

Abnormal Activation of Temporoparietal Language Areas During Phonetic Analysis in Children With Dyslexia

Joshua I. Breier, Panagiotis G. Simos, Jack M. Fletcher, Eduardo M. Castillo, Wenbo Zhang, and Andrew C. Papanicolaou
The University of Texas Health Science Center at Houston

Event-related magnetic fields were recorded using magnetoencephalography in children with ($n = 12$) and without ($n = 11$) dyslexia while they discriminated between pairs of syllables from a voice onset time series (*/ga/-/ka/*). Nonimpaired readers exhibited left-hemisphere predominance of activity after the resolution of the N1m, whereas children with dyslexia experienced a sharp peak of relative activation in right temporoparietal areas between 300 and 700 ms post-stimulus onset. Increased relative activation in right temporoparietal areas was correlated with reduced performance on phonological processing measures. Results are consistent with the notion that deficits in appreciating the sound structure of both written and spoken language are associated with abnormal neurophysiological activity in temporoparietal language areas in children with dyslexia.

Dyslexia, a developmental disorder that affects up to 17% of the school-age population depending on the sample and how it is defined (Lyon, 1995; B. A. Shaywitz & Shaywitz, 1994), is characterized by difficulty in single-word decoding that is not the result of general developmental disability or sensory impairment (B. A. Shaywitz, Fletcher, & Shaywitz, 1995). Children with dyslexia also exhibit deficits in perception of speech at the phoneme level (Adlard & Hazan, 1998; Brady, Shankweiler, & Mann, 1983; Breier, Gray, et al., 2001; de Gelder & Vroomen, 1998; Godfrey, Syrdal-Lasky, Millay, & Knox, 1981; Manis et al., 1997; McBride-Chang, 1995, 1996; Mody, Studdert-Kennedy, & Brady, 1997; Reed, 1989). According to one view, these perceptual deficits are closely related to a difficulty in developing an awareness of the phonological structure of speech that is typically observed in children with dyslexia. In turn, well-developed phonological awareness skills are a prerequisite to acquiring normal reading skills (McBride-Chang, 1995, 1996; Reed, 1989).

Recent evidence from functional brain imaging studies indicate that both children and adults with dyslexia consis-

tently exhibit decreased activation of temporoparietal language areas in the left hemisphere during word recognition and phonological decoding (Paulesu et al., 2001; Pugh et al., 2000; Rumsey et al., 1992; B. A. Shaywitz et al., 2002; S. E. Shaywitz et al., 1998; Simos, Breier, Fletcher, Bergman, & Papanicolaou, 2000; Simos, Brier, Fletcher, Foorman, et al., 2000). This region largely overlaps with Wernicke's area, encompassing three major sites within the posterior portion of the superior temporal gyrus and often extending into the supramarginal gyrus: an area anterior to Heschl's gyrus, the supratemporal plane that extends posterior to Heschl's gyrus, and cortex on the dorsal bank of the superior temporal sulcus (Binder et al., 2000; Jancke, Wustenberg, Scheich, & Heinze, 2002; Wise et al., 2001). These areas are known to be engaged in tasks that require analysis of the sound structure of both written (Breier, Simos, Zouridakis, & Papanicolaou, 1999; Moore & Price, 1999; Rumsey et al., 1997; B. A. Shaywitz et al., 2002; Simos, Brier, Fletcher, Foorman, et al., 2000; Simos, Breier, et al., 2001) and spoken (Booth et al., 2002; Burton, Small, & Blumstein, 2000; Celsis et al., 1999; Demonet et al., 1992; Hickok, 2001; Kober et al., 2001; Newman & Twieg, 2001; Poldrack et al., 2001; Wong et al., 2002) language. Although anterior and posterior regions of the left hemisphere are observed to be engaged during the phonological analysis of both speech and print (Breier, Simos, Zouridakis, & Papanicolaou, 1999; Burton et al., 2000; Zeffiro & Eden, 2000), it is believed that this region supports neurophysiological processes that are crucial for the integration of orthographic and phonological word representations during reading (Booth et al., 2001; Gernsbacher & Kaschak, 2002; Moore & Price, 1999; Nakada, Fujii, Yoneoka, & Kwee, 2001; Simos et al., 2002; Simos, Breier, Wheless, et al., 2000). To the extent that engagement of a given cortical area in a particular cognitive function can be indexed by the degree of neurophysiological activity observed in that area, measures of temporoparietal activation during speech perception could potentially shed

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Joshua I. Breier, Panagiotis G. Simos, Eduardo M. Castillo, Wenbo Zhang, and Andrew C. Papanicolaou, Department of Neurosurgery, Division of Clinical Neurosciences, The University of Texas Health Science Center at Houston; Jack M. Fletcher, Department of Pediatrics, The University of Texas Health Science Center at Houston.

This work was partially supported by National Institutes of Health (NIH) Grant RO1 HD35938 to Joshua I. Breier and by National Science Foundation Grant REC-9979968, NIH Grant NS37941-01, and National Institute of Child Health and Human Development Grant DA10715 to Andrew C. Papanicolaou.

Correspondence concerning this article should be addressed to Joshua I. Breier, Department of Neurosurgery, Division of Clinical Neurosciences, The University of Texas Health Science Center at Houston, The Institute for Rehabilitation and Research, 1333 Moursund Street, Suite H114, Houston, Texas 77030. E-mail: joshua.i.breier@uth.tmc.edu

light on the relationship between reading disability and deficits in phonological processing and speech perception.

