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Neural Correlates of Symbolic Number Comparison in Developmental Dyscalculia

Christophe Mussolin[1], Anne De Volder[2], Cécile Grandin[2], Xavier Schlögel[2], Marie-Cécile Nassogne[2], and Marie-Pascale Noël[1]

[1]Université Catholique de Louvain, Louvain-la-Neuve, Belgium

[2]Louvain School of Medicine, Brussels, Belgium

Developmental dyscalculia (DD) is a deficit in number processing and arithmetic that affects 3–6% of schoolchildren. The goal of the present study was to analyze cerebral bases of DD related to symbolic number processing. Children with DD aged 9–11 years and matched children with no learning disability history were investigated using fMRI. The two groups of children were controlled for general cognitive factors, such as working memory, reading abilities, or IQ. Brain activations were measured during a number comparison task on pairs of Arabic numerals and a color comparison task on pairs of nonnumerical symbols. In each task, pairs of stimuli that were close or far on the relevant dimension were constituted. Brain activation in bilateral intraparietal sulcus (IPS) was modulated by numerical distance in controls but not in children with DD. Moreover, although the right IPS responded to numerical distance only, the left IPS was influenced by both numerical and color distances in control children. Our findings suggest that dyscalculia is associated with impairment in areas involved in number magnitude processing and, to a lesser extent, in areas dedicated to domain-general magnitude processing.

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Abstract

■ Developmental dyscalculia (DD) is a deficit in number processing and arithmetic that affects 3–6% of schoolchildren. The goal of the present study was to analyze cerebral bases of DD related to symbolic number processing. Children with DD aged 9–11 years and matched children with no learning disability history were investigated using fMRI. The two groups of children were controlled for general cognitive factors, such as working memory, reading abilities, or IQ. Brain activations were measured during a number comparison task on pairs of Arabic numerals and a color comparison task on pairs of nonnumerical symbols. In each task, pairs of stimuli that were close or far on the relevant dimension were constituted. Brain activation in bilateral intraparietal sulcus (IPS) was modulated by numerical distance in controls but not in children with DD. Moreover, although the right IPS responded to numerical distance only, the left IPS was influenced by both numerical and color distances in control children. Our findings suggest that dyscalculia is associated with impairment in areas involved in number magnitude processing and, to a lesser extent, in areas dedicated to domain-general magnitude processing. ■

INTRODUCTION

Developmental dyscalculia (DD) is a specific learning disability affecting the processing of numerical and arithmetical information in the context of normal intelligence (American Psychological Association, 1994), with prevalence estimates in the order of 3–6% (Shalev, 2004; Shalev & Gross-Tsur, 2001; Gross-Tsur, Manor, & Shalev, 1996). Several hypotheses have been proposed to account for DD. Some of them postulate a deficit of a general cognitive system such as working memory (Geary, Hoard, & Hamson, 1999; McLean & Hitch, 1999; Swanson, 1993; Geary, Brown, & Samaranayake, 1991; Hitch & McAuley, 1991; Siegel & Ryan, 1989), retrieval of information from long-term memory (Geary, Hamson, & Hoard, 2000; Geary, 1993), or visuospatial abilities (Rourke & Conway, 1997; Rourke, 1993). On the other hand, recent behavioral data support the hypothesis of a specific deficit with number processing in DD (Landerl, Bevan, & Butterworth, 2004; Butterworth, 1999). It was postulated that people with learning disabilities in mathematics could have problems in the construction of the mental number line (Bachot, Gevers, Fias, & Roeyers, 2005) or in the access to this internal representation of magnitude from symbolic notation (Rousselle & Noël, 2007; Rubinsten & Henik, 2005).

In agreement with the pioneer Gerstmann (1940) and Henschen (1919) works based on brain-damaged patients' evaluation, neuroimaging studies in healthy adults have repeatedly demonstrated the implication of parietal lobes in number processing. In particular, the bilateral intraparietal sulcus (IPS) seems to be consistently activated in numerical tasks such as number comparison (Pesenti, Thioux, Seron, & De Volder, 2000; Pinel et al., 1999) or calculation (Zago et al., 2001; Chochon, Cohen, van de Moortele, & Dehaene, 1999). The activation of IPS appears independently of the notation (Venkatraman, Ansari, & Chee, 2005; Pinel, Dehaene, Riviere, & LeBihan, 2001) and even in the absence of explicit processing of number magnitude (Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003). Furthermore, the activation of the IPS has been found to be modulated by numerical distance (Moyer & Landauer, 1967), whereby there is an inverse relationship between distance and levels of activation (Pinel et al., 2001). On the basis of these results, it is assumed that this region, especially the horizontal segment of the IPS (hIPS), might hold the abstract representation of number magnitude (Dehaene, Piazza, Pinel, & Cohen, 2003; Dehaene, Dehaene-Lambertz, & Cohen, 1998). Recently, some studies analyzed differences in brain activation dedicated to number processing between children and adults. Using an adaptation paradigm with nonsymbolic numerical quantities, Cantlon, Brannon, Carter, and Pelphrey (2006) observed that both adults and 4-year-old children showed IPS activation in response to a change in the number of visual elements, even if the clusters activated in adults tended to be more extensive than in children. During number comparison, it was also found that, compared with adults, children showed weaker parietal activation but a stronger

[1]Université Catholique de Louvain, Louvain-la-Neuve, Belgium, [2]Louvain School of Medicine, Brussels, Belgium

recruitment of right frontal areas (Ansari & Dhital, 2006; Ansari, Garcia, Lucas, Hamon, & Dhital, 2005).

Relatively few studies have attempted to investigate the cerebral bases of learning disabilities in mathematics. Using a voxel-based morphometric technique, Isaacs, Edmonds, Lucas, and Gadian (2001) showed that impaired calculation ability in adolescents, who had been very low birth weight infants, was associated with less gray matter density in the left IPS. An insufficient recruitment of the right IPS was also observed in adults with Turner syndrome during approximate calculation (Molko et al., 2003). Although these findings are interesting, they were based on people with mathematical learning disability following prematurity or genetic disorder. More convincing evidence was provided by the comparison of brain activation in participants with pure DD and age-matched controls during active numerical tasks. Using ERPs, it was found that the time course related to the numerical distance slightly differed between DD adolescents and age-matched or adult groups without dyscalculia while they compared Arabic numerals to the reference standard 5 (Soltész, Szücs, Dékány, Márkus, & Csépe, 2007). During later window interval (about 340–430 msec), the topography of the distance effect differed over the left hemisphere between adults and dyscalculic adolescents. Moreover, there was a distance effect on the right parietal electrodes in controls but not in the dyscalculic group. Combined with the less steep slope of the behavioral distance effect in dyscalculic adolescents compared with adults, these ERP differences could reflect an abnormal processing of number magnitude conveyed by single-digit numbers. Another study reported similar frontal-parietal network in DD and control children during approximate calculation, exact calculation, and nonsymbolic comparison (Kucian et al., 2006). No group differences in cerebral activity were observed during exact calculation and nonsymbolic comparison, whereas brain activations during approximate calculation were slightly weaker in the IPS and in the inferior and middle frontal gyrus for children with DD than for control children. Finally, Price, Holloway, Räsänen, Vesterinen, and Ansari (2007) found a weaker modulation of the right IPS in children with pure DD relative to control peers in response to nonsymbolic number comparisons.

