0.3 U). Enzymes were inactivated at 80°C for 20 min.

Primers for single base extension reactions (SBE) were designed with photocleavable bases (Kirsten et al., 2006). All SBE primers were obtained from Biotez (Berlin, Germany). SBE reactions were performed under the following conditions: Initial denaturation at 95°C for 4 min, 44 cycles with denaturation at 94°C for 10 s, primer hybridization at 60°C for 30 s, and elongation at 72°C for 10 s. Reactions consisted of 1 µl buffer C 10×, 1 µl $MgCl_2$ 100 mM, 0.2 TermiPol (all from Solis Biodyne, Tartu, Estonia), 0.9 µl ddNTP 4×10 mM (Carl Roth GmbH), 12 µl digested PCR-product, completed to 18 µl with primer and aqua bidest. SBE products were detected using MALDI-TOF mass spectrometry (Bruker Daltonics, Leipzig, Germany) according to standard protocols. Genotype calling was done using *GenoTools* (Pusch et al., 2001) and in-house software.

The 2,445-bp deletion was detected by PCR using the above given conditions with primers as published (Meng et al., 2005). PCR products were detected using 2% agarose gels (Carl Roth GmbH) stained with ethidium bromide.

Occurrence of the homozygous deletion was always confirmed by sequencing (Eurofins MWG Gmbh; data not shown). Randomly chosen samples genotyped as heterozygous for the deletion and wild-type samples were also confirmed by sequencing (5% of samples).

Statistics

All genotypes were analyzed for association with dyslexia applying standard statistics for allelic odds ratio and Lathrop genetic relative risk calculations (Lathrop, 1983). Analysis of Hardy–Weinberg equilibrium in controls was used to evaluate genotyping quality. For haplotype analysis, the software *Haploview 4.1* was used (Barrett et al., 2005). To test significance of differences in allele frequencies, chi-square statistics or, if appropriate, Fisher's Exact Test was used. For differences of haplotypes, Fisher's Exact Test was used, and *p* values were corrected according to Bonferroni for the number of haplotypes (five). We confirmed haplotype analyses using HAPLORE, a program for haplotype reconstruction in individuals without recombination (Zhang et al., 2005). Minimum posterior probability of a correct haplotype was set to >90%. Haplotypes were successfully assigned to 95% of individuals with an average posterior probability of >99.7%. *Haploview 4.1* and HAPLORE results were similar and therefore HAPLORE results are shown.

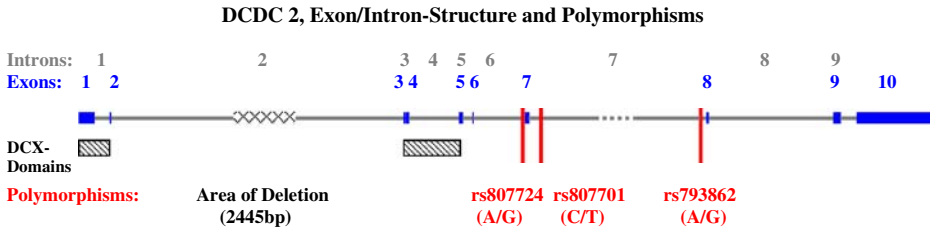

Fig. 1 Schematic view of DCDC2. The exon (coding regions)/intron (noncoding regions) structure of DCDC2. *Short vertical lines* indicate exons, *gray areas* introns. A *crossed area* marks the examined deletion, the examined polymorphisms are marked by *long vertical lines*. *Hatched areas* indicate doublecortin domains. (Meng et al. 2005, modified)

Table 1 Distribution of genotypes in cases and controls for all samples, respectively

Genotypes	Cases *n* (%)	Controls *n* (%)	Total *n* (%)	Association GRR or OR [CI95] (*p*-value)	
				GRR	OR
Deletion	*n*=72	*n*=184	*n*=256		
Deletion/deletion	2 (3)	0 (0)	2 (1)	18.7 [4.2–84.1] ($p<0.001$)	2.6 [1.2–5.3] ($p=0.010$)
Deletion/wild type	11 (15)	16 (9)	27 (11)	2.1[0.9–4.6]$p=0.079$	
Wild type/wild type	59 (82)	168 (91)	227 (89)	0.4 [0.2–0.9] $p=0.024$	
rs793862	*n*=72	*n*=177	*n*=249		
A/A	10 (14)	10 (6)	20 (8)	2.2 [1.1–4.7] ($p=0.038$)	
A/G	20 (28)	74 (42)	94 (38)	0.6[0.4–1.0] $p=0.077$	
G/G	42 (58)	93 (53)	135 (54)	n.s.	n.s
rs807701	*n*=72	*n*=171	*n*=243		
C/C	14 (19)	14 (8)	28 (12)	2.2 [1.2–4.4] ($p=0.019$)	
C/T	24 (33)	80 (47)	104 (43)	n.s.	
T/T	34 (47)	77 (45)	113 (47)	n.s.	n.s.
rs807724	*n*=72	*n*=177	*n*=249		
G/G	7 (10)	8 (5)	15 (6)	n.s.	
G/A	17 (24)	68 (38)	85 (34)	0.6 [0.3–1.0] ($p=0.044$)	
A/A	48 (67)	101 (57)	149 (60)	n.s.	n.s.