Functional brain imaging studies have provided mixed results regarding the involvement of auditory association areas, located near the temporoparietal junction of the left hemisphere, in speech perception. Simos, Breier, Fletcher, Bergman, & Papanicolaou (2000), using magnetoencephalography (MEG), found no evidence for decreased activation of left temporoparietal areas during a simple word recognition task. In a functional magnetic resonance imaging (MRI) study, Corina et al. (2001) reported reduced hemodynamic signal in the supratemporal plane in the context of a task that placed more explicit demands on phonological processing (rhyme matching with pseudowords). Studies using positron emission tomography provide similarly diverse results. Rumsey et al. (1992) found reduced activity in left temporoparietal areas in adults with dyslexia during an auditory word rhyming task. Flowers, Wood, and Naylor (1991) found a similar reduction during a task in which participants monitored a stream of concrete nouns for words that were four letters in length. In contrast, Hagman et al. (1992) found a reduction in activity in basal temporal areas bilaterally during a phoneme detection task, and McCrory, Frith, Brunswick, and Price (2000) found a decrease in right superior temporal activation during real and pseudoword repetition tasks. Differences in imaging modalities, data reduction and analysis procedures, stimulus characteristics, task requirements, and participant selection criteria and demographics likely all contribute to the diversity of findings across studies.

In the current study, we used MEG to determine the functional state of temporoparietal language areas of the left hemisphere during a simple speech perception task in children with and without dyslexia. MEG is a completely non-invasive method of functional brain imaging that provides a direct measure of neuronal activity by detecting regionally elevated levels of intracellular electrical currents in large neuronal aggregates (Lewine, 1990; Papanicolaou, 1998; Papanicolaou & Tarkka, 1996). We have previously established the spatiotemporal patterns of brain activation specific to spoken word recognition (Breier, Simos, Zouridakis, & Papanicolaou, 1998; Breier, Simos, Zouridakis, & Papanicolaou, 1999; Papanicolaou et al., 1999, 2001; Simos, Breier, Zouridakis, & Papanicolaou, 1998a, 1998b) and have verified their stability or reproducibility over time (Breier, Simos, Zouridakis, & Papanicolaou, 1999; Breier, Simos, Zouridakis, & Papanicolaou, 2000). Moreover, in a series of investigations (Papanicolaou et al., 1999; Simos, Papanicolaou, et al., 1999), the validity and topographical specificity of these maps have been established by comparing them with the results of direct cortical stimulation mapping (Papanicolaou et al., 1999; Simos, Castillo, et al., 2001; Simos, Papanicolaou, et al., 1999) and with the results of the intracarotid amytal (Wada) procedure in more than 80 consecutive patients (Breier, Simos, et al., 2001; Breier, Simos, Zouridakis, Wheless, et al., 1999; Maestu et al., 2002; Szymanski et al., 2001). In the current study we applied these methods to study the spatiotemporal profile of neurophysiological activity in temporoparietal language ar-

reas during the discrimination of pairs of tokens from a voice onset time (VOT) series (/ga/-/ka/) in children with and without dyslexia. Adult readers without impairment exhibit a large increase in the degree of activation in left as compared with right auditory association areas after the resolution of the N1m during the same task (Papanicolaou et al., 2003). We predicted significantly reduced relative activation of left-hemisphere auditory association areas in children with dyslexia, a profile similar to that found during tasks that involve phonological decoding of print.

Method

Participants

Twenty-three children, ranging in age from 8.4 to 12.6 years ($M = 10.8$, $SD = 1.4$), served as participants. The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was administered to estimate intellectual abilities. In order to eliminate children with below average intelligence, a Full Scale IQ above 79 was required for participation in the study. All children had normal hearing in both ears, as assessed with pure-tone threshold audiometric screening at 250, 500, 1000, 2000, 4000, and 8000 Hz at 20 dB HL (American Speech-Language-Hearing Association Audiologic Assessment Panel, 1997), a normal tympanogram (used to assess middle ear function), English as the primary language, and no history of neurological disorder. All children were right-hand dominant as indicated by a score of +4 or greater on the Edinburgh Handedness Inventory (Oldfield, 1971). The protocol used in this study received full approval from the Institutional Review Board of the University of Texas Health Science Center at Houston. Potential participants were identified through contacts maintained by the authors with parents, advocacy groups, and professionals who work with the local school districts and private agencies. Parents initiated contact with the authors, and children were tested after parents had given informed consent and children had given informed assent.

Children were identified as having dyslexia based on several achievement measures, including (a) the Basic Reading Cluster of the Woodcock Reading Mastery Tests—Revised (Woodcock, 1998), which consists of the Word Attack (decoding of pseudowords) and Word Identification (decoding of real words) subtests; (b) the Spelling subtest of the Wechsler Individual Achievement Test (Wechsler, 1992); and (c) the Test of Word Reading Efficiency (Torgesen & Wagner, 1999) which measures speed of word reading and decoding. Standard scores on these three measures were averaged to form a composite. Children were placed into the RD group on the basis of a composite score at or below 90, with at least two of the three tests being at or below this cutoff (Breier, Gray et al., 2001). This criterion is similar to that used in other studies (Fletcher et al., 1994; Foorman, Francis, Fletcher, & Lynn, 1996; Joanisse, Manis, Keating, & Seidenberg, 2000; Manis et al., 1997; Post, Swank, Hiscock, & Fowler, 1999; B. A. Shaywitz & Shaywitz, 1994; Stanovich & Siegel, 1994). Using these methods, we identified 12 children as having dyslexia and 11 as having no impairment (NI). In addition to the above tests, all children were administered the phoneme elision, memory for digits, and rapid letter naming subtests of the Comprehensive Test of Phonological Processing (CTOPP; Wagner, Torgesen, & Rashotte, 1999) as measures of phonological processing skills. The Hollingshead two-factor index of social position (Hollingshead, 1975) was used to assess socioeconomic status (SES). Children were also screened for specific language impairment (SLI) using the Concepts and Directions and Recalling Sentences subtests of

the Clinical Evaluation of Language Functions —3 (Semel, Wiig, & Secord, 1995) as well as the Vocabulary subtest of the WASI. Children with a scaled score below 7 on all three tests were identified as having SLI and excluded from the study (Joanisse et al., 2000).