Together, the data derived from participants with DD suggest a deficiency in the recruitment of regions in and around the IPS. Yet, none of these previous studies investigating cerebral bases of dyscalculia have controlled for the possible cognitive factors that could influence the performance of participants. Dyscalculia is frequently associated with a variety of disorders, such as dyslexia, attention deficit/hyperactivity disorder, and poor working memory, that could possibly explain some differences in the pattern of brain activation (Lewis, Hitch, & Walker, 1994). For instance, brain activation in the IPS was found to be modulated by spatial working memory (Culham & Kanwisher, 2001), which could be needed to perform nonsymbolic number comparison tasks as the one used by Price et al. (2007). Therefore, a complete behavioral testing of children's capacities to be related to the functional imaging results is necessary to understand the exact role of the areas activated. Finally, although recent behavioral works suggest a specific deficit for Arabic numbers comparison in DD (Rousselle & Noël, 2007; Rubinsten & Henik, 2005), no functional imaging study examined this hypothesis.

The main purpose of the present study was to further investigate cerebral bases of dyscalculia. We wanted to examine brain activations related to symbolic number processing in children with and without learning difficulties in mathematics using fMRI. To this end, children with DD and control children matched on IQ, reading abilities, and working memory capacities performed a comparison task on pairs of Arabic numerals (see Figure 1). The numerical distance between numerals was manipulated to point out cerebral areas for which activation varied with that dimension in each group. A color detection performed on pairs of nonnumerical symbols was also used as a control task. If DD is associated with an impairment in the representation of number magnitude, as suggested by recent behavioral data, we might expect differences between children with and without DD in parietal activations dedicated to the numerical distance, especially in the IPS. Moreover, the color task enables to test to what extent the potential differences in brain activation are specific to numbers.

METHODS

Participants

Fifteen children with DD (8 girls and 7 boys, mean age = 10.5 ± 1.6 years) and 15 control children with no learning disability history (6 girls and 9 boys, mean age = 10.9 ± 1.6 years) participated in a block-design fMRI study. A 2-year delay in a mathematical battery (Simonart, 1998) without literacy problems and with a verbal and a nonverbal IQ above 85 (Wechsler Intelligence Scale for Children, Third Edition; Wechsler, 1996) was the clinical criterion for referring patients, who were further assigned to the DD group based on their scores on neuropsychological tests. Written informed consent for the participation in this study was obtained from the legal guardians of the children. None of these children suffered from any other neurological, psychiatric, or any other developmental or learning disorder (attention deficit/hyperactivity disorder and dyslexia) (Gross-Tsur et al., 1996). The study was approved by the local ethics committee based on the World Medical Association's Declaration of Helsinki (World Medical Association, 2002).

Neuropsychological Testing

All the children assigned in the group with mathematical disabilities were diagnosed as having DD by the neuropediatric department. We confirmed this diagnosis by using

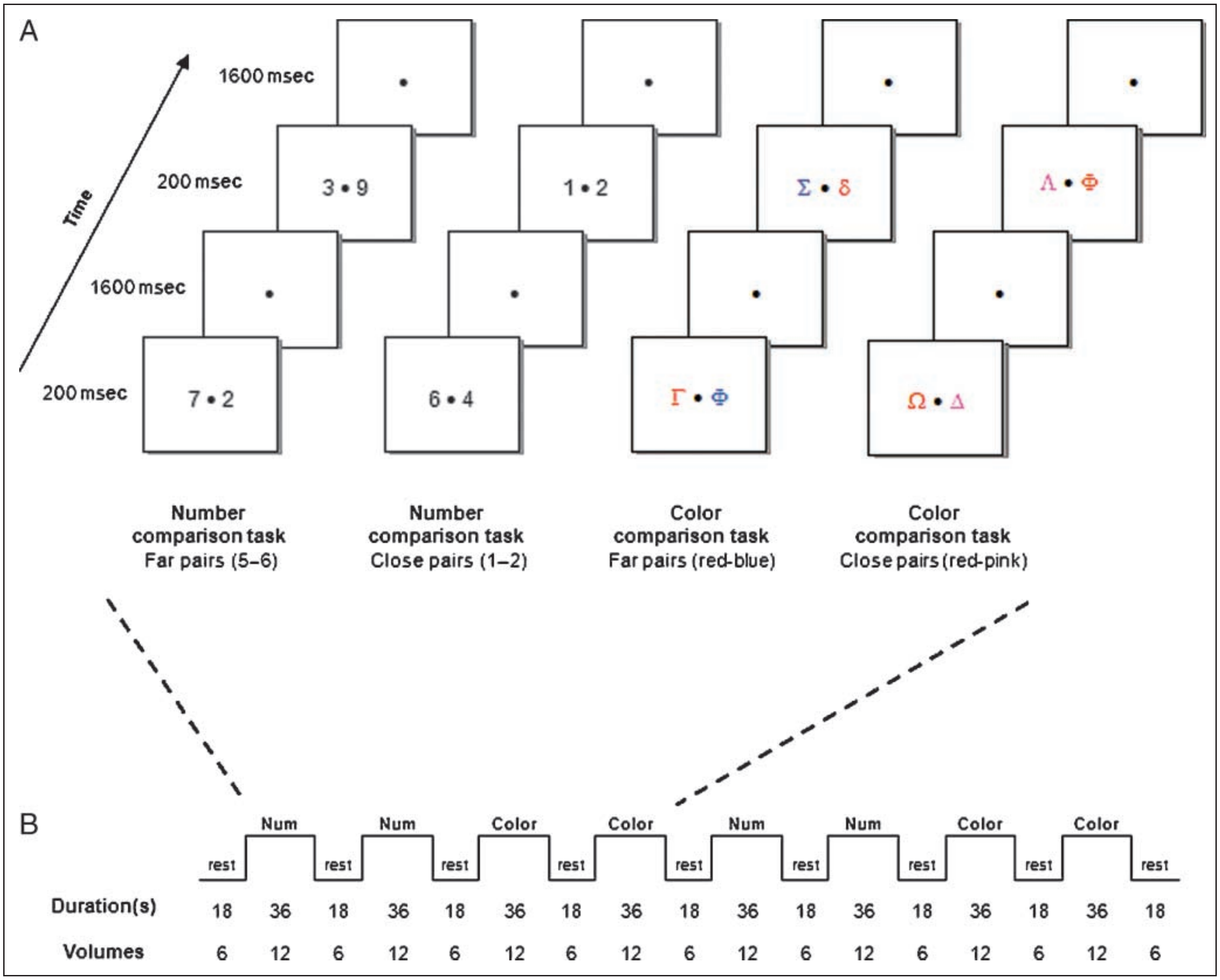

Figure 1. (A) Task design. (B) Sample sequence of blocks used. Three such sequences were presented in pseudorandom order including four blocks of number comparisons (Num) and four blocks of color comparisons (Color) alternating with fixation (rest) periods.

