Abnormal Auditory Cortical Activation in Dyslexia 100 msec after Speech Onset

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Abstract

■ Reading difficulties are associated with problems in processing and manipulating speech sounds. Dyslexic individuals seem to have, for instance, difficulties in perceiving the length and identity of consonants. Using magnetoencephalography (MEG), we characterized the spatio-temporal pattern of auditory cortical activation in dyslexia evoked by three types of natural bisyllabic pseudowords (/ata/, /atta/, and /a a/), complex nonspeech sound pairs (corresponding to /atta/ and /a a/) and simple 1-kHz tones. The most robust difference between dyslexic and non-reading-impaired adults was seen in the left supratemporal auditory cortex 100 msec after the onset of the vowel /a/. This N100m response was abnormally strong in dyslexic individuals. For the complex nonspeech sounds and tone, the N100m response amplitudes were similar in dyslexic and nonimpaired individuals. The responses evoked by syllable /ta/ of the pseudoword /atta/ also showed modest latency differences between the two subject groups. The responses evoked by the corresponding nonspeech sounds did not differ between the two subject groups. Further, when the initial formant transition, that is, the consonant, was removed from the syllable /ta/, the N100m latency was normal in dyslexic individuals. Thus, it appears that dyslexia is reflected as abnormal activation of the auditory cortex already 100 msec after speech onset, manifested as abnormal response strengths for natural speech and as delays for speech sounds containing rapid frequency transition. These differences between the dyslexic and nonimpaired individuals also imply that the N100m response codes stimulus-specific features likely to be critical for speech perception. Which features of speech (or nonspeech stimuli) are critical in eliciting the abnormally strong N100m response in dyslexic individuals should be resolved in future studies. ■

INTRODUCTION

Reading problems are the most obvious, and, in many cases, the first, behavioral manifestation of developmental dyslexia. Both reading acquisition and the attainment of fluency of reading that could be expected, based on age or intelligence, are abnormal in dyslexia. Even in adult age, dyslexic individuals remain slow and error-prone readers (Leinonen et al., 2001; Scarborough, 1984). These persistent problems in word recognition are also manifested in reading-related cortical activation measured with electroencephalography (EEG; Brandeis, Vitacco, & Steinhausen, 1994), magnetoencephalography (MEG; Helenius, Salmelin, Service, & Connolly, 1999; Helenius, Tarkiainen, Cornelissen, Hansen, & Salmelin, 1999; Salmelin, Service, Kiesilä, Uutela, & Salonen, 1996), functional magnetic resonance imaging (fMRI; Temple et al., 2001; Shaywitz et al., 1998), and positron emission tomography (PET; Brunswick, McCrory, Price, Frith, & Frith, 1999; Rumsey et al., 1997). Converging evidence from these different techniques suggests that posterior cortical areas are underactivated in developmental dyslexia while inferior frontal areas show increased level of activation (for a review, see Pugh et al., 2000).

The ability to perceive and manipulate the sounds, phonemes, of a spoken language is highly correlated to reading. Preschool phonological abilities predict reading and spelling skills in the first school years (Muter, Hulme, Snowling, & Taylor, 1997; Bradley, 1988; Lundberg, Olofsson, & Wall, 1980). Further, training of phonological skills improves reading performance (Bradley & Bryant, 1983). It has been intensely debated whether phonological deficits in dyslexic individuals could be secondary to a general, even multimodal, impairment that hampers the processing of all sensory information ensuing in rapid succession (Tallal, 1980). Deficits in processing rapidly changing auditory verbal and nonverbal stimuli are particularly profound in language-learning-impaired children who have difficulties in understanding and producing spoken language in addition to reading problems (Tallal & Piercy, 1973, 1974). Impaired auditory resolution and poor reading is also correlated in adult population (Ahissar, Protopapas, Reid, & Merzenich, 2000).

Compared with reading, functional imaging studies of auditory processing in dyslexia have been relatively

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scarce and diverse, despite the central role of auditory/phonological problems in dyslexia. Hagman et al. (1992) reported increased glucose use in medial temporal areas in dyslexic individuals during syllable discrimination. Rumsey et al. (1992) found that, unlike non-reading-impaired adults, dyslexic individuals failed to show significant increase of blood flow in the left superior temporal cortex while performing a rhyming task. A recent functional MR spectroscopy study by Richards et al. (1999) reported an increased area of lactate elevation in the left anterior brain regions in dyslexic children as compared with nonimpaired children when they performed a rhyming task. Using fMRI, Temple et al. (2000) showed increased left prefrontal activation in control but not in dyslexic adults to rapidly changing relative to slowly changing nonspeech stimuli. No differences were found in the activation of the auditory cortex in the abovementioned blood flow studies. Owing to poor temporal resolution of hemodynamic measures, subtle differences between impaired and nonimpaired individuals during distinct time windows could be masked if the overall level of activation would be comparable between groups. The sensitivity of these techniques could also be relatively poor to transient synchronous responses, like the robust neural activation at about 100 msec, readily detected with event-related potentials (ERPs) and MEG (for reviews on electric N100 response and magnetic N100m/M100 response, see Hari, 1990; Näätänen & Picton, 1987).

Auditory word processing is composed of several hierarchical operations including acoustic, phonetic, phonological, lexico-semantic, and syntactic analysis. The correspondence between evoked responses peaking during distinct time windows and perceptual/cognitive subcomponents of speech processing are still unclear. MEG studies have indicated that at around 150–200 msec after stimulus onset, the phonological categories have already been accessed (Phillips et al., 2000; Vihla, Lounasmaa, & Salmelin, 2000). It is thus plausible that the neural populations underlying the N100m response could already be involved in phonetic/phonological processing.

ERP studies have indicated that during dichotic listening of consonant–vowel syllables, the N100 amplitude distribution over the left and right hemispheres differs between dyslexic and nonimpaired children (Brunswick & Rippon, 1994). The cortical basis of this difference is unclear, as special source-modeling techniques were not used, which would have allowed to differentiate between responses from the two hemispheres (Scherg, 1990). In a typical MEG experiment, the center of the neuronal population generating the N100 response can be localized to supratemporal auditory cortex with an accuracy of a few millimeters. Moreover, the time behavior of the response in each hemisphere can be followed with millisecond resolution. A recent MEG study by Heim et al. (2000) failed to find significant differences between dyslexic and control children in the amplitudes of the evoked fields peaking at 80 and 210 msec for consonant–vowel syllables. However, this study used relatively rapid presentation rate that can totally abolish the N100m response in young children (Paetau, Ahonen, Salonen, & Sams, 1995). Nagarajan et al. (1999) reported abnormally weak left hemisphere N100m response evoked by brief rapidly successive nonspeech stimuli in dyslexic adults.

As N100m response is likely to have an important, yet poorly known, role in speech processing, we used MEG to determine whether the auditory N100m response evoked by various slowly or rapidly successive speech or complex nonspeech sounds reveals differences between dyslexic and non-reading-impaired adults. Behavioral studies have shown that the perception of the identity of consonants is impaired in dyslexic individuals. Normally, consonants are perceived categorically meaning that speech sounds, for example, in a continuum from /ba/ to /da/, are heard as members of one category or the other rather than as ambiguous. In dyslexic individuals, the phonological category boundaries appear to be less sharply defined (Richardson, Leppänen, Leiwo, & Lyytinen, submitted; Reed, 1989). Further, dyslexic children are impaired in discriminating consonant–vowel syllables like /ba/ and /da/ in a task where they have to indicate the presentation order of the syllables (Reed, 1989). These syllables are only differentiated by a 40-msec transitional period at the beginning of the syllable during which the frequencies, formants, change rapidly over time. Thus, in the current experiment, we manipulated the presence of transitions in speech sounds (/a/ followed by /ta/ vs. /a/ followed by /a/; active speech task) and in the corresponding complex nonspeech sounds (complex sound task) to investigate whether the neural activation evoked by brief frequency transitions is normal in dyslexia. As the amplitude of the N100m response has been reported to increase with attention at high presentation rates (Woldorff et al., 1993), the subjects were asked to actively discriminate between the stimuli to maximally engage the neuronal populations involved.