Demographic data and group means on IQ measures are presented in Table 1. Group means on achievement and phonological processing measures are presented in Table 2. Group comparisons for continuous variables were performed using two-sample *t* tests with a Welch–Satterthwaite correction for nonhomogeneity of variance. Fisher’s exact test was used to test for differences in distributions between groups for categorical variables. There were no significant differences between the NI and dyslexic groups in age, SES, or ethnicity. The percentage of females was higher in the NI group ($p < .05$). Two children in the dyslexic group had a history of diagnosis with attention-deficit/hyperactivity disorder—predominantly inattentive type. These children did not take their usual daily dosage of psychostimulant medication (methylphenidate) until after MEG imaging had been performed. Both groups had mean Full Scale IQ scores within the average range; however, children with dyslexia had significantly lower Full Scale ($p < .01$) and Verbal IQ ($p < .001$) scores. These findings are not surprising as lowering of language functions is commonly found in children with dyslexia (B. A. Shaywitz, Fletcher, & Shaywitz, 1995). The groups did not differ on Performance IQ. As expected, children with dyslexia performed significantly below those without dyslexia on academic achievement tests used for group placement as well as the phonological processing measures.

Table 1
Demographic and IQ Data by Group

	Measure	No impairment (<i>n</i> = 11)	Dyslexia (<i>n</i> = 12)
	Age (in years)		
	<i>M</i>	11.2	10.4
	<i>SD</i>	1.2	1.4
AQ: 7	Sex		
	Female	6	1
AQ: 8	Male	5	12
	Socioeconomic status (Hollingshead Social Class)		
	I	2	1
	II	4	3
	III	3	8
	IV	2	0
	Race		
	White	7	11
	Black	2	1
	Hispanic	2	0
	Attention-deficit/hyperactivity disorder	0	2
	WASI Full Scale IQ (standard score)		
	<i>M</i>	109.3	101.2
	<i>SD</i>	7.6	9.5
	WASI Verbal IQ (standard score)		
	<i>M</i>	113.2	98.2
	<i>SD</i>	8.3	7.5
	WASI Performance IQ (standard score)		
	<i>M</i>	104.5	104.3
	<i>SD</i>	11.1	14.2

Note. WASI = Wechsler Abbreviated Scale of Intelligence.

Table 2
Academic Achievement and Phonological Processing Test Data by Group

Measure	No impairment (<i>n</i> = 11)	Dyslexia (<i>n</i> = 12)
WRMT–R Basic Reading Cluster		
<i>M</i>	105.3	86.7
<i>SD</i>	9.0	5.4
WRMT–R Word Identification		
<i>M</i>	105.7	86.2
<i>SD</i>	9.5	5.4
WRMT–R Word Attack		
<i>M</i>	103.8	89.8
<i>SD</i>	8.0	7.0
Test of Word Reading Efficiency		
<i>M</i>	99.6	62.3
<i>SD</i>	11.4	12.1
Wechsler Individual Achievement Test—Spelling		
<i>M</i>	105.5	81.3
<i>SD</i>	11.0	6.9
CTOPP–phoneme elision		
<i>M</i>	108.9	89.3
<i>SD</i>	6.3	15.1
CTOPP–immediate memory for digits		
<i>M</i>	97.1	80.3
<i>SD</i>	19.0	13.3
CTOPP–rapid letter naming		
<i>M</i>	106.8	80.0
<i>SD</i>	6.6	18.8

Note. WRMT–R = Woodcock Reading Mastery Tests—Revised; CTOPP = Comprehensive Test of Phonological Processing.

Stimuli

Seven consonant–vowel tokens that formed a velar voicing series with VOT values ranging from 0 to 60 ms in 10-ms steps served as stimuli. The syllables were prepared using the cascade branch of the Klatt88 software synthesizer. Variation of VOT was achieved by broadening the bandwidth of F1 and exciting F2 and F3 with a noise source during the period between stimulus onset and voicing source onset. The fundamental frequency (F0) was constant at 120 Hz for all syllables. The nominal formant frequencies at stimulus onset were 300 Hz, 1840 Hz, and 1960 Hz and changed linearly across a 55-ms transition period to 768 Hz, 1333 Hz, and 2522 Hz. The transitions were followed by a 200-ms steady state segment resulting in a total stimulus length of 255 ms. In addition, the relative balance of low-frequency energy in the voicing source was enhanced by setting the spectral tilt parameter of the Klatt synthesizer to 10 along the entire length of the syllable. Finally, the voiced portions of the stimuli were low-pass filtered at 3200 Hz.

Stimuli were presented binaurally in pairs with an onset-to-onset interval of 2 s between pair members. The first stimulus in every pair was an endpoint stimulus (either a /ga/ with a 0-ms VOT or a /ka/ with a +60-ms VOT), with an equal number of trials for each stimulus. In one half of the trials the second stimulus was a token from the series at least four steps away in VOT (e.g., 40-, 50-, or 60-ms VOT when the first stimulus was a /ga/ and 0-, 10-, or 20-ms VOT when the first stimulus was a /ka/), randomly chosen. On the other half of the trials the first stimulus was repeated. Match and mismatch trials were randomly interspersed. Children were familiarized with the task using five pairs of endpoint stimuli in the MEG unit under the same conditions as the test. During both

training and the MEG recordings, children were asked to decide if the two tokens in each pair were the same or different, responding by raising their right (or left) index finger if the tokens were the same. The responding hand was counterbalanced across participants. The interval between stimulus pairs was varied randomly across trials between 3 and 4 s. Stimulus delivery was accomplished via two 5-m-long plastic tubes terminating in ear inserts, and sound intensity was 80 dB SPL at the participant's outer ear. Event-related magnetic fields (ERFs) were recorded to the first stimulus of each pair to ensure that the observed neurophysiological activity reflected processes involved in the analysis of the speech stimuli rather than the cognitive and motor processes involved in the participant's response. There was no significant difference in accuracy ($p > .4$) between the RD ($M = 77\%$, $SD = 5\%$) and NI ($M = 77\%$, $SD = 6\%$) groups.