two pencil-and-paper arithmetic tests: the Kortrijk Rekenen Test (KRT; Cracco et al., 1994), which is a normalized test including complex calculations and mathematical problems; and a timed calculation test in which children were required to solve a maximum of simple calculations for each operation (additions, subtractions, and multiplications) in 1 min.

In addition, other general cognitive abilities were assessed. Intellectual capacities were evaluated using the Similarities and Images Completion subtests of the Wechsler Intelligence Scale for Children, Third Edition (Wechsler, 1996), which enabled to calculate an estimate of IQ for both DD and control children. Reading ability was assessed by the L3 task (Lobrot, 1980) and the 1-min reading task (Khomsi, 1998). In the L3, children have 5 min to read silently a maximum of 36 sentences and complete them with one of five given words, involving rapid reading and comprehension. The 1-min test is a standardized reading task in which children are required to read as many words as they can on a list within 1 min. Four measures of short-term memory were also obtained. In the word span tasks, children are presented with increasingly longer series of words and are asked to repeat them in the actual presentation order (forward word span) or in the reverse order (backward word span). The Corsi block-tapping test provided a measure of spatial short-term memory. In this task, children are asked to reproduce the same sequence of block pointing as shown by the examiner. The listening span (adapted from Daneman & Carpenter, 1980) was used to evaluate the central executive component of the working memory. In this test, the experimenter read sets of sentences (from two to four), and the child is required to indicate whether each sentence is true or not. Then, at the end of the set, the child has to recall the last word of each of the sentences included in the set.

As reported in Table 1, the comparison between the two groups revealed significant differences in all arithmetical tasks. Children with DD had lower scores than controls on KRT, addition, subtraction (ps $< .001$), and multiplication ($p < .05$) problems. On the contrary, no significant

Table 1. Neuropsychological Testing

	Control Children	*DD Children*	*Normative Data*	*t*
Descriptive Information				
n	15	15		
Sex (male/female)	9/6	7/8		
Age (months)	131.5 (19.6)	126.1 (18.3)		0.44
IQ				
Similarities (raw scores)	13.5 (2.6)	11.9 (1.9)	10.1 (2.6)	1.93
Images completion (raw scores)	11.7 (2.8)	11.2 (2.8)	9.8 (3.2)	0.45
IQ estimated	114.9 (12.7)	108.9 (10.5)		1.40
Mathematics				
KRT score	17.7 (5.9)	5.3 (3.6)	14 (P50)	6.91***
1-min addition	25.3 (5.7)	14.3 (6.6)	–	4.87***
1-min subtraction	21.9 (6.0)	11.0 (6.1)	–	4.89***
1-min multiplication	18.5 (5.9)	10.5 (6.5)	–	3.51*
Reading				
L3 (correct sentences)	27.2 (7.9)	23.5 (6.6)	23.1 (6.4)	1.40
1-min reading (correct words)	78.9 (21.7)	67.9 (17.7)	72 (16.1)	0.94
Working Memory				
Forward span words	4.1 (0.5)	3.9 (0.3)	–	1.34
Backward span words	3.3 (0.5)	3.0 (0.4)	–	1.74
Corsi blocks span	5.5 (0.9)	5.3 (1.2)	5.3 (0.9)	0.51
Listening span	3.9 (0.7)	3.1 (0.6)	2.5 (0.7)	1.20

Mean, *SD*, and *t* test for age, performance in the mathematical tests, IQ subtests, reading tests, and working memory tests for children in the control and the DD groups.

*SD*s or percentiles (P) are shown in parentheses.

*$p < .05$.

***$p < .001$.

differences were observed in reading, memory, and IQ subtests (all *p*s > .05).

Tasks and Stimuli

Before scanning, the participants were carefully instructed about the procedure and they had to solve four blocks of practice trials on a computer outside the scanner to gain familiarity with the tasks.

Participants were instructed to keep their eyes on a fixation point at the center of the screen throughout the experiment and to avoid movements as much as possible. They held a response button in each hand. Two experimental tasks were performed: a number comparison task and a color comparison task. During both comparison tasks, a pair of (numerical or nonnumerical) symbols was flashed for 200 msec at the center of the screen, followed by a 1600-msec blank screen interval during which the child had to produce his or her response. In the number comparison task, children were presented with two Arabic numerals ranging from 1 to 9 and had to select the larger numeral of each pair by pressing the corresponding button as quickly as possible. Two numerical distances were contrasted: small (1 or 2) and large (5 or 6). In the color comparison task, pairs of nonnumerical symbols (selected among the symbols Λ, Δ, Ω, Σ, Γ, δ, &, Φ) were presented. We have chosen to avoid numerical symbols to prevent automatic activation of the number magnitude related to Arabic numerals (Rubinsten, Henik, Berger, & Shahar-Shalev, 2002; Girelli, Lucangeli,

& Butterworth, 2000), which could in turn lead to brain activation around the IPS (Pinel, Piazza, Le Bihan, & Dehaene, 2004). The target symbol was red and the color of the other symbol was either far (i.e., blue) or close (i.e., pink). The children had to select the red symbol by pressing the corresponding button. The position of the correct response was counterbalanced for each task. During the rest periods, children were asked to look at the fixation point without any head or eye movement. Stimuli were presented using a video projector and a translucent screen. The experiment was programmed and responses were recorded using E-Prime 1.1 software (Schneider, Eschmann, & Zuccolotto, 2002).

Data Acquisition

Structural brain imaging was obtained in each subject by three-dimensional MRI in the bicommissural orientation on a 1.5-T magnetic resonance imager (Gyroscan, Philips Medical Systems; Best, The Netherlands), using a T1-weighted gradient-echo sequence (fast field echo, repetition time = 30 msec; echo time = 3 msec; flip angle = 30°; slice thickness = 1.5 mm). The head was restrained by foam pads.

