Functional Abnormalities in the Dyslexic Brain: A Quantitative Meta-Analysis of Neuroimaging Studies

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Abstract: This study used foci from 17 original studies on functional abnormalities in the dyslexic brain to identify brain regions with consistent under- or overactivation. Studies were included when reading or reading-related tasks were performed on visually presented stimuli and when results reported coordinates for group differences. Activation likelihood estimation (ALE) was used for quantification. Maxima of underactivation were found in inferior parietal, superior temporal, middle and inferior temporal, and fusiform regions of the left hemisphere. With respect to left frontal abnormalities, we found underactivation in the inferior frontal gyrus to be accompanied by overactivation in the primary motor cortex and the anterior insula. Tentative functional interpretations of the activation abnormalities are provided. *Hum Brain Mapp 30:3299–3308, 2009.* © 2009 **Wiley-Liss, Inc.**

Key words: dyslexia; reading; magnetic resonance imaging; positron-emission tomography; cerebral cortex

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INTRODUCTION

Over the last 12 years, a substantial number of studies have examined functional brain abnormalities of children and adults who suffer from severe reading difficulties, and several reviews of the imaging findings were published [Démonet et al., 2004; Grigorenko, 2001; Habib, 2000; Heim and Keil, 2004; McCandliss and Noble, 2003; Pugh et al., 2000; Sandak et al., 2004; Shaywitz and Shaywitz, 2005; Temple, 2002]. A main conclusion of these reviews is that developmental dyslexia is associated with underactivation in posterior regions of the left hemisphere which, in skilled reading, forms a highly organized cortical system for visual word processing. Following Sandak et al.'s [2004] theorizing, this word processing system includes two posterior subsystems. The function of the dorsal (temporoparietal) reading system is to map letters (graphemes) of a visual word onto phonological segments in an attentionally controlled manner. This function is important in early phases of learning to read and, in skilled readers, it is involved in the processing of unfamiliar visual words. Underactivation of this dorsal system in dyslexic readers is interpreted as reflecting a phonological impairment, specifically an impairment to access phonological segments associated with graphemes. The second posterior reading subsystem is referred to by Sandak et al. [2004] as ventral (occipito-

temporal). Its main function is considered to be fast automatic processing of familiar visual words or frequent letter strings within words. It appears to be late developing in reading acquisition and is aptly referred to as the occipitotemporal "skill zone" [Grigorenko, 2001; Sandak et al., 2004; Schlaggar and McCandliss, 2007; Shaywitz et al., 2002, 2007]. Accordingly, underactivation of this ventral system in dyslexic readers is interpreted as reflecting an impairment with fast effortless visual word recognition. Some authors see the deficit with fast visual word processing—reflected in left ventral underactivation—as secondary to the primary dysfunction of the dorsal system involved in controlled grapho-phonological word processing [McCandliss and Noble, 2003; Pugh et al., 2000].

A further common theme in the mentioned reviews is that dyslexic readers exhibit abnormal overactivation in frontal and/or right hemisphere regions to compensate for the dysfunctional left posterior reading systems. Specifically, overactivation in left inferior frontal regions is interpreted as reflecting covert articulatory word guessing based on contextual or visual cues and—more generally— as reflecting increased effort during reading. Abnormal engagement of right hemisphere temporoparietal regions was also interpreted as compensation for the corresponding left temporoparietal dysfunction [Démonet et al., 2004; Pugh et al., 2000; Sandak et al., 2004; Shaywitz and Shaywitz, 2005].

This study extends the mentioned narrative reviews by quantitatively meta-analyzing 17 studies which reported brain regions with abnormal under- or overactivation (in relation to nonimpaired readers). Studies were included when reading or reading-related tasks were performed on visually presented stimuli and when results reported coordinates for group differences. A main goal was to provide specific information on brain loci with activation abnormalities (in terms of x-, y-, z-coordinates), which in the mentioned reviews are globally characterized as temporoparietal or occipitotemporal. A further goal was to clarify inconsistent findings on abnormalities in left frontal brain regions for which both over- and underactivations are reported. More generally, the quantitative meta-analytic approach provides an objective synthesis of the findings of the 17 imaging studies on functional abnormalities associated with dyslexia. This synthesis may also lead to the identification of previously overlooked functional abnormalities. The resulting statistical brain map may serve as a mask for small volume corrections or as starting point for studies of dyslexic abnormalities in effective connectivity between regions of interest.