MEG Procedures

MEG recordings were conducted with a whole-head, 148-channel Magnes WH 2500 neuromagnetometer array (4-D Neuroimaging, San Diego, CA) housed in a magnetically shielded chamber. The magnetic flux measurements were filtered with a bandpass filter between 0.1 and 20 Hz and digitized at 250 Hz. Intrinsic noise in each channel was less than 10 fT/ $\sqrt{\text{Hz}}$. The amount of magnetic noise produced by remote sources was further reduced by submitting the MEG data to an adaptive noise reduction procedure that is part of the signal analysis software. This procedure uses the magnetic flux recordings obtained online from nine "reference sensors" (three magnetometers, three first-order axial gradiometers, and three second-order axial gradiometers) located at a distance of approximately 30 cm above the array of 148 magnetometers. The distance between these reference sensors and the intracranial generators of magnetic flux ensures that they record only "extraneous" flux (i.e., flux that is not due to neuronal currents). Following each recording session, the magnetic flux values recorded at each time point within each epoch are, in essence, subtracted from the corresponding magnetic values measured by each of the 148 magnetometers. A minimum of 60 single-trial ERF segments were averaged separately for each sensor after excluding those containing eye movement (as indicated by a peak-to-peak amplitude in the electrooculogram in excess of 50 μV), myogenic, or mechanical artifacts. Finally, the averaged epochs were adjusted relative to the mean amplitude in the 150-ms prestimulus period to remove direct current offset.

The intracranial generators of the observed ERFs at successive 4-ms intervals were modeled as equivalent current dipoles (ECDs) by using the nonlinear Levenberg-Marquardt algorithm on a spherical head model. This method was used to search for the ECD source that was most likely to have produced the observed magnetic field distribution at a given point in time (according to the Biot-Savart law; e.g., Sarvas, 1987). ECD solutions were considered as satisfactory if they were associated with a correlation coefficient of at least .90 between the observed and the "best" predicted magnetic field distribution. The source estimation algorithm was applied to the magnetic flux measurements obtained from a group of 34–38 channels, always including both magnetic flux extrema. Source location was computed in reference to a Cartesian coordinate system defined by a set of three anatomical landmarks (fiducial points): the right and left external meatuses and the nasion. The line passing through the right and left external meatuses served as the y -axis. The line between the nasion and the midpoint of the y -axis defined the x -axis, and the line perpendicular to the x - y plane, passing through the intersection of the x -axis and y -axis, defined the z -axis. The position of the magnetometers relative to the participant's head was precisely determined using

five coils, three of which were attached to the fiducial points and two on the forehead. The coils were turned on briefly at the beginning and again at the end of the recording session, and their precise location in three-dimensional space was determined using a localization algorithm built into the system. During the recording session, a fiber-optic motion detector was used to ensure that the participant did not change position relative to the sensor.

Orthogonal coronal, sagittal, and axial T1-weighted structural MRI images were obtained using a Signa 1.5 system (General Electric, Fairfield, CT) (repetition time = 13.6 ms, echo time = 4.8 ms, recording matrix 256×256 pixels, 1 excitation, 240-mm field of view, and 1.4-mm slice thickness). Precise coregistration of the MEG coordinate system with structural MRI images was achieved by aligning MEG fiducial points with high contrast cod liver capsules (3 mm in diameter), which were affixed to the participant's nasion and inserted in the external meatus prior to MRI scan.

The total number of successive activity sources that accounted for the ERF components between 200 ms and 1,000 ms post-stimulus offset was used to estimate the degree, or total duration, of stimulus-locked neurophysiological activation in a particular area. Studies from our group and others (Breier, Simos, et al., 2001; Breier, Simos, Zouridakis, Wheless, et al., 1999; Papanicolaou et al., 1999; Simos, Breier, et al., 1999; Simos, Breier, Zouridakis, & Papanicolaou, 1998a, 1998b; Simos, Papanicolaou, et al., 1999) support the concurrent validity of this procedure for constructing brain activation profiles. These studies have shown that this procedure is sufficiently accurate for identifying (a) the hemisphere that is more prominently involved in basic linguistic functions and (b) specific regions within the dominant hemisphere that are indispensable for particular cognitive processes such as decoding and encoding of spoken and printed words.

The construct validity of the measure of brain activation used in this procedure reflects the degree to which the measure provides an accurate representation of both the spatial and the temporal extent of regionally elevated levels of neurophysiological activity. A neurologically plausible rationale for using the number of sequential activity sources as one such measure can be summarized as follows. Processing of an incoming auditory stimulus requires engagement of neurophysiological processes in primary auditory and nearby association cortices. These processes involve instantaneous increases in neuronal signaling in one or more neuronal populations. This, in turn, produces a time-limited increase in intracellular currents which, integrated, can be represented as an electrical dipole. The greater the strength of the dipole (i.e., the magnitude of intracellular current) at each point in time, the greater the strength of the resulting magnetic flux. Given the dipolar nature of the source, which is concurred by the dipolar appearance of the recorded magnetic flux distribution (or contour map), the greater the strength of the recorded magnetic flux, the higher the likelihood that the parameters of the underlying source will be computed with a sufficient degree of confidence by the dipole-fitting algorithm. The correlation coefficient between the observed and an ideal or hypothesized underlying source is a widely used index of the degree to which the computed source solution approximates that of a dipolar source. In fact, the vast majority of activity sources were associated with correlations of .95 or greater. This measure of goodness of fit reflects how well the computed dipole parameters account for the observed distribution of magnetic flux recorded by the 148 magnetometer sensors at each 4-ms time slice. This correlation criterion was derived empirically in the context of the validation studies mentioned above.