Blood oxygen level-dependent fMRI data were acquired using a multislice T2*-weighted gradient EPI sequence (repetition time = 3000 msec; echo time = 50 msec; flip angle = 90°) with 33 axial slices, 3.6-mm slice thickness (isotropic voxel), in the bicommissural orientation (i.e., in the plane of the anterior and posterior commissures). The matrix was 64 × 64, and the field of view was 210 × 210 mm.

The fMRI paradigm consisted of three runs of eight alternating epochs of comparison tasks and fixation (36 sec per epoch). Two number comparison conditions (small distances and large distances) and two color comparison conditions (close colors and far colors) were blocked and presented in a pseudorandom order. Stimuli were projected onto a skill screen placed at the rear of the magnet bore. Participants viewed the stimuli via an angled mirror fastened to the head coil. Each run comprised the acquisition of 144 volumes and contained 160 trials (20 trials × 4 conditions × 2 blocks of each condition per run). Stimulus onset was synchronized with the acquisition of the first slice. The participants received instructions before each sequence and were not warned of the alternation between tasks and conditions.

Data Analysis

Data were processed and analyzed using Statistical Parametric Mapping (SPM 2, The Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ac.uk/spm), implemented in Matlab (Mathworks Inc., Sherborn, MA). The first six volumes of each run were discarded to allow for T1 equilibration. The individual structural brain volume was realigned to the first remaining functional brain volume of the corresponding participant to correct for within- and between-run motion, coregistered with the anatomical scan, and further spatially normalized using the MRI template supplied by the Montreal Neurological Institute (MNI). This procedure resulted in normalized fMRI scans with a cubic voxel size (2 × 2 × 2 mm) for the group analysis. Next, a spatial smoothing with a Gaussian kernel of 8 mm (FWHM) was applied to reduce the residual anatomical and functional variability across participants. The means (*SD*) of head movements in the x, y, and z plane were 0.1 (0.3), 0.6 (0.8), and 1.3 (1.4) mm, respectively, for the control children and those of children with DD were 0.2 (0.4), 0.8 (1.2), and 1.7 (0.7) mm. No significant differences in head motion were found between the two groups (all ps > .05).

Condition-related changes in regional brain activity were estimated for each participant by a general linear model in which the responses evoked by each condition of interest were modeled by a standard hemodynamic response function. The contrasts of interest were computed at the individual level to identify the cerebral regions significantly activated by each condition. Significant cerebral activations were then examined at the group level in random-effect analyses using one-sample t tests, with the statistical threshold set at $p_{\text{corrected}} < .05$ (FWE) and extending to at least 20 contiguous voxels. Considering the high interindividual variability in brain activation related to number processing (Kadosh, Kadosh, Kaas, Henik, & Goebel, 2007), an uncorrected statistical threshold of $p_{\text{uncorrected}} < .001$ at the voxel level was also applied. Only the activation of cortical brain regions was reported (for further details, see Table S1). Finally, anatomical labels were given based on the classification of the automated anatomical labeling atlas (Tzourio-Mazoyer et al., 2002).

ROI Analysis

To further investigate potential group differences in brain activation for the number comparison task, we extracted ROIs using MarsBar toolbox (MarsBar, Matthew Brett). ROIs were defined by significantly activated clusters in the random effect analysis of all children for the number comparison task (including small and large numerical distances) versus fixation at an FWE corrected level of $p_{\text{corrected}} < .05$. Only brain regions for which we had a priori hypothesis were considered (Dehaene et al., 2003). This analysis resulted in two parietal clusters around the IPS: one in the left superior parietal lobule (coordinates: −24, −60, 48; 1171 voxels) and one in the right inferior parietal lobule (coordinates: 50, −50, 58; 1139 voxels). We applied a similar voxel size to each parietal cluster using a box of 10 mm around the peak of activation. The contrast values were computed within these ROIs for all participants during small versus large distance in both number and color comparisons. Then, we analyzed the Distance × Task interaction for each child using the contrast (small numerical distance vs. large numerical distance) minus (small color distance vs. large color distance). These individual contrasts were then entered in a two-sample group analysis to assess differences between DD and control children (for a detailed method, see Henson & Penny, 2003). To ensure that the potential group differences were not the consequence of lower activation levels throughout the whole brain in DD participants, we performed similar ROI analyses on left (−10, −77, 3) and right (20, −73, 2) hemisphere primary visual areas (see Amunts, Malikovic, Mohlberg, Schormann, & Zilles, 2000).

RESULTS

Behavioral Data

Mean error rates and median RTs in each task for the two groups are summarized in Table 2. Accuracy data were analyzed using a 2 comparison tasks (number vs. color) × 2 distances (small vs. large) × 2 groups (DD vs. control children) repeated measures ANOVA. The analysis revealed no group effect ($p > .05$), showing that error rates were not significantly different between children with DD and controls. The main effect of task was significant, $F(1,28) = 23.09$, $p < .001$, corresponding to higher error rates for number comparison than for color comparison. Although the main effect of distance was highly significant, $F(1,28) = 33.49$, $p < .001$, it appeared in the numerical task, $F(1,28) = 51.51$, $p < .001$, but not in the color task ($F < 1$), as revealed by the Task × Distance interaction, $F(1,28) = 32.49$, $p < .001$.

The analysis of median RTs (for correct trials only) revealed that the group was not significant and did not interact with any other variable (all ps $> .05$), indicating no difference between the two groups of children in latencies. The main effect of task appeared significantly, $F(1,28) = 109.07$, $p < .001$, indicating that the number comparison task was processed slower than the color comparison task. The main effect of distance was significant, $F(1,28) = 122.67$, $p < .001$, and interacted with the task, $F(1,28) = 44.88$, $p < .001$, indicating a stronger distance effect in the number comparison task, $F(1,28) = 110.06$, $p < .001$, than in the color comparison task, $F(1,28) = 9.69$, $p = .004$.

Functional Imaging

Table S1 summarizes the anatomical localization and MNI coordinates of activated voxels clusters within each contrast for children with and without DD.

Number Comparison versus Color Comparison

During number relative to color comparisons, the only activation was found in the left postcentral gyrus for children with DD at the uncorrected threshold.

Numerical Distance

At the uncorrected threshold, control children showed stronger activation for small than large numerical distance trials in the banks of the right IPS, with additional activations in the right middle frontal gyrus and the middle cingulate gyrus. For the same contrast, children with DD activated the left supramarginal gyrus and the middle frontal gyrus.