Previous studies have also indicated that dyslexic children make more errors than nonimpaired children in a temporal order judgment task of two different tones when these tones are separated by less than 400 msec (Reed, 1989). The duration of the silent period inside an auditory input also codes features critical for speech perception such as length of a consonant. For example, in the Finnish language, a vowel /a/ separated by a 95-msec silent period from a syllable /ta/ is perceived as the pseudoword /ata/ with a short consonant in the middle. When the silence between /a/ and /ta/ is prolonged to at least 175 msec, a long consonant is always perceived, instead (i.e., pseudoword /atta/). Dyslexic individuals, however, occasionally perceive a short consonant even when the silent gap is 175 msec, unlike

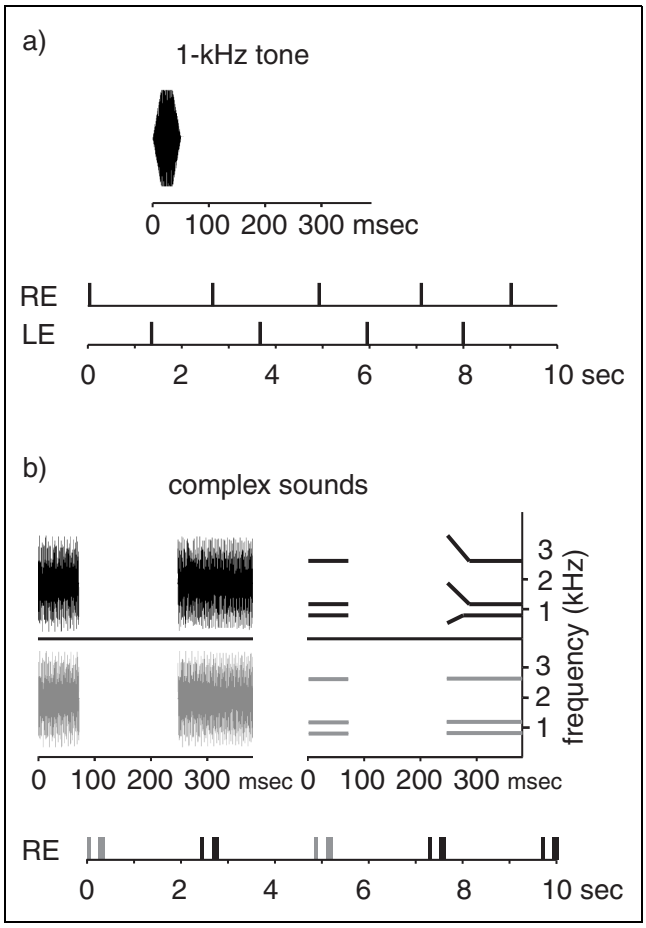

Figure 1. The 1-kHz tone (a) and the complex sound stimuli (b) used in the simple tone and complex sound tasks. Schematic presentation of the stimulus sequence over a 10-sec time interval is shown below the stimuli. The tone was presented alternately to the right ear (RE) and left ear (LE), and the complex sounds only to the right ear.

non-reading-impaired adults (Richardson, 1998; Richardson et al., submitted). Babies of dyslexic parents also show abnormal mismatch responses evoked by rarely occurring pseudoword /atta/ in a series of frequently presented pseudoword /ata/ (Leppänen et al., in press). In the present study, we employed these same pseudowords, with the silent gap between the vowel /a/ and syllable /ta/ either 95 or 175 msec, corresponding to silence durations in short and long consonants in the Finnish language. These short or long consonant pseudowords were presented with equal probability (ignored speech task) or as high-probability standards and low-probability deviants (mismatch task). To optimize the comparability of these two tasks with existing literature (Pihko, Leppäsaari, Leppänen, Richardson, & Lyytinen, 1997) and each other, the subjects were ignoring the stimuli. Our dyslexic participants were recruited from the population of the Jyväskylä Longitudinal Study of Dyslexia (Lyytinen, 1997), and they all had at least one close relative with developmental dyslexia.

RESULTS

The stimuli in the MEG experiment comprised simple tones, complex nonspeech sound pairs, and natural speech sounds (see Figures 1 and 2). The speech stimuli were bisyllabic pseudowords presented in three different conditions: active discrimination, ignored speech, and mismatch task.

Activation Associated with Simple Tones

Simple 50-msec 1-kHz tones elicited prominent activation 80–90 msec after tone onset in the temporal cortices (Figure 3a). The two subject groups did not show any differences in N100m peak strength (Table 1). The responses evoked by tones presented to the contralateral ear, for example, responses in the left hemisphere to right-ear stimulation, evoked stronger response [$F(1,17) = 32.8$, $p < .0001$] than ipsilateral stimulation, for example, responses in the left hemisphere to left-ear stimulation. A significant hemisphere by stimulated ear interaction indicated that the contra- versus ipsilateral difference was especially prominent in the right hemisphere [$F(1,17) = 5.7$, $p < .03$].

The peak latencies of the N100m responses did not show differences between the subject groups. The

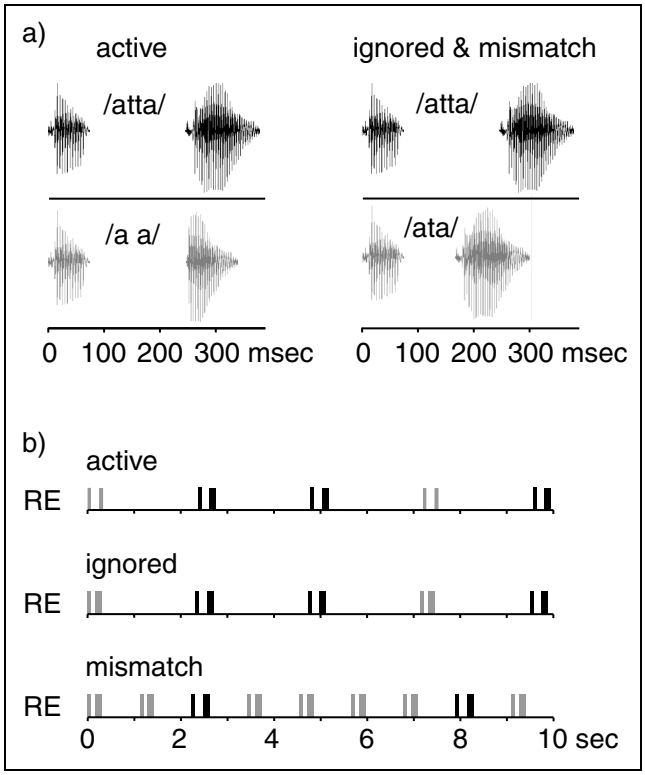

Figure 2. (a) The speech stimuli used in the active discrimination, ignored speech, and mismatch tasks. (b) Schematic presentation of the stimulus sequence over a 10-sec time interval in the active, ignored, and mismatch tasks. The stimuli were presented only to the right ear (RE).