It should be pointed out that this is a simplified account, as in reality other factors also contribute to the strength of the recorded

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magnetic flux, such as the depth and orientation of the cortical patch containing the active neurons relative to the plane of each magnetometer sensor and, of course, the characteristics of background noise, or magnetic flux produced by sources not related to the neurophysiological activity that processing of the stimuli entails. The empirically established concurrent validity of this measure (Breier, Simos, et al., 2001; Breier, Simos, Zouridakis, Wheless, et al., 1999; Maestú et al., 2002; Papanicolaou et al., 1999; Simos, Breier, et al., 1999; Simos et al., 1998a; Simos et al., 1999), however, lends credence to the plausibility of the claim that the duration of focal cortical activity may be a measure of the "degree of engagement" of a particular cortical region in a given task. This measure is complementary to other similarly derived measures used by other imaging modalities, such as the spatial extent of cortex that shows differential hemodynamic modulation across two different tasks.

Results

Localization of MEG Activity Sources

As expected, analyses indicated typical early and late components in all children (see Figure 1). The early portion of the ERF was dominated by the N1m component, which typically extended to about 200 ms post-stimulus onset. Sources of this early N1m component were generally distributed bilaterally on the floor of the Sylvian fissure in children from both groups. As these sources reflect activa-

tion of primary auditory cortex (Nakasato et al., 1997; Pantev & Lutkenhoner, 2000; Zouridakis, Simos, Breier, & Papanicolaou, 1998), they are not considered further in these analyses.

MEG activity occurring after the resolution of the N1m component (i.e., between approximately 200 and 1,000 ms post-stimulus onset) is generally associated with activation of auditory association cortex (Breier, Simos, et al., 2001; Breier, Simos, Zouridakis, Wheless, et al., 1999; Papanicolaou et al., 1999; Papanicolaou et al., 2003; Simos, Castillo, et al., 2001; Simos et al., 1999). Late MEG activity sources (after 200 ms post-stimulus onset) were found in every child in the left and/or right temporoparietal language areas (primarily in Brodmann's area 22). This region included cortex within the supratemporal plane and the dorsal bank of the superior temporal sulcus in the posterior portion of the superior temporal gyrus, often extending into nearby supramarginal gyrus. Activity sources were also observed in approximately half of the children in the mesial temporal lobe (7 of 12 children with dyslexia, 6 of 11 NI children) and the middle temporal gyrus (6 of 12 children with dyslexia, 7/11 NI children) in the left and/or right hemispheres. Occasional activity was observed in the angular, inferior frontal, and/or inferior temporal gyri in the left and/or right hemispheres. Because of the lack of consistent activation in these other areas, and as we were specifically

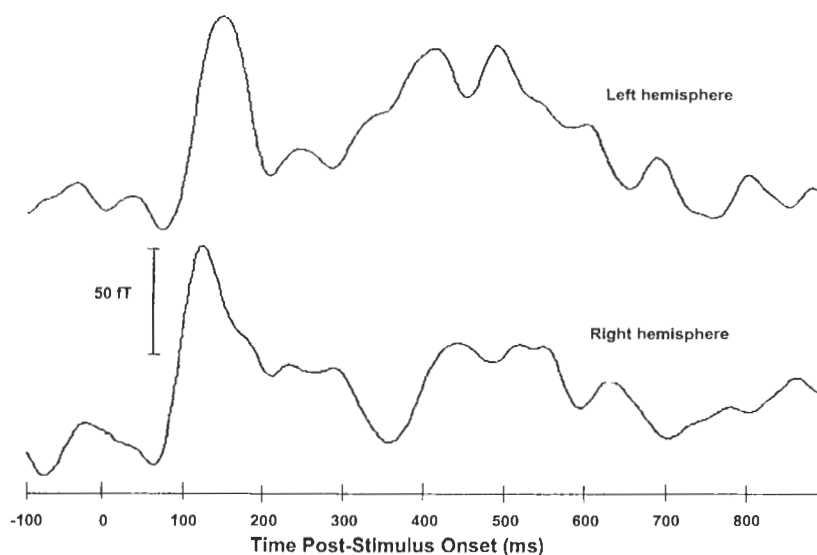


Figure 1. Sample event-related magnetic field (ERF) waveforms to the consonant-vowel stimuli from a child in the group with no impairment. Both waveforms were recorded at the sites of maximum magnetic outflux at the peak of the N1m component (first major deflection) over the left (top line) and right (bottom line) hemispheres. Stimulus onset is at zero. The magnitude of early ERF components (usually between 60 and 200 ms) is bilaterally symmetrical with activity sources localized at or near the primary auditory cortex. Later components (after 200 ms or the resolution of the N1m component) are usually greater in amplitude over the left as compared with the right hemisphere and are associated with a greater number of consecutive activity sources localized primarily in auditory association cortices, although some activity sources are also found in the supramarginal and middle temporal gyri and mesial temporal cortex.

interested in interhemispheric asymmetries in activity occurring in temporoparietal cortices, we restricted analyses to this region.

Hemispheric Asymmetries in MEG Activity in Temporoparietal Areas

Individual MEG scans from a representative NI child (top) and a child with dyslexia (bottom) are presented in Figure 2. The activation profile displayed by children in the NI group is characterized by a dense concentration of activity sources in the left hemisphere, with relatively sparser activity in homotopic areas of the right hemisphere. In contrast, the profile associated with dyslexia consists of a well-formed map in the right hemisphere. Although activity is also observed in left temporoparietal areas, it is somewhat more diffuse and the map is not as well-defined.