Quantitative meta-analysis was introduced to the field of neuroimaging by activation likelihood estimation (ALE) that was concurrently developed by Turkeltaub et al. [2002] and Chein et al. [2002]. It is based on the fact that the majority of functional imaging studies report the foci of brain activity in terms of 3D (x, y, z) coordinates in standardized stereotactic space. In ALE, the foci of brain activity in a set of studies are analyzed for concordance by modeling each reported focus as center of a Gaussian probability distribution. These distributions are then combined to create a whole-brain statistical map (ALE map) that estimates the likelihood of activation for each voxel. We used a recent extension of this method by Laird et al. [2005], which makes it possible to perform statistical comparisons of ALE maps. For this study, this approach led to three ALE maps: one presenting brain regions with underactivation in dyslexic readers, one presenting regions with overactivation and, finally, a subtraction map which allows a formal assessment of differences between the two maps.

MATERIALS AND METHODS

To identify relevant studies, we performed several Medline searches with the keywords "dyslexia" and "imaging". Criteria for the selection of fMRI and PET studies were the following: (1) stimuli were letter strings of words or pseudowords, or single letters, (2) tasks were reading or reading-related (e.g., rhyme judgements), and (3) group comparisons (dyslexics vs. controls) were reported in a standard stereotactic space (Talairach or MNI). Because of the third criterion, several studies could not be included [e.g. Shaywitz et al., 1998, 2002]. These studies typically presented group differences using brain figures and reference to Brodmann's areas or presented activation differences for regions of interest only. One study [Brunswick et al., 1999] was excluded in favor of a more recent one [Paulesu et al., 2001] that examined the same (and additional) participants with the same tasks. On the basis of the mentioned criteria, 17 studies (12 fMRI and 5 PET) with a total number of 595 participants (294 dyslexics and 301 controls) were included. Data are current with December, 2008. We also included the most recent study from our lab [Wimmer et al., manuscript submitted for publication]. The selected studies and their main characteristics are listed in Table I.

From the 17 studies altogether 128 foci of reliable group differences were extracted (69 for dyslexic underactivation and 59 for dyslexic overactivation). For each study, group differences for only a single contrast of an experimental condition against baseline (simple fixation or low-level visual control) were included. However, one study identified foci by correlation with reading ability [Meyler et al., 2007]. Because of limitation to one contrast per study, all foci included in the meta-analysis stem from independent samples. The majority of studies reported group differences for only one such baseline-contrast [Booth et al., 2007; Brambati et al., 2006; Cao et al., 2006; Grünling et al., 2004; Hoeft et al., 2006, 2007; Ingvar et al., 2002; Kronbichler et al., 2006; McCrory et al., 2005; Paulesu et al., 2001; Schulz et al., 2008; Temple et al., 2001]. For studies which reported group differences for more than one contrast, we only used foci reported for the "phonological" task, that is pseudoword reading [Georgiewa et al., 1999; Rumsey et al., 1997; Wimmer et al., manuscript submitted for

TABLE I. Main characteristics of the included studies and number of foci used in the meta-analysis