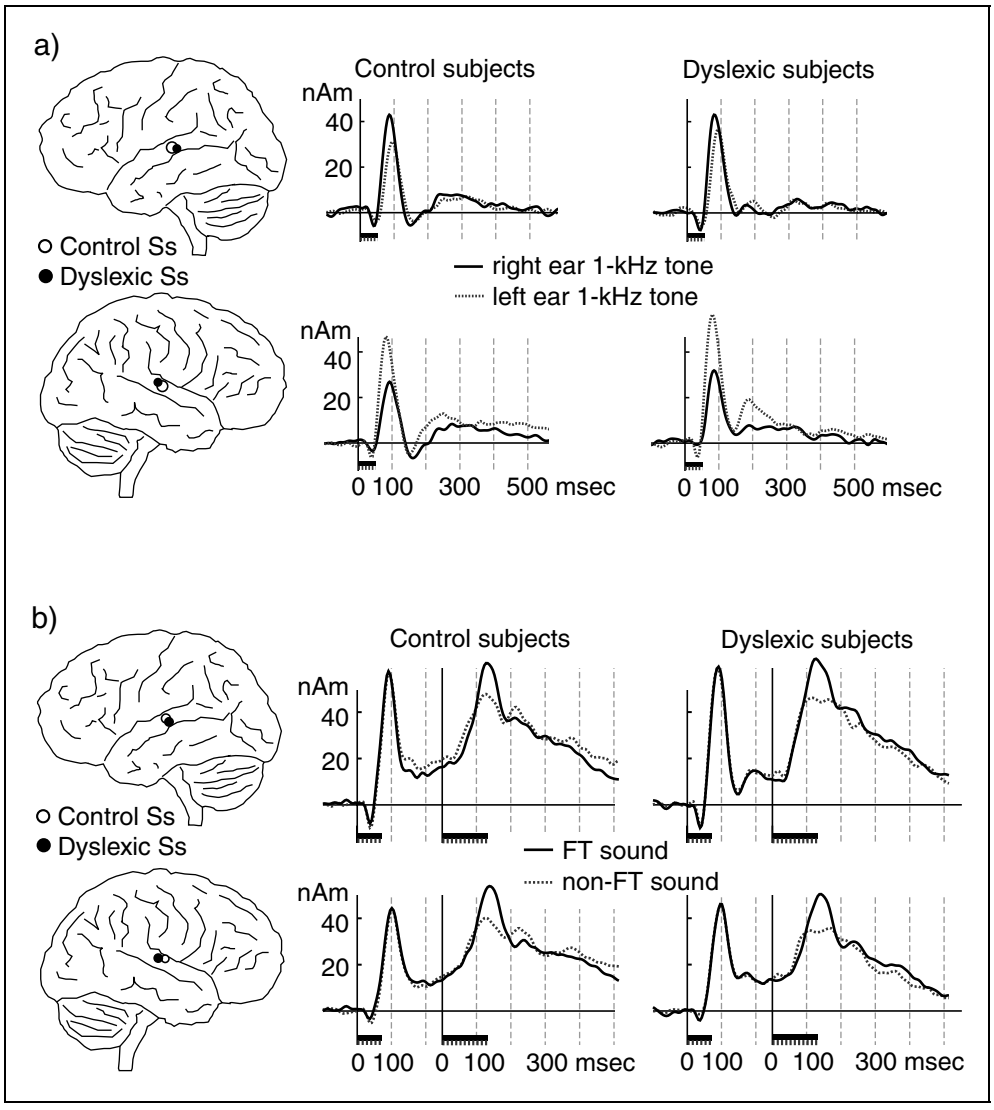

Figure 3. The center of activation of the N100m responses evoked by 1-kHz tones (a) and complex sounds (b) in the left (upper row) and right hemisphere (lower row) and the activation strengths as a function of time averaged across all control and dyslexic participants. The mean N100m source areas in control (white circle) and dyslexic participants (black circle) are shown on the schematic surface images of the brain, with the radius of the circle indicating one standard error of mean. (a) For 1-kHz tones, the activation evoked by right ear stimulation is shown as a solid line and left ear stimulation as a dotted line. (b) The activation evoked by the pair of complex sounds that contained a frequency transition (FT) in the beginning of the second sound is shown as a solid line and the activation evoked by the sound pair that did not contain a frequency transition as a dotted line. The duration of the stimuli is indicated on the time scale.

contralateral responses peaked earlier than the ipsilateral responses [$F(1,17) = 63.4$, $p < .0001$] and the contra- and ipsilateral responses peaked on average 4 msec earlier in the right than left hemisphere [$F(1,17) = 6.6$, $p < .02$]. The amplitude and latency differences between the contra- and ipsilateral responses are in agreement with earlier studies (Salmelin et al., 1999; Mäkelä et al., 1993; Pantev, Lütkenhöner, Hoke, & Lehnertz, 1986; Elberling, Bak, Kofoed, Lebech, & Saermark, 1982).

The mean location of the neuronal population generating the N100m response was identical in the two subject groups. The contra- and ipsilateral response locations did not differ, whereas a significant main effect of hemisphere was found in the N100m response location [$F(1,17) = 23.1$, $p < .0002$]. Subsequent analysis revealed that the right hemisphere N100m responses were located on average 7 mm anterior [$F(1,17) = 20.8$, $p < .0003$] and 3 mm lateral [$F(1,17) = 11.8$, $p < .003$] to left hemisphere responses. The pronounced anterior–posterior differences in the source locations between the right and the left hemisphere is commonly detected (Salmelin et al., 1999; Pantev, Ross, Berg, Elbert, & Rockstroh, 1998; Vasama, Mäkelä, Tissari, & Hämäläinen, 1995; Mäkelä et al., 1993; Elberling et al., 1982), but the subtle lateral–medial difference has been reported by only a few studies (Pantev, Ross, et al., 1998; Vasama et al., 1995).

To summarize, for the simple 1-kHz tones, the results are highly compatible with the current literature on the effects of contra- and ipsilateral stimulation on N100m strength and latency and the difference in the source locations of the N100m in the two hemispheres. These general features of the N100m response were replicated in the other tasks for the first sound of each stimulus pair and are not separately mentioned below. For the second sounds of the stimulus pairs, however, the results were less robust, because in the active, passive, and ignored speech tasks, either the strength and/or the latency difference between the contra- and

Table 1. N100m Source Strengths and Latencies in the Left and Right Hemisphere in Dyslexic and Control Subjects for Simple Tones and for the First Sound of Each Stimulus Pair (mean ± *SEM*)

	Strength (nAm)			*Latency (msec)*		
	Control Ss	*Dyslexic Ss*	*p*	*Control Ss*	*Dyslexic Ss*	*p*
Left hemisphere						
Tone, 1 kHz						
Right ear (RE)	45 ± 4	47 ± 7	*ns*	86 ± 2	86 ± 6	*ns*
Left ear (LE)	33 ± 4	41 ± 7	*ns*	91 ± 2	93 ± 8	*ns*
Complex sound (RE)	59 ± 6	62 ± 10	*ns*	87 ± 1	86 ± 2	*ns*
Complex sound (RE)	59 ± 6	60 ± 9	*ns*	88 ± 2	84 ± 2	*ns*
Vowel /a/, active (RE)	42 ± 3	58 ± 4	.006	91 ± 2	95 ± 5	*ns*
Vowel /a/, active (RE)	40 ± 3	58 ± 4	.004	92 ± 2	97 ± 6	*ns*
Vowel /a/, ignored (RE)	40 ± 5	60 ± 5	.01	93 ± 2	100 ± 6	*ns*
Vowel /a/, ignored (RE)	39 ± 6	58 ± 5	.02	93 ± 2	100 ± 7	*ns*
Vowel /a/, mismatch (RE)[a]	12 ± 3	22 ± 4	*ns*	95 ± 3	106 ± 7	*ns*
Vowel /a/, mismatch (RE)[b]	14 ± 3	24 ± 4	.055	95 ± 3	103 ± 7	*ns*
Right hemisphere						
Tone, 1 kHz						
Right ear (RE)	28 ± 3	36 ± 5	*ns*	90 ± 2	91 ± 5	*ns*
Left ear (LE)	49 ± 4	61 ± 6	*ns*	80 ± 2	81 ± 5	*ns*
Complex sound (RE)	47 ± 4	49 ± 4	*ns*	95 ± 3	93 ± 3	*ns*
Complex sound (RE)	47 ± 4	49 ± 4	*ns*	98 ± 4	91 ± 3	*ns*
Vowel /a/, active (RE)	25 ± 2	35 ± 4	.04	101 ± 5	102 ± 6	*ns*
Vowel /a/, active (RE)	26 ± 2	35 ± 4	*ns*	102 ± 5	103 ± 6	*ns*
Vowel /a/, ignored (RE)	30 ± 5	35 ± 4	*ns*	104 ± 6	102 ± 7	*ns*
Vowel /a/, ignored (RE)	28 ± 4	35 ± 4	*ns*	106 ± 6	102 ± 7	*ns*
Vowel /a/, mismatch (RE)[a]	12 ± 3	15 ± 3	*ns*	98 ± 5	109 ± 9	*ns*
Vowel /a/, mismatch (RE)[b]	12 ± 3	17 ± 3	*ns*	103 ± 7	111 ± 10	*ns*