Group differences in relative activity in left and right temporoparietal areas were analyzed by forming a hemispheric asymmetry index (AI) for each child according to the following formula:

$$\frac{(\text{number of sources in right temporoparietal areas} - \text{number of sources in left temporoparietal areas})}{\text{total number of sources in left and right temporoparietal areas}}$$

AI scores were submitted to a one-way analysis of variance (ANOVA) with group membership (dyslexic, NI) as the independent variable. Full Scale IQ and gender were included as covariates, as the NI and RD groups differed on these two factors. There was a significant effect of group, $F(1, 19) = 4.57, p < .05 (\eta^2 = .19)$. There were no significant effects for IQ ($p > .35$) or gender ($p > .8$). The mean AI for each group is presented in Figure 3. A more negative number indicates more relative activity in left temporoparietal areas. Whereas NI children exhibited more activity in left as compared with the right temporoparietal areas, children with dyslexia showed, on average, more bilaterally equivalent activity.

Timing of Relative Activation of Left and Right Temporoparietal Areas

A separate index of the degree of hemispheric asymmetry in temporoparietal activity was computed for each of the eight successive 100-ms time windows, beginning at the resolution of the N1m component (200–299 ms post-stimulus onset, 300–399 ms post-stimulus onset, etc.). Mean asymmetry indices for each group are plotted as a function of time in Figure 4. Group effects for these AIs were evaluated using a multivariate approach to a repeated measures ANOVA with time window as the within-subjects factor



Figure 2. Individual magnetoencephalography scans from a child in the group with no impairment (NI; top) and a child in the group with dyslexia (bottom). Late activity sources (i.e., those occurring after 200 ms post-stimulus onset) are represented by orange circles. As can be seen, the NI profile consists of a well-formed map of activity in the left temporoparietal region with relatively reduced activity in homotopic areas of the right hemisphere. In contrast, the profile associated with dyslexia consists of a well-formed map in the right temporoparietal region with equivalent but more diffuse activity in homotopic areas of the left hemisphere.

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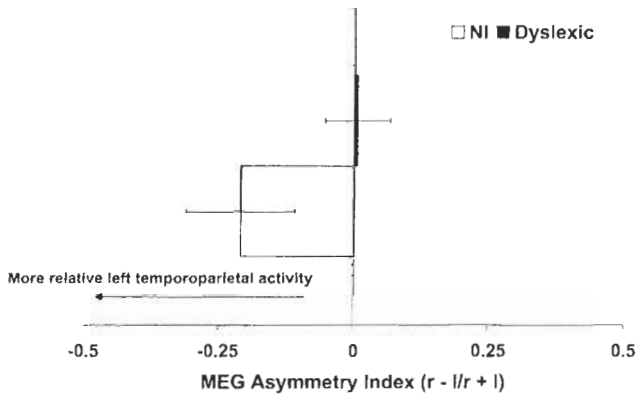


Figure 3. Relative number of late magnetoencephalography (MEG) activity sources in right (r) as compared with left (l) temporoparietal areas [(right - left)/(right + left)] for children with no impairment (NI) and children with dyslexia. A more negative number indicates more relative activity in left temporoparietal areas (error bars indicate standard errors of the mean).

and group (dyslexic, NI) as the between-subjects factor. Full Scale IQ and gender served as covariates. There was a significant Time Window \times Group interaction, $F(7, 13) = 3.38, p < .028 (\eta^2 = .65)$, indicating that group differences on AI scores varied with time. There were no significant main or interaction effects for IQ or gender. Follow-up analysis within each time window using a critical value of $p < .0063 (.05/8)$ indicated significant effects for the two time windows between 400 ms and 600 ms post-stimulus onset. As can be seen in Figure 4, NI children exhibit left-hemisphere lateralization of MEG activation across the later portions of the recorded epoch. After the resolution of the N1m, however, children with dyslexia exhibit a relative increase in MEG activity in the right hemisphere beginning at about 300 ms to 400 ms and lasting until about 600 ms to 700 ms post-stimulus onset.

The Relationship Between Abnormal Activity in Temporoparietal Areas and Phonological Processing Skills

As expected, children with dyslexia exhibited significant deficits on phonological processing tasks, including phoneme elision, immediate phonological memory, and rapid automatized naming (see Table 2). We therefore examined the relationship between the amount of relative activation in right temporoparietal areas between 300 and 700 ms post-stimulus onset, the time window for the sharp peak of abnormal activation in dyslexic children observed in the above analyses, and the performance on phonological processing tasks using regression analyses with gender and Full Scale IQ score as covariates. To evaluate statistical significance, we used a nominal alpha of .0167 (.05/3) to maintain familywise Type I error rate at .05.

Analyses indicated a significant correlation between the AI for temporoparietal activity occurring between the 300-ms and 700-ms time window and the phoneme elision

($pr = -.52, p < .016$) subtest of the CTOPP, a measure of phonemic awareness. There was also a marginally significant correlation between the MEG AI and rapid letter naming ($pr = -.49, p = .025$). The correlation between the AI scores and the scores on the immediate phonological memory for digits ($p > .20$) were not significant. Age- and gender-adjusted phoneme elision scores are plotted as a function of the MEG asymmetry index in Figure 5. Poorer performance on the measure of phonological awareness (indicated by a lower z score) is associated with increased relative activity in right temporoparietal areas (indicated by a more positive number).