Year	First author	Imaging	N	Dys	Con	Native language	Age range	Task type	Contrast	No. of foci (under-/ overactivation)
2008	Wimmer	fMRI	39	20	19	German	15–34	Phonological lexical decision	Nonwords > fixation	3/10
2008	Schulz	fMRI	34	12	22	German	10–12	Silent reading of sentences with semantically conguous or incongruous endings	Sentence reading > fixation	5/0
2007	Booth	fMRI	32	15	17	English	9–15	Semantic association judgement	Related word pairs > fixation	1/1
2007	Hoeft	fMRI	53	23	30	English	7–16	Word rhyme judgement	Rhyme > fixation	3/4
2007	Meyler	fMRI	67	41	26	English	8–11	Sentence comprehension	Correlation between reading ability and neural activation	3/0
2006	Brambati	fMRI	24	13	11	Italian	13–63	Silent reading	Reading (words and pseudowords) > false font string observation	5/0
2006	Cao	fMRI	28	14	14	English	8–14	Word rhyme judgement	Conflicting trials > fixation	6/0
2006	Hoeft	fMRI	30	10	20	English	8–12	Word rhyme judgement	Rhyme > fixation	6/0
2006	Kronbichler	fMRI	28	13	15	German	14–16	Sentence comprehension	Reading > false font string comparison	2/10
2005	McCrory	PET	18	8	10	English	(Mean) 20	Word reading and picture naming	Reading > false font string comparison	1/0
2004	Grünling	fMRI	38	17	21	German	(Mean) 13	Pseudoword rhyme judgement	Pseudoword rhyme > letter sting judgment	3/22
2002	Ingvar	PET	18	9	9	Swedish	20–28	Reading silently and aloud	Reading words silently > rest	2/2
2001	Paulesu	PET	72	36	36	English, Italian, French	(Mean) 24	Reading aloud	Reading (words and pseudowords) > rest	4/0
2001	Temple	fMRI	39	24	15	English	8–12	Visual letter matching and line matching	Matching letters > matching lines	5/1
1999	Georgiewa	fMRI	34	17	17	German	9–17	Silent reading	Silent pseudoword reading > letter string observation	2/2
1997	Rumsey	PET	31	17	14	English	18–40	Reading aloud	Nonword > fixation	13/7
1996	Paulesu	PET	10	5	5	English	(Mean) 26	Letter pair rhyme judgement	Letter pair rhyming > shape similarity judgment	5/0
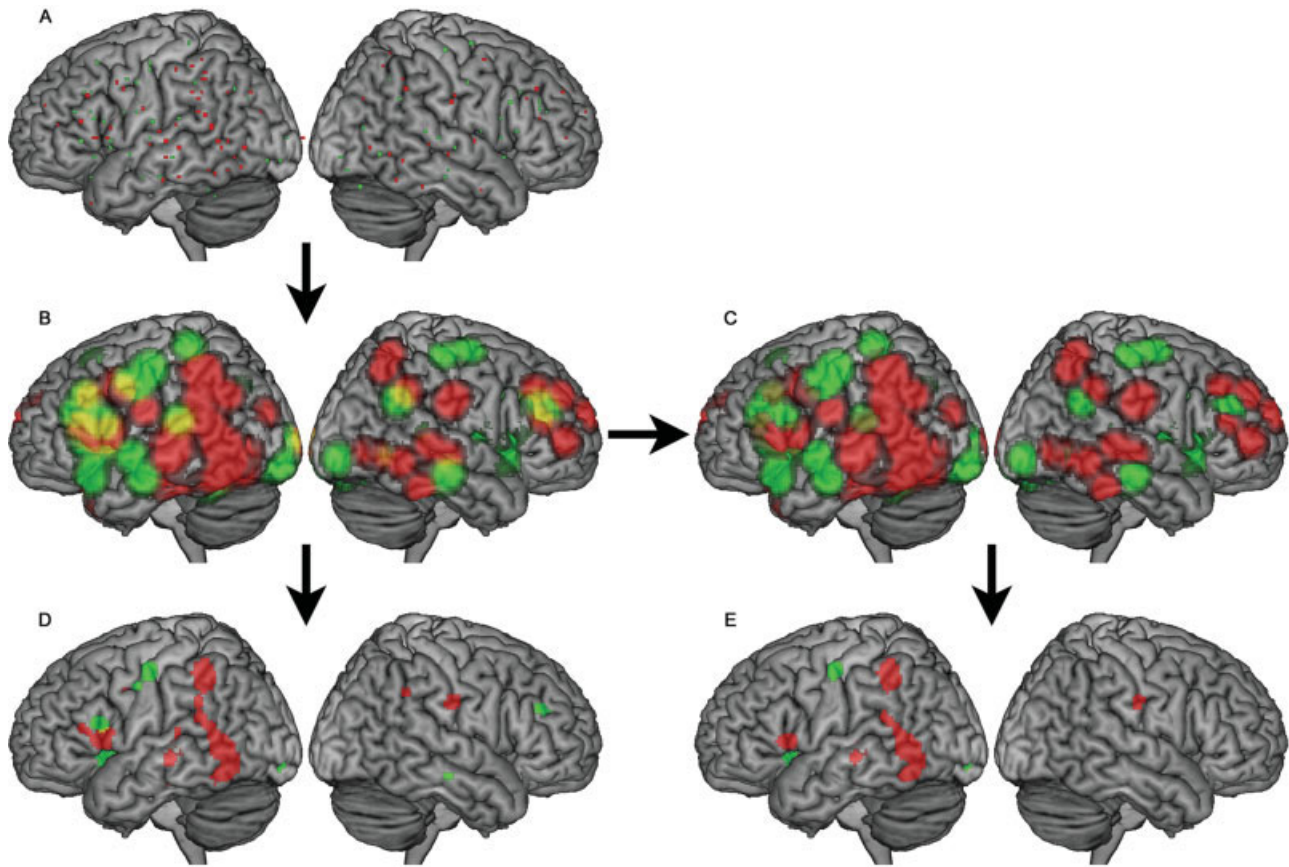
Figure 1.