In the complex sound task and in the active, ignored, and mismatch speech tasks, the response strengths and latencies are shown separately for the identical first sounds of the two types of stimulus pairs.

[a]Vowel /a/ in deviant condition, i.e., followed by syllable /ta/ after 175 msec.

[b]Vowel /a/ in standard condition, i.e. followed by syllable /ta/ after 95 msec.

the ipsilateral responses failed to reach statistical significance.

Activation Associated with Complex Sounds

In the complex sound task, the first sound of the stimulus pair was a steady-state sound, while the second sound either contained a frequency transition in the beginning or was a steady-state sound. The N100m response elicited by the first sound of the pair peaked around 85 msec after the sound onset in the left (contralateral) and around 95 msec in the right (ipsilateral) hemisphere (Figure 3b; Table 1). For the first sound of a pair, neither the response strength, latency, nor location differed between the two subject groups.

The N100m response elicited by the second sound in a pair peaked around 120–130 msec after the sound onset in the left hemisphere and 10 msec later in the right ipsilateral hemisphere (Table 2). Both the strength and latency of the N100m response failed to show any differences between the two subject groups. The N100m response was significantly stronger [$F(1,17) = 43.5$,

Table 2. N100m Source Strengths and Latencies in the Left and Right Hemisphere in Dyslexic and Control Subjects for the Second Sound of Each Stimulus Pair (mean ± *SEM*)

	Strength (nAm)			*Latency (msec)*		
	Control Ss	*Dyslexic Ss*	*p*	*Control Ss*	*Dyslexic Ss*	*p*
Left hemisphere						
Complex FT sound	64 ± 8	65 ± 12	*ns*	133 ± 5	134 ± 5	*ns*
Complex non-FT sound	49 ± 7	53 ± 9	*ns*	119 ± 5	118 ± 8	*ns*
/ta/ 175-msec gap, active	29 ± 4	32 ± 5	*ns*	113 ± 4	126 ± 7	*ns*
/a/ 175-msec gap, active	30 ± 5	35 ± 4	*ns*	116 ± 5	110 ± 6	*ns*
/ta/ 175-msec gap, ignored	20 ± 3	28 ± 4	*ns*	109 ± 4	113 ± 8	*ns*
/ta/ 95-msec gap, ignored	14 ± 2	20 ± 4	*ns*	111 ± 4	127 ± 7	*ns*
/ta/ 175 ms gap, mismatch[a]	17 ± 4	22 ± 4	*ns*	109 ± 7	120 ± 7	*ns*
/ta/ 95-msec gap, mismatch[b]	9 ± 2	16 ± 4	*ns*	116 ± 4	124 ± 5	*ns*
Right hemisphere						
Complex FT sound	57 ± 5	52 ± 7	*ns*	141 ± 4	142 ± 4	*ns*
Complex non-FT sound	42 ± 5	40 ± 5	*ns*	118 ± 5	137 ± 9	*ns*
/ta/ 175-msec gap, active	19 ± 3	22 ± 3	*ns*	113 ± 4	130 ± 6	.03
/a/ 175-msec gap, active	22 ± 3	22 ± 3	*ns*	107 ± 3	107 ± 7	*ns*
/ta/ 175-msec gap, ignored	21 ± 4	18 ± 3	*ns*	111 ± 4	113 ± 7	*ns*
/ta/ 95-msec gap, ignored	17 ± 5	19 ± 2	*ns*	126 ± 2	128 ± 7	*ns*
/ta/ 175-msec gap, mismatch[a]	15 ± 4	17 ± 3	*ns*	121 ± 5	124 ± 5	*ns*
/ta/ 95-msec gap, mismatch[b]	14 ± 4	17 ± 3	*ns*	124 ± 4	129 ± 4	*ns*

FT = frequency transition.

[a]Deviant.

[b]Standard.

$p < .0001$] and peaked later [$F(1,17) = 6.6, p < .02$] for those complex sounds that contained a frequency transition than for the steady-state sounds.

To summarize the results for all the nonspeech sounds used in the current study, we found no evidence for differences in cortical processing of simple 1-kHz tones or complex sounds (containing brief frequency transition or not) between dyslexic and non-reading-impaired individuals, as indicated by latency, strength, and location of the N100m response.

Activation Associated with Active Discrimination of Speech Sounds

In the active discrimination task a vowel /a/ was followed after 175 msec by either a syllable /ta/ or a modified version of the same syllable from which the initial formant transition was removed. The N100m response elicited by the vowel /a/ peaked around 95 msec after the sound onset in the left (contralateral) and around 100 msec in the right (ipsilateral) hemisphere (Figure 4a; Table 1). For the response strength, a significant main effect of subject group was revealed [$F(1,17) = 11.2$, $p < .004$]. The N100m response evoked by the vowel /a/ was about 30% stronger in dyslexic than non-reading-impaired individuals. When analysis was conducted separately for each hemisphere, only the left hemisphere showed a significant difference between the groups [$F(1,17) = 10.7$, $p < .005$], while for the right hemisphere, the difference between groups only approached significance [$F(1,17) = 4.1, p < .06$]. No differences were detected in the latency or in the location of the N100m response between the two subject groups.

The N100m response elicited by the second syllable /ta/ or by the modified version of the same syllable peaked around 110–130 msec after the sound onset in the left contra- and right ipsilateral hemispheres (Table 2). The strength of the N100m failed to reveal any differences between the two stimuli or subject groups. The peak of the response was delayed for the