Discussion

In the current study, children with dyslexia demonstrated aberrant profiles of neurophysiological activity during the perceptual analysis of speech stimuli. Although activity in temporoparietal auditory association areas was observed bilaterally in virtually all children, NI children exhibited relatively greater activity in the left hemisphere as compared with the right hemisphere, a profile similar to that observed in adults performing the same task (Papanicolaou et al., 2003). In contrast, children with dyslexia generally exhibited a reduced degree of lateralization of activity to the left auditory association cortices, with a sharp increase in relative activation of homotopic areas of the right hemisphere between 300 ms and 700 ms post-stimulus onset. These findings were independent of IQ and gender.

A large body of evidence suggests that posterior temporal cortex plays a crucial role in phonological analysis. However, the precise functional organization of this region, which is part of the auditory association cortices, is not

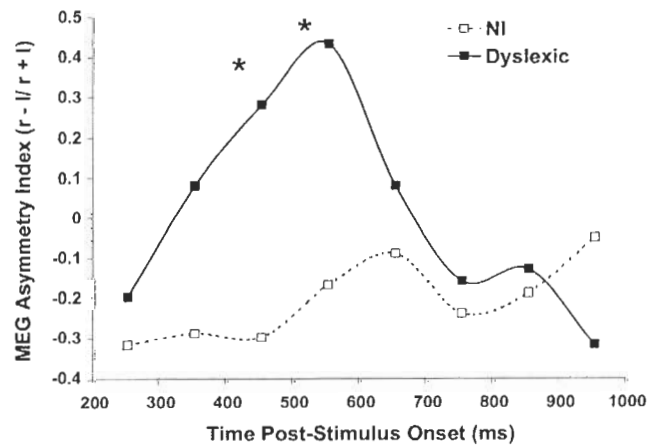


Figure 4. Relative number of late magnetoencephalography (MEG) activity sources in right (r) as compared with left (l) temporoparietal areas [(right - left)/(right + left)] for children with no impairment (NI) and children with dyslexia for successive 100-ms time windows beginning after the resolution of the N1m. A more negative number indicates more relative activity in the left hemisphere. Time windows with significant group differences ($p < .05$) are marked by asterisks.

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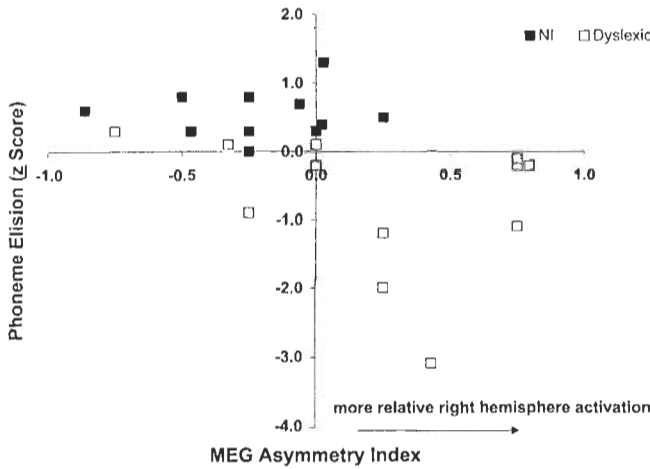


Figure 5. Plot of performance on a measure of phonological awareness, the phoneme elision subtest of the Comprehensive Test of Phonological Processing (a more negative number indicates worse performance), as a function of hemispheric asymmetries in temporoparietal activation (a more positive number indicates greater lateralization of activity to the right hemisphere) for children with no impairment (NI) and children with dyslexia. Increased lateralization of activity to the right hemisphere is associated with poorer performance on this measure of phonological awareness.

clear. According to one view, auditory association cortices in the left hemisphere can be subdivided, on the basis of functional criteria, into three subregions: an area anterior to Heschl's gyrus, the supratemporal plane that extends posterior to Heschl's gyrus, and a cortex located on the dorsal bank of the superior temporal sulcus (e.g., Binder et al., 2000; Gernsbacher & Kaschak, 2002; Poeppel, 2001; Price, 2000). Although predominant activation in one or more of the aforementioned superior temporal loci in the left hemisphere has been reported by some investigators in response to speech stimuli (Binder et al., 2000; Burton et al., 2000; Demonet et al., 1992; Vouloumanos, Kiehl, Werker, & Liddle, 2001), others have failed to find hemispheric asymmetries in task-related changes in blood flow in this region (Belin, Zatorre, & Ahad, 2002; Jancke et al., 2002). Using MEG, which measures neurophysiological activity in a more direct fashion than hemodynamic imaging methods, we found evidence for bilaterally symmetric activation of primary auditory cortices during the early stages of processing of simple speech stimuli (~0–200 ms after stimulus onset), immediately followed by predominantly left-hemisphere activation of auditory association cortices in adults without reading problems (Papanicolaou et al., 2003). As in this study, Papanicolaou et al. (2003) observed early activity primarily in the vicinity of the primary auditory cortex, in and around Heschl's gyri. Later activity was found in all three major subregions of posterior temporal cortex listed above. Furthermore a comparison of the degree of activity between speech sounds and nonspeech analogs suggested that speech sounds receive specialized processing by neurophysiological mechanisms located in the posterior part of

the left superior temporal gyrus even when the stimuli have no lexical referents. In the Papanicolaou et al. (2003) study, activation profiles associated with the perception of speech and nonspeech stimuli were distinguishable on the basis of both anatomical and temporal features. Thus, both speech sounds and nonspeech analogs activated left posterior temporal areas to the same extent, during the early stages of stimulus processing. Regional activation was greater, however, in response to speech than to nonspeech stimuli during the later stages of processing. Other studies have shown that as the demands for lexical–semantic processing increase, activation appears to spread to more ventral areas, notably the middle temporal gyrus (Binder et al., 2000; Binder, Frost, Hammeke, Rao, & Cox, 1996; Booth et al., 2002; Castillo et al., 2001). Thus, data from MEG studies support the notion that auditory association areas along the left superior temporal gyrus are specialized for the analysis of spoken language. Evidence for such specialization, in the form of lateralized neurophysiological activity occurring between approximately 200 ms and 1,000 ms post-stimulus onset, has been found in both adults and children who are normal readers.