(**A**) Surface rendering of all 128 input foci with underactivation in red and overactivation in green. (**B**) Overlays of the separate ALE maps for under- (red) and overactivation (green), respectively. Regions contained in both maps are shown in yellow. (**C**) Surface rendering of the difference map (after subtracting the ALE values for underactivation from the ALE values for overacti-vation). The blurred coloring results from discrepant activations at surface and deeper regions. (**D**) Composite surface rendering of the two thresholded independent ALE maps for under- and overactivation, respectively. (**E**) Surface rendering of the thresholded difference map. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

publication] or rhyme judgement [Paulesu et al., 1996]. The meta-analysis used the peak coordinates of the clusters identified by the group comparisons. When a cluster included several anatomically distinct regions, the reported local maxima for these subregions were also used.

In preparation for the meta-analysis, Talairach-coordinates were transformed into MNI-space using icbm2tal [Lancaster et al., 2007]. Figure 1A shows all 128 input foci (red for underactivation, green for overactivation) rendered on left and right hemisphere brain surfaces, respectively.

In the next step, two separate ALE maps were generated by modeling each input focus as center of a Gaussian probability distribution. One map was generated for the 69 foci representing underactivations and the other for the 59 foci representing overactivations. Figure 1B shows the separate under- and overactivation maps rendered onto the surface of the left and the right hemisphere. Regions included in both the under- and the overactivation map are represented in yellow.

To examine statistical significance, each of these maps was contrasted with a noise map based on 10,000 sets of random foci. These random sets consisted of the same number of foci (i.e., 69 vs. 59 for under- and overactivation maps, respectively) as the to-be-tested maps. The noise maps make it possible to examine the probability of the ALE value of each voxel under the null-hypothesis that ALE values are distributed randomly and uniformly in the brain. For these analyses, GingerALE software version 1.2b1 [Laird et al., 2005] was used with a FWHM of 12 mm and 10,000 permutations. To correct for multiple comparisons, false discovery rate (FDR) was set at $q = 0.05$, and the threshold for cluster extent was set at a volume of 120 mm^3 (equivalent to 15 voxels). These are standard val-

ues recommended by the authors of the software. The thresholded separate under- and overactivation maps are rendered in Figure 1D.

In addition to the two separate maps, a difference map was computed by subtracting the ALE values for underactivation from the ALE values for overactivation. The resulting map presents positive ALE values for over- and negative values for underactivations. Figure 1C shows a surface rendering of these ALE values. The blurred color for some surface regions is caused by discrepant activations, for example, an overactivation in a deeper region is shining through the underactivation in the surface region. This subtraction map was contrasted with a noise map based on 10,000 sets of random foci. Each of these random sets consisted of 128 foci (i.e., 69 vs. 59 for negative and positive values, respectively). Further analysis (computation of corrected *p*-values and thresholding) was done with the same parameters as for the primary maps. The final thresholded difference map is rendered in Figure 1E.