Color Comparison versus Number Comparison

During color comparisons relative to number comparisons, control children showed activations at the uncorrected threshold in the precuneus and the fusiform gyrus, bilaterally, as well as in the left superior frontal gyrus and the lingual gyrus. Additional activations in the right hemisphere were found in the superior parietal lobule, the angular gyrus, and the superior occipital gyrus. In children with DD, activations were restricted to the fusiform gyrus of both hemispheres.

Table 2. Behavioral Data

	Control Children		*DD Children*	
	RT (msec)	*% Errors*	*RT (msec)*	*% Errors*
Number comparison task	416 (25)	5.1 (1.2)	464 (24)	6.8 (1.1)
Small distance	468 (29)	8.1 (1.4)	508 (28)	9.2 (1.4)
Large distance	365 (22)	2.1 (1.1)	420 (22)	4.5 (1.1)
Color comparison task	299 (25)	1.9 (0.8)	335 (25)	4.3 (0.8)
Small distance	306 (27)	2.0 (1.0)	347 (26)	4.4 (1.0)
Large distance	292 (25)	1.7 (0.8)	323 (24)	4.1 (0.8)

Mean accuracy and response times on number and color comparison tasks for each group of children.

*SD*s are shown in parentheses.

Color Distance

At the uncorrected threshold, control children showed stronger activation for close relative to far color trials in the left inferior temporal gyrus, the lingual gyrus, and the superior and middle occipital gyri. In children with DD, no region was activated for the same contrast.

Group Comparison

Differences between DD and control children were examined using two-sample t tests for each contrast. These analyzes revealed no differences in any contrast when correcting for multiple comparison (at $p_{corrected} < .05$). As summarized in Table 3, a few areas showed significant

Table 3. Differences in Brain Activation between DD and Control Children for Each Contrast (at $p_{uncorrected} < .001$, >20 voxels)

	MNI Coordinates				
	x	*Y*	*z*	K_E	*Z*
Number Comparison (vs. Fixation)					
Control children > DD children			No suprathreshold cluster		
DD children > control children					
Right postcentral gyrus	28	−30	42	64	3.84
Right supramarginal gyrus	46	−32	34	20	3.82
Left thalamus	−2	−20	−12	71	3.70
Number vs. Color Comparison					
Control children > DD children			No suprathreshold cluster		
DD children > control children			No suprathreshold cluster		
Numerical Distance (Small vs. Large Pairs)					
Control children > DD children					
Right middle frontal gyrus	30	36	36	21	3.42
Left superior parietal lobule	−18	−64	52	39	3.91
Right IPS	42	−46	54	29	3.50
Left middle cingulate gyrus	−12	−28	46	34	3.85
DD children > control children			No suprathreshold cluster		
Color Comparison (vs. Fixation)					
Control children > DD children			No suprathreshold cluster		
DD children > control children			No suprathreshold cluster		
Color vs. Number Comparison					
Control children > DD children			No suprathreshold cluster		
DD children > control children			No suprathreshold cluster		
Color Distance (Close vs. Far Pairs)					
Control children > DD children					
Left lingual gyrus	−10	−76	−6	68	4.07
Right lingual gyrus	16	−64	0	36	3.74
Left cuneus	−2	−80	30	52	3.61
DD children > control children			No suprathreshold cluster		

Coordinates are reported in MNI space as given by SPM2 and correspond only approximately to Talairach and Tournoux (1988) space. Anatomical labels are based on the automated anatomical labeling atlas (Tzourio-Mazoyer et al., 2002).

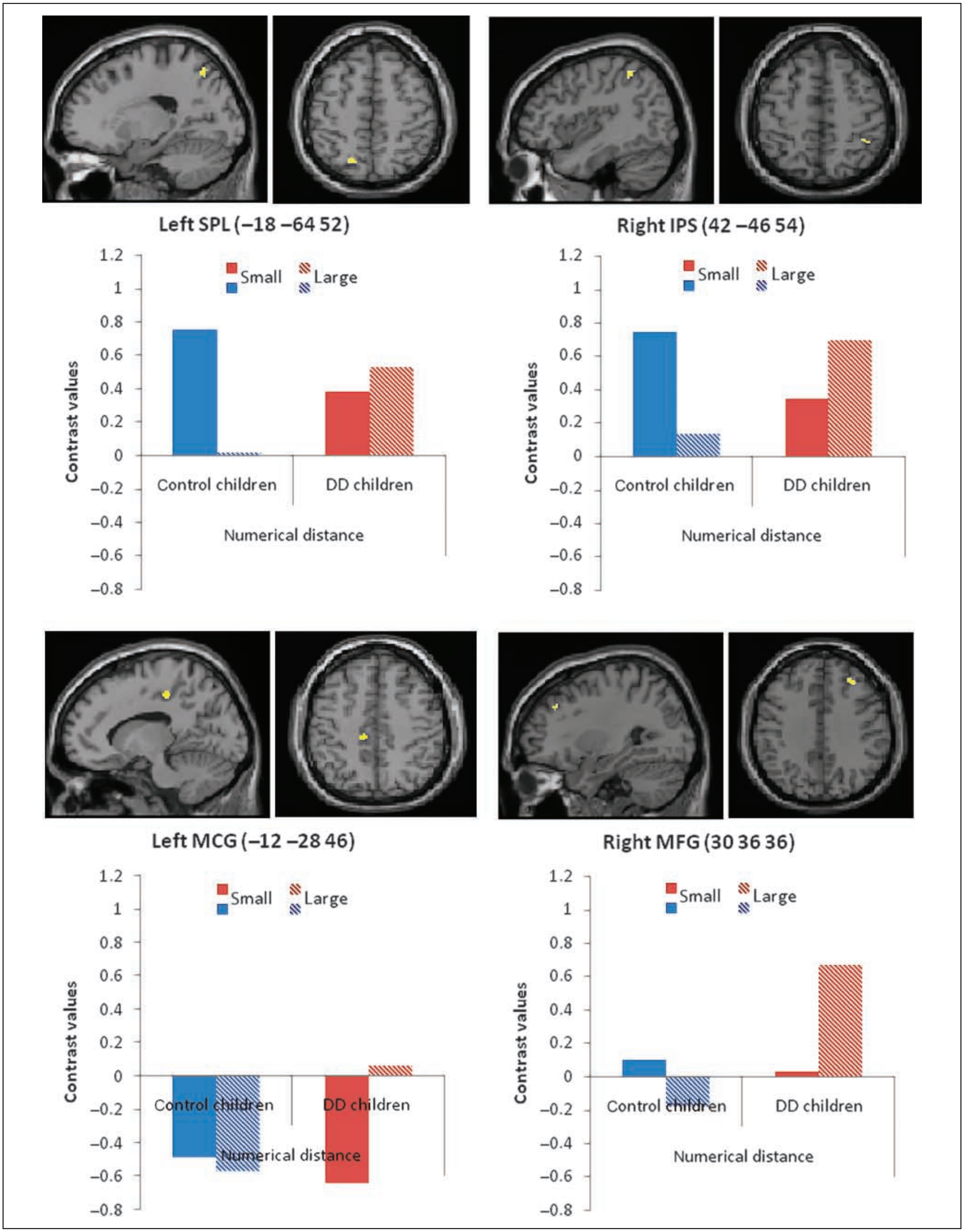

Figure 2. Localization of brain areas showing more activation for control children than children with DD in the contrast between small relative to large numerical distance from the random whole-brain analysis ($p_{uncorrected} < .001$). Bar charts depict modulation of brain activation (mean contrast values) for this contrast, as computed in these regions for both control and DD children. IPS = intraparietal sulcus, MCG = middle cingulate gyrus, MFG = middle frontal gyrus, SPL = superior parietal lobule.