A detailed analysis of all single markers can be seen in appendix II.

GRR genetic relative risk of homozygous genotype versus all other genotypes, *OR* allelic odds ratio, *CI95* 95% confidence interval, *n* number of individuals, *n.s.* not significant

Results

DCDC2 was investigated for association with dyslexia and dyslexia subgroups. We studied four polymorphisms: three SNPs (rs807724 in intron 6, rs793862 and rs807701 in intron 7) and a 2,445-bp deletion in intron 2 (Fig. 1), as well as resulting haplotypes.

A significant association was observed for all three DCDC2 SNPs as well as the deletion:

rs793862 (GRR[1] A/A: 2.2 [CI95[2] 1.1–4.7] $p<0.05$)
rs807701 (GRR C/C: 2.2 [1.2–4.4] $p<0.05$)
rs807724 (GRR G/A: 0.6 [0.3–1.0] $p<0.05$)
Deletion (GRR del/del: 18.7 [4.2–84.1] $p<0.001$; allelic OR[3]: 2.6 [1.2–5.3] $p<0.01$) (see Table 1 for details)

The heterozygous genotype of the deletion was found in 15% of all cases and 9% of controls (Table 1). The increased frequency of the deletion was of statistical significance in all cases, as well as in the severe, the nonsevere, and the nondysphonetic subgroup. Dysphonetics showed the same tendency, with the deletion-allele more frequent in cases than controls, but were not significant (Table 2).

[1] Genotype relative risk

[2] Confidence interval 95%

[3] Allelic odds ratio

Table 2 Distribution of genotypes and alleles associating in all samples within subgroups

	Controls (n=184)	All cases (n=72)	Severe cases (n=25)	Nonsevere cases (n=43)	Dysphonetic cases (n=34)	Nondysphonetic cases (n=34)
Deletion genotype del/del	0%	3%***	0%	4.7%***	0%	6%***
Deletion alleles	4%	10%**	8%*	13%**	7%	15%***
rs793862 genotype A/A	5.6%	13.9%*	8%	16.3%	8.8%	17.6%*
rs807701 genotype C/C	8.2%	19.4%*	16%	20.9%	17.6%	20.6%*
rs807724 genotype G/A	38.4%	23.6%*	28%	23.3%	29.4%	20.6%

p values for genotypes are according to the genotype relative risk (GRR) of shown genotype vs all other genotypes (Lathrop, 1983). p values for the deletion are for allelic differences between cases and controls.

n number of individuals

*p<0.05; **p<0.01; ***p<0.005

All other tested DCDC2 variants also showed evidence for association in our study. Subgroup analysis revealed a further increased GRR for rs793862 and rs807701 in the nonsevere (GRR of 2.7 [1.2–6.3] and 2.5 [1.1–5.4], respectively) and the nondysphonetic (GRR of 3.0 [1.2–7.4] and 2.5 [1.0–5.8], respectively) subgroup. The third SNP, rs807724, showed no association in either of the subgroups (Table 2).

Additionally, haplotype analysis revealed a risk-haplotype with evidence for association. This haplotype contained the A, T, and A alleles from rs793862, rs807701, rs807724, and the deletion. It was present in 8% of cases and 2% of controls ($p_{\text{corrected}}$<0.05). The frequency of this haplotype was further increased in the nonsevere and the nondysphonetic subgroups (Table 3).

Table 3 Distribution of haplotypes and the deletion in all samples and subgroups

	Controls (n=368)	Cases (n=144)	Severe cases (n=50)	Nonsevere cases (n=86)	Dysphonetic cases (n=68)	Nondysphonetic cases (n=68)
rs793862/rs807701 (A/T)	3%	8%	4%	10%*	3%	13%**
rs793862/rs807701 (A/C)	23%	20%	18%	21%	24%	16%
Deletion	4%	10%**	8%*	13%**	7%	15%**
rs793862/rs807701/ rs807724/deletion (A/T/A/deletion)	2%	8%*	4%	10%**	3%	13%***

p values of haplotypes are corrected after Bonferroni; p values represent frequency differences between cases and controls.

*p<0.05; **p<0.01; ***p<0.005

n number of alleles/haplotypes

Discussion

Individuals with dyslexia experience severe problems with reading and writing, resulting in severe disadvantages for their development if left unattended. Strong evidence for a genetic component in the causes of dyslexia has been reported. The concrete genetic causes still remain to be found. To contribute to the search for susceptibility genes in German dyslexics, we aimed to replicate and refine the findings on DCDC2 (Meng et al., 2005; Schumacher et al., 2006; Harold et al., 2006; Brkanac et al., 2007).