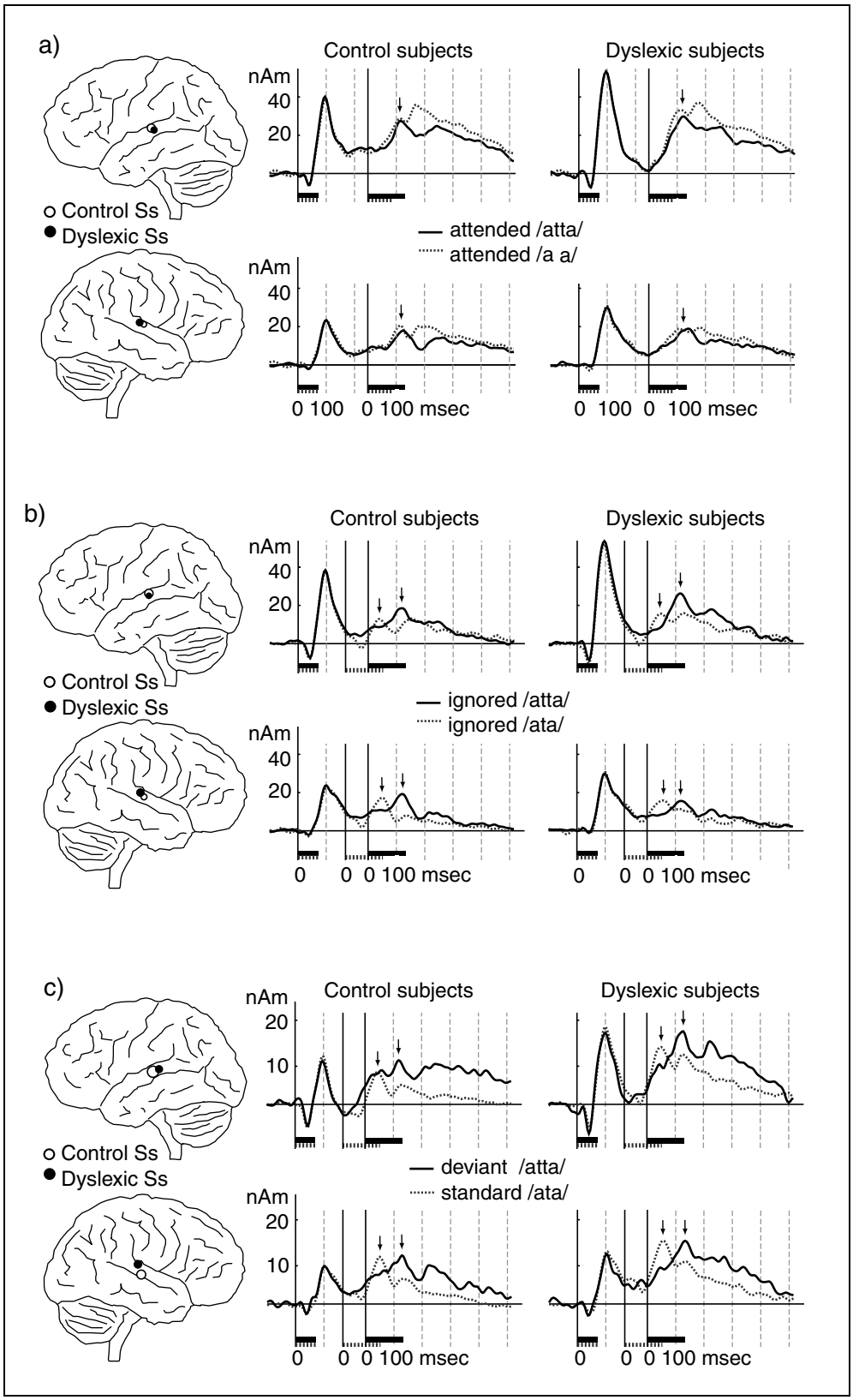

Figure 4. The center of activation of the N100m responses evoked by vowel /a/ in the left (upper row) and right hemisphere (lower row) in the active discrimination task (a), in the ignored speech task (b), and in the mismatch task (c). The radius of the circle indicates one standard error of mean. The activation strengths in each task are shown as a function of time averaged across all control and dyslexic participants. The N100m responses evoked by the second syllable of the pseudoword (/ta/ or modified /a/) are shown with an arrow. (a) The mean activation evoked by vowel /a/ followed by syllable /ta/ after 175 msec is shown as a solid line and the activation evoked by vowel /a/ followed by another vowel /a/ (modified from /ta/) as a dotted line. (b) The mean activation evoked by vowel /a/ followed by syllable /ta/ after 175 msec is shown as a solid line and the activation evoked by vowel /a/ followed by syllable /ta/ after 95 msec as a dotted line. (c) The mean activation evoked by vowel /a/ followed by syllable /ta/ after 175 msec (deviants, 20% of all sounds) is shown as a solid line and the activation evoked by vowel /a/ followed by syllable /ta/ after 95 msec (standards) as a dotted line. Note the more sensitive strength scale in (c) compared to (a) and (b).

syllable /ta/ compared with /a/, but this significant main effect was largely due to the dyslexic individuals, as indicated by a significant stimulus type by subject group interaction [$F(1,17) = 5.9, p < .03$]. Subsequent analysis, conducted separately for the two types of stimuli, revealed that the response evoked by syllable /ta/ was delayed by about 15 msec in dyslexic subjects compared with non-reading-impaired individuals [$F(1,17) = 4.3$,

$p < .055$]. This effect of subject group was extremely subtle and reached statistical significance only in the right ipsilateral hemisphere [$F(1,17) = 5.7$, $p < .03$].

Activation Associated with Ignored Speech Sounds

In the ignored speech task, the duration of the silent period between the vowel /a/ and a syllable /ta/ was either 95 or 175 msec. The N100m response elicited by the vowel /a/ peaked around 95 msec after the sound onset in the left (contralateral) and around 105 msec in the right (ipsilateral) hemisphere (Figure 4b; Table 1). For the response strength, a significant main effect of subject group was detected [$F(1,17) = 4.6$, $p < .05$]. In accordance with the attended condition, the N100m response evoked by the ignored vowel /a/ was about 30% stronger in dyslexic than non-reading-impaired individuals, with the difference reaching statistical significance only in the left hemisphere [$F(1,17) = 7.2$, $p < .02$]. In the right hemisphere, the responses were equally strong in the two groups. No differences were detected in the latency or in the location of the N100m response between the two subject groups.

The N100m response evoked by the syllable /ta/ following the vowel /a/ after 175 or 95 msec peaked around 110–125 msec after the sound onset in the left contralateral and right ipsilateral hemisphere (Table 2). No difference between the subject groups was detected either for the strengths or for the latencies. The N100m response was weaker [$F(1,17) = 15.6$, $p < .001$] and peaked 10 msec later [$F(1,16) = 16.5$, $p < .001$] when the duration of the silent period was 95 msec than when the silence was 175 msec. A significant stimulus type and hemisphere interaction [$F(1,17) = 4.4$, $p < .05$] indicated that this difference in amplitude was only seen in the left hemisphere.

Activation Associated with Mismatch Speech Task

In the mismatch speech task, an identical vowel /a/ was followed by a syllable /ta/ after a silent period of either 95 msec (probability = .8) or 175 msec (probability = .2). The interpair interval was only 0.8 sec compared with 2.0 sec in the other two speech tasks. The N100m response elicited by the vowel /a/ peaked around 100 msec after the sound onset in the left (contralateral) and around 105 msec in the right (ipsilateral) hemisphere (Figure 4c; Table 1). The response strength, latency, and location failed to reveal statistically significant differences between groups; however, in the left hemisphere, the effect of subject group on the response strength approached significance [$F(1,16) = 4.4$, $p < .057$].

The N100m response elicited by the syllable /ta/ following the vowel /a/ after 175 or 95 msec peaked around 115–125 msec after the sound onset in the left contralateral and right ipsilateral hemisphere (Table 2). No difference between the two subject groups was detected either for the strengths or for the latencies. The N100m response was weaker when the silent gap was 95 msec than when it was 175 msec [$F(1,16) = 12.3$, $p < .003$]. The difference in amplitude was only seen in the left hemisphere, as indicated by a significant stimulus type by hemisphere interaction [$F(1,16) = 7.9$, $p < .01$].