Our group and others have shown that specific cortical sites within the auditory association cortex in the left hemisphere are functionally specialized for, and serve as indispensable components of the brain circuit that supports, phonological processing of both spoken and printed linguistic stimuli. This notion is clearly supported by evidence that (a) word stimuli presented in either the visual or the auditory modality activate the same superior temporal loci at the same latencies (e.g., Simos et al., 1998b), (b) electrical interference with these sites selectively impairs the ability to process speech (Simos, Papanicolaou, Breier, et al., 1999), and (c) electrical currents applied transiently to the same cortical locations impair the ability to extract phonological information from pronounceable letter strings that lack lexical referents (pseudowords; Simos, Breier, Wheless, et al., 2000). It is therefore not surprising that children and adults with severe reading disability (a) have pronounced difficulties in tasks that require mental manipulation of the phonological representations of spoken utterances and (b) show significantly reduced activation in left-hemisphere posterior temporal cortices during tasks that involve phonological decoding of print (Horwitz, Rumsey, & Donohue, 1998; Paulesu et al., 2001; Pugh et al., 2000; Shaywitz et al., 1998; Simos, Breier, Fletcher, Bergman, & Papanicolaou, et al., 2000; Simos, Breier, Fletcher, Foorman, et al., 2000). An associated increase in activity in homotopic areas of the right hemisphere has been observed in a number of studies as well (Pugh et al., 2000; Simos, Breier, Fletcher, Bergman, et al., 2000; Simos, Breier, Fletcher, Foorman, et al., 2000).

The present study extends findings, from studies using reading tasks, by providing evidence that children with dyslexia may lack the predominant involvement of left-hemisphere auditory association cortices exhibited by children and adults without reading problems during the performance of a simple speech perception task. The task used in the current study was specifically chosen to isolate the

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neurophysiological processes involved in the acoustic and phonetic analysis of speech, minimizing memory-related and lexical processes. Event-related magnetic activity was recorded in response to the first stimulus of each pair to further ensure that the brain activity recorded corresponded to speech perception and did not reflect the additional cognitive operations that matching of the stimuli entails. The lack of engagement of auditory association cortices during speech perception noted in the current study is consistent with previous reports of aberrant changes in hemodynamics during engagement in other speech-processing tasks in individuals with reading difficulties (Corina et al., 2001; Flowers et al., 1991; Rumsey et al., 1992).

Whether the late increase in right-hemisphere engagement characteristic of the present dyslexia group represents compensatory engagement of right-hemisphere auditory association areas in speech processing or the result of the use of alternative perceptual strategies, which are normally supported by the right hemisphere, cannot be determined with certainty at present. However, evidence suggests that reduced activity in left-hemisphere and increased activity in right-hemisphere auditory association areas is a marker of the core functional deficit in reading disability and not an epiphenomenon. Children with dyslexia exhibit consistent deficits on tasks requiring knowledge of the segmental structure of speech, or phonological awareness, and these deficits likely have a role in the etiology of dyslexia (Bradley & Bryant, 1983; Fletcher et al., 1994; Shankweiler & Crain, 1986; Stanovich & Siegel, 1994; Wagner et al., 1994). Children with dyslexia also show deficits in tasks that tap into acoustic or phonetic processing abilities (Adlard & Hazan, 1998; Brady et al., 1983; Breier, Gray, et al., 2001; de Gelder & Vroomen, 1998; Godfrey et al., 1981; Manis et al., 1997; Mody et al., 1997; Reed, 1989). In the current study, a significant relation was found between the degree of hemispheric asymmetry in the activation of auditory association cortices and measures of phonological processing, including phonemic awareness. Increased relative activity in right posterior temporal areas was associated with reduced ability to segment spoken utterances as well as slowed access to letter sounds. These relationships appeared to be specific to children with dyslexia, suggesting that there may be a continuum of dysfunction in left temporoparietal areas in children with dyslexia and that variance in phonemic awareness in NI children may be related to other factors.

Although the speech signal is a complex quasicontinuous event without intrinsic linguistic structure, representations occur in phonological store as discrete, ordered segments with distinct phonetic features (Liberman, Mann, Shankweiler, & Werfelman, 1982). Thus, the process by which the phonetic structure of the speech signal is extracted is central not only to acquiring phonemic awareness but also, as the beginning reader must learn to map graphemes onto these discrete segments (Treiman, Broderick, Tincoff, & Rodriguez, 1998; Wagner & Torgesen, 1987; Wagner et al., 1994), to learning to read. This hierarchical relationship between perceptual analysis, phonemic awareness, and reading has received empirical support from behavioral

studies (Breier et al., 2001; McBride-Chang, 1996; Watson & Miller, 1993). It is therefore of significant interest that current findings suggest that children with dyslexia and normal readers differ in the brain mechanisms underlying the appreciation of the sound structure of spoken as well as written language. Although these results support hypotheses that deficits in phonetic analysis may provide a more fundamental basis for phonological processing deficits and ultimately difficulty in acquiring reading skills, alternative explanations must also be considered. Phonetic analysis, phonological processing, and reading disability in children with dyslexia may be correlated through a common cause: abnormal neurophysiological function in areas of the brain specialized for these purposes. Further brain-imaging, genetic, and behavioral studies are needed to explore the direction of the relationships between abnormalities in brain and behavioral function in dyslexia.

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Received January 28, 2002

Revision received February 20, 2003

Accepted February 21, 2003 ■