When All Hypotheses are Right: A Multifocal Account of Dyslexia

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Abstract: Many hypotheses have been proposed about the brain underpinnings of developmental dyslexia, but none of them accommodates the variable deficits observed. To address the issue of anatomical deficits in dyslexia; total and partial volumes, lateralization indices (LI), and local gray matter volumes (LGMV) were measured. Analyses were performed in large samples of control and dyslexic subjects, and in correlation with their performance on phonological, reading, and spelling tests. Results indicate an absence of net differences in terms of volumes but significant continuities and discontinuities between groups in their correlations between LI, LGMV, and performances. Structural connectivity also highlighted correlations between areas showing (dis)continuities between control and dyslexic subjects. Overall, our data put forward the idea of a multifocal brain abnormalities in dyslexia with a major implication of the left superior temporal gyrus, occipital-temporal cortices, and lateral/medial cerebellum, which could account for the diverse deficits predicted by the different theories. *Hum Brain Mapp* 30:2278–2292, 2009. © 2009 Wiley-Liss, Inc.

Key words: dyslexia; reading; superior temporal gyrus; VBM; fusiform gyrus; cerebellum

INTRODUCTION

Developmental dyslexia consists of a specific and persistent failure to acquire efficient reading skills despite conventional instruction, adequate intelligence, and socio-cultural opportunity [American Psychiatric Association, 1994; World Health Organization, 1993]. Three main groups can be distinguished among the many neuro-cognitive hypotheses about dyslexia [see Démonet et al., 2004 for a review]:

the phonological, the visual, and the cerebellar hypotheses. Phonological hypotheses postulate deficits related to the access and/or the manipulation of phonemic information [e.g. Ramus, 2004; Shaywitz and Shaywitz, 2005] in relation with abnormalities of the left superior temporal and inferior frontal cortex [Dufor et al., 2007]. These deficits would either be genuine or linked to impaired basic auditory processing, preventing efficient learning of graphemes/phonemes correspondences that are crucial to reading. Supporting such ideas, studies have shown reduced performances for short-term verbal memory tasks or phonemic awareness in dyslexia [Ramus et al., 2003], deficit in phonemic categorization [Serniclaes et al., 2001], or in rapid acoustic transition perception [Tallal et al., 1985]. The visual hypothesis posits the existence of low level visual disorders related to abnormal thalamic magno-cells [Livingstone et al., 1991] such as dyslexic subjects show increased thresholds on detection of low contrast, low spatial or high temporal frequencies [Lovegrove et al., 1980], and poor sensitivity to visual motion [Demb et al., 1998].

Additional Supporting Information may be found in the online version of this article.

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In addition, the visual magnocellular pathway is involved in directing attention, eye movements and visual search, all three processes being relevant to reading [Stein and Walsh, 1997]. Neural correlates of visual deficits would therefore also involve the thalamus (lateral geniculate nuclei), the primary visual cortex, and dorsal visual areas that receive magnocellular inputs [i.e. MT and dorsal regions—Demb et al., 1997, 1998]. In addition to this primary visual deficit, additional areas more directly involved in reading and visual word encoding/decoding have also been suggested to be altered in dyslexic subjects: inferior-temporal cortex, angular/supramarginal gyri and inferior frontal gyrus [Démonet et al., 2004; Hoeft et al., 2007; Paulesu et al., 2001; Pugh et al., 2000]. Finally, the cerebellar hypothesis relates dyslexia to a general learning disorder, including failure to automatize reading and writing skills [Nicholson et al., 2001]; i.e. an impaired automatization of sensory-motor procedures essential in reading that would reflect abnormal function in the lateral cerebellum [Doyon et al., 2002].

In line with these hypotheses, Galaburda and colleagues first described microscopic abnormalities in the auditory [Galaburda and Kemper, 1979] and then in the frontal and perisylvian areas [Kaufman and Galaburda, 1989] of dyslexic subjects. Subsequent works also revealed soma atrophies of the thalamic lateral [Livingstone et al., 1991], and medial geniculate nuclei [Galaburda et al., 1994]. This was followed by the identification of abnormalities in the visual primary cortex [Jenner et al., 1999] and the cerebellum [Finch et al., 2002]. These microanatomical anomalies represent anatomical markers that fit with above-mentioned hypotheses on dyslexia. Morphometric studies partially confirmed these discoveries revealing differences between dyslexic and control subjects mainly located in the left inferior frontal, superior-temporal, temporo-parietal, medial occipital regions, and the cerebellum [Eckert, 2004]. However, inconsistencies across studies that typically involved 10 to 20 subjects suggest that results might be affected by a large inter-individual heterogeneity even in normal subjects. In addition, depending on studies, structural abnormalities were either directly related to morphological differences between unimpaired and dyslexic readers or correlated with reading skills; leading to hypothesized both genuine and experience-based cortical variations. To distinguish between these two hypotheses, absence of correlation in dyslexic readers vs. significant correlation in controls is needed such as one can hypothesize that brain abnormalities do not allow the environmentally-driven modulation to develop as in normal subjects. Here, we examined high resolution MRI T1 images of a large sample of subjects ($N = 77$) to address how the distribution of language performance across subjects in each group and between groups could be related to that of local gray matter volume (LGMV) in the brain and cerebellum. Volumetric analyses (regional volumes, lateralization, and voxel-based morphometry [Ashburner and Friston, 2000]) were performed using a multiple regression approach involving reading related performances assessed by standard cognitive tests [Paulesu et al., 2001] as

regressors. These tests were designed to target the different cognitive components impaired in dyslexia [Coltheart et al., 1993]: phonological awareness, lexical access, grapheme-phoneme conversion and visual reading skills.

METHODS

Subjects

Seventy-seven subjects (38 dyslexic subjects: four women; mean age 27.25 years, SD 7.92 years—and 39 control subjects: four women; mean age 27.83 years, SD 5.75 years) participated in this study. All subjects were native French speakers, had 12 years or more of school education (equal or superior to French “baccalaureat”) and were free from any history of sensory deficits, neurological or psychiatric illness, or medical treatment. Seven subjects were left-handed and the remaining subjects were right-handed (minimal score + 65% on Edinburgh inventory test [Oldfield, 1971]. The Toulouse local ethic committee approved the different study’s protocols in which subjects were involved and all subjects gave informed written consent.

Neuropsychological Assessment

The diagnosis of developmental dyslexia was established using both inventory and testing procedures in accordance with the guidelines of the ICD-10 Classification of Mental and Behavioral Disorders. The clinical examination included a clinical interview, regular, irregular, and “loan” (foreign words which are used in French and primarily call upon addressing, lexical reading procedure) and pseudo-word reading tasks, a rapid digit-strings reading task, phonological and metaphonological tasks (syllabic deletion, phoneme deletion, spoonerisms, phonologically incongruent word search, phonological-based rime decision from visual stimuli) and spelling tasks of irregular words and pseudowords [see Paulesu et al., 2001 for details]. In addition, the IQ was controlled using either the full WAIS-IVR battery or the vocabulary, similarity, blocks, and assembly subtests from the WAIS-IVR. Performance and RTs of each subject were classified according to normalized scores. A participant was diagnosed as dyslexic and included into the study if his/her performance was two standard deviations below the average on at least 10 out of twenty one scales of the clinical tests (scores or RTs) whereas his/her IQ was within the normal range. Data used in the subsequent analyses correspond to the clinical tests on which data were recorded for all participants and no dyslexic participant failed and/or stopped (e.g. as in spoonerism).

Imaging Parameters

High-resolution T1-weighted MRI images (MPRAGE acquisition) were recorded for all subjects using one of the two scanners available. Fifty-two subjects (25 dyslexic and 27 control readers) were scanned on a 1.5 tesla Magnetom Vision Siemens scanner (TR 9.7 TE 4 flip angle 8° FOV

300 mm, matrix 256×256 , voxel size 1.17 mm^3) and the other twenty-five subjects (13 dyslexic and 12 control readers) were scanned on a 2 tesla Magnetom Vision Siemens scanner (TR 9.7 TE 4 flip angle 12° FOV 256 mm, matrix 256×256 , voxel size 1 mm^3 for eight subjects and matrix 162×256 , voxel size 1.58 mm^3 for the other 17 subjects).

Spatial Processing

Images were automatically segmented into gray- and white-matter and CSF, and simultaneously bias corrected and warped into a standard space using SPM5¹ (R186) software and Matlab[®] 7 (R14) with a resampling at 2 mm^3 using a trilinear interpolation.² Automatic segmentation was chosen as i) manual segmentation is prone to inter-rater variability and ii) some brain areas such as the occipito-temporal cortex may be hard to define and trace manually [Eckert, 2004]. The resulting outputs were maps in which the value in each voxel was the probability that a particular voxel belonged to that class and data were thresholded such as only probabilities superior to 0.2 were kept. As part of the process the probability values were modulated by the local stretching and compression induced by the warps such that the total content of any tissue class was the same in the warped images as it would have been in their original space. This procedure [Ashburner and Friston, 2005] outperforms previous methods that executed these steps successively. To check equal segmentation and registration between groups, the sum square distances of each image from the average image across groups and from the gray matter template used for segmentation/normalization were computed. Results showed no significant difference between groups either from the mean image ($t(75) = -0.65$ $P = 0.5$ for non smoothed images and $t(75) = -1.4$ $P = 0.16$ for smoothed images) or from the template ($t(75) = -0.37$ $P = 1$ for nonsmoothed images and $t(75) = -1.4$ $P = 0.16$ for smoothed images). This ensured that possible differences between groups were not related to a bias toward one group or the other during image preprocessing. Examples of segmented images (worst and best representative) are provided as supporting information along with a plot of the sample homogeneity, i.e. the sum square distances. The mean image per group is also presented allowing estimating the spatial resolution achieved (Supporting Fig. 1).

Statistical Analyses

(A) Neuropsychological data: *t*-tests were performed on each task separately to compare the normal and dyslexic reader groups; the alpha level was adjusted for multiple comparisons, i.e. $\alpha = 0.0036$ (B) Volumes analyses: The

total and regional volumes of gray and white matter were computed for each group counting the number of voxels and using the Jacobian determinant of the normalization field. Regional volumes were computed the same way within atlas masks for the different brain areas [Maldjian et al., 2003, 2004; Tzourio-Mazoyer et al., 2002]. Total gray and white volumes were compared between groups using a two-sample *t*-test (α 5% two-sided) whereas MANOVAs were conducted for each lobe with the hemispheres (left/right) and areas as repeated factors and the groups as independent factor. Lateralization indices were also computed for each area (left-right/left+right) and MANOVAs and multiple regression analyses were carried out. The alpha level was adjusted for the multiple analyses performed over the four brain lobes (frontal, parietal, temporal, occipital) and the cerebellum, i.e. $\alpha = 1\%$. For each analysis/region, the alpha level was kept at 1% because the MANOVA takes into account the covariance between factors (areas). For the multiple regression analyses, the same predictors as those used in the VBM analyses were adopted (see below) including the confounding factors (i.e. age, scanner origin, total volume). The alpha level was also set to 1%. (C) VBM: To allow statistical tests, tissue class images were smoothed with a 8 mm FWHM isotropic Gaussian kernel to render data more normally distributed [Salmond et al., 2002]. Importantly, the cerebrum and the cerebellum were smoothed separately. Normalized tissue class images of the cerebrum and cerebellum were separated using masks of the standard brain [Maldjian et al., 2003, 2004; Tzourio-Mazoyer et al., 2002], then smoothed and finally re-assembled together (see Supporting Fig. 2 for an example of masked images). This procedure was used to ensure a greater independence between the cerebellar tissue and the surrounding occipital cortex. All effects (partial correlations) were evaluated through multiple regression analyses for gray and white matter volumes. To test for group differences, a matrix including only the two groups, plus the age, scanner origin and gray or white matter global volume of each participant (each of these components being potentially confounding factors) was made up. Differences between groups were tested using classical inferential *t*-tests (probability to find a difference under the hypothesis that the two groups are similar, i.e. testing H_0) and using empirical Bayes estimates [likelihood to have a real difference given the initial difference in the data, i.e. testing H_1 —Friston and Penny, 2007]. For the correlation analysis with reading/language performances, another matrix was set up and the regressors used in this case corresponded to the group origin (control or dyslexic), age, scanner origin and gray or white matter global volume of each participant and performances recorded during the neuropsychological assessment. First, all scores and reaction times were normalized (demeaned and scaled to unity variance) equalizing the weight of each variable. Second, principal component analyses (PCA) were performed on the phoneme deletion, syllabic deletion, sound categorization, word reading and pseudo-word reading tasks as

¹<http://www.fil.ion.ucl.ac.uk/spm/>

²Parameters used to perform the analyses were "light regularization" and 60 mm full-width at half maximum (FWHM) cutoff for bias correction, two Gaussian functions per tissue class for segmentation, 25 mm warp-field cutoff for normalization.

TABLE I. Mean scores and RTs (in sec) for the different clinical tests used to diagnose dyslexic subjects and corresponding *T* and *P* values from the two-sample *t*-tests (*df* = 75)

Clinical test	Dyslexics	Controls	<i>T</i> and <i>P</i> values
Phoneme deletion scores/40	33.36 ± 6.18	38.23 ± 2.95	-4.41 < .001
Phoneme deletion RTs	170.89 ± 74.12	136.56 ± 49.53	2.39 < .001
Syllabic deletion scores/20	17.68 ± 2.99	19.28 ± 0.94	-3.17 < .001
Syllabic deletion RTs	132.52 ± 65.45	90.76 ± 14.81	3.88 < .001
Sound categorization scores/20	14.36 ± 2.99	16.35 ± 1.93	-3.47 < .001
Sound categorization RTs	261.13 ± 74.55	235.64 ± 73.61	1.5 n.s.
Irregular word spelling scores/15	8.63 ± 2.91	13.12 ± 1.32	-8.75 < .001
Pseudo-word spelling scores/15	13.55 ± 1.55	14.2 ± 1	-2.19 < .01
Loan word reading scores/30	25.84 ± 4.01	29.33 ± 0.86	-5.3 < .001
Word reading scores/40	32.63 ± 9.43	35.71 ± 8.16	-1.53 n.s.
Word reading RTs	737.06 ± 182.36	517.26 ± 62.87	7.1 < .001
Pseudo-word reading scores/40	28 ± 9.97	34.74 ± 8.28	-3.23 < .001
Pseudo-word reading RTs	1031 ± 330	619 ± 112	7.36 < .001
Rapid digit naming RTs	20.15 ± 3.21	14.87 ± 2.03	-8.45 < .001

both scores and reaction times were recorded for these tests, giving partially redundant measurements (see Supporting Fig. 3). The respective part of variance explained by the 1 st PCA component was 65, 54, 70, 55, and 59%. Confirmatory analyses using a two sample *t*-tests ($\alpha = 0.01$ two-sided) between groups performed on each of the 1 st PCA components showed significant differences between groups ensuring conformity with initial data. Hence these components were used as covariate in the regression analyses instead of original scores and reaction times. Finally, an analysis of partial correlation coefficients was conducted between the different covariates to ensure linear independence. The analysis of partial correlation coefficients between covariates revealed only one high partial correlation ($r = 0.89$) between the word and nonword reading tasks such as more than 50% of the variance was shared between covariates. The word reading task was thus removed from the VBM analysis. The choice of removing the word reading regressor instead of the pseudo-word reading one was motivated by the fact that i) word reading scores (though not RT) did not differed between groups (see Table I) and II), apart from the visual analysis, the pseudo-word reading task relies more heavily on the grapheme-to-phoneme conversion than the word reading task. Therefore, removing the word reading task allowed a better analysis/interpretation than removing the pseudo-word reading task, and this process is critically affected in dyslexia. Performance regressors were split into two groups (see Supporting Fig. 3 for an example of matrix) thus allowing testing (F-contrasts) for correlations across groups (pooling regressors from control and dyslexic subjects) and testing for differences between groups in the way performances correlated with LGMV. Sixteen F-maps were therefore obtained (eight across groups and eight “between groups” maps— $P = 0.003$ corrected for multiple contrasts and $q = 0.05$ FDR corrected for multiple testing across voxels [Genovese et al., 2002]). Within group maps were also computed to better understand the quali-

tative (rather than statistically quantitative) nature of the data. For these analyses, data are reported at $P = 0.05$ FDR corrected. (D) Structural Connectivity Analysis: To assess which brain regions follow similar patterns of volume distribution as the ones revealed by the VBM analysis, we used the same framework as functional connectivity, i.e. a multiple regression analysis has been performed using the volume distributions obtained for four regions of interest [Wilke et al., 2003]. These regions of interest were obtained from the VBM results. Specifically, LGMV values were obtained for each subject from the first eigenvariate computed across voxels included in 6 mm³ spheres [Büchel and Friston, 2000] centered over the left STG (-60 -20 6 BA41), left fusiform gyrus (-32 -80 -16 BA19) and left cerebellar declive (-26 -68 -26) and pyramis (0 -70 -36). The multiple regression analysis was performed with these eight regressors (4 ROI × 2 groups), as well as the groups, age, scanner origin and total gray matter volumes. *T*-tests were performed looking at positive and negative correlations across groups and differences between groups ($P = 0.003$ corrected for multiple contrasts and $q = 0.05$ FDR corrected for multiple testing across voxels).

For VBM as well as the connectivity analyses, clusters have been corrected for nonisotropic smoothness [Worsley et al., 1999; Hayasaka et al., 2004]. Only clusters of a minimum of 160 mm³ (20 voxels for the VBM analysis) or 120 mm³ (15 voxels for the connectivity analysis) corresponding roughly to the number of expected voxels per cluster were considered. The anatomical labeling was performed automatically using the Talairach Daemon³ database server [Lancaster et al., 1997] transforming MNI to Talairach coordinates using M. Brett’s algorithm⁴ and compared with a reference atlases for the brain [Mai et al., 2004] and

³<http://ric.uthscsa.edu/resources>

⁴<http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml>

Figure 1.

Regional gray matter volume lateralization in control and dyslexic readers. (A) Volumes of gray and white matter for the left and right cerebellum and cerebrum in control (blue) and dyslexic (red) subjects. Box sizes represent the lower and upper quartile with the median indicated in the middle. The whiskers show the extent of the data (1 interquartile) with outliers indicated by the red crosses. Notches represent the robust estimate of the uncertainty about the median. (B) Pattern of lateralization in control and dyslexic subjects obtained from the LI. (C) and (D) Graphs of corre-

lations between the LI of the superior temporal gyrus (STG) and the pseudoword reading performance and between the LI the inferior frontal gyrus (IFG) and the loan word reading performances. Blue dots represent the control subjects and red triangles the dyslexic subjects. Significant correlations are indicated by a regression line: in black across groups (control and dyslexic subjects together) and in blue or red within group (control or dyslexic subjects). Note that only a significant across group effect was observed on the IFG demonstrating a weak correlation.

the cerebellum [Schmahmann et al., 1999]. Coordinates of maximum intensities for each SPM cluster are reported in the MNI space. Figures are reported in neurological convention and data were either projected onto the MNI152 or mapped onto the individual Colin brain [Van Essen et al., 2001].

RESULTS

Neuropsychological Data

Comparison of behavioral variables between groups revealed lower scores and longer RTs in the dyslexic group than in the control group for all tasks but RTs in sound categorization and scores in word reading (Table I).

Volumes Analyses

Control versus dyslexic subjects

No differences in total gray matter (0.71 ± 0.07 vs. 0.72 ± 0.09 ; $t(75) = 0.45$ $P = 0.65$), white matter (0.55 ± 0.07 vs. 0.54 ± 0.07 ; $t(75) = -0.29$ $P = 0.76$)—or partial (anatomical areas) gray volumes were observed between control and dyslexic subjects (Fig. 1A).

Lateralization analyses

No main group effects (α corrected or not, 1 or 5%) were observed on lateralization indices for the MANOVAs performed lobe by lobe. Only a Group $\times$ Hemisphere $\times$ ROI interaction ($\lambda = 0.7$ $F(7,69) = 3.12$ $P = 0.006$) was observed for the parietal lobe. Post hoc tests (Newman-

Keuls $P < 0.05$) revealed that in controls there were significant volume differences between the left and right angular gyri, superior parietal lobules (left > right $P = 0.02$ and 0.03), paracentral lobules, posterior cingulate gyri, and postcentral gyri (right > left $P = 0.00002$; $P = 0.03$ and $P = 0.00002$). For the dyslexics subjects, similar hemispheric differences were observed for the angular gyri (left > right $P = 0.01$), paracentral lobules and postcentral gyri (right > left $P = 0.00002$). However, in contrast with the control subjects, they did not show significant differences for the posterior cingulate gyri ($P = 0.053$) and superior parietal lobule ($P = 0.08$) but instead showed a volume asymmetry for the inferior parietal lobule ($P = 0.00002$).⁵ These lateralization effects were however only relative, i.e. differences were observed between areas for each group, and lateralization indices did not differ between groups when computed for each area in turn (with or without multiple comparison correction—Fig. 1B).

Regression analyses between LI and behavioral variables

Significant effects were observed in the regression analyses performed between lateralization indices and behavioral variables. The more left lateralized the superior temporal gyrus was, the better the performance in pseudoword reading, i.e. orthographic encoding and grapheme-to-phoneme conversion ($R^2 = 0.31$ $F(12,64) = 2.41$ $P = 0.01$; partial correlation 0.4 $P = 0.0008$ —Fig. 1C). Similarly, the more left lateralized the inferior frontal gyrus was, the better the performance in loan word reading, i.e. lexical access ($R^2 = 0.33$ $F(12,64) = 2.71$ $P = 0.005$; partial correlation 0.25 $P = 0.03$ —Fig. 1D). Those effects were observed across groups and no significant differences between groups were observed. Nevertheless, regression analyses performed on each group separately revealed distinct contributions of each regressor according to the group. In controls, left lateralization of the STS significantly correlated with the syllabic deletion (partial correlation— 0.39 $P = 0.03$), phonemic deletion (partial correlation 0.47 $P = 0.008$) and pseudoword reading performances (partial correlation 0.47 $P = 0.0008$) as well as with the total gray matter volume (partial correlation 0.52 $P = 0.003$ — $R^2 = 0.75$ $F(11,27) = 3.3$ $P = 0.005$). The analysis of regression performed over the IFG was not significant ($R^2 = 0.53$ $F(11,27) = 0.9$ $P = 0.48$) and no regressor showed a significant effect. In dyslexics, this was the regression analysis performed over the STS that was not significant ($R^2 = 0.58$ $F(11,26) = 1.26$ $P = 0.29$), with however a significant

effect for pseudoword reading (partial correlation 0.39 $P = 0.019$). Finally, although the overall regression model was significant for the IFG lateralization ($R^2 = 0.72$ $F(11,26) = 2.65$ $P = 0.019$), no behavioral variables significantly correlated with the IFG lateralization except dyslexic's age (partial correlation -0.34 $P = 0.017$). These results thus suggest that left lateralization of the STS is strongly correlated with phonological performances in both groups whereas only a weak correlation exists between the lateralization of the IFG and lexical access.

Voxel Based Morphometry

Control versus dyslexic subjects

As for the regional analysis, no significant differences between groups were observed between the local gray matter volumes (LGMV—voxel based analysis, $P = 0.05$ FDR corrected). This absence of difference between groups was confirmed using posterior probability maps (i.e. looking at the likelihood of a difference given the data).

Regression analyses between LGMV and behavioral variables

While there were only weak evidences for absolute differences in LGMV between groups, strong correlations ($P < .05$ FDR corrected) between language performance and LGMV were observed within each group (intra-group correlations) and across groups (control and dyslexic subjects pooled together). Differences in the way language performances and LGMV correlated were also observed between groups (stronger/weaker correlations in control vs. dyslexic subjects). No effect was observed in the white matter. Noteworthy, whereas performances of all the cognitive tests were incorporated into a multiple regression model, only three tests targeting the main cognitive components of reading (i.e. phonemic deletion, pseudoword reading, and irregular word spelling—partial correlations of respectively -0.2 , 0.2 , and 0.36 , Supporting Fig. 3) showed significant correlation with the LGMV. Among the auditory tests (auditory input/verbal output), only the phoneme deletion test showed significant correlations, which may reflect that this test necessitates heavier phonological manipulations (more detailed phonological analysis) than the others, thus better capturing morphological variations correlated with phonological awareness. Among the reading tests (visual input/verbal output), only pseudoword reading showed significant correlations with LGMV, suggesting that LGMV variations captured by this test were related to orthographic decoding and/or grapheme-to-phoneme conversion or association rather than visual encoding per se (which would be reflected for instance in rapid digit naming). Finally, for the spelling from dictation tests (auditory input/written output), only irregular word spelling showed significant differences across groups in their correlations with the LGMV. This finding might

⁵Although it is common use to define the supramarginal gyrus and angular gyrus as part of the inferior parietal lobule, the automated anatomical labeling atlas (Tzourio-Mazoyer et al., 2002) used here to delineate our areas, defines the inferior parietal lobule as the part of the brain located between the postcentral gyrus and the supramarginal gyrus.

TABLE II. MNI coordinates of maximum FDR corrected P values ($q < 0.05$) with cluster size, z -value, and anatomical label of gray matter voxels showing significant correlation differences between groups for the phoneme deletion task

MNI coordinate	Cluster size	Z-value	Label
4-74-16	2189	4.89	Left/Right cerebellum: left inferior semilunar lobule (VIIB), left/medial pyramis (VIII A), left/right declive (VI) and right centralis/culmen (III, IV, V) Left/Right posterior occipital/fusiform gyri
-32-72 44	27	3.40	Left precuneus/superior parietal lobule
14-80-50	31	3.14	Right inferior semilunar lobule (VIIB)
-60-16 18	374	4.03	Left transverse and superior temporal gyri Left pre/post central gyri
-60-8 32	72	3.85	Left precentral gyrus
-44-30 56	69	3.13	Left postcentral gyrus
-52-26 36	67	3.70	Left postcentral gyrus
-10-34 74	42	4.13	Left pre/postcentral gyrus
-44-36 20	74	3.71	Left inferior parietal lobule
-54 20 14	39	3.38	Left inferior frontal gyrus (pars triangularis)
-48 6 30	127	3.88	Left precentral gyrus (inferior)
-4 36-22	75	3.37	Gyrus rectus
10 44-4	46	3.40	Anterior cingulate
34 34-14	41	3.14	Right middle/inferior frontal gyrus border

Height threshold: $F = 9.57$, $P = 0.003$, Extent threshold: $k = 20$ voxels, Expected voxels per cluster, $\langle k \rangle = 17.92$, Resel = 149.07 voxels. The upper part of the table corresponds to voxels negatively correlated with the phoneme deletion performance for controls vs. no effect in dyslexic subjects (therefore control < dyslexic), whereas the lower part corresponds to voxels positively correlated with the phoneme deletion performance for controls vs. no effect in dyslexic subjects (therefore control > dyslexic). Only clusters with a minimum size of 160 mm³ (20 voxels) were taken into account.

relate to impaired lexicon access (or ill-formed lexicon) in dyslexic subjects relative to control readers, rather than a more fundamental spelling problem in the former group (which would be reflected in pseudoword spelling).

Phoneme Deletion

Control subjects showed significant stronger correlations between LGMV and the phoneme deletion performances than dyslexics (Fig. 2A—Table II). For control subjects, smaller gray matter volumes corresponded to increased (better) performance in the infero-temporal cortex bilaterally, the cerebellum (pyramis, declive, culmen, inferior semi-lunar) and the left precuneus. By contrast, no significant correlations were observed in dyslexic readers for these areas (i.e. dyslexics (no correlation) > controls (negative correlation)). Similarly, greater LGMV were observed for increased performances in the left lateral fronto-temporal cortex (STG, IFG), along with the left inferior parietal lobule and the right IFG/insula for control subjects vs. again no significant correlations in dyslexic readers (i.e. controls (positive correlation) > dyslexics (no correlation)).

Irregular Word Spelling

Control and dyslexic subjects showed significant opposite (reversed) effects (Fig. 2B—Table III). In the left transverse and superior temporal gyri, the left/right orbital/

frontal gyri, anterior and posterior cingulate and visual cortex, the greatest LGMV corresponded to the highest spelling performance in dyslexic subjects whereas the greatest LGMV corresponded to the lowest performance in control subjects (i.e. dyslexics (positive correlation) > controls (negative correlation)). By contrast, in the left/right cerebellum and ventral visual areas, the highest LGMV corresponded to the best spelling performance in control subjects whereas the highest LGMV corresponded to lowest performances in dyslexic subjects (i.e. controls (positive correlation) > dyslexics (negative correlation)). Note that at variance with the phonological deletion task, no significant correlation was observed within either group.

Pseudoword Reading Performances

Only significant correlations across groups were observed (i.e. no differences between groups—Fig. 2C, Table IV). Greater LGMV as pseudoword reading performance increased were observed in the left perisylvian areas (superior temporal gyrus, inferior/medial frontal), right middle/superior and medial frontal gyri, posterior cingulate gyrus, left/right paracentral lobules, and visual cortex. Conversely, smaller LGMV for an increased performance (negative correlation) were observed in inferior-temporal (inferior/middle occipital, fusiform, parahippocampal) and cerebellar areas. Interestingly, within-group effects re-

Figure 2.

Between and across-groups gray matter volumes/performances correlations. Brain renders show areas with significant differences between groups in the way LGMV and phonological (A— $F_{critic} = 9.57$) and spelling performances (B— $F_{critic} = 10.01$) correlated, areas showing significant correlations LGMV/pseudoword reading performances across groups (C— $F_{critic} = 8.47$), and the overlap between these three results (D—reading in red,

spelling in green and phonological deletion in blue). Corresponding slices of the cerebellum and occipito-temporal cortex are displayed from $z = -14$ to $z = -24$. Plots show the correlations between LGMV and performances over the left superior temporal gyrus, left fusiform gyrus, the left declive and the pyramis for control (blue) and dyslexic (red) subjects.

TABLE III. MNI coordinates of maximum FDR corrected P values ($q < 0.05$) with cluster size, z -value and anatomical label of grey matter voxels showing significant correlation differences between groups for the irregular word spelling task

MNI coordinate	Cluster size	Z-value	Label
-54-14 10	128	3.65	Left transverse and superior temporal gyrus
-4 38-14	108	3.72	Left/Right orbital gyri
-4 34 16	159	3.82	Left anterior cingulate
-8-40 48	33	3.62	Left precuneus
-12-44 60	70	3.67	Left paracentral lobule—precuneus
4-52 22	457	3.89	Posterior cingulate, precuneus, cuneus
8 44 6	23	3.26	Right anterior cingulate
14 68 14	28	4.71	Right superior frontal gyrus
10-44 62	53	3.37	Right paracentral lobule—precuneus
-26-88-16	1584	4.45	Cerebellum: Culmen (IV), Declive (VI), Uvula (IX), Left Inferior semi-lunar lobule (VIIIB), fusiform gyri, and left inferior occipital gyrus
-26-42-46	22	3.23	Left cerebellar tonsil (VIIIB)
32-82-46	91	3.89	Right Inferior semi-lunar lobule (VIIIB),
-26-42-46	42	3.23	Left cerebellar tonsil, nodulus (X)

Height threshold: $F = 10.01$, $P = 0.003$, Extent threshold: $k = 20$ voxels, Expected voxels per cluster, $\langle k \rangle = 16.731$, Resel = 149.07 voxels. The upper part of the table corresponds to voxels negatively correlated with the score in the irregular word spelling task for controls and positively correlated for dyslexics (control < dyslexic). The lower part of the table corresponds to reversed effects, i.e. positive correlation in control subjects and negative correlations in dyslexic subjects (control > dyslexic). Only clusters with a minimum size of 160 mm³ (20 voxels) were taken into account.

vealed that in the cerebrum (inferior-temporal cortex, visual cortex and right parietal) the positive correlations were driven by control subjects vs. no significant within-group effect for dyslexic subjects. In the cerebellum, control subjects were driving the negative correlations in the posterior/medial parts (declive) whereas effects were more marked in dyslexics for the inferior/lateral part

(left inferior semilunar and tonsil/tuber—Supporting Fig. 4).

Structural Connectivity

VBM results revealed significant effects in a number of overlapping areas (Fig. 2 and Supporting Fig. 5). Of special

TABLE IV. MNI coordinates of maximum FDR corrected p values ($q < .05$) with cluster size, z -value and anatomical label of grey matter voxels showing significant correlation across groups for the pseudoword reading task

MNI coordinate	Cluster size	Z-value	Label
-36-58-22	4338	5.25	Cerebellum: left/right tonsil, inferior semi-lunar lobules (VIIIB), uvula (IX), pyramis (VIII A), declive (VI), culmen (IV), and left tuber Left middle occipital and fusiform gyrus, Right lingual, parahippocampal and fusiform gyrus
-22-20 12	20	2.92	Left parahippocampal gyrus
52-28-8	28	3.31	Right middle temporal gyrus
-26 42-14	44	3.26	Left orbito-frontal gyrus
-40 28-4	26	3.25	Left inferior frontal gyrus, pars orbitalis
-64-20 4	132	3.63	Left superior temporal gyrus
-54 18 6	298		Left inferior frontal gyrus, pars triangularis, Precentral gyrus
8-64 10	1043	4.63	Left/right cingulate gyrus, posterior cingulate, Precuneus, cuneus
-10-40 48	200	4.62	Left paracentral lobule—middle cingulate cortex
-6-58 50	29	3.19	Left precuneus
-14-6 72	27	3.72	Left superior frontal gyrus
10-40 52	215	4.10	Right paracentral lobule—middle cingulate cortex
30 40-14	32	3.27	Right orbito-frontal gyrus
42 -68 38	75	3.72	Right angular gyrus

Height threshold: $F = 8.47$, $P = 0.005$, Extent threshold: $k = 20$ voxels, Expected voxels per cluster, $\langle k \rangle = 21.686$, Resel = 149.07 voxels. The upper part of the table corresponds to voxels negatively correlated with performance, whereas the lower part corresponds to voxels positively correlated with performance (no difference between groups). Only clusters with a minimum size of 160 mm³ (20 voxels) were taken into account.

Figure 3.

Connectivity pattern as measured from LGMV distributions. Brain renders show positive and negative correlations for the left STS (T_{critic} 3.27), fusiform (T_{critic} 3.16), declive (T_{critic} 2.69) and pyramis (T_{critic} 2.9).

interest were areas relevant to dyslexia as the various theories suppose a dysfunction of these regions: left inferior frontal gyrus ($-65\ 17\ 10$), left superior temporal gyrus ($-61\ -20\ 6$), left/right fusiform gyri ($-44/42\ -65\ -18$) and visual cortex and the cerebellum (from left declive $-20\ -72\ -26$ to pyramis $0\ -67\ -34$). Noteworthy, not only did the left STG, fusiform and cerebellum show expected significant effects in relation to with specific language performances (e.g. superior temporal gyrus with phonology, fusiform with reading and cerebellum with spelling) but also with other tasks. Based on these observations, we asked whether these effects might relate to performance/structure relationships in functional systems distributed over the cerebrum and cerebellum and performed a structural connectivity analysis with the left STS, left fusiform gyrus, the left cerebellar declive and cerebellar pyramis as seed regions. Only across groups' correlations were observed, i.e. there was no significant difference between groups in the way gray matter volumes covaried.

LGMV variations measured over the left STG were positively correlated with other voxels of the STG and this effect spread over the left pre/postcentral gyri and the middle temporal gyrus. In the right hemisphere, correlations were observed with the right STG and right precen-

tral gyrus (Fig. 3A). Another significant correlation was observed over the left STG but from the cerebellar pyramis as seed area. In fact, the LGMV of the pyramis negatively correlated, not only with the left STS, but also the left anterior middle temporal gyrus, left/right anterior parahippocampal area, inferior/medial frontal gyrus, anterior cingulate and right visual cortex. Positive correlations were also observed between the pyramis volumes bilaterally and the left/right uvula, the left postcentral gyrus, right pre/postcentral gyri, right anterior STG, right inferior/lateral temporal gyrus, right anterior STG, right inferior/lateral temporal gyrus, right anterior STG (Fig. 3B). From the left (posterior) declive area, only positive correlations were observed: with the left tuber, right declive as well as with the left fusiform, left/right parahippocampal areas, left anterior cingulate, left middle temporal gyrus and right lateral occipital cortex (Fig. 3D). Finally, from the left fusiform gyrus, positive correlations were observed with the left declive, left/right medial occipital gyrus, precune, left inferior parietal/supramarginal gyrus, medial frontal and lateral middle frontal gyri. Negative correlations were observed with the left inferior declive (different region from the previous positive correlation from the left declive to the fusiform, see Fig. 3C), the right inferior semi-lunar lobule, left/right visual cortex (cuneus, lingual), right fusi-

form, left/right thalamus, right STG and right superior frontal.

DISCUSSION

No total (all brain) or partial (lobes) volume difference and lateralization difference could be observed in our large sample between control and dyslexic subjects. The absence of volume difference was confirmed in the voxel-based analysis under both H0 and H1. However, when *p* values uncorrected for multiple comparisons were used ($P < .01$ —Supporting Table I, Supporting Fig. 6), differences could be observed. Although one needs to keep in mind that uncorrected *p* values cannot be used with certainty as some results may be false positives (hence the False Discovery Rate FDR correction), it is important that most of the differences observed with uncorrected *p* values were in accordance with the literature [Eckert, 2004]. These differences concerned the left frontal areas (dyslexic > control subjects) and the left/right temporal cortices (control > dyslexic subjects). The fact that only uncorrected statistics gave these trends, and in almost all previously reported regions, suggests that by using smaller samples, individual variability may have been under- or overestimated by previous studies biasing results toward significance in some regions and not in others.

In contrast with the absence of volume difference, significant correlations LGMV/language performances across groups and/or differences of correlations between groups were observed in three main territories: the cerebellum, the ventral visual cortex and several parts of (mainly) left and dorsal hemispheric brain areas (superior frontal, medial parietal areas, and superior temporal). Those results are in line with the cerebellar, visual and phonological hypotheses on dyslexia [Démonet et al., 2004]. Only the left angular/supramarginal gyri were not observed as showing significant correlations between LGMV and performances (although correlated with the LGMV of the left fusiform gyrus) whereas functional imaging studies have shown functional differences over this region in dyslexic subjects [e.g. Dufor et al., 2007; Ruff et al., 2002, for a review Temple, 2002]. One possible explanation is that this region is only affected by a functional deficit in dyslexia and/or that structural abnormalities in this region are weak or localized in the white matter. Abnormalities of the white matter were not observed here but it is known that T_1 signal intensities do not correlate well to white matter integrity. This can be seen for instance in disorders such as multiple sclerosis, in which white matter T_1 signal intensities remain normal even in severely damaged tissue [Filippi et al., 2001]. Indeed, analyses based on diffusion images that are more sensitive to white matter signals suggest structural differences between control and dyslexic readers in this region [see Beaulieu et al., 2005; Deutsch et al., 2005; Klingberg et al., 2000].

Before turning onto more details about the localization of the observed effects and their possible interpretations, one

needs to question the validity of the results. Because LGMV differences between groups were small (not significant), the significant correlations between LGMV and language performances may be explained, at least partly, by the significant differences in performances between groups. For all behavioral tests, dyslexic subjects showed a larger variance than control subjects did and it is therefore possible that correlations were driven by this difference in performance distributions. Such an effect is likely for instance for the correlation between loan word reading (lexical access) and the lateralization of the IFG (Fig. 1D). For the VBM analysis, whereas phonological scores for dyslexics ranged from -4.6 to 1.1 (mean -0.5 SD 1.35) versus -1.8 to 1.4 (mean 0.49 SD 0.7) for control subjects, only control subjects showed significant correlations with the LGMV. This result goes in the opposite direction as one can predict from variance distributions, i.e. that larger variance in performance leads to stronger correlations with the LGMV. For reading, no difference between groups was observed even though, again, variances were different. In addition, both groups showed intra-group significant correlations but with different spatial distributions. In both cases, it thus seems unlikely that correlations were only due to higher variances in the dyslexic group. Finally, for spelling, because only group differences were observed and scores of controls were quite narrow (ceiling effect in controls), it is possible, even likely, that effects were related to higher score variations in the dyslexic group than in the control group. One thus should be cautious when interpreting this particular result.

Cerebellar Discoveries

The most striking differences were observed in the cerebellum (see Fig. 2), which is usually associated with skill acquisition and automatization. According to Nicolson and collaborators [Nicolson and Fawcett, 2007], dyslexics would show an impaired reading fluency as a consequence of poor automatization of sensory motor associations, including speech-script transcoding, and this deficit would be associated with motor deficits. Although not investigated in this study, none of our subjects reported motor problems during the clinical interview, which ties up with studies showing that motor deficits are not systematically associated with dyslexia [Chaix et al., 2007; Raberger and Wimmer, 2003]. Indeed cognitive deficits may be observed after cerebellar damage without motor deficits [Marien et al., 2001] suggesting a genuine involvement of the lateral cerebellum in language functions.

It has been hypothesized that cognitive processes rely on cerebellar/prefrontal loops such that the cerebellum would support routine operations leaving prefrontal circuits free to process new or challenging tasks [Rammani, 2006]. This functional specialization of the cerebellum might be reflected by the LGMV pattern we observed in relation with efficient processing of unknown stimuli or nonroutine tasks such as those involved in pseudoword reading or phoneme deletion tasks. In particular, best performers in

control subjects exhibited the highest LGMV in the left IFG, right orbital part of the middle frontal gyrus and anterior cingulate and the lowest in the cerebellum; which agrees with the negative correlation (structural connectivity) observed between the pyramis and anterior cingulate gyrus. Aside of those observations, we also observed a disorganization of the performances/LGMV correlations in dyslexia. Whereas control subject showed correlations between the left declive and the performances in phonological deletion and pseudoword reading, no such correlation existed in dyslexics for phonological performance. In addition, a remapping toward the left inferior semilunar lobule/tuber (Supporting Fig. 4) was observed for pseudoword reading. Finally, cautious is needed in the interpretation of this part of the study (see above), irregular word spelling, which calls upon more routinized long-term memory based functions such as access to orthographic lexicon, yielded a reverse correlation pattern between group and areas: best performers in control subjects showed an increase in LGMV in the frontal areas vs. decrease in the cerebellum and the reverse for dyslexic subjects. This result is in accordance with the idea of disorganization of fronto/cerebellar loops in dyslexia (Nicolson and Fawcett 2007). Fine-grained anatomical connections between cerebral cortical areas and the cerebellum are only poorly specified in Humans, but different tracks have been identified in macaque monkeys. Tracks have been identified between the cerebellum and frontal areas (especially pre/post rolandic areas and the lateral prefrontal cortex) but also between the cerebellum and the superior temporal sulcus and posterior parietal association areas, either via the pontine nuclei [Schmahmann and Pandya, 1997a, b] and/or the thalamus [Middleton and Strick, 1997]; homolog structures in Humans might account for our results.

Visual Cortex Correlations

Significant correlations across groups for pseudoword reading, and differences in correlations between groups for irregular word spelling were observed mainly over the visual cortex (around the calcarine sulcus) and the occipito-temporal cortices. According to the hypothesis relating dyslexia to abnormalities in the M cell system, we would have expected differences in the thalamus, visual cortex, and related dorsal areas like MT. Here, correlations linked to the visual system did not involve these regions except BA17/18. One possibility is that differences in areas like MT are more functional than structural. Another possibility is that local volume measurements are not sensitive enough to capture variations in cell density and size [Livingstone et al., 1991], which may exist in dyslexia [for a discussion, Bishop, 2002]. In contrast with the M hypothesis, strong effects were observed over the left and right infero-temporal cortex [Kronbichler et al., 2007], which agree with the hypothesis of a “visual reading deficit” originating from left fusiform abnormalities. In fact, not

only reading disorders occur after left infero-temporal lesions [e.g. Damasio and Damasio, 1983] but also spelling disorders [Rapczak and Beeson, 2004]. Volumes variations in this area may thus reflect altered visual processes in dyslexia although these deficits likely concern their high-level components [Pernet et al., 2006]. This is also in agreement with the connectivity analysis that revealed that LGMV of the left fusiform gyrus covaried negatively with other ventral visual areas and the thalamus vs. positive correlation with the supramarginal gyrus, medial frontal and lateral middle frontal gyri; regions that are known to be involved in higher level reading processes [Price, 2000]. This connection pattern seems likely as the thalami, cuneus, precuneus are the natural pathways of the visual system, the left and right fusiform gyri are known to be connected via splenium fibers, and fusiform and inferior frontal (but not middle frontal) are connected via the inferior frontal-occipital fasciculus [Catani, 2006]. More surprisingly, than the reading and spelling correlations, we also observed significant correlations between visual ventral areas and performances in phonological deletion [see Kronbichler et al., 2007 for similar result]. In the left fusiform gyrus, effects elicited by the three tasks overlapped largely, whereas in the right hemisphere, phonological performances were correlated with LGMV in regions located more caudally than those correlated with reading or spelling performances (Fig. 2). Physiological [Gibson and Maunsell, 1997; Poremba et al., 2003] and functional fMRI [Cohen et al., 2004; von Kriegstein et al., 2005] studies have indeed shown auditory responses of the infero-temporal cortex. Of particular relevance here, Cohen and co-workers [Cohen et al., 2004] reported the existence of a multimodal area in the left fusiform gyrus (lateral infero-temporal multimodal area—LIMA) that is involved in phonology and in word decoding. Our results partly agree with Cohen et al. as reading and phonological performances correlated with LGMV in the “LIMA” region, whereas reading, spelling and also phonological performances correlated with LGMV in the visual word form area (VWFA).

Of particular importance here, was the ability to discriminate between infero-temporal and cerebellar gray matter as both showed correlations with performances. Special care has been taken in this respect as the cerebrum and cerebellum have been smoothed separately; thus, ensuring greater independence of neighboring voxels. To adjust the statistics to differences in smoothness between regions, a correction for nonisotropic smoothness has also been applied [Haya-saka et al., 2004; Worsley et al., 1999]. Registration errors could also have occurred thus mixing fusiform and cerebellar tissues: using SPM5, the mean displacement errors are estimated to be about 4.5 mm [Crinion et al., 2007] and thus cannot really account for effects located more than 15 mm apart (such as the distance between fusiform and declive regions) as observed on our data. Indeed, comparison of volume distributions computed over the left fusiform gyrus and left declive show that they are different

measurements ($t(76) = 41.48$ $P < .0001$). In addition, no difference between groups can be observed in terms of distance relative to template (Supporting Fig. 1) suggesting that there was no bias toward on group or the other. Finally, careful inspection of the results and excluding from the analysis a 8 mm-wide tissue strip along the cerebral/cerebellar border (Supporting Fig. 7) revealed that even in this case performances were correlated with LGMV in both regions. We are thus confident that both the infero-temporal and the superior cerebellum correlate independently with the three tasks (phonological deletion, pseudoword reading and irregular word spelling).

Left Superior Temporal Gyrus

In agreement with most conceptualizations of the neural underpinnings of spoken language [Hickok and Poeppel, 2004; for reviews Démonet et al., 2005; Wise, 2003], we observed significant LGMV/performance correlations over the left STG with phoneme deletion task in normal readers but not in dyslexic subjects. Within the same region, other clusters also showed correlations with pseudoword reading and irregular word spelling. Considering the absence of significant effects in the dyslexia group, this finding might be accounted for by the auditory/phonological hypothesis. It may be that in dyslexic subjects, who show very limited phonological awareness abilities, the cortical architecture in the left association auditory cortex/superior temporal gyrus is deeply disorganized so that no systematic performance/LGMV relationship could arise at the group level. This effect may also be reflected in findings related to grapheme/phoneme performances (no intra group correlation with the pseudoword reading and end of the distribution/continuum in the across group analysis) and more generally in tasks involving speech decoding such as in irregular word spelling to dictation task. Connectivity analysis revealed connection with the right STS, which is expected as those regions are connected via the corpus callosum [Catani et al., 2002] and are believed to be both involved in speech/phonological processing [Hickok and Poeppel, 2004]. Another significant correlation was observed over the left STS but from the cerebellar pyramis as seed area. Anatomical connections between the STS and the cerebellum are not known in Humans but several authors have postulated an involvement of the cerebellum in phonological processing and dyslexia [e.g. Georgiewa et al., 2002]. The absence of any systematic association between LGMV and performance on phoneme deletion in dyslexic subjects as well as the absence of within group modulation of the LGMV of the cerebrum by the performance on pseudoword reading suggests strongly disorganised structure/function relationships for phonological skills. Causal structural anomalies may well lay in the left superior temporal gyrus (STG), an hypothesis that is further supported by the correlations we observed, in the control group only, between leftward lateralization of this region and increased performance in phonological processing. Microstructural abnormal-

ities (e.g. microgyria) observed in some cases of dyslexia in these regions might explain the difference in lateralization [Eckert, 2004] and seem to be, in this case, linked to genotypic characteristics [Galaburda et al., 2006].

CONCLUSION

Almost all sites proposed to be involved in dyslexia by the different theories were observed in this work on LGMV. Previous studies typically did not report all expected involved sites possibly because of too small group sizes, biasing the statistics, and/or because performances in the different components of reading (visual, phonological, lexical, spelling skills) were not all controlled. Here, using sufficiently large sample and correlating gray matter volumes with reading related skills, we observed differences mainly around the left IFG, the left STG, the fusiform gyri and the lateral superior, and inferior medial cerebellum. These findings lend support to a multifocal explanation of behavioral deficits observed in dyslexia. However, the total absence of correlation with the phonological deletion task over the whole brain and with the pseudoword reading task over the cerebrum in dyslexic subjects suggest that brain areas involved in or related to phonological processing (STG, IFG, and possibly left fusiform) are primarily altered in dyslexia.

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