RESULTS

Figure 1 illustrates the results of the processing steps from the input foci in Figure 1A to the final thresholded ALE maps in Figure 1D,E. A first observation from Figure 1A is that 80 input foci are localized in the left hemisphere and only 48 in the right hemisphere with 58% of the left and 48% of the right hemisphere foci being underactivation foci. The renderings in Figure 1B visualize the separate ALE maps for the underactivation and the overactivation foci before thresholding. Because of the spatial proximity of similar input foci (shown in Fig. 1A) and the 12-mm-FWHM of the Gaussian probability distributions, large coherent brain regions are represented in each of the two maps. Inspection of the renderings shows that underactivation dominates in left occipitotemporal and temporoparietal regions, whereas overactivation dominates in bilateral occipital and left frontal regions. Regions contained in both maps (yellow) are localized in left inferior frontal and precentral gyri. Corresponding to the smaller number of input foci, the regions of under- and overactivation in the right hemisphere are less extended. The subtraction map in Figure 1C is similar to the composite of the under- and overactivation maps of Figure 1B. Overlaps of under- and overactivations are not longer present.

Figure 1D shows that the extended regions in the under- and overactivation maps of Figure 1B shrink massively when mentioned height and extent thresholds are applied. However, the thresholded underactivation map in Figure 1D still contains a large cluster in the left hemisphere reaching from dorsal inferior parietal to ventral occipitotemporal regions. It also includes underactivations in left temporal and left inferior frontal regions. The thresholded overactivation map contains several left hemisphere regions (anterior insula, primary motor cortex, inferior frontal gyrus, lingual gyrus, caudate nuclei, thalamus) and

also a number of right hemisphere regions (medial frontal cortex, middle temporal gyrus, caudate nuclei). Of interest is that the left inferior frontal overactivations are in close proximity to the underactivation cluster.

The thresholded difference map of Figure 1E provides a more conservative assessment of activation abnormalities than the separate over- and underactivation maps. However, the majority of activation abnormalities identified by the separate maps are still present in the conservative thresholded difference map. This applies to the large left hemisphere underactivation reaching from dorsal inferior parietal to ventral occipitotemporal regions and to the middle temporal and the inferior frontal underactivation. The difference map also identified the majority of the clusters of the separate overactivation map (left hemisphere: anterior insula, primary motor cortex, lingual gyrus, caudate nuclei, thalamus; right hemisphere: medial frontal cortex). Details of the MNI-coordinates of the maxima and the extent of the under- and overactivations are provided in Table II.

For additional evaluation of convergence across studies, we examined for each cluster of under- or overactivation of the subtraction meta-analysis how many of the 17 studies contributed to its identification. For this evaluation, an input focus was assigned to a region, or to a local maximum within a region, when it fell within a sphere of 20 mm radius around the maximum. Table III shows substantial convergence for the large left posterior underactivation with altogether 8 of the 17 studies contributing. Some convergence, with at least four studies contributing, was also given for the local maxima within the large left posterior underactivation. For the clusters with overactivation, it has to be noted that only nine studies reported foci for overactivations. In relation to this small number, there was substantial convergence for the left anterior insula and the left primary motor area with contribution from five and four studies, respectively. Interestingly, 13 of the 19 contributions to clusters with overactivation stemmed from three German-based studies [Grünling et al., 2004; Kronbichler et al., 2006; Wimmer et al., manuscript submitted for publication]. Rather limited convergence with contributions from at most two studies is given for the underactivation clusters in the left anterior inferior temporal gyrus and the right postcentral gyrus and for the overactivation clusters in the left thalamus and the right medial frontal cortex.