To our knowledge, this is the first report of the 2,445bp DCDC2 deletion (Meng et al., 2005) in a German population, expanded by the investigation of three SNPs and the resulting haplotypes. Looking at single markers, we found evidence for association of dyslexia with the 2,445bp deletion and all three SNPs. In previous studies, two of the four polymorphisms (rs807701 and rs793862) also showed association with dyslexia in German-speaking subjects (Schumacher et al., 2006). We could partially replicate the findings of Schumacher et al. (2006) for association of rs793862 (A/A) and rs807701 (C/C), where Schumacher found a trend for association. The SNP rs807724, not studied by Schumacher et al. (2006), showed significant association for the heterozygous genotype G/A. This genotype was decreased in cases that might be at least partially the consequence of the nonsignificant increase of the homozygous genotype.

In American and British cohorts, the results for polymorphisms of DCDC2 were ambiguous, sometimes associating with dyslexia (Meng et al., 2005), but also showing a trend for an association ($p<0.1$; Harold et al., 2006; Brkanac et al., 2007) or no association at all (Harold et al., 2006; Brkanac et al., 2007). Of all polymorphisms, the deletion showed the most consistent results. Our study confirms the prominent role of the deletion and, interestingly, strongest evidence for association was found in the nonsevere and nondysphonetic subgroups. This might hint to a specific role of DCDC2 in the etiology of these dyslexia subtypes. Furthermore, all analyzed DCDC2 variants were not increased in our severe case group compared with the nonsevere case group.

Functional subgroups of dyslexia are well established (Boder, 1971). We carried out subgroup analyses of associating DCDC2 polymorphisms and haplotypes for the dysphonetic subtype, as well as the nondysphonetic counterpart (Table 2). In the dysphonetic subgroup, none of the studied polymorphisms showed association. In the nondysphonetic subgroup, the deletion, rs793862, and rs807701 associated significantly, whereas rs807724 did not. This subgroup mainly consists of another dyslexia subtype: dyseidetics (surface dyslexia) (Boder, 1971; Coltheart et al., 1983; Schulte-Körne et al., 1993). While the dysphonetic subtype is characterized by problems in differentiation and synthesis of sounds, the dyseidetic subtype has problems with visual perception concerning the discrimination of written words. These results indicate a possible role for DCDC2, perhaps even the deletion itself, in the development of the dyseidetic subtype.

We also investigated haplotypes for the DCDC2 variants in all dyslexics and functional subgroups. A risk-haplotype consisting of rs793862 (A), rs807701 (T), rs807724 (A), and the deletion showed association (8%/2%, $p_{\text{corrected}}<0.05$) in all cases, as well as in the nonsevere subgroup (10%/2%, $p_{\text{corrected}}<0.05$) and the nondysphonetic subgroup (13%/2%, $p_{\text{corrected}}<0.05$). Severe and dysphonetic cases showed no association with this haplotype (Table 3). We also examined two marker haplotypes studied in Schumacher et al. (2006), but we could not replicate their results. While Schumacher found the A/C haplotype, consisting of rs793862 and rs807701, to be associating, we found the A/T haplotype to be associating in the nondysphonetic and nonsevere subgroup only. Our findings might probably be a consequence of the linkage between the A/T alleles and the deletion, the

strongest risk factor. Additionally, since frequency ratios of deletion and ATA-del haplotype are comparable, it can be speculated that the deletion itself might be a causative factor of dyslexia, especially for the dyseidetic subtype.

Our results suggest a role of DCDC2 in the development of dyslexia in Indo-Germanic languages. The inconsistency in different publications concerning that role could possibly be caused by the considerable difference in the distribution of risk alleles among functional subgroups as observed in our data. If the distribution of these subgroups within dyslexics differed between these studies, different frequencies of the risk alleles between dyslexics might be expected.

Furthermore, different grades of regularity concerning the grapheme–phoneme correspondence occur in different languages, e.g., the English language is more irregular than the German language and, therefore, might be more vulnerable to dysphonetic components of dyslexia. Thus, we might expect that the ratio of functional subgroups within dyslexics may differ in both languages. In consequence, language might introduce a language-specific sampling bias when studies of German- and English-speaking dyslexics are compared.

Additionally, the most severe cases are often mixed forms of the different functional subtypes (e.g., dysphoneidetics). In our group of severe cases, most of them (84%) had a strong dysphonetic component. In concordance to the findings in the dysphonetic vs nondysphonetic groups, association within severe vs nonsevere group was decreased. Thus, the discrepancy between the results of Schumacher et al. (2006) and Brkanac et al. (2007), who found an increased association for some variants in more severe cases, and our study could be explained: A lower proportion of dysphonetics in their studies might be a reason for these differences.

Hence, the application of functional subgroup classification should be used in addition to severity classification. This observation of possible different genetic backgrounds for different forms of dyslexia should be confirmed by further investigation of subgroups in larger cohorts.

The presented evidence for genetic association of DCDC2 with dyslexia in conjunction with functional evidence for the role of DCDC2 in neuronal migration during brain development (Karl, 2004) may suggest that impaired neuronal migration may play a role in the etiology of dyslexia, possibly especially in mechanisms leading to the dyseidetic form of the disease. The study of these mechanisms and the identification of further susceptibility genes are important steps towards the development of genetic tests for early identification of children with a high risk for dyslexia. Earlier detection could open the possibility of earlier support and, thus, decrease problems at school age (Schneider et al., 1999). In addition, identification of subgroup-specific traits in children might allow for customized mentoring.

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