The very same stimuli were used in the mismatch task and in the ignored speech task, the only differences being the relative probability of the 175 and 95 msec silent periods and the interpair interval. A comparison of the source waveforms in these conditions suggested that the response to the deviant syllable /ta/ exhibited two features that were specific to the mismatch task. The waveforms to the deviant stimuli showed in the left hemisphere of control subjects an additional response, at about 100 msec after the expected onset of the standard syllable /ta/, apparently evoked by the omission of the standard stimuli. A similar phenomenon has been reported in non-reading-impaired adults using ERPs (Pihko et al., 1997). To quantify this effect, the strength of the response evoked by the deviant syllable /ta/ in the left hemisphere was measured from individual N100m response waveforms at the time where the N100m response peaked for the standard syllable /ta/. A mixed-model ANOVA (stimulus type as within-subjects factor and subject group as between-subjects factor) revealed a significant stimulus type by subject group interaction [$F(1,16) = 4.6$, $p < .05$]. In the control subjects, the activation was equally strong to the deviant and standard stimuli [$F(1,8) = .4$, *ns*]. The clear response to the deviant stimulus within this unusual time window is apparently an omission response to the high-probability stimulus. This interpretation is corroborated by the findings in the ignored speech condition, where the activation at this time point was significantly weaker for the /ta/ preceded by a 175-msec silent period than for the /ta/ with the 95-msec silence [$F(1,8) = 6.5$, $p < .03$]. In dyslexic subjects, however, the response in the mismatch speech task was significantly stronger to the standard stimulus than to the deviant stimulus [$F(1,8) = 16.8$, $p < .03$]. Thus, unlike the control subjects, dyslexic individuals did not show an omission response to the missing standard stimulus /ta/ at the expected latency.

In addition to the omission response, the deviant syllable seemed to evoke a later broad response peaking well after the offset of the entire syllable. The mean strength of this broad response was quantified in the left hemisphere at 100–300 msec after the termination of the syllable from the individual response waveforms. Unlike the omission response, this later broad deflection failed to reveal any significant main effect or interaction between the two subject groups (mixed-model ANOVA, stimulus type as within-subjects factor and subject group as between-subjects factor). The late response was stronger to the deviant than standard stimuli [$F(1,16) = 18.6$, $p < .0005$].

Comparisons of the Active and Ignored Speech Tasks

The same speech stimulus /ata/ with identical stimulus parameters were used both when subjects were actively discriminating between the speech stimuli and ignoring them. The effect of attention on the strength and latency of the N100m response evoked by the vowel /a/ and the syllable /ta/ was tested using a mixed-model ANOVA (attentional level, hemisphere, and stimulus type as within-subjects factors and subject group as between-subjects factor). For the response strength, the analysis revealed a significant interaction between attentional level and stimulus type [$F(1,17) = 4.9$, $p < .04$], indicating that the attentional level of the subject affected only the response evoked by the syllable /ta/. The effect of attentional level on the N100m strength for the syllable /ta/ reached statistical significance in the left hemisphere [$F(1,17) = 7.0$, $p < .02$].

Figure 5 illustrates the N100m strength in the left hemisphere for vowel /a/ (right) and syllable /ta/ (left) in the active discrimination and ignored speech tasks. In the upper row, the mean strength of the N100m response is depicted across all subjects and in the lower row the individual response strengths in the attended condition are plotted against ignored condition. The strength of the N100m response for vowel /a/ reveals a robust difference between dyslexic and non-reading-impaired individuals both in active discrimination and ignored conditions, and this difference is clearly seen over individual subjects. The attentional level of the subject does not reliably modulate the response strength for vowel /a/, while for the syllable /ta/, the strength of the N100m response is increased by attention. For syllable /ta/, the responses of the two subject groups are practically overlapping.

The attentional level of the subject also affected the latency of the response. The N100m response evoked by /ta/ was delayed by about 10 msec when subjects were attentively listening to the stimuli; also, this effect reached statistical significance only in the left hemisphere [$F(1,17) = 4.4$, $p < .05$].

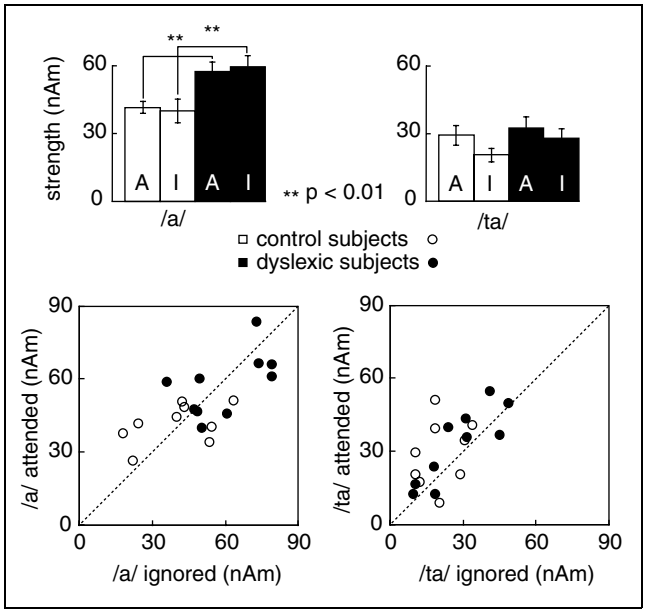

Figure 5. The N100m strength in the left hemisphere for vowel /a/ (left) and syllable /ta/ (right) in active discrimination (A) and ignored speech (I) tasks. In the upper row, the mean (± *SEM*) strength of the N100m response across all control (white bars) and dyslexic participants (dark bars). In the lower row, the response strength for the active versus ignored speech tasks is plotted for each control (white circles) and dyslexic individual (dark circles).

DISCUSSION

We studied auditory cortical activation evoked by natural bisyllabic pseudowords, complex nonverbal sound pairs, and 1-kHz tones in dyslexic and non-reading-impaired individuals. Our most robust finding was that the left hemisphere N100m response, peaking around 100 msec in the supratemporal auditory cortex, was abnormally strong in dyslexic individuals for the vowel /a/ in the beginning of the pseudowords. The difference between groups was detected irrespective of whether the subjects were actively listening to the pseudowords or ignoring them and was reproducible within the same condition. On the other hand, the N100m response evoked by the complex sound that was composed of the peak F1, F2, and F3 formant frequencies of the vowel /a/ was similar between groups in strength and in latency. Nor were any group differences detected for the 1-kHz tone.

Intracranial recordings have indicated that auditory input reaches primary auditory cortex already about 10–15 msec after stimulus onset (Liégeois-Chauvel, Musolino, & Chauvel, 1991; Celesia, 1976). The middle-latency responses (N19m, P30m, and P50m) peaking 10–50 msec after sound onset can be detected with MEG although several hundreds to thousands of averages have to be gathered in each subject (Mäkelä, Hämäläinen, Hari, & McEvoy, 1994; Pelizzone et al., 1987). The N100m response is part of the long-latency auditory-evoked responses. It is the most prominent and reproducible auditory-evoked response and seems to be elicited by any abrupt acoustic input or change in the auditory environment (Hari, 1990). Intracranial measurements have shown that auditory responses around 100 msec after sound onset originate both from secondary auditory areas in the lateral parts of Heschl's gyrus and from the planum temporale (Liégeois-Chauvel, Musolino, Badier, Marquis, & Chauvel, 1994). The activation is larger in the planum temporale, suggesting that it is the main source of the N100 response measured outside the scalp (Liégeois-Chauvel et al., 1994). This interpretation is supported by high-precision MEG recordings (Lütkenhöner & Steinstrater, 1998).

MEG studies have indicated that by the time the mismatch response reaches its maximum around 150–200 msec after stimulus onset, the phonological categories have already been accessed (Phillips et al., 2000; Vihla et al., 2000). The neural populations underlying the N100m response could thus already be involved in phonetic/phonological processing. During normal development, some of the N100m related neural populations could become tuned to phonetic contrasts of the native language. Previous studies have shown that phonological categories are less sharply defined in dyslexic individuals (Reed, 1989). As the strength of the MEG response depends on the amount of synchronously activated neural cells, one highly speculative interpretation of the abnormally strong N100m response in dyslexic individuals is that speech evokes activity in an abnormally large, nonspecialized, neural population. While it is possible that the abnormally strong N100m response in dyslexic individuals is related to phonological problems, some unknown acoustic parameters of the speech stimuli could have triggered the difference as well, e.g., continuous amplitude modulation not present in our nonspeech sounds.