DISCUSSION

The present meta-analytic results make it possible to specify the rather broad anatomical characterization of brain dysfunctions that are given in the narrative reviews of functional neuroimaging studies on dyslexia [Démonet et al., 2004; Grigorenko, 2001; Habib, 2000; Heim and Keil, 2004; McCandliss and Noble, 2003; Pugh et al., 2000; Sandak et al., 2004; Shaywitz and Shaywitz, 2005; Temple, 2002]. In the Introduction, we referred to the review by

TABLE II. Regions showing under- or overactivation in dyslexic readers as identified by the subtraction meta-analysis

Region	Volume (mm³)	Range x	Range y	Range z	Local maxima x	Local maxima y	Local maxima z
Nonimpaired > dyslexic readers							
L posterior regions	5,248	−66/−40	−66/−40	−20/24			
Superior temporal g.					−52	−44	20
Superior temporal s.					−54	−50	14
Middle temporal g.					−60	−56	2
Inferior temporal g.					−52	−62	−8
Fusiform g.					−46	−50	−16
L inferior parietal lobule	1,856	−60/−46	−52/−38	36/56	−52	−46	44
L inferior frontal g., opercular	1,240	−58/−42	12/24	2/10	−46	16	6
L middle temporal g.	1,080	−58/−44	−32/−20	−8/6	−52	−28	0
L inferior temporal g.[a]	448	−46/−40	−32/−20	−22/−16	−44	−26	−20
R postcentral g.[a]	472	50/60	−20/−14	26/34	54	−18	30
Dyslexic > nonimpaired readers							
L anterior insula	376	−36/−30	12/22	−8/0	−34	18	−4
L primary motor cortex	784	−58/−46	−16/−8	44/54	−50	−12	50
L lingual g.	528	−20/−12	−94/−84	−12/−6	−16	−88	−8
L caudate nuclei	608	−24/−16	−6/4	18/24	−20	0	20
L thalamus[a]	168	−8/−2	−16/−12	6/14	−4	−14	8
R medial frontal c.[a]	536	20/30	34/42	18/26	24	38	22

[a] Regions showing small convergence across studies.

Sandak et al. [2004] which, similar to the other reviews, distinguished between a dysfunctional dorsal (temporoparietal) reading system and a dysfunctional ventral (occipito-temporal) reading system with the former being engaged by the phonological reading route (i.e., by attentionally controlled grapho-phonological processing of unfamiliar letter strings) and the latter being engaged by the visual reading route (i.e., by fast automatic processing of familiar visual words or frequent letter strings within words). A third left inferior frontal system was described as exhibiting overactivation due to covert articulatory processes and—more generally—was assumed to reflect increased dyslexic effort during reading. In the following, we relate the present meta-analytic findings to the broad anatomical localizations of the reading systems in the narrative reviews.

Dorsal (Temporoparietal) Reading System

In the review by Sandak et al. [2004], this system is anatomically characterized as including "the angular gyrus and supramarginal gyrus in the inferior parietal lobule, as well as the posterior aspect of the superior temporal gyrus (Wernicke's area)" (p. 275). McCandliss and Noble [2003] summarized the evidence as speaking for a "dysfunction of left perisylvian structures, typically implicating the posterior superior temporal gyrus, and sometimes the angular gyrus and the insula" (p. 197). Démonet et al. [2004] referred to a left dorsal reading pathway as "including mainly the angular and supramarginalis gyri" (p. 1454). We note further that several MEG studies found dyslexic abnormalities (delayed or reduced activity) in posterior

portions of the left superior temporal gyrus/sulcus [review by Salmelin and Helenius, 2004].

Our meta-analysis provides partial support for these anatomical characterizations. The thresholded difference map found maxima of underactivation in posterior parts of the left superior temporal gyrus/sulcus, and the separate underactivation map found an additional maximum in the supramarginal gyrus. However, there was no support for a dysfunction of the angular gyrus. This region was not identified by the subtraction meta-analysis, and it was also not included in the less conservative underactivation map. This finding is remarkable, because the left angular gyrus—starting with nineteenth century neurological conceptions [Dejerine, 1891, 1892]—was considered to be the critical brain site for reading competence and for loss of reading ability. The present failure to identify the angular gyrus as dysfunctional in dyslexic readers is consistent with recent neuroimaging research which questioned the importance of the angular gyrus in reading [Price, 2000].

A main finding of the present meta-analysis was underactivation in the left inferior parietal lobule which typically is not included in anatomical characterizations of the temporoparietal reading system. The center of this underactivation is close to the intraparietal sulcus, and quite distant from the temporoparietal junction. The functional role of this region in reading is not clear. Cao et al. [2006] proposed that competent readers exhibit increased inferior parietal activation in response to conflicting orthography-phonology information in a rhyme judgement task. Cohen et al. [2008] found activation of bilateral parietal regions when unfamiliar (e.g., vertical) displays of words required serial, attention demanding letter processing. However, the

TABLE III. Convergence across studies

Year	First author	Underactivations										Overactivations					
		L superior temporal g.	L superior temporal s.	L middle temporal g.	L inferior temporal g.	L fusiform g.	L inferior parietal lobule	L inferior frontal g., opercular	L middle temporal g.	L inferior temporal g.	R postcentral g.	L anterior insula	L primary motor cortex	L lingual g.	L caudate nuclei	L thalamus	R medial frontal c.
2008	Wimmer	X			X	X	X	X				X	X		X		X
2008	Schulz	X					X										
2007	Booth							X									
2007	Hoeft						X					X			X		
2007	Meyler		X	X													
2006	Brambati		X					X									
2006	Cao		X	X	X			X		X							
2006	Hoeft						X										
2006	Kronbichler	X	X	X	X		X					X	X	X	X	X	
2005	McCrory					X											
2004	Grünling								X			X	X	X			X
2002	Ingvar																
2001	Paulesu	X	X	X	X	X											
2001	Temple																
1999	Georgiewa							X									
1997	Rumsey	X							X	X	X	X	X	X		X	
1996	Paulesu								X								
	Total	5	5	4	4	3	5	5	3	2	1	5	4	3	3	2	2

For each local maximum, studies contributing to that maximum are marked with an X.

superior parietal regions, identified by Cohen et al. [2008] as engaged by serial reading, are more posterior and more medial than the presently identified left inferior parietal local maximum.

An interesting interpretation of the underactivation in the left inferior parietal lobe is offered by the conceptualization of the dorsal visual pathway as including a visuomotor integration system [Milner and Goodale, 1995]. From this perspective, the left inferior parietal region may serve as a visuo-articulatory interface where grapheme codes activate articulation of phonemic segments in left frontal language regions, and the presently found underactivation may reflect a dysfunction of this interface area.

Ventral (Occipitotemporal) Reading System

Sandak et al. [2004] localized this fast visual word processing system in left inferior occipitotemporal/fusiform regions and with extension into the middle and inferior temporal gyri. Similarly, Démonet et al. [2004] localized the ventral reading system in the posterior fusiform gyrus and in inferior temporal and occipital regions. A more specific localization was proposed by McCandliss and Noble [2003] who, following the Visual Word Form Area (VWFA) hypothesis of Cohen et al. [2002], localized the ventral system in the left mid-fusiform gyrus.

The present meta-analysis provides support for a dysfunction of the VWFA. To examine how the presently found local maximum of underactivation in the fusiform gyrus relates to the localization ($x = -43$, $y = -54$, $z = -12$; Talairach space) of the VWFA of Cohen et al. [2002], we transformed our MNI coordinates into Talairach space using icbm2tal [Lancaster et al., 2007]. The resulting coordinates of our fusiform maximum at around $x = -44$, $y = -47$, $z = -15$ showed an Euclidean distance of only 8 mm (three voxels) to the classical VWFA coordinates. As noted in the Introduction, several authors suggested that the left fusiform region is progressively recruited for fast visual word recognition in the course of reading development. Consistent with this developmental interpretation, all three studies that contributed specifically to the identification of the fusiform maximum in the present meta-analysis were done with adolescents or adults and not with children [McCrory et al., 2005; Paulesu et al., 2001; Wimmer et al., manuscript submitted for publication]. For interpretation of the dyslexic underactivation in the left fusiform region, it may be of interest that there are somewhat different interpretations of the function of the VWFA in the left fusiform region. The original interpretation of the VWFA by Cohen et al. implies that dyslexic readers suffer from a deficit in fast parallel processing of legal letter strings. Our research group proposed that the VWFA is engaged by efficient visual-orthographic word recognition [Kronbichler et al., 2004] and suggested that a dysfunction of the left fusiform region affects the build-up or the use of an orthographic word lexicon in recognition [Wimmer et al., manuscript submitted for publication]. From the position of Price and Devlin [2003] and Devlin et al. [2006], it

would follow that the underactivation of the VWFA reflects a general impairment to link visual or other sensory information to higher-order representations.

Consistent with the anatomical characterization of the ventral occipitotemporal reading system by Sandak et al. [2004], we found local maxima of underactivation not only in the VWFA but also in the posterior portion of the inferior temporal gyrus and the middle temporal gyrus. A further cluster of underactivation in the left middle temporal gyrus was localized anterior to the posterior local maximum. These inferior and middle temporal regions may not be engaged by visual-orthographic processes but by lexical-semantic processes [Bookheimer, 2002; Booth et al., 2007; Cao et al., 2006; Price et al., 1997; Vigneau et al., 2006]. A recent review of speech processing also described these brain structures as a lexical interface region which links auditory-phonological representations in the posterior superior temporal sulcus with widely distributed conceptual representations [Hickok and Poeppel, 2004, 2007]. From this perspective, the presently found underactivations in middle and inferior temporal regions may reflect impaired access to lexical-semantic representations and this may be a consequence of a primary dysfunction with visual word processing. Consistent with this interpretation, two recent studies that relied on sentence comprehension found marked dyslexic underactivation in the left middle temporal region [Kronbichler et al., 2006; Meyler et al., 2007].

Anterior (Inferior Frontal) Reading System

This subsystem with overactivation in dyslexic readers was localized by narrative reviews in posterior aspects of the left inferior frontal gyrus and was assumed to reflect compensatory reliance on effortful pronunciations in word recognition [Démonet et al., 2004; Sandak et al., 2004]. Consistent with the reviews, the overactivation map included a region in the left inferior frontal gyrus, but this region was no longer present in the more conservative subtraction map. Regions with overactivation were identified in the primary motor cortex and the anterior insula. The former region is close to the mouth area [Fox et al., 2001], and activation in this region may reflect compensatory reliance on articulatory-based access to phonological word representations. A main new finding is underactivation of the opercular part of the left inferior frontal gyrus. This underactivation may reflect a dysfunction in efficient access to lexical and sublexical phonological output representations. A recent reformulation of the dominant phonological deficit explanation of dyslexia suggested that the deficit may have less to do with the quality of phonological representations but more with access to these representations [Ramus and Szenkovits, 2008].

Additional Findings

Not mentioned in the narrative reviews is the presently found overactivation of the left lingual gyrus. This brain

region is assumed to be engaged by low-level visual processes [Dien, 2009; Jobard et al., 2003; Mechelli et al., 2000], and the presently found overactivation may reflect prolonged visual processing when dyslexic readers are confronted with reading or a reading-related task.

An interesting negative finding was the absence of a group difference in the cerebellum but not all of the included studies acquired functional data from this structure. A dysfunction of the cerebellum is assumed by the automaticity deficit hypothesis [Nicolson et al., 1999]. Several voxel-based morphometric studies found reduced gray matter density in the cerebellum of dyslexic readers [Brambati et al., 2004; Brown et al., 2001; Eckert et al., 2005; Kronbichler et al., 2008].

A further negative finding from the subtraction meta-analysis is that no clusters with overactivation were identified in the right hemisphere. Such overactivations in some original studies were interpreted to reflect compensatory processes in these regions [Démonet et al., 2004; Pugh et al., 2000; Sandak et al., 2004; Shaywitz and Shaywitz, 2005]. Although there were a number of right hemisphere input foci showing overactivation, these foci were rather scattered and no reliable clustering was observed.

CONCLUSION

We used ALE based on 128 foci from 17 original neuroimaging studies to identify brain regions with under- and overactivation in dyslexic readers. Maxima of underactivation were found in inferior parietal, superior temporal, middle and inferior temporal, and fusiform regions of the left hemisphere. The localization of the maxima specified the broad anatomical characterizations of the narrative reviews. New findings were provided on left frontal abnormalities. Here, we found underactivation in the inferior frontal gyrus to be accompanied by overactivation in the primary motor cortex and the anterior insula. The assessment of group differences by the conservative subtraction method failed to identify dyslexic abnormalities in the right hemisphere and in the cerebellum.

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