group differences in activation at the uncorrected threshold ($p_{uncorrected} < .001$, voxels > 20). During number comparison relative to fixation, differences in brain activation between DD and control children were found in the right postcentral gyrus and the supramarginal gyrus. In fact, the analysis of the mean contrast values in these regions revealed that differences in brain activation were due to a deactivation in reference to the baseline (fixation) period for control children but not for children with DD. However, no group differences were observed when number was contrasted with color comparisons in any area. Considering the comparison between small and large numerical distance, control children showed greater activation than children with DD in the left superior parietal lobule and the right IPS. Additional activations were found in the right middle frontal gyrus and the left cingulate gyrus. Cerebral activity in all of these regions showed modulation by numerical distance for controls but not for children with DD. As illustrated in Figure 2, although brain activation in the left and right parietal regions increased with the decreasing numerical distance, the frontal and the cingulate gyri showed higher deactivation for large relative to small numerical distance in controls.

Regarding color comparison relative to fixation or number comparison, DD and control children activated essentially the same regions. With respect to color distance, higher activation for control than children with DD was observed in the bilateral lingual gyrus and in the left cuneus only.

We also examined the interaction between group, distance, and task in the two parietal ROIs,[1] which had been extracted from the random analysis. As depicted in Figure 3, it was found that the Distance × Task interaction differed significantly between both groups in the right IPS, $t(28) = 1.95$, $p_{corrected} < .05$. The brain activity in this region showed a strong modulation for small relative to large numerical distance in controls, $t(14) = 2.4$, $p_{corrected} < .05$, but not in DD children, $t(14) = -0.65$, $p_{corrected} > .05$. No differences in brain activation were observed between the two groups of children with respect to color distance at the same threshold. A similar trend was observed in the left IPS whose response differed between control and DD children at a less stringent threshold, $t(28) = 1.26$, $p_{corrected} = .1$. In controls, the cerebral activity of the left IPS was significantly modulated by numerical distance, $t(14) = 3.7$, $p_{corrected} < .001$, as well as by color distance although less strongly, $t(14) = 1.93$, $p_{corrected} < .05$, whereas in children with DD, this region was not influenced by numerical distance or color distance (all $p_{corrected} > .05$). Moreover, the lack of group effect for Task × Distance interaction in the left and right primary visual areas (all $p_{corrected} > .05$) indicated that the aforementioned differences between children with and without DD were not explained by lower brain activation level.

DISCUSSION

The present article explored cerebral bases of number processing in children with pure DD. To the best of our knowledge, only three previous studies investigated differences in brain activity related to dyscalculia. Compared with controls, DD adolescents showed a delayed ERP time course related to the numerical distance over the left hemisphere and no distance effect on right parietal electrodes (Soltész et al., 2007). In another study, Kucian et al. (2006) found weak group differences in brain activation during approximate calculation, but not during nonsymbolic magnitude comparison and exact calculation. However, the approximate calculation task could require strong demands on attention and working memory to keep in mind the correct sum and compare it to closest of the two propositions. It is thus difficult to distinguish between differences in activation related to these general nonnumerical factors and those related to specific functional deficits in

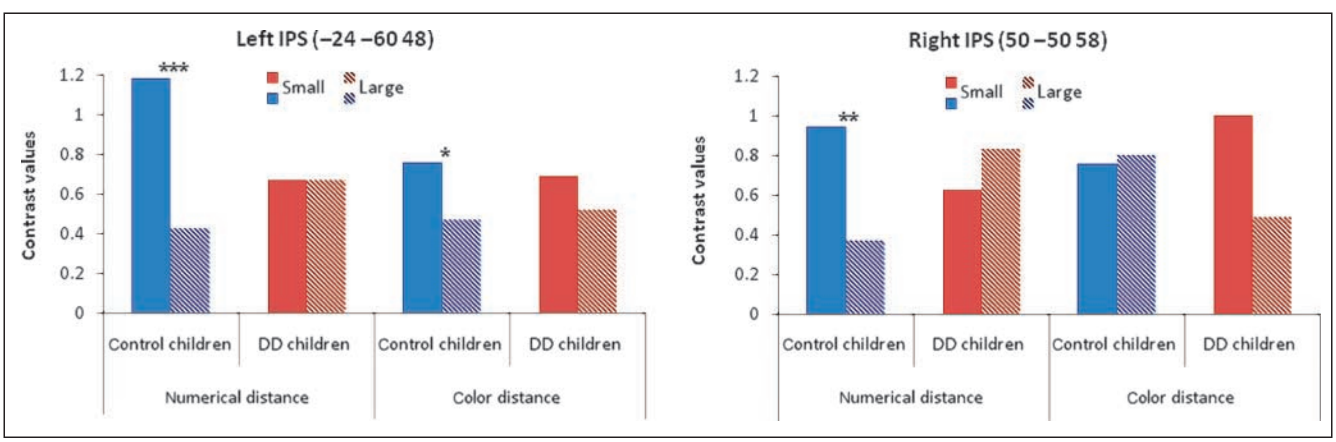

Figure 3. ROI analysis. Bar charts depict modulation of brain activation (mean contrast values) in left and right IPS during numerical and color distances, as computed in these regions for both control and DD children. Significant group differences are marked with one (*$p_{corrected} < .05$), two (**$p_{corrected} < .01$), or three asterisks (***$p_{corrected} < .001$), corrected for multiple comparisons.

number processing. Indeed, there is a large body of evidence that DD is frequently associated with weak working memory (Geary et al., 1991, 1999; McLean & Hitch, 1999; Swanson, 1993; Hitch & McAuley, 1991; Siegel & Ryan, 1989) and visuospatial abilities (Rourke & Conway, 1997; Rourke, 1993). In addition, the lack of group differences during nonsymbolic magnitude comparison in Kucian et al. (2006) could be due to the influence of perceptual variables varying with the numerosity (e.g., Clearfield & Mix, 1999). Finally, they found weak activations in children with DD compared with healthy children in the right insula and parahippocampal gyrus. Yet, none of these regions was previously seen to be modulated by numerical distance or to be specifically implicated in number magnitude processing. Using more controlled stimuli, Price et al. (2007) reported a weak modulation of the IPS in children with DD relative to normally developed children when they had to compare sets of squares. Nevertheless, some research has shown that symbolic comparison might be more affected than nonsymbolic comparison in dyscalculia (Rousselle & Noël, 2007).

In the current study, we focused on the magnitude comparison of symbolic numbers. The cognitive performance of children with DD was assessed to ensure that they did not differ from control children on IQ, working memory, or reading abilities. At the behavioral level, no significant differences in latencies and accuracy and comparable numerical and color distance effects were found between the two groups of children. The fact that distance influenced latencies in color task indicates that children based their judgment on the comparison of both colors rather than on the detection of the target color only. Our main result is to reveal particular differences in brain activation between children with and without DD related to symbolic numerical distance. The whole-brain analysis revealed that control children showed greater activation than children with DD in and around the IPS bilaterally. Subsequent ROIs analyses confirmed these findings and revealed a stronger modulation of these regions by numerical distance for controls relative to children with DD. Previous brain-imaging studies have demonstrated the crucial role of these regions in number processing, such as calculation (Venkatraman et al., 2005; Gruber, Indefrey, Steinmetz, & Kleinschmidt, 2001), approximation (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999), number comparison (Kaufmann et al., 2005; Pinel et al., 2001, 2004), unconscious numerical priming (Naccache & Dehaene, 2001), and numerosity change detection (Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004), as well as subitizing and counting (Piazza, Mechelli, Butterworth, & Price, 2002; Sathian et al., 1999). More importantly, this area was found to be implicated in numerical distance conveyed by symbolic (Ansari et al., 2005; Kadosh et al., 2005; Pinel et al., 1999, 2001) and nonsymbolic numerical quantities (Price et al., 2007; Ansari & Dhital, 2006). Beside the parietal lobe, we found that children with DD exhibited weaker activations than control peers in the right middle frontal gyrus and in the left cingulate gyrus. A modulation of frontal activation by numerical distance was previously observed in healthy children, particularly in the right hemisphere (Ansari & Dhital, 2006; Ansari et al., 2005). Although more rarely observed than parietal regions, the posterior cingulate gyrus was also found to be correlated with numerical distance (Ansari & Dhital, 2006; Ansari, Dhital, & Siong, 2006; Pinel et al., 2001).

Voxel-based morphometry studies have revealed a structural deficiency of the IPS in people with mathematic disorders. Compared with controls, adolescents with very low birth weight (Isaacs et al., 2001), adults with Turner syndrome (Molko et al., 2003), and recently children with DD (Rotzer et al., 2008) showed a reduction of gray matter volume in the IPS. Therefore, subtle disturbances at the level of neural organization in the IPS might be the substrate of impaired arithmetical skills. Further support for this hypothesis was provided by Kadosh, Kadosh, Schuhmann, et al. (2007) who found that virtually lesioning the right parietal cortex in healthy adults by means of transcranial magnetic stimulation impaired automatic access to symbolic numerals and led to DD like performance in healthy adults. This favors a causal role between the right IPS and the dyscalculic profile. Together, brain-imaging results found here and elsewhere are in line with recent behavioral evidence which showed that people with DD could have a deficit in activating internal representation of magnitude. Adults with DD engaged in a Stroop-like numerical task did not present the classic size congruity effect when they had to judge perceptual characteristics (grayness, height, or physical size) of Arabic numerals (Rubinsten & Henik, 2005). In another study, no Spatial-Numerical Association of Response Codes (SNARC) effect that refers to a spatial preference for left-hand responses to small numbers and right-hand responses to large numbers (Dehaene, Bossini, & Giraux, 1993) was found in children with both arithmetical and visuospatial problems during a number comparison task (Bachot et al., 2005). This was interpreted by the authors as reflecting an abnormal representation of number magnitude on the oriented mental number line. Finally, we observed that, compared with age-matched controls, children with mathematical disabilities had difficulties in comparing symbolic and nonsymbolic numbers close from each other in magnitude (Mussolin & Noël, submitted). In the present study, there was also a trend to slower latencies and higher error rates for DD children relative to controls especially during the number comparison task. The age of the participants seems to play a crucial role in this respect, as a significant slowdown in the context of DD was previously reported in young children of 7–9 years old (Rousselle & Noël, 2007; Bachot et al., 2005; Landerl et al., 2004) but not in older participants (Soltész et al., 2007; Kucian et al., 2006). It is possible that, with increasing experience, performance improves in comparing number magnitude over time, and DD children finally achieve a level of skill that is not quantitatively different from that of control children.

The weak differences in performance pattern between the two groups of children only cannot explain the changes in IPS activity. First, given that brain response in the IPS was positively correlated with the level of difficulty (Göbel, Johansen-Berg, Behrens, & Rushworth, 2004), more activation in this region is expected for DD children who exhibited more difficulties than their control peers during number comparison. However, the reverse pattern is observed with a greater modulation of the IPS in control relative to DD children. Second, DD children also tended to be slower and more error prone than control children during color comparison, but these behavioral differences did not lead to similar changes in brain activation. Furthermore, the two comparison tasks were controlled for known nonnumerical factors showing IPS modulation such as response selection (Jiang & Kanwisher, 2003; Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Corbetta & Shulman, 2002; Wojciulik & Kanwisher, 1999), spatial working memory (Culham & Kanwisher, 2001), or attention (Jiang & Kanwisher, 2003; Culham & Kanwisher, 2001; Wojciulik & Kanwisher, 1999) requirements. Although eye movements were not recorded in the fMRI scanner, it is very unlikely that saccade rates would produce task-specific activation differences given the short presentation time of the stimuli. The group differences reported at the whole-brain level were found only when liberal uncorrected statistical threshold was used. However, previous neuroimaging studies in both healthy (Ansari & Dhital, 2006; Cantlon et al., 2006; Ansari et al., 2005) and DD children (e.g., Kucian et al., 2006) or in individuals with different levels of mathematical competence (e.g., Grabner et al., 2007; Menon et al., 2000) have shown that number-related differences in brain activation are much more subtle than task differences.

Our study included a nonnumerical task that allowed us to examine the extent to which differences in brain activation between children with and without DD were specific to number processing. In children with DD, brain activity differed in the left postcentral gyrus but was due to less deactivation for number than color comparisons. In control children, higher activation for color relative to number comparisons was found in the ventral pathway, including the fusiform gyrus, the lingual gyrus, the angular gyrus, and the superior occipital gyrus. These regions play a crucial role in color perception as previously demonstrated in neuroimaging studies in healthy adults (McKeefry & Zeki, 1997; Gulyas & Roland, 1994; Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991) and brain-damaged patients (Damasio & Frank, 1992; Zeki, 1990). The bilateral precuneus, the left superior frontal gyrus, and the right superior parietal lobule, which were also more activated in color than number comparisons, were involved in a fontro-parietal network for maintaining internal representations and could reflect a more intense storage and/or refreshing of information (Cornette, Dupont, Salmon, & Orban, 2001). However, we failed to report any differences between DD and control children when number and color comparisons were contrasted. These results are in agreement with recent fMRI experiments that showed an involvement of dorsal parietal regions, especially the IPS, not only in number processing but also during color discrimination (Claeys et al., 2004). In particular, it was found that some parts of the IPS were implicated not only in number magnitude but also in several tasks involving nonnumerical magnitude (for a discussion, see Kadosh, Lammertyn, & Izard, 2008). The hIPS reacted almost identically when numbers were processed according to their numerical value, physical size, or luminance (Pinel et al., 2004). In a very similar study (Kadosh et al., 2005), only a region in the left anterior IPS showed a distance-specific effect for numbers whereas an overlap of the three distance effects was observed in the posterior part of the left IPS. In the same vein, it was found that the comparison of angles, lines, or two-digit numbers involved a similar region in the left IPS (Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003). More support for a relative common substrate for number and color magnitudes was provided by Shuman and Kanwisher (2004). They observed no specific activation for nonsymbolic numerical quantities in any of the parietal regions (including the hIPS) previously identified as involved in number processing when compared with color processing on the same stimuli.

Differences between DD and control children were observed regarding numerical and color distance effects. Control children showed a significant modulation of brain activity in the right IPS by numerical distance, but not by color distance. On the contrary, the right IPS did respond to neither numerical distance nor color distance in DD children. Crucially, this region is within a few millimeters of the hIPS coordinates described by Dehaene et al. (2003), which is supposed to hold an abstract representation of number magnitude. A different pattern appeared in the left IPS, which was influenced by numerical distance and, to a lesser extent, by color distance in controls only. Together, this indicates a distinct role of the left and the right parietal cortices in number processing during typical development. Whereas the right IPS might be specifically involved in number processing, the left IPS could respond to more general magnitude (Walsh, 2003). Compared with controls, children with DD showed not only a smaller activation of areas dedicated to numerical distance but also a weaker involvement of regions sensitive to color distance. The left and the right lingual gyri, which have been consistently observed during color discrimination (e.g., Gulyas & Roland, 1994; Corbetta et al., 1991), were less activated in DD than control children. Furthermore, the left IPS that responded to both numerical and color distances in controls was not significantly modulated by any distances in children with DD. Thus, it seems that the lack of IPS sensitivity in dyscalculia concerns domain-specific and domain-general magnitudes. Up to now, there is, however, little empirical evidence for a nonnumerical magnitude deficit in DD children. Although Rousselle and Noël (2007) observed slower latencies for children with both math and reading difficulties relative to controls in comparing the physical size of two identical Arabic numerals, Landerl et al. (2004) reported no group difference during the same kind of task. Furthermore, these performances were based on two different sizes rather than on a continuum as numbers. More behavioral and brain-imaging investigation is needed to examine potential impairment in DD during nonnumerical magnitude processing.

Another question is whether other brain regions tended to compensate for the deficient parietal activation during numerical task. Compared with controls, children with DD did not activate any frontal regions classically found to be involved in executive functions. By contrast, differences in brain activation were observed between the two groups in the right postcentral gyrus and supramarginal gyrus, corresponding to deactivation in reference to fixation period for controls but not for children with DD. The postcentral gyrus was previously implicated in number processing (Kadosh et al., 2005; Kaufmann et al., 2005; Pinel et al., 1999), but its role is yet unclear. Possibly, activation of this region could reflect the sensorimotor demands of the task requiring, as the visual identification of Arabic numerals and the selection of the appropriate response (Pinel et al., 1999). The supramarginal gyrus has been considered as the anatomical locus of information storage in working memory. Activation in the upper part of the right supramarginal gyrus (near the dorsal pathway) has been preferentially detected during visuospatial working memory tasks, whereas the lower part of the left supramarginal gyrus seems dedicated to the phonological storage of the verbal working memory (Smith & Jonides, 1998; Smith, Jonides, & Koeppe, 1996; Paulesu, Frith, & Frackowiak, 1993). Therefore, one interpretation of the activation of the right supramarginal gyrus in DD children but not in control children is that they needed stronger demands on visuospatial working memory to perform the task. Although our measure of visuospatial working memory did not reveal any impairment in children with DD, previous studies suggest that children performing poorly on mathematical tasks could have difficulties with visuospatial abilities (e.g., Rourke, 1993). Activation of the supramarginal gyrus was also found in number processing, especially in calculation (Zago et al., 2001; Cowell, Egan, Code, Harasty, & Watson, 2000). This region has been considered as playing a role in the spatial representation of numbers. For instance, the supramarginal gyrus was activated in adults when they had to decide whether close Arabic numerals are or are not in the correct ordinal sequence (Fulbright, Manson, Skudlarski, Lacadie, & Gore, 2003). Finally, transient neural disruption of the supramarginal gyrus using repetitive transcranial magnetic stimulation affected the comparison of Arabic numerals (Göbel & Walsh, 2001). Consequently, this area was postulated to play a crucial role for the representation of small numbers, which are learned early in the development and used by young children for verbal and finger counting. Together, the fact that the right supramarginal gyrus was activated in the dyscalculic group only might suggest some immature engagement of general- or specific-related visuospatial processes during the comparison of symbolic numbers.

Conclusion

The major contribution of this article is to reveal a weak involvement of areas dedicated to number magnitude in dyscalculia. The left and the right IPS was typically modulated by symbolic numerical distance in controls but not in DD children. These differences in brain activation could not be explained by nonnumerical cognitive factors generally associated with dyscalculia. Rather, the present findings indicate a functional perturbation in children with DD of brain regions that support the representation of domain-specific and, to a lesser extent, domain-general magnitude processing.

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Reprint requests should be sent to Christophe Mussolin, Unité CODE, Faculté de Psychologie, Université Catholique de Louvain, 10 Place C. Mercier, 1348 Louvain-la-Neuve, Belgium, or via e-mail: christophe.mussolin@uclouvain.be.

Note

1. A similar analysis was conducted at the whole-brain level but failed to reveal significant clusters, probably due to the small number of participants and the low statistical power of third level interaction analyses.

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