Previous MEG studies have found relatively little evidence for speech-specific activation around 100 msec after sound onset. For instance, Eulitz, Diesch, Pantev, Hampson, and Elbert (1995) compared the N100m responses evoked by a vowel /a/ and a 1-kHz tone and discovered that the latency of the response was longer for the vowel than for the tone, while no difference was found in the response strength. In a study by Tiitinen, Sivonen, Alku, Virtanen, and Näätänen (1999), a simple tone was carefully matched to vowel /a/ in F2 formant frequency and amplitude. The authors failed to detect a significant difference in the strength of the N100m response, but the latency was again delayed for speech. Thus, it seems that in non-reading-impaired adults, the latency but not the strength of the N100m response shows differences between speech and nonspeech stimuli. It is worth noting, that, although MEG can accurately localize the center of activation underlying the measured signal, far-field ERPs are blind to specific micropatterns of neuronal activity in a given area (Näätänen & Picton, 1987). Thus, the specific topographical parameter maps elicited by complex auditory stimuli can only be detected with single neuron or multiple unit recording (Schreiner, 1998).

It is not, however, totally inconceivable that normally absent differences in the strength of the N100m response between different stimuli could appear in populations with exceptional auditory perceptual capabilities. This possibility is supported by a study comparing N100m response strength in musicians and nonmusicians; only musicians showed differences between simple tones and piano tones, while in nonmusicians, the response strengths to these two sounds where equal (Pantev, Oostenveld, et al., 1998).

While the abnormally strong response for the speech sound /a/ was seen quite consistently across dyslexic individuals, it should be kept in mind that dyslexia is a heterogeneous condition. In a study by Adlard and Hazan (1998), only 30% of the dyslexic children had speech perception deficits that impaired the detection of a variety of phonetic contrasts, not only those with rapid acoustic changes. Thus, depending on the subject selection, the N100m abnormality might or might not appear. All our dyslexic individuals had also family history of reading difficulties that could be critical for the elicitation of the observed effect. Language-learning impairment might as well be manifested in the amplitude of the N100m response, perhaps even more clearly than dyslexia.

The N100m response evoked by consonant–vowel syllable /ta/ was normal in strength but slightly delayed in dyslexic subjects, when the duration of the silent period between a vowel /a/ and subsequent syllable /ta/ was 175 msec. The delayed response was seen when subjects were attentively listening to speech. When the stimulus parameters were the same but the subjects were ignoring the speech stimuli, no latency difference was detected. It is, however, unlikely that the latency delay in the dyslexic individuals for the syllable /ta/ would be solely related to attentional factors. First, in the active discrimination task, the latency difference between groups was abolished when the consonant was removed from the beginning of the syllable. Further, the two subject groups also showed different pattern of activation in the mismatch task when the subjects were ignoring the stimuli. In the mismatch task, the frequently presented pseudoword /ata/ with 95 msec of silence between the syllables was occasionally replaced by a pseudoword with a 175-msec silent gap between the syllables. The omission response evoked by the missing syllable /ta/ at the expected latency was not detected in dyslexic individuals. Behavioral studies have shown that dyslexic individuals occasionally continue to perceive the consonant as short even when the silent gap between /a/ and /ta/ is 175 msec, while the nonreading-impaired adults always perceive a long consonant (Richardson, 1998; Richardson et al., submitted). Thus, the current observations, a delayed response to /ta/ at 175-msec gap duration and the missing omission response to the same syllable, are in agreement with behavioral findings, indicating that there are subtle difficulties in the perception of consonants in dyslexia.

In the current study, our rapidly successive nonspeech sounds failed to reveal any difference between dyslexic and nonreading impaired individuals. In a previous MEG study (Nagarajan et al., 1999), reporting reduced N100m strength in dyslexic individuals the stimuli were pairs of 20-msec sounds separated by a 200-msec silent gap. Our stimuli were longer (72 and 133 msec), and this might be the reason for the apparent discrepancy between the current study and that of Nagarajan et al. (1999).

Furthermore, we did not preselect our dyslexic participants according to difficulties in rapid auditory processing as was done in the study by Nagarajan et al. (1999).

Both the dyslexic and non-reading-impaired individuals showed a stronger N100m response to the complex sound beginning with a frequency transition than to the same sound without the transition. Thus, the presence of a brief transition in the beginning of a steady-state sound seemed to be adequately processed in dyslexic adults as reflected in the N100m response, at least using the current stimulus setup. It is also worth noting that in dyslexic individuals, problems have not been reported in detection of frequency transitions as such but rather in discrimination between different types of transitions, e.g., between speech sounds /ba/ and /da/ (see, e.g., Reed, 1989). Thus, in the future, more sensitive paradigms are clearly warranted to study the processing of frequency transitions and consonants in dyslexia.

In summary, the current study indicates that in adults with familiar type of dyslexia the left auditory cortex is abnormally activated already 100 msec after speech onset. It therefore appears that the auditory N100m response, originating in the supratemporal auditory cortex, also codes some stimulus-specific features likely to be critical for speech perception. In a recent fMRI study by Belin, Zatorre, Lafaille, Ahad, and Pike (2000), the upper bank of the superior temporal sulcus, including planum temporale, was significantly more activated by all human-made vocal sounds than by nonvocal sounds. The authors suggest a parallel with this area and the inferior occipito-temporal areas containing neural populations that seem to be favoring certain types of visual objects such as faces or words (for review see, e.g., Allison, McCarthy, Nobre, Puce, & Belger, 1994). It has further been demonstrated that intensive training can elicit specialized responses in the occipito-temporal areas for new objects (Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999). It is currently unknown whether such functional specialization and exposure related changes could be detected in the N100m response. Future studies should resolve what is the relationship between N100m response and language/reading acquisition and which features of speech (or nonspeech stimuli) are critical in eliciting the abnormally strong N100m response in dyslexic individuals. This would be of great importance not only for obtaining a better understanding of dyslexia but also for further clarifying the functional role of the N100m response.

METHODS

Subjects

We studied 10 adults with a history of developmental dyslexia (five women, five men; age 28–50 years, mean 35.6 years) and 9 non-reading-impaired control subjects (five women, four men; age 28–40 years, mean 34.8 years). The dyslexic individuals were recruited from the population of the Jyväskylä Longitudinal Study of Dyslexia (JLD) (Lyytinen, 1997). Control subjects were either spouses of the dyslexic participants ($n = 6$) or age-matched adults ($n = 3$). Informed consent was obtained from all subjects.

The inclusion criteria used in the JLD study are self-reported persistent reading or writing difficulties starting from early school years. In addition, the test performance of the included individuals had to be below 1 standard deviation in at least three independent reading and spelling tasks. Individuals with sensory or neurological abnormalities, or intelligence quotient (IQ) below 80 (Raven, Court, & Raven, 1992), were excluded. All the dyslexic individuals had at least one close relative with dyslexia.

The dyslexic individuals were tested with the standard behavioral test battery used in the JLD study (Leinonen et al., 2001). Control subjects were also tested for IQ and reading and spelling performance. The subject groups did not differ in IQ (Raven et al., 1992), but compared with control subjects, the dyslexic participants were significantly slower [$t(16) = 7.5$, $p < .0001$] and more error prone [$t(16) = 4.7$, $p < .0002$] in reading aloud text passages and made more errors in spelling aloud words and pseudowords presented auditorily [$t(16) = -2.7$, $p < .02$]. In phonological awareness tasks (phoneme deletion and syllable reversal), 70% of the dyslexic individuals performed at least 2 standard deviations below the mean of a normative sample (100 adults, see Leinonen et al., 2001).

Stimuli in the MEG Experiments

The stimuli in the MEG experiment comprised simple tones, complex nonspeech sounds, and natural speech sounds. Monoaural stimulation produces stronger responses in the contra- than ipsilateral hemisphere (Pantev et al., 1986). To maximally engage the language dominant left hemisphere, the speech and complex sounds were presented to the right ear.

In the simple tone task, stimuli were sinusoidal 1-kHz 50-msec tones with 15-msec rise and fall times (Figure 1a). Tones were delivered alternately to the left and right ear using randomized stimulus onset asynchrony (SOA) of 0.9–1.3 sec. Subjects read a self-selected book, ignoring the stimuli.

In the complex sound task, stimuli were two types of sound pairs (Figure 1b). The first sound was identical in both sound pairs: It was composed of 817, 1181, and 2632 Hz sinusoidal tones corresponding to the peak F1, F2, and F3 formant frequencies of the vowel /a/ (Steinschneider, Arezzo, & Vaughan, 1982). The duration of the first sound was 72 msec. The second sound was either (i) composed of the same three steady-state frequencies as the first sound or (ii) the three steady-state frequencies were preceded by a frequency transition corresponding

to peak F1, F2, and F3 formant frequency transitions in speech sound /ta/ (Steinschneider et al., 1982). Transitions were created by linearly changing the tone frequencies from 526 to 817 Hz, 1835 to 1181 Hz, and 3439 to 2632 Hz. The duration or the transition was 30 msec for the lowest frequency and 40 msec for the other two frequencies. The total duration of the second sound was 133 msec. The first and the second sound were separated by a 175-msec silent period. The steady-state sound pair and the sound pair containing the frequency transition were presented with equal probability in a randomized order using a constant 2.0-sec interpair interval (silent gap between the end of second sound of a sound pair and the beginning of the first sound of a next sound pair). During the experiment, subjects were instructed to covertly discriminate between the two types of stimuli.

The speech stimuli were bisyllabic natural pseudowords presented in three different conditions: active discrimination, ignored speech, and mismatch task (Figure 2). In every condition, the first speech sound was always the same vowel /a/. The duration of the vowel was 72 msec. In the active discrimination task, the vowel /a/ was followed by 175 msec of silence and then by either (i) a 133-msec-long syllable /ta/ or (ii) a modified version of the same syllable from which the first 40 msec had been removed. The former (i) was perceived as speech sound /atta/ and the latter (ii) as (a slightly odd) speech sound /a a/. In the ignored speech task, the duration of a silent period between the vowel /a/ and a syllable /ta/ was either 95 or 175 msec, resulting in perception of either a short or a long consonant (/ata/ vs. /atta/). Both in the active discrimination and ignored speech tasks, the equiprobable stimuli were presented in a randomized order with using a constant 2.0-sec interpair interval (Figure 2b). In the mismatch speech task, 80% of the stimuli were speech sounds perceived as /ata/ (silent gap between vowel and syllable 95 msec; standards) and 20% of the stimuli were speech sounds perceived as /atta/ (gap 175 msec; deviants). Standards and deviants were presented in a randomized order ensuring that maximally two deviants occurred in a row using a 0.8-sec interpair interval (Figure 2b). During the active discrimination task, the subjects were instructed to covertly discriminate between the two types of stimuli and in the ignored and mismatch speech tasks to pay no attention to the stimuli while reading a self-selected book.

The stimulus intensities of these three extremely different types of auditory stimuli were adjusted so that subjectively, they were perceived as pleasant and about equally loud. Compared with the mean intensity of the simple tone, the mean intensity of the complex sound was 2 dB and word 9 dB lower at the output of the sound delivery system.

Measurements were conducted in a magnetically shielded room. The stimuli were presented to the subject through a plastic tube and an ear piece. Measurement always started with finding the hearing threshold of each individual for the simple sounds and then increasing the volume to 70 dB above hearing level. The simple tone experiment was conducted first. Then either the two active discrimination tasks (complex sounds and active discrimination of speech sounds) or the two passive tasks (ignored and mismatch speech) were presented. The presentation order of the tasks was also randomized within the active and passive conditions.

MEG Recordings and Analysis

MEG is based on detecting cerebral magnetic fields associated with synchronous activation of thousands of nerve cells (for reviews see, e.g., Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993). The MEG measurements in the present study were conducted using the Neuromag Vectorview whole-head system (Neuromag, Helsinki, Finland). The device contains 102 triple sensor elements composed of two orthogonal planar gradiometers and one magnetometer. Neuromagnetic signals were averaged on-line from 200 msec before stimulus presentation to 800 msec after. Signals were bandpass filtered to 0.03–200 Hz and sampled at 0.6 kHz. Both horizontal and vertical eye movements were recorded on-line (bandpass 0.03–200 Hz), and epochs contaminated by eye or eyelid movements were rejected. For each stimulus category, 80–100 artefact-free responses were gathered.

Individually, for each subject, the neuromagnetic signals detected by the planar gradiometers were reduced into time behavior of distinct brain areas using equivalent current dipole (ECD) analysis (Hämäläinen et al., 1993). An ECD represents the mean location and strength of activation in a given brain area and the orientation of current flow therein. Dipoles were determined using standard selections of 23 gradiometer pairs that covered the auditory field pattern optimally in the left and right hemispheres. In the simple tone task, ECDs were found separately for the ipsi- and contralateral responses in the left and right hemisphere at the time of the maximum deflection around 100 msec after tone onset. In the active speech, ignored speech and complex sound tasks, the evoked responses to the two types of stimuli in each task were first averaged together and ECDs were then determined at the time of the peak deflection around 100 msec evoked by the first sound of a pair. The ECDs in the left and right hemisphere were then introduced into a multidipole model, keeping their orientations fixed but allowing the amplitudes to vary to achieve maximum explanation of the measured whole-head data over the entire averaging period, separately for the two types of stimuli. In the complex sound task, the left and right hemisphere N100m dipoles evoked by the first sound of a pair explained over 80% of the measured signal also during

the peak of the activation evoked by the second sound of a pair. In the mismatch task, dipole modeling was carried out for the signals evoked by the standard stimuli (the higher number of averages resulted in a superior signal-to-noise ratio compared with that for the deviant stimuli). In the analysis, the geometry of the head was approximated by average female and male spherical head models.

The location of sources is defined in head coordinates that are set by the nasion and two reference points anterior to both ear canals: x axis is directed from the left (negative) to the right (positive) preauricular point, y axis towards the nasion, and z axis towards the vertex. The locations of four head position indicator coils attached to the subject's head with respect to the anatomical reference points were measured using a 3-D digitizer. The locations of the coils with respect to the MEG helmet were determined in the beginning of each session.

Statistical Analysis

The peak strengths and latencies of the contra- and ipsilateral N100m responses were measured in each individual subject from the source waveforms. In the simple tone task, the N100m peak strength and latency were tested separately using a mixed-model analysis of variance (ANOVA) with hemisphere (left and right) and stimulated ear (contralateral and ipsilateral) as within-subjects factors and subject group (control and dyslexic subjects) as between-subjects factor. The mean location of the neuronal population generating the N100m response was tested using a mixed-model ANOVA with hemisphere and stimulated ear and head coordinates as within-subjects factors and subject group as between-subjects factor. In the complex sound, active speech, ignored speech, and mismatch speech tasks the N100m response strength and latency were tested separately for the first part and second part of each sound pair using a mixed-model ANOVA (hemisphere and stimulus type as within-subjects factors and subject group as between-subjects factor). The location of the activation was tested using a mixed-model ANOVA (within-subjects factors hemisphere and head coordinates and between-subjects factor subject